DATA ASSIMILATION FOR CARDIAC ELECTRICAL DYNAMICS

Elizabeth M. Cherry[1], Darby I. Cairns[1], Nathan Holt[1], Nicholas S. LaVigne[2], Flavio H. Fenton[3], and Matthew J. Hoffman[1]

[1] School of Mathematical Sciences, Rochester Institute of Technology, Rochester, NY, {excsma, dic4597, nxh7119, mjhsma}@rit.edu
[2] Center for Applied Mathematics, Cornell University, Ithaca, NY, nsl42@cornell.edu
[3] School of Physics, Georgia Institute of Technology, Atlanta, GA, flavio.fenton@physics.gatech.edu

SUMMARY

New insights into the mechanisms underlying cardiac arrhythmias may be possible from a greater understanding of variables unobserved in experimental settings. When experimental observations are sparse, data assimilation can be effective at recovering a more complete system state estimate. We have recently shown using synthetic observations of one- and three-dimensional cardiac tissue that data assimilation can be used to recover state variables observed sparsely in space and time or unobserved. Here we extend these findings to show that data assimilation remains effective in reconstructing cardiac states with underlying system spatial heterogeneity and in the presence of significant model error.

Key words: *data assimilation, cardiac arrhythmias, alternans*

1 INTRODUCTION

Cardiac arrhythmias remain an important health problem, largely because an incomplete understanding of their underlying dynamics remains elusive. A quantitative understanding of cardiac electrical dynamics is difficult to achieve: although measurements of voltage at high spatial and temporal resolution through recordings of fluorescence from voltage-sensitive-dye-perfused cardiac tissue (optical mapping) [1] are achievable, the resolution still is not at the level of an individual cell, and many important variables other than voltage are not or cannot be observed. Thus, most simulations of cardiac electrical dynamics aim to achieve qualitative (e.g., type of dynamics) or high-level quantitative (e.g., dominant frequency) agreement with observations. We previously showed that data assimilation [2], a technique borrowed from weather forecasting, holds promise for allowing a more quantitative reconstruction of dynamics during complicated cardiac arrhythmias like fibrillation. Here we extend these results to show that data assimilation remains useful for reconstructing states of discordant alternans in one-dimensional rings from synthetic observations when intrinsic spatial heterogeneity and more significant model error are considered.

2 METHODOLOGY

We closely follow the methodology of Hoffman et al. [2]. For data assimilation, the Local Ensemble Transform Kalman Filter (LETKF) [3] was used. The model of cardiac action potentials used in the algorithm was the Fenton-Karma (FK) model [4] with the same parameter values as in Ref. [2] except where noted otherwise to ensure spatial discordant alternans in a 1D ring geometry (periodic boundary conditions), which corresponds to a propagating wave state with persistent oscillations in wavelength. Numerical integration of the model differential equations was performed using the explicit Euler method with time steps of 0.05ms and a spatial resolution of 0.025cm. For the LETKF, we used 20 ensemble members to characterize covariance of the model-derived (background) forecast. Observations were assimilated every 5ms. As in Ref. [2], multiplicative inflation was used to artificially inflate the estimated covariance, and additive

inflation in the form of scaled differences of 5-ms forecasts was used to extend the subspace spanned by the ensemble. Initial states for the ensemble members were drawn randomly from states visited during a 500-ms model run, which ensured physical consistency of the initial ensemble. Synthetic observations were generated using either the FK model or the Beeler-Reuter (BR) model [5] by coarsening the true 2-second state to 5ms-intervals (100 time steps) and 0.075cm spacing (3 grid points) and then adding random Gaussian error (mean zero, standard deviation 0.05).

3 RESULTS AND CONCLUSIONS

We extend results from Ref. [2] by showing that the LETKF can recover discordant alternans states in 1D with spatial heterogeneity in the truth as well as with more significant model error. We also show preliminary results of fitting parameters to experiments; improved alignment of simulations with experiments should further extend the conditions under which data assimilation is useful.

