

Available Student Research Projects in the Laboratory for Computational Physiology (LCP)

Fall, 2009

Contents

1. UROP Projects	2
1.1 Heart rate variability and sepsis in neonates	2
1.2 De-identification quality control	2
1.3 Time of death in the ICU	2
1.4 Mortality analysis of a large ICU population	3
1.5 Intensivist staffing patterns and patient outcome	3
1.6 Determining the significance of blood pressure drops (hypotensive events) in the ICU	3
2. Advanced Projects (MEng, SM, PhD)	3
2.1 Develop predictive algorithms for hemodynamic instability	3
2.2 Extracting pathophysiologic interpretations from raw data	3
2.3 Physiologic effects of hypotension	4
2.4 Is respiratory modulation of ABP a useful indicator of vascular volume and cardiac filling pressure?	4
2.5 An investigation of an integrated physiology abnormality score (IAPS)	4
2.6 Reduce false alarm rates for apnea/bradycardia in the NICU	5
2.7 Predictive alerts	5
2.8 AKI prediction of outcomes in critically ill	5
2.9 Septic shock: providing early warnings through multivariate logistic regression models	6
2.10 Reduction of false arrhythmia alarms	6

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1. UROP Projects

1.1 Heart rate variability and sepsis in neonates

The LCP has considerable experience in the analysis of heart rate variability (HRV). Over the last year we have collected thousands of hours of ECG, respiration and pulse oximetry data from several hundred neonates. The objective of this project is to run our existing heart rate variability (HRV) tools (together with some novel approaches, such as phase rectified signal averaging and heart rate turbulence) to determine if any of the HRV metrics are markers of, or predictive of sepsis in neonates. Background reading can be found here:

<http://www.physionet.org/events/hrv-2006/moorman.pdf>

<http://www.physionet.org/tutorials/hrv-toolkit/>

<http://www.physionet.org/tutorials/hrv/>

Required skills include Matlab, some knowledge of statistics and basic signal processing knowledge, although these can be learned on-the-job. Some knowledge of bash and C is useful but not essential.

1.2 De-identification quality control

We have developed software that automatically de-identifies free text (discharge summaries, nursing notes, etc). We wish to develop a procedure for routine human-aided evaluation of the quality of the de-identification. It is necessary to monitor the occurrence of false negatives—protected health information (PHI) that has escaped de-identification. A web-based application is required that will select and present de-identified text from the MIMIC II database to two or more human reviewers. False negative PHI must be marked by each reviewer, scores need to be collected, disagreements need to be adjudicated, and final statistics must be calculated.

1.3 Time of death in the ICU

When do patients in the ICU die? How and why do they die? Clearly many deaths are a result of decisions to withdraw life supportive care and switch to comfort measures. These decisions are usually made in a family conference held after morning work rounds, and deaths follow later. Other deaths occur despite maximal therapeutic efforts. Can the database answer these questions of when and why? Are there physiologic factors that are involved in ICU deaths, or are deaths more related to work flow patterns?

1.4 Mortality analysis of a large ICU population

We have death statistics for patients within the ICU or during their hospital stay, however we have not explored what happened to the patients after they were discharged from the hospital. The purpose of this project is to review Social Security Administration master death records to figure out the probability of survival after discharge from the hospital, and potentially identify significant factors involved in survival. This project could also investigate the impact of gender on outcomes in certain patient subsets (diagnostic classes).

1.5 Intensivist staffing patterns and patient outcome

At some point in time there was a change in staffing patterns in the BIDMC ICUs. In January 2004 the hospital instituted a staffing pattern that put an intensivist on call for all ICU beds during the night, thus assuring 24 hour attending coverage. Is there any evidence of a change in patient care or outcome as a result of the increased senior clinician coverage? (Mortality, procedures and complications, etc.?)

1.6 Determining the significance of blood pressure drops (hypotensive events) in the ICU

Drops in blood pressure are known to be predictors of instability and markers of ill health in the ICU. The purpose of this project is to determine if significant blood pressure drops (MBP < 60 mmHg for > 1/2h) have any independent association with mortality and length of stay in the ICU. Is the degree of hypotension, or the number of episodes of prognostic value?

