Combined State and Parameter Estimation of Human Intracranial Hemodynamics

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Abstract

We describe an application of probabilistic modeling and inference framework that is capable of analyzing sensor data in an intensive care unit setting. We are specifically interested in the intracranial hemodynamics. We show that using a probabilistic description of the system and sensor models in addition to the state-of-the-art statistical learning machinery can lead to an accurate real-time decision support mechanism.

1 Introduction

An estimated five million critically ill patients are admitted to intensive care units (ICUs) in the United States every year, at a cost of nearly $100 billion, and roughly half a million of them die, [6]. Advances in clinical decision-making for critically ill patients, therefore, can have a significant human and financial impact.

Decisions on testing and treatment in the ICU are often made under considerable uncertainty. Despite what may appear to be a plethora of information from continuous patient monitoring, key pathophysiological states (vasospasm, sepsis, subarachnoid hemorrhage, failure of autoregulation, etc.) are not directly measurable and must be inferred from the history of observations. The problem is further complicated by the variability in physiology across patients, by the complexity of the disease pathways and injury processes in ICU patients, and by the abundance of artifacts in measured data.

A patient in an ICU is continuously monitored by various sensors, while many interventions, tests, and additional measurements are done asynchronously. The sensory data are usually displayed in real time, and can, if continuously observed, provide an expert physician with a great deal of insight into a patient's condition. In most ICU settings, however, data are reduced to an hourly paper chart generated by a nurse and reviewed daily by the physician. It seems plausible, therefore, that standards of care might be improved by automated data analysis and decision support systems. At present, however, deployed systems are limited to automated alarms based on simple rules; their false-alarm rate often exceeds 90% and generally ICU staff ignore the alarms [11].

This abstract describes a decision support methodology that can deal with high-frequency, artifact-ridden data, variability in patient physiology, and unknown disease states. Our particular focus is on neurocritical care for traumatic brain injury (TBI), which is the developed world's leading cause of morbidity and mortality for individuals under the age of 45 [16]. TBI patients may exhibit a multitude of primary and secondary brain injury pathways, and their obtunded state adds to the difficulty of clinical assessment. The physiological mechanism of interest for such patients is the

intracranial hemodynamics system, for which the key variable is the intracranial pressure (ICP)—the pressure of the cerebrospinal fluid that surrounds the brain tissue. We are interested in inferring critical physiological events and states using from ICP data and other measurements, as well as estimating ICP itself in a non-invasive manner.

Our approach is based on the classical theory of state estimation, i.e., calculation of a probabilistic estimate of patient state at each time point given the complete observation history up to that point. The calculation is based on system, sensor, and parameter models. The system model describes how the intracranial dynamics evolve over time as well as giving the probability of occurrence and likely effects of disease events (hematoma, vasospasm, autoregulation failure, etc.) and clinical interventions. The sensor model describes the measurement process, including noise, artifacts, drift, etc.; the parameter model describes the a priori uncertainty about physiological parameters of the individual patient.

We represent these models using dynamic Bayesian networks [2], which allow for uncertainty in all aspects of the model. We use the physiological model described in [15, 12, 13, 14] and further developed in [10] as basis of our system model. Inference is performed from the observed sensor data using sequential Monte Carlo algorithms, allowing us to learn patient parameters, estimate patient state, and detect clinically important events.

Our probabilistic model is still incomplete, as we don't have a complete sensor model yet. A complete sensor model is necessary, since the data is buried in non-Gaussian, highly persisting random artifactual noise.

2 Related Work

Deterministic modeling of human physiology has a very long history. One highlight is the work of Guyton [5], who describes the human circulation system in terms of 354 interconnected subsystems. For intracranial hemodynamics, Ursino and his colleagues have provided a deterministic differential equation system which is capable of describing various important physiological phenomena [15, 12, 13, 14]. Whereas standard ICP measurement requires cranial drilling, recent work [7, 8] builds on a simplified version of Ursino's model to estimate ICP non-invasively from blood pressure and Doppler measurements of cerebral blood flow velocity.

