

# Kalman Meets Neuron: The Emerging Intersection of Control Theory with Neuroscience

Steven J. Schiff

*Abstract*—Since the 1950s, we have developed mature theories of modern control theory and computational neuroscience with almost no interaction between these disciplines. With the advent of computationally efficient nonlinear Kalman filtering techniques, along with improved neuroscience models that provide increasingly accurate reconstruction of dynamics in a variety of important normal and disease states in the brain, the prospects for a synergistic interaction between these fields are now strong. I show recent examples of the use of nonlinear control theory for the assimilation and control of single neuron dynamics, the modulation of oscillatory wave dynamics in brain cortex, a control framework for Parkinsonian dynamics and seizures, and the use of optimized parameter model networks to assimilate complex network data – the ‘consensus set’.

## I. INTRODUCTION

MODEL based predictor-controller systems employ a computational model to observe a dynamical system, assimilate data through sensors, reconstruct and estimate the remainder of the unmeasured variables and parameters using the model, and then calculate a control vector to generate a desired manipulation of the system. The result of the actual system dynamics is then compared with the predicted outcome, the expected errors within the model are updated and corrected, and the process repeats iteratively. This extremely powerful recursive control engineering framework has never been applied to the range of significant applications to bio-medical applications that it warrants.

Model based predictor-controller algorithms were developed in parallel with the US space program in the 1960s. The most prominent of such strategies was the Kalman filter [1], which for linear systems is a maximum likelihood estimator

that gives the optimal tracking of system state and calculation of control vectors to modulate such states. The dual theorems of observability and reachability for such systems have been considered one of the most important developments in mathematics of the 20th century [2]. Observability and reachability theorems essentially state that if you can observe a system’s state variables, you can optimally control it (reach a given state). Incredibly, these theoretical concepts have been largely absent in the observation and control of complex biological systems.

Of course the linearized equations of motion of missile guidance are a far cry from more complex biological system applications. In the decades since Kalman’s seminal work in the 1960s, the extended (linearized) Kalman filter approaches for nonlinear systems have met with mixed success. Even the simplest of nonlinear system dynamics, such as sine and cosine functions to convert bearings to common coordinates, are notorious for being terrible candidates for linearized Kalman approaches [3].

It was the advent of true nonlinear predictor-controller algorithms that has opened for us an entirely new set of possibilities for biological systems. These methods have been in large part driven by the meteorological use of nonlinear convection models of the atmosphere in data assimilation and weather prediction, termed ensemble Kalman filtering [4-5]. In parallel with this meteorological work, Julier and Uhlmann [3,6] published a nonlinear Kalman strategy termed the unscented Kalman filter (UKF). These strategies were based on using fundamental nonlinear models directly, while iterating the noise and error expectations through these nonlinear equations. The Bayesian framework for updating predictions with measurements remains the same

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S. J. Schiff is with the Departments of Engineering Science and Mechanics, Neurosurgery, and Physics, of the Pennsylvania State University, University Park, PA 16802 (phone: 814-863-4210, e-mail [sschiff@psu.edu](mailto:sschiff@psu.edu)).

as linear Kalman filtering. By employing an optimized sparse sampling of the possible dynamics, the UKF can be computationally efficient.

The UKF can be viewed as a very efficient and selective ‘particle filter’. Particle filtering creates a large number of initial conditions based upon the probability distribution function of the errors in a system, and iterates all of the ‘particles’ through the linear or nonlinear equations of the system. This brute force Monte Carlo scheme can be extremely powerful, but is computationally very inefficient. There have been a wide variety of schemes for selecting subsets of initial conditions (reviewed nicely in [7]). There are several computational neuroscience applications of particle filtering in recent years including [8] and [9], each nicely outlining the natural links with Bayesian state estimation. But as [7] exhaustively demonstrates, UKF is not only more efficient, but often more accurate, than particle approaches.

It is truly remarkable how well UKF methods can estimate state in highly nonlinear, even nondifferentiable systems. Although heavily used now in robotics [10], this nonlinear filtering work has been developed in almost complete isolation from biology and medicine. It was a groundbreaking study by [11] that demonstrated a clear strategy for applying UKF to a model single neuron. In their work, [11] were not at all optimistic that spatiotemporal applications of cell-to-cell interactions would be tractable.

Simultaneous with the work of [11], we demonstrated that mammalian cortex can generate a wide variety of spatiotemporal structures to accompany typical oscillation frequencies observed in motor, sensory, and navigational cognitive phenomena [12]. In this work, we also demonstrated that a fundamental model of general cortical dynamics, the networked differential equations of Wilson and Cowan [13-14], can replicate all of the qualitative dynamics seen in these experiments: ring, plane, spiral, and irregular waves.

We have recently extended the work of [11] to cell-to-cell interactions in a spatiotemporal system [15]. Our control system was designed to speed

up, slow down, or quench spatiotemporal oscillations in cortex. We performed this work using a model of the middle layers of cortex, reflecting cellular dynamics as well as cell-to-cell communications, and we incorporated an ‘observer’ model to track and filter the real system, as well as generate the control vector to modulate the system. We proved that the use of an observer system is a substantial improvement in the tracking and control of such systems when noise is sufficiently high [15]. It is now increasingly recognized that transient cortical oscillations, seen ubiquitously in sensory and motor cortices, reveal spatiotemporal wave patterns when modern multisite optical [16] or electrical [17] measurements are made. We are unaware of any previous nonlinear state estimation for such spatiotemporal neuronal data.

Nevertheless, incorporating the results of [15] directly into real-time experiments is premature. In order to stabilize our algorithms, we needed to empirically adjust the covariance of the estimated state. This is a universal problem in all nonlinear ensemble Kalman filters, and even the seminal work of [6] incorporated a multiplier to adjust estimated covariance. Later, in the meteorological literature, [18-19] termed this strategy covariance inflation, and we followed the formalism of [20] in adjusting our covariance estimate of state. There have been a variety of additional schemes suggested for adjusting covariance inflation, and an efficient method for handling real-time biological systems awaits development.

We have explored taking the foundational ionic dynamical equations of neuronal excitability, the Hodgkin-Huxley equations [21], and incorporated them into an ensemble Kalman framework [22]. We found that not only can we measure voltage alone and reconstruct the entire set of parameters and variables in the setting of significant noise, but we can deliberately damage this model (assuming constant values of the sodium rate variable), and still get adequate reconstruction. Assigning such trivial dynamics is what [11] did with neuronal threshold, and works because of the iterative nature of the UKF framework. What happens is that in UKF constant parameters with

trivial dynamics can be tracked if the iteration time constant is fast compared with the dynamical parameter being tracked. Obviously one can only carry this so far in a model, but again, the potential robustness of ensemble Kalman filters to model inadequacy is quite intriguing.

We have also done considerable work to explore the metabolic dynamics of potassium flow into and out of cells and compartments during neuronal activity [23-24]. We found that combining such dynamics with biophysical neuron dynamics was possible, and showed how measuring voltage could permit reconstruction of potassium dynamics in the extracellular space, and vice versa [22].

Another finding is that such use of a Bayesian assimilation of data, combined with UKF, offers the prospect of an improvement in dynamic clamp approaches [22], where the typical data assimilation technique of direct insertion [25] has been shown to be non-optimal compared with an optimized ensemble Kalman strategy.

Lastly, all neurons are different – we therefore need to account for significant parameter variations in our model systems. We need a method that treats heterogeneity in neurons formally, and our solution is what we term the ‘consensus set’ of parameters. It turns out that it is straightforward in ensemble Kalman filters to let the filters seek a local mean field for model parameter averaging. Surprisingly, such local mean fields frequently converge to values close to the true mean values, but it is not at all clear that such convergence to the true values is necessary. I say this because we need to track dynamics, and not validate models in systems where we can never truly replicate the full underlying biophysics. We therefore developed a consensus set to optimize the mean field parameters for a region in space, and afford tracking of this noisy heterogeneous system [26].

There are a variety of disease dynamics for which such strategies are of potential use. These include epilepsy and Parkinson’s disease, as well as modulation of oscillatory wave dynamics in brain. I will show a variety of numerical and experimental results representing such work in

progress.

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