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# Real-time Multidimensional Temporal Analysis of Complex High Volume Physiological Data Streams in the Neonatal Intensive Care Unit

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**Abstract**

*The intensive care of immature preterm infants is a challenging, dynamic clinical task that is complicated because these infants frequently develop a range of comorbidities as they grow and develop after their premature birth. Earliest reliable condition onset detection is a goal within this setting and high frequency physiological analysis is showing potential new pathophysiological indicators for earlier onset detection of several conditions. To realise this, a platform for multi-stream, multi-condition, multi-feature risk scoring is required. In this paper we demonstrate our multi-stream online analytics approach for condition onset detection and demonstrate a user interface approach for patient state that can be available in real-time to support condition risk scoring.*

***Keywords***

Critical Care, Neonatal Intensive Care, Physiologic Monitoring, Patient Monitoring.

## Introduction

Preterm birth is a significant global phenomenon with reported rates from 5 to 12%. The intensive care of the critically ill preterm infant may be complicated at any time by the onset of one or more of the recognised comorbidities of prematurity. The earlier detection and treatment of these conditions should be associated with better short and long term outcomes.

Recent research demonstrates the potential to monitor and analyse high frequency physiological data from critical care neonatal patients for earlier onset detection of a range of conditions such late onset neonatal sepsis [1], pneumothorax [3], intraventricular haemorrhage [4] [5], and periventricular leukomalacia [6]. Within these research studies, however, there has been a limitation of considering conditions in isolation and a predominance of the analysis of ECG and derived heart rate only. Preterm neonates can develop multiple conditions concurrently or over time. Each condition has its unique set of pathophysiological behaviours. An infrastructure that can process multiple higher frequency physiological data to support the earlier condition onset detection for multiple conditions would improve clinical support greatly. Such a solution requires a multidimensional approach as there are multiple conditions and multiple streams of data for which multiple behaviours can exist. The seamless integration of key clinical data is also a key factor for the provision of relevant context to facilitate clinical decision-making and improving outcomes for newborn infants [7].

Infection is a major concern for clinicians who care for preterm infants in neonatal intensive care units. Nosocomial infection (NI), an infection that occurs during hospitalisation but was not present or incubating at the time of admission [8], is one of the most important causes of morbidity among hospitalised newborns [9]. Intrinsic biological risk factors for NI include the relative immunodeficiency of the prematurely born infant together with the immature barrier function of the skin and gastrointestinal tract. Medical interventions, invasive procedures, and contact with medical devices are important extrinsic risk factors. The early diagnosis of a NI is difficult because the clinical signs of infection are usually vague, non-specific and subtle until the infection is well established. Although biological markers for inflammation are available to assist clinicians in making an early diagnosis of infection, there has not been widespread adoption of this biotechnology.

This paper presents the application of our multi-stream online analytics approach for condition onset detection and provides example results from a research study for earlier onset detection of late onset neonatal sepsis (LONS). We have devised a multi-stream, multi-feature risk scoring approach to model patient state over time and to demonstrate an approach for the graphical user interface to visually represent the patient state.

## Materials and Methods

### Dynamic, real-time analytics with Artemis

In support of this research study the Artemis platform was utilised. Artemis is a platform for online health analytics that enables concurrent multi-patient, multi-stream, and multi-diagnosis and temporal analysis in real-time to support clinical management and research. The platform architecture is shown in Figure 1.

The Data Acquisition component facilitates the extraction of real-time medical device generated physiological data streams together with the extraction of necessary information from the Clinical Information System. Those data are then forwarded to the Online Analysis component which performs the analysis of the data in real-time; that is, before it reaches the database storage. For this real-time component, Artemis employs IBM's InfoSphere Streams, a streaming middleware system that processes streaming data in real-time. Once processed, the original data, together with the newly generated analytics, are stored within the Data Persistency component. Artemis is capable of processing and then storing the raw data and derived data from multiple infants at the rate they are generated [7], [10].

**Late Onset Neonatal Sepsis Case Study**

Preterm infants admitted to the Neonatal Intensive Care Unit (NICU) at The Hospital for Sick Children, Toronto, constituted the population for the prospective cohort study from which the patient case presented to demonstrate the user interface of our risk scoring approach in this paper is drawn. Patients were enrolled if they were located within an Artemis bed space, of which there were 8 within the 36 bed NICU, provided they satisfied the inclusion and exclusion criteria. The Hospital's Research Ethics Board approved the study together with a waiver for informed parental consent.

***LONS research aims***

LONS may be modeled as a dynamic continuum of five sequential phases, each associated with a corresponding clinical state:

- Phase 0: no infection present.
- Phase 1: infection present but no detectable clinical symptoms and signs.
- Phase 2: subtle clinical symptoms and signs present.
- Phase 3: definite clinical symptoms and signs present.
- Phase 4: very obvious clinical symptoms and signs present.

Since there is a relationship between phase of LONS [LONS_phase] and clinical status [LONS_status] of the neonate, it is possible to assign a corresponding clinical state to the neonate [state 0 . . . state 4].

There is also a temporal dimension because the clinical state changes as LONS progresses from phase 1 through to phase 4. The clinical status of the neonate may be documented by capturing the LONS_status at time *t*.

Robust risk identification of LONS from the analysis of physiological data during the preclinical Phase 1 would provide the greatest benefit to clinicians and their patients. If identification is delayed until Phase 2 or 3, then there might be clinical utility as the selection of LONS from other potential differential diagnoses. However, identification at phase 4 does not represent an improvement on current clinical practice. As a result, our overall research aim is to develop robust risk identification of LONS from the analysis of physiological data during the preclinical Phase 1.

Preterm infants (24 weeks < gestational age (GA) < 37 completed weeks), expected to survive for more than 48 hours after admission to the NICU, constituted the study population for the prospective cohort study provided none of the following were present at admission to the NICU:

1. Established infection, necrotising enterocolitis, or a haemodynamically significant patent ductus arteriosus requiring surgical ligation.
2. Any acute injury to the central nervous system that is likely to be associated with fluctuations of cardiorespiratory physiological data streams.
3. Any congenital abnormality that is likely to be associated with fluctuations of cardiorespiratory physiological data streams.

***Data collection***

The demographic data that was extracted from the Clinical Information System included gestational age at birth, birth weight, gender, admission diagnosis, and postnatal age at entry to the study. Information from the Admission/Discharge/Transfer table was initially integrated manually on a daily basis and then through automated polling every 20 minutes to provide up-to-date patient bed space information for the Artemis bed spaces.

The physiological data collected by Artemis that is presented in this paper is a subset of all the streams collected. The streams of relevance for this work together with their respective frequencies were:

- Electrocardiogram (ECG) (1000 Hz);
- Heart rate (HR) (1 Hz);
- Transcutaneous blood oxygen saturation ($SpO_2$) (1 Hz);
- Respiration rate (RR) (1 Hz);
- Blood pressure [systolic, diastolic, and mean] (BP) (1Hz).

Standard clinical care within this NICU includes the continuous monitoring of ECG and pulse oximetry resulting in constant availability of the ECG together with the derived HR, RR, and also the $SpO_2$. BP real-time streaming was only available when the neonate's clinical condition required its continuous monitoring.

