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Model-Based Data Integration in Clinical Environments

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Abstract— As a result of improved hospital information-technology infrastructure and declining costs of storage media, vast amounts of physiological waveform and trend data can now be continuously collected and archived from bedside monitors in operating rooms, intensive care units, or even regular hospital rooms. The real-time or off-line processing of such volumes of high-resolution data, in attempts to turn raw data into clinically actionable information, poses significant challenges. However, it also presents researchers — and eventually clinicians — with unprecedented opportunities to move beyond the traditional individual-channel analysis of waveform data, and towards an integrative patient-monitoring framework, with likely improvements in patient care and safety. We outline some of the challenges and opportunities, and propose strategies for model-based integration of physiological data to improve patient monitoring.

I. INTRODUCTION

Advances in sensor technology, computer power, and digital storage media permit increasingly copious amounts of clinical data to be continuously collected and archived, not only as part of specific research projects but also during the routine clinical management of patients [1]. For example, archiving a full patient-day of eight waveform signals, trend information, and monitoring alarms in uncompressed format might be well less than 200 MB, though much smaller storage requirements can even be achieved with adequate compression. The collection and storage of large volumes of high-resolution waveform and trend data from bedside monitors is therefore no longer a rate-limiting step in scientific investigations or clinical practice, and vendors have begun marketing commercial products that provide for such options. However, despite the availability now of overwhelming amounts of clinical data, the use of this data in typical clinical decision making has not advanced correspondingly over the past decades.

Although the interfaces may be more sophisticated, what the bedside monitor presents to the clinician is still quite basic information. The monitor might pull together and displays signals from various devices, each dedicated to a particular measurement modality; it may generate and plot maxima, minima, and simple short-term averages of these signals where appropriate; and it implements alarms and alerts that are usually only based on single-channel analysis. The analysis is most sophisticated in the case of ECG-derived critical alarms, but otherwise is largely based on checking simple high/low threshold conditions.

The clinical staff currently gathers data from disparate sources (monitors, lab results, radiology reports, clinical notes, ...), retrospectively screens the data for important events, and uses clinical experience to synthesize the information and formulate differential diagnoses and treatment plans. This obviously puts an enormous burden on the staff. Consequently, most of the data gathered is only screened for overt, clinically important abnormalities, and – in the absence of such events – is rapidly lost from active consideration, even if it is archived. This leads to neglect of potentially valuable information that could otherwise be used to understand the integrity of the patient's physiological systems. Ever more pressing, therefore, is the need to aid clinicians in turning the vast amounts of raw data into clinically actionable information – preferably in real-time – to improve the efficiency, efficacy, timeliness, and safety of clinical decision-making [2], [3].

This problem of data overload is most prevalent in operating rooms and critical-care units, where multiple channels of very dynamic waveform data are acquired at high rates and continuously streamed to bedside monitors, as well as to nurses' central stations. However, current monitoring technology is largely focused on data display, and on separately analyzing individual channels of data to generate trends and alarms. Thus, the task of extracting important but subtler waveform features, and the synthesis of such information across multiple data channels in order to arrive at a comprehensive assessment of patient state, falls to the clinician where humanly possible, but otherwise is unsupported. Current monitoring technology tends to ignore the functional relationship among physiological variables, and the consequent redundancy of information, though these could be leveraged to reduce false monitoring alarms [4], and to extract physiological parameters more robustly.

Here, we advocate the interpretation of monitoring data in the context of appropriately chosen mathematical models derived from physiological understanding. We summarize our vision of model-based data integration, give specific examples of model-based approaches to aid clinical monitoring, and point to current research challenges in systematically obtaining models (often reduced models from more detailed ones) that are well structured for the task at hand. We also outline some practical impediments to model-based data integration in the critical care and perioperative environments.