2. Advanced Projects (MEng, SM, PhD)

2.1 Develop predictive algorithms for hemodynamic instability

Mohammed Saeed's doctoral thesis (<http://hdl.handle.net/1721.1/40507>) demonstrated the feasibility of classifying the temporal patterns of physiologic variables (ABP, HR, CO) into "unstable" vs "stable" classes. His work suggested that hemodynamic instability could be predicted up to 2 hours in advance. This work needs to be extended in many directions—more patients, more variables included in the predictive algorithm, different feature sets (perhaps simpler) should be evaluated, etc. The verification of a robust predictor of hemodynamic deterioration would be a valuable contribution to critical care decision-making. We now have a larger population on which we can attempt to evaluate these methods. We would also like to analyze the possibility of adding other factors to the prediction such as fluid balance and signal quality.

2.2 Extracting pathophysiologic interpretations from raw data

Extensive data is collected from ICU patients on a continuous basis, including: physiologic waveforms, streams of measurements based on such waveforms (ABP, HR, PAP, CVP, etc.), laboratory tests, imaging reports, fluid balance, ventilator settings and arterial blood gases, medication records, and clinical notes. This project would explore the feasibility of using the available data to estimate and track the physiologic state of the patient. For example, is it possible to explain

the likely pathophysiologic basis of a hypotensive event? (Is it due to pump failure, rhythm disturbance, volume depletion, vascular resistance drop, medication effect, etc.?) The project would involve modeling, natural language processing, expert systems, and signal processing. The work would be done using the MIMIC II Database.

2.3 Physiologic effects of hypotension

ICU patients may experience considerable variation in arterial blood pressure, and considerable effort is focused on controlling ABP using fluids and vasoactive medications. It would be interesting to investigate the relationship between ABP and organ function. It is clear that very low blood pressure leads to inadequate perfusion of organs and subsequent damage evidenced by biomarkers of kidney and hepatic cell damage, for example. The MIMIC II DB (includes >30,000 records of ICU patient admissions) could be used to explore this question.

2.4 Is respiratory modulation of ABP a useful indicator of vascular volume and cardiac filling pressure?

A number of publications have noted that the modulation of pulse pressure (SBP-DBP) by the respiratory cycle (especially in ventilated patients) is related to the level of the central venous pressure. Low CVP levels correlate with increased amplitude modulation of PP, and hypotensive patients showing this seem to respond better to volume replacement than patients with less modulation amplitude. In determining the etiology of hypotensive episodes it is important to assess vascular volume in a non-invasive manner. We would like to explore the effectiveness of respiratory modulation of PP in our large MIMIC database [CCM 2009, 37:2570–2575, and editorial on p. 2662].

One challenge is that some blood pressure waveforms in the database are sampled with a low amplitude resolution (only 8 bits) which leads to heavy quantization and poor estimation of the cyclic variation in the pulse pressure. It is therefore necessary to restore the original pulse waveform in order to preserve features such as respiratory modulation. The project will begin by taking high quality data and degrading it through quantization and clipping, then applying various methods such as cubic spline interpolation and fitting of Gaussian functions to restore the original waveform.

Once the signal processing techniques are established, measures of respiratory pulse pressure variation may be correlated with estimates of vascular volume in patients with hypotension treated with volume replacement. Required skills include Matlab, and basic signal processing knowledge, although these can be learned on the job.

2.5 An investigation of an integrated physiology abnormality score (IAPS)

This project is aimed at creating a descriptor of organ function similar to the simplified acute physiology score (SAPS), but one that captures the temporal characteristics of the abnormalities. By developing a multidimensional descriptor of normality we can measure the distance of this descriptor from a target value and integrate the difference over time to provide a measure of risk for the patient, in terms of how long and how badly the organ function has been damaged. For example, what is the relationship between mortality and the “integrated abnormal physiology score” (IAPS)

for certain variables such as: lactate, SpO₂, pH, creatinine, mean arterial pressure (MAP), etc. The IAPS is the area between a physiologic variable (such as mean arterial pressure) and a threshold that defines the limit of normality. This score may also be used to study its relation to end organ function.