3.1 Data assimilation in the presence of tissue spatial heterogeneity

Real cardiac tissue is likely to contain spatial variations in electrophysiological properties. We tested whether the LETKF could perform well in recovering the truth state when one model parameter, τ_{si}, was varied spatially in the truth data. This parameter scales the slow inward current of the FK model, and small differences can have large effects on wavelength and alternans propensity (see Fig. 1). We used a single sinusoid scaled to fit the 14-cm ring; the maximum and minimum values of τ_{si} were set to 29.3 and 28.7, so that the average value of τ_{si} was 29.0, the same as in the numerical model used in the LETKF. The spatially heterogeneous truth state clearly exhibited spatial variations in wavelength on top of the discordant alternans dynamics.
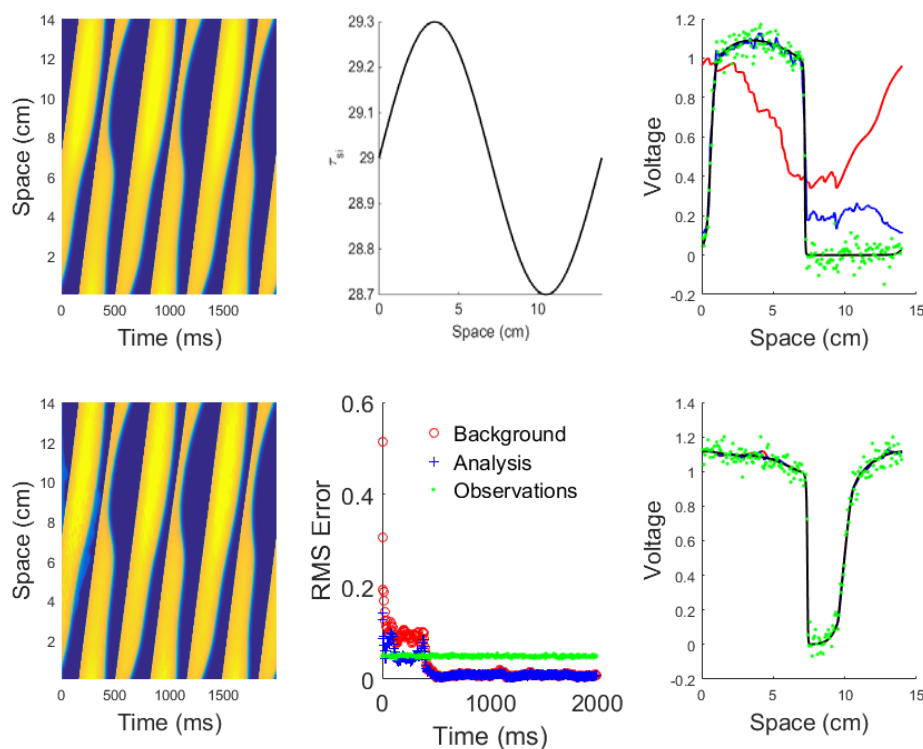

Figure 1. Upper left: space-time plot of truth voltage including spatial heterogeneity; colormap ranges from dark blue (lowest voltage) to red (highest voltage). Upper center: true spatial heterogeneity in parameter τ_{si}. Upper right: before the first assimilation of observations, true wave profile (black), observation points (green), initial estimate of wave profile obtained by averaging initial ensemble members (background, red), and improved estimate after incorporating data (analysis, blue). Lower left: estimated voltage showing excellent agreement after 500 ms. Lower center: root-mean-square error for background and analysis, with values below the observation error after 500 ms. Lower right: wave profile after 1000 ms, with truth, background, and analysis essentially superimposed within the envelope of the observations (green).

Although the LETKF had no awareness of the spatial variation in the truth and used a spatially invariant value for τ_{si}, it nevertheless obtained excellent agreement with the truth, as shown in Fig. 1. Within the first assimilation cycle, the forecast improved from a largely featureless average of the ensemble members (initialized to random model states) to a recognizable wave with correct location and wavelength. Small errors resulting from a slightly elevated resting voltage value (lighter blue in space-time plots) were corrected within about 500ms, corresponding to one period of the discordant alternans. Within the same time, the root-mean-square error dropped below the level of noise added to the observations and approached zero.