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II. MODEL-BASED DATA INTEGRATION

Mechanistic mathematical models reflect our understanding of the functional relationships among the variables and parameters that determine the overall behavior of the system under investigation. Such models provide the opportunity to estimate unmeasured model variables and parameters from experimental data, possibly in real-time. The level of abstraction or detail of the model is chosen with an eye on the characteristics of the data streams that the model is intended to represent. Conversely, the knowledge that data of better quality could allow more to be inferred from a particular model might cause one to attempt the collection of better data (for instance at a higher sampling rate, and/or with more amplitude resolution, and/or with more attention to characterizing and filtering out various sources of noise).

By casting our understanding of physiology and pathophysiology in the mathematical framework of deterministic or stochastic dynamical systems, we enable quantitative predictions to be made, and to be compared against results from clinical measurements. In the context of model-based integration of bedside monitoring data, mathematical modeling provides constraints that may allow us to relate readily observable data streams (such as waveforms of ECG, arterial blood pressure, or cerebral blood flow velocity) to physiological variables and parameters that are unmeasured but more directly reflective of changes in pathological state (such as cardiac output, cardiac contractility and ejection fraction, peripheral resistance, or intracranial pressure).

Augmenting the number of available monitoring signals through model-based estimation of unmeasured physiological quantities can permit more comprehensive monitoring. This might in turn allow earlier differentiation of competing diagnoses, more timely identification of disease progression or deterioration, and more accurate titration of therapy.

III. MODELING CHALLENGES

Among the challenges in model-based patient monitoring are the following:

- careful time-stamping of data obtained from different devices;
- automated assessment of signal quality as a function of time, so estimation is only attempted where the data permits it to be done with confidence;
- determination of suitable model structures and estimation algorithms for the available data and estimation objectives;
- validation of estimation results;
- presentation to and acceptance by clinicians.

We address some of these and related issues below and in the sections that follow (though not in the same order as listed above).

Mathematical models of physiological systems tend to be built at a level of complexity that captures the system's dynamic behavior over a wide range of time and length scales. Modules might be added that represent more of the relevant physiology, in attempts to improve the fit of the models

to particular experimental data. The Physiome Project, for example, advocates a multiscale modeling approach to integrate experimental data from the subcellular to the organism level [5]. However, increasing the complexity of a model can also significantly work against its usefulness in other respects: parameter values are harder to pick reliably, because many different combinations of parameter values can lead to model responses that are essentially indistinguishable, given the level of noise in the data; simulation times are increased; and it becomes difficult to understand in a fundamental way what parts of the model — and ultimately what aspects of the physiology — actually contribute to a particular dynamic response, and how. Appropriately reducing the complexity of a model may actually make for a more effective representation of experimental data, particularly for real-time monitoring applications.

It would be desirable to have a systematic methodology for exploring complex models from this point of view: to deduce where aggregation or simplification or reduction of a model may be possible or required; where refinement or elaboration might be desirable or necessary; and how to then accomplish these tasks in a way that preserves the physiological interpretability of the model. Though the literature does not provide anything quite so comprehensive, there are approaches and tools that can be useful [6], and some of these are outlined in the next section. By contrast, the most widely studied model-order reduction schemes in the current control literature [7] make no attempt to preserve the interpretability of the variables and parameters that specify the reduced-order model, thus limiting their applicability in clinical monitoring and decision-making processes.

IV. EXAMPLES OF MODEL-BASED APPROACHES TO PATIENT MONITORING

While a general theory is currently lacking, specific examples of model-order reduction and model-based data integration for clinical monitoring have been successfully implemented. We give three examples, labeling them in each case by the analytical approach that underlies the construction of the reduced model. Analytical approaches that are not mentioned in more detail here, but that can provide powerful structural insights into a model, include the use of participation factors [6], [8] to analyze the linear, time-invariant model obtained by linearizing a nonlinear, time-invariant model around an equilibrium point.