2.6 Reduce false alarm rates for apnea/bradycardia in the NICU

Resolution of apneic episodes is one important criterion for discharging patients from the neonatal intensive care unit (NICU). Reliable automated detection of apnea is a desirable goal. At present the very low positive predictivity (high FP rates) of such alarms make them almost useless. Is it possible to improve monitoring and alarm performance for apnea/bradycardia in neonates? Using a new method of robust respiration rate estimation from multiple physiologic sensors (ECG, pulse oximeter and respiratory bands), this project aims to determine if a more sensitive and specific method of detecting apnea can be developed. By correlating drops in heart rate and O₂ saturation in a short time window after a suspected apnea, it may be possible to provide an early warning alert of potentially hazardous hypoxic events post-apnea, without the numerous false alarms that currently pervade the ICU. Algorithm development could be done using MIMIC II 7-channel data. [Conceivably the final algorithm could be tested using a single bedside monitor, the RS-232 port and a second computer.]

2.7 Predictive alerts

Develop predictive alerts and validate them using the MIMIC II database, with the intention of performing clinical evaluation of promising algorithms. Prediction of the following events would be of great interest:

- Impending sepsis or septic shock (additional work needed)
- Hypotensive episodes (additional research needed)
- Need for intubation or re-intubation for respiratory failure (new area)
- Renal failure

2.8 AKI prediction of outcomes in critically ill

Barrantes et al (Acute kidney injury criteria predict outcomes of critically ill patients, Critical Care Medicine. 36(5):1397–1403, May 2008) demonstrated that “The Acute Kidney Injury Network definition of acute kidney injury predicts hospital mortality, need for renal replacement therapy, and prolonged hospital stay in critically ill patients. An increment of serum creatinine ≥ 0.3 mg/dL in 48 hrs alone predicts clinical outcomes as well as the full Acute Kidney Injury Network definition.” This project aims to verify these results (evaluated on only 496 patients), using our larger database of over 18,000 patients. If discrepancies are found, an exploration of the differences will be performed. For more information on the research database see <http://mimic.mit.edu>.

2.9 Septic shock: providing early warnings through multivariate logistic regression models

Early goal-directed therapy (EGDT) in severe sepsis and septic shock has shown to provide substantial benefits in patient outcomes. However, these preventive therapeutic interventions are contingent upon an early detection or suspicion of the underlying septic etiology. Detection of sepsis in the early stages can be difficult, as the initial pathogenesis can occur while the patient is still displaying normal vital signs. In a preliminary study our group developed an early warning system (EWS) to provide clinicians with a forewarning of an impending hypotensive crisis—thus allowing for EGDT intervention. Multivariate logistic regression EWS models were trained to differentiate between 107 high-risk sepsis patients of whom 39 experienced a hypotensive crisis and 68 who remained stable. The models were tested using 7-fold cross validation; the mean area under the receiver operating characteristic (ROC) curve for the best model was 0.940 ± 0.038 . This project will attempt to extend this work and apply it to a much larger population. See Shavdia D. Septic shock: Providing early warnings using logistic regression models. M.Eng. Thesis, Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, MA, Sept. 2007 for more information.

2.10 Reduction of false arrhythmia alarms

A large fraction of arrhythmia alarms in the ICU are false. The alarms are generally based on the ECG signal alone. Major reductions in the rate of false critical arrhythmia alarms have been achieved by fusing information from both the ECG and the blood pressure waveforms. (See Aboukhalil A, Nielsen L, Saeed M, Mark RG, Clifford GD. Reducing false alarm rates for critical arrhythmias using the arterial blood pressure waveform. *J Biomed Inform*, 41(3):442-451, June 2008. Available online March 21st 2008. (doi:10.1016/j.jbi.2008.03.003).) However, only about 60% of ICU patients have intra-arterial catheters to monitor arterial BP waveforms. Virtually all patients, however, have pulse oximeters which produce a photoplethysmographic (PPG) signal. Preliminary work has been done in this lab investigating the use of the ECG and PPG to reduce false alarms. (See Deshmane AV. False arrhythmia alarm suppression using ECG, ABP, and photoplethysmogram. M.Eng. Thesis, Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, MA, Sept. 2009.) This project's goal is to continue work toward a successful algorithm to reduce false alarms by fusing ECG, PPG, and ABP data.

If any of these topics or related projects interest you, please contact Prof. Roger Mark (rgmark@mit.edu).