The basic techniques for detecting events in critical-care monitoring using dynamic Bayesian networks have been presented by Aleks and his colleagues [9]. They detect sensory artifacts in blood-pressure measurement and estimate the underlying true blood pressure accurately using particle filtering. Some preliminary work on modeling of critical hemodynamic events using the methods described here has been presented previously at a clinical meeting [10].

3 Probabilistic Inference

The main task of the ICU monitoring system is to estimate the physiological states of a patient given a sequence of observations. Recent trends in machine learning suggest a data-driven approach that is model agnostic. However, such an approach is not the best fit due to following reasons.

- The data is complex and high-dimensional and is buried under artifactual noise which is persisting over long time periods. Furthermore, there is missing data from some or all sensors for extended time periods.
- The underlying physiological model is known and sensory processes can be explained stochastically. Being agnostic to this information is not reasonable.

Furthermore, results in [9] show that model-based approaches can do far better than purely data-driven ones.

3.1 Probabilistic Modeling: Dynamic Bayesian Networks

As mentioned before, most physiological models are described in terms of deterministic differential equations. However, this is not a good fit for real life applications as system parameters are unknown

most often the time and most physiological variables show stochastic behavior. Furthermore, measurements are available through noisy and artifactual sensors; hence we believe that only stochastic models can describe the intrinsic uncertainty, stochastic variation and sensor noise.

We represent the intracranial dynamics using a dynamic Bayesian network (DBN). A portion of the model is illustrated in the appendix, see Figure 3. DBNs are concise descriptions of discretized stochastic differential equations that can handle discrete and continuous variables, [2]. For stochastic modeling of intracranial dynamics and the associated DBN representation, see [10]. Figure 1(a) and 1(b) illustrate some elementary simulations and show how our model can express physiological events (like hypotension, 1(a)) or ICU interventions (like jugular vein compression test, 1(b)). Our model is capable of explaining various stochastic physiological and clinical scenarios.

3.2 State Estimation

ICU monitoring systems should be capable of inferring and predicting the underlying hidden patient physiological states. State estimation is the task of calculating posterior probability densities over the states, given a sequence of observations. It is one of the widely studied problems in statistics, control theory and artificial intelligence. Exact state estimation is tractable only in limited situations, and for nonlinear, non-Gaussian models such as ours, approximation schemes are necessary. One such approximation scheme is the sequential Monte Carlo (SMC) framework. Particle filtering is one example of the SMC framework that has been successfully used in various state estimation tasks, [1, 3].

We use particle filtering for the state estimation task in our intracranial hydrodynamics model. In an unpublished work of ours, successful inference of various physiological phenomenon like hematoma, vasospasm, autoregulation failure has been achieved using the described framework under the assumption that system parameters are fully known. Figure 2(a) illustrates the inference of autoregulation failure. Autoregulation failure is very hard to infer unless there is a physiological event or clinical intervention happening. Our approach, however, is capable of doing proper inference using the information buried in high-frequency data. Red line in figure 2(a) shows the belief state on the autoregulation. After a short gap, particle filter is able to detect the autoregulation failure and changes its belief state properly.

3.3 Parameter Estimation

Our intracranial model is parametrized by a high-dimensional parameter set. Each human has a unique combination of parameters and estimating these parameters is a crucial part of our application. Failing to estimate these parameters properly may lead to very poor state estimation and prediction. However, most state-of-the-art algorithms cannot handle our model as it is very high-dimensional both in parameter and state spaces.

Online parameter estimation in nonlinear and non-Gaussian systems is a challenging task. It is still an open research problem in the SMC community. Russell's group at UC Berkeley has an ongoing algorithmic research effort in the direction of high-dimensional parameter estimation, (for instance, [4]) and there are some promising results for the intracranial dynamics model using the recent particle Markov Chain Monte Carlo (PMCMC) framework. Figure 2(b) illustrates the one dimensional parameter estimation of the autoregulation speed parameter. For this one dimensional simple estimation problem, a plain bootstrap particle filter is sufficient to track the posterior.