A. Subset Selection

As mentioned above, mathematical representations of physiological systems can often be quite elaborate, including tens if not hundreds of states and parameters that need to be specified. A classic example is the Guyton model of cardiovascular and fluid-electrolyte regulation [9]. Consequently, a discrepancy commonly exists between the high resolution and rich dynamic behavior of the model, and the limited dynamic behavior of the small number of measurements that can be made. This disparity leads to parameter estimates that are overly sensitive to even slight variations (noise) in the

experimental data, if one attempts to estimate all or a large number of the model parameters.

It turns out that in many such cases the parameter space can be systematically split into two groups: a small set of parameters that can be estimated robustly; and the remaining parameters being less reliably identifiable and therefore fixed at *a priori* values. Fixing a large fraction of parameters at nominal values will introduce a bias in the resultant estimates of the remaining parameters. The advantage to be gained, however, is the robust identification of this remaining small number of parameters, which significantly influence the fit of the model output to the available data.

An algorithm for such subset selection has been described in [10] and evaluated by [11], in the context of understanding the hemodynamic response to changes in posture. The full model in [11] contained over 140 parameters. Subset selection identified four significant parameters that could be identified reliably from time series of heart rate and arterial blood pressure recorded during changes of posture.

B. Averaging

Sometimes one might be interested in isolating the dynamic behavior on a particular time scale, rather than carrying forward the full dynamic response of a model. In particular, one might not be interested in the instantaneous value of a particular physiological variable, but rather in the response of the variable's short-term average to perturbations in model parameters. This is especially the case for the cyclic or quasi-periodic waveforms typically found in physiological settings. Such responses generally tend to occur over time scales that are large compared to the fastest characteristic time constant in the model. In these cases, a cycle-averaged model that tracks the cycle-to-cycle dynamics rather than the intra-cycle dynamics seems desirable [12], [13]. One might expect simulation times to be reduced, and the cycle-averaged model to exhibit a structure that simplifies the analysis of its dynamic behavior. Frequency selective averaging generalizes the notion of averaging to isolate dynamics at particular frequencies [14].

The work in [15], [16] applied cycle-averaging to the well-known Windkessel model, to use intra-beat and inter-beat information of the arterial blood pressure waveform for beat-by-beat estimation of cardiac output and total peripheral resistance. The earlier work in [17] exploited beat-to-beat variability in a different way to estimate these same quantities.

C. Time-scale Separation

In some circumstances, one seeks to keep track of dynamic responses on two very different time scales: a very fast dynamic behavior associated with "fast variables;" and a very slow response of "slow variables." Following standard singular perturbation methods [18], we can consider the slow variables to be essentially constant over the time scale of the fast dynamics. Conversely, the fast variables can be considered to have settled to a quasi-steady-state over the characteristic time scale of the slow dynamics.

The work in [19], [20] exploited this idea when developing a model-based data-integration and estimation algorithm that uses peripheral arterial blood pressure and cerebral blood flow velocity measurements to noninvasively estimate intracranial pressure and cerebrovascular resistance and compliance. Since the time scale for cerebrospinal fluid formation is very long compared to the characteristic time constant of cerebrovascular blood flow, mean intracranial pressure can be considered constant within a beat, but varying from beat to beat. The resulting model is considerably simpler than that of [21]. Intra-beat waveform analysis yields the desired parameters of resistance, compliance and intracranial pressure, whose estimation on a sliding window allows variations in the estimates from one beat to the next.

V. TECHNICAL CHALLENGES

Apart from the model-reduction challenges outlined above, several technical challenges exist in implementing a model-based patient monitoring paradigm in critical care and perioperative care environments.

A key technical problem relates to integrating data from multiple bedside monitoring devices into a single computer for time-locked archiving or real-time processing. Most modern stand-alone bedside monitoring devices do not provide analog or digital output streaming of raw or processed data. Rather, they might provide the option to save raw or processed data to a local hard drive for later recovery and analysis. Since manufacturers generally do not provide an option for sending an external timing signal into these monitoring devices, time-locked data streaming or time-locked data archiving from all bedside monitoring devices is therefore generally impossible at present.