3.2 Data assimilation in the presence of significant model error

To further test whether data assimilation could recover more realistic truth states, we used the BR model to generate a truth state of discordant alternans in a 12.5-cm ring while continuing to use the FK model within the LETKF. This case posed a considerable challenge because the action potentials of the BR model, and thus those in the truth state and synthetic observations, had a spike-and-dome morphology, whereas the action potentials of the FK model, and thus those produced by the LETKF algorithm, did not. Despite the differences in wave shape arising from the different action potential shapes, within 500ms (one discordant alternans period) the LETKF matched wavefront location and produced good estimates for wavelength and conduction velocity, as can be seen in Fig. 2. As expected, the RMS error was higher (above the level of the noise added to the truth) because of differences in action potential shape; these differences can be seen in Fig. 2 as areas of elevated voltage (light blue) that persist along the wavefront after the first 500ms. In general, although differences in wave shape confined to a narrow area of the wavefront cannot be matched because the model used in the LETKF cannot achieve such shapes on its own, the LETKF performed well in matching the salient features of the truth state, including the location, speed, and dynamically varying width of the wave.
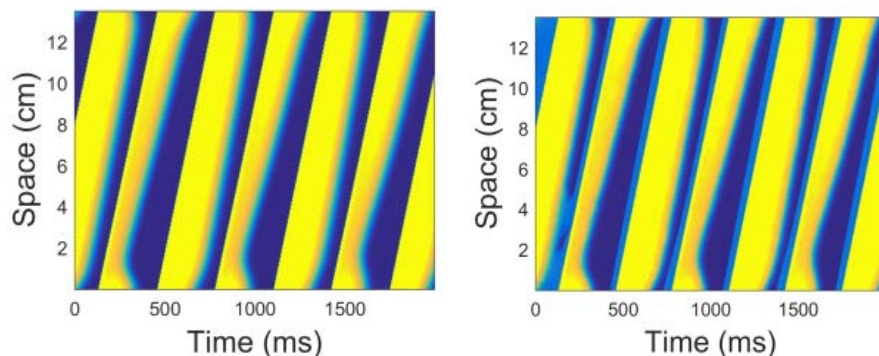

Figure 2. Performance of data assimilation in the presence of significant model error. Left: truth voltage from the BR model. Right: reconstructed voltage showing excellent agreement in wavelength, wave speed, and wave location after the first 500 ms. Colormap ranges from dark blue (lowest voltage) to red (highest voltage).

3.3 Customizing model parameterizations from experimental data

Better agreement between observations with spike-and-dome action potential morphology and forecasts produced by the LETKF algorithm could be achieved by substituting a model capable of reproducing wave shapes, such as the model of Bueno-Orovio et al. [6]. However, finding parameter values for these models that fit specific experimental data is challenging because of the large number of parameters, biological variability, and the highly nonlinear nature of the problem. Because spatial heterogeneity may make it necessary to perform multiple parameterizations for a single experiment, computational efficiency is also important. We have implemented a genetic algorithm to find parameterizations to fit the Bueno-Orovio et al. model to experimental data from microelectrode recordings. Like the FK model, the Bueno-Orovio et al. model is a flexible phenomenological reaction-diffusion model that can reproduce a broad range of cardiac dynamics, but unlike the FK model, it can reproduce action potential shapes. We find that the genetic algorithm works well in many cases, including for experimental data, even when fitting many parameters, provided that the bounds on parameters are not excessively large. Figure 3 shows an

example of fitting to experimental action potentials from microelectrode recordings of both endocardium and epicardium. We permitted the algorithm to vary 18 of 28 parameters. The algorithm was able to find good parameterizations in both cases, including good agreement for the distinctive action potential shapes. This approach, which has been used by others previously [7,8], shows promise for finding model parameterizations and should be useful in developing customized and spatially heterogeneous models for use in the LETKF to increase its range of applicability.
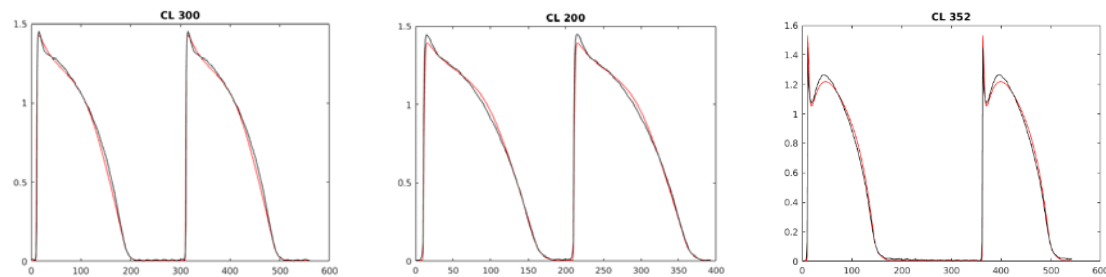

Figure 3. Parameter fitting (red) of the Bueno-Orovio et al. model to endocardial and epicardial microelectrode data (black). Cycle lengths of 300 and 200 ms (left and center) fit simultaneously are shown for endocardial data. One cycle length of 352 ms is shown for epicardial data.

3.4 Conclusion

We find that our data assimilation approach [2] continues to perform well for estimating states of cardiac discordant alternans in one-dimensional rings even when intrinsic spatial heterogeneity in the truth state is not included in the LETKF model and even when model error is increased by obtaining synthetic observations from a different model than that used within the LETKF. Future work includes verifying our one-dimensional results with spatial heterogeneity and large model error in three-dimensional simulations of scroll waves as well as estimating parameters as part of data assimilation, developing heterogeneous models to use within the LETKF, and applying our methods to data from cardiac tissue experiments.

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