4   Conclusion

We have described a probabilistic framework that is capable of modeling a highly complex physiological behavior. Using this framework and recent statistical learning machinery, we are able to do state estimation and system identification. This inference mechanism which can infer unmeasurable states and pathological events can be used to build a decision support system for ICU physicians.

We need to build a better and complete sensor model that can explain the artifactual noise stochastically. Parameter estimation still poses issues as the parametrization of interest is very high-dimensional. However, there are promising results that were obtained using the offline PMCMC framework. As a future research direction; such inference can be used for decision making over

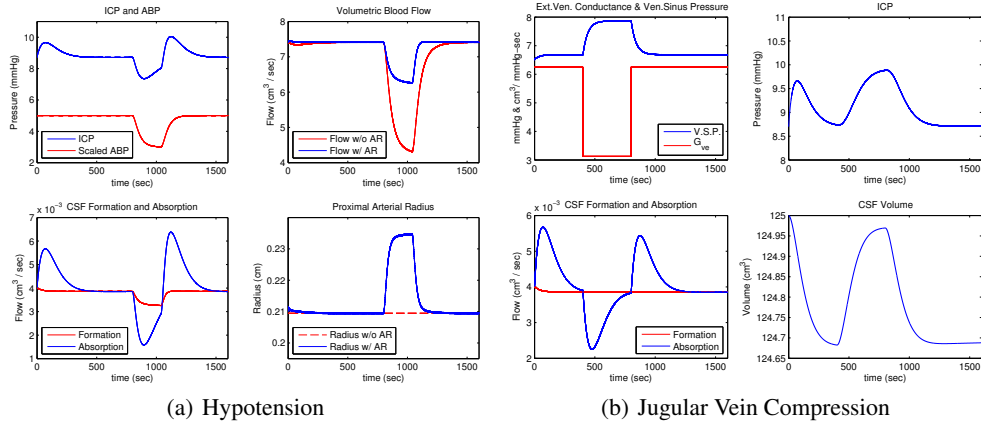(a) Hypotension   (b) Jugular Vein Compression

Figure 1: Simulating Intracranial Dynamics, (a)-Hypotension: The simulated behavior of intracranial variables around a 4 min period in which the ABP drops from 100 to 60 mmHg. Top left: ICP falls and rises with ABP. Top right: CBF stays within a tight range when autoregulation is intact, but decreases markedly when it is impaired. Bottom left: CSF absorption drops below formation as the reduction in ICP decreases its pressure gradient. Bottom right: Proximal arterial radius increases during hypotension, but only if autoregulation is intact. (b)-Jugular vein compression: Simulated behavior during jugular compression. Top left: Venous sinus pressure (VSP) rises as jugular vein is compressed. Top right: ICP rises as jugular compression prevents venous outflow. Bottom left: CSF absorption rate drops below formation rate as rise in VSP decreases its pressure gradient. Bottom right: CSF volume rises while CSF formation exceeds absorption.

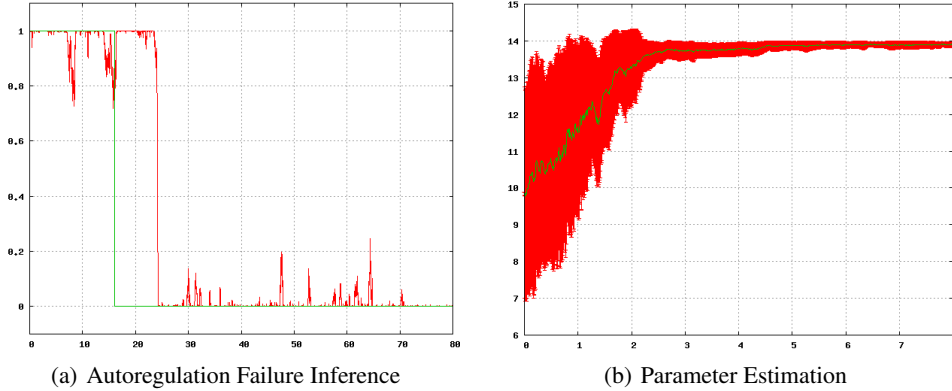(a) Autoregulation Failure Inference   (b) Parameter Estimation