Apart from this lack of interoperability, a further major obstacle for research and implementation in advanced patient monitoring is the proprietary format by which each vendor stores its data. Vendors tend to be very reluctant to make their data formats available to researchers. An inordinate amount of time is therefore spent on decoding individual proprietary data formats to get to the raw data that is being recorded by the device.

Many bedside monitors were designed years ago, when the bandwidth of the hospital information technology infrastructure and storage capacity were much more limited than today. Consequently, compromises were made with regards to the sampling frequency and amplitude resolution of waveforms that were streamed or archived. Some hemodynamic monitors, for example, stream data at comparatively low sampling rates ($\sim$ 100 Hz) and amplitude resolution ($\leq$ 10 bits), though the sampling frequency and amplitude resolution internal to the monitor are generally much higher. Such reduced data quality can be rather limiting even for routine applications for neonates and premature neonates, in whom heart rates commonly hover above 150 beats/minute. Furthermore, algorithms that rely on analyzing fine intra-cycle features of waveforms might encounter suboptimal performance due to quantization errors or insufficient temporal resolution of the streamed data.
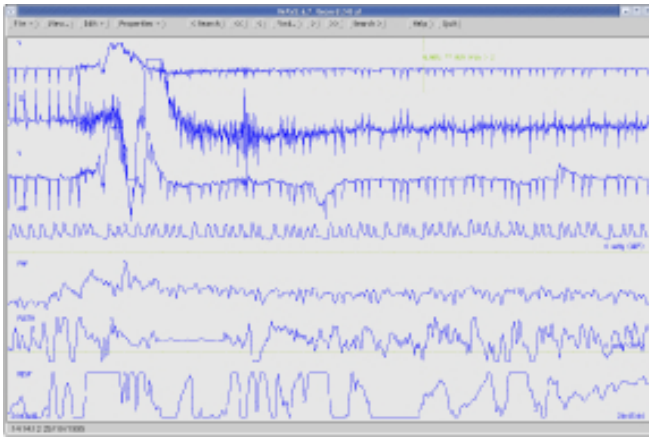
Fig. 1. Multiparameter recording from a patient in critical care (from the MIMIC-II database, [1]). Significant artifacts exist in all recorded waveforms. Top to bottom: three channels of ECG, arterial blood pressure, pulmonary artery pressure, plethysmogram, respiration.

In the development phase of our model-based algorithms, we have also encountered the more mundane problem of clinical staff needing to be sensitized to steps that are critical to making use of archived data, e.g. logging the medical record number or name of the patient into the bedside monitoring devices, and discharging the patient from the monitors at the end of their hospital stay. This is needed for matching of data from bedside monitors with other clinical information from the hospital's electronic medical record systems, e.g., associating information on medication or intervention with a particular record.

Finally, waveform data — especially the pressure and flow waveforms — tend to be noisy and prone to artifacts, see Figure 1. Automated signal-quality assessment is therefore an important pre-processing step in developing model-based patient monitoring algorithms [2]. Some very promising work in the area of multi-signal processing has begun to address the problem of automated signal processing and validation for the arterial blood pressure waveform [4], and some extensions have been applied to the electrocardiogram [22].

VI. CONCLUSIONS

The abundance of physiological waveform data from a patient's bedside provides the opportunity to extend the current monitoring framework (focused on single-channel analysis) to one that interprets the available data in the context of physiological models that encapsulate our current understanding. We thereby harness functional physiological relationships to estimate unmeasured but physiologically important variables, and thus augment the information available to the care provider for improved rational clinical decision making. A primary research challenge in the field of model-based patient monitoring is the development of structured model-reduction methodologies that preserve the clinical interpretability of the variables and parameters in reduced models. Such interpretability is imperative for model-based methods to be adopted clinically. Technical impediments to this program include: proprietary data formats; the lack of interoperability of different bedside monitors; and the lack of accurate time synchronization of different devices. Despite these challenges, however, we are convinced that model-based data integration and interpretation will improve the way clinicians diagnose, track, and treat disease conditions in data-rich clinical environments.

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