Figure 2: State and Parameter Estimation, (a)-State estimation (autoregulation inference): Green line shows the exact autoregulation behavior. Autoregulation failure happens around the 15th second whereas the particle filter infers the failure correctly around the 25th second. Red line is the mean of the particles, showing approximately the probability of active autoregulation mechanism. (b): Parameter estimation: Correct autoregulation speed parameter is $\tau = 14$ seconds. Bootstrap filter with $N = 5000$ particles correctly learns the parameter. The green line and the red errorbar shows the mean and the standard deviation of the particles that represent the posterior distribution, respectively.

long time scales. The decision of administering an additional test, intervention or drug can be described as a partially observable Markov decision process (POMDP) in an effort to find optimal or sub-optimal control strategies.

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A   DBN for Intracranial Pressure

We have developed differential equations for various sets of physiological variables. For instance, ICP can be expressed mathematically as follows.

$$
\begin{aligned}
\dot{P}_{ic} &= \left(\frac{2G_1}{C_{ic}}\right) P_a + \left(\frac{-2G_1}{C_{ic}}\right) P_1 + \left(\frac{-2G_2}{C_{ic}}\right) P_2 + \left(\frac{2G_2 + G_{pv}}{C_{ic}}\right) P_c + \left(\frac{-G_{pv} - G_{vs}}{C_{ic}}\right) P_v \\
&+ \left(\frac{G_{vs}}{C_{ic}}\right) P_{vs} + \left(\frac{G_f}{C_{ic}}\right) (P_c - P_{ic})_+ - \left(\frac{G_0}{C_{ic}}\right) (P_{ic} - P_{vs})_+
\end{aligned}
$$

where C_1, C_2, G_f, and G_0 are static parameters and P_a, P_1, P_2, P_c, P_v and P_{vs} are various pressures inside the intracranial compartment.

$$
\begin{aligned}
C_{ic} &= \frac{1}{(K_E \times P_{ic})} \\
C_{vi} &= \frac{1}{K_v(P_v - P_{ic} - P_{v1})}
\end{aligned}
$$

K_E, K_v and P_{v1} are static parameters as well. The complete model has more than 10 dynamic state variables and more than 25 static parameters.

Figure 3 illustrates the aforementioned differential equation graphically. Due to space constraints as well as highly interconnected DBN structure, we will not illustrate the whole intracranial dynamics structure here.
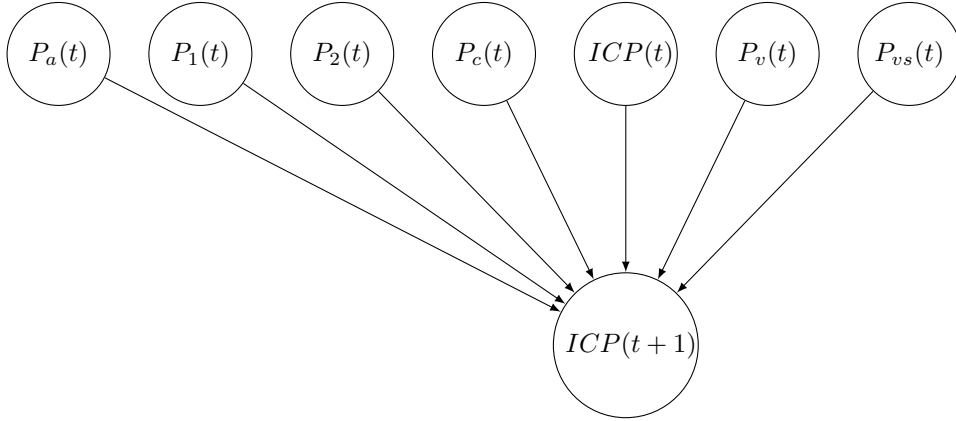

Figure 3: A portion of the DBN that illustrates the transition for the intracranial pressure $ICP(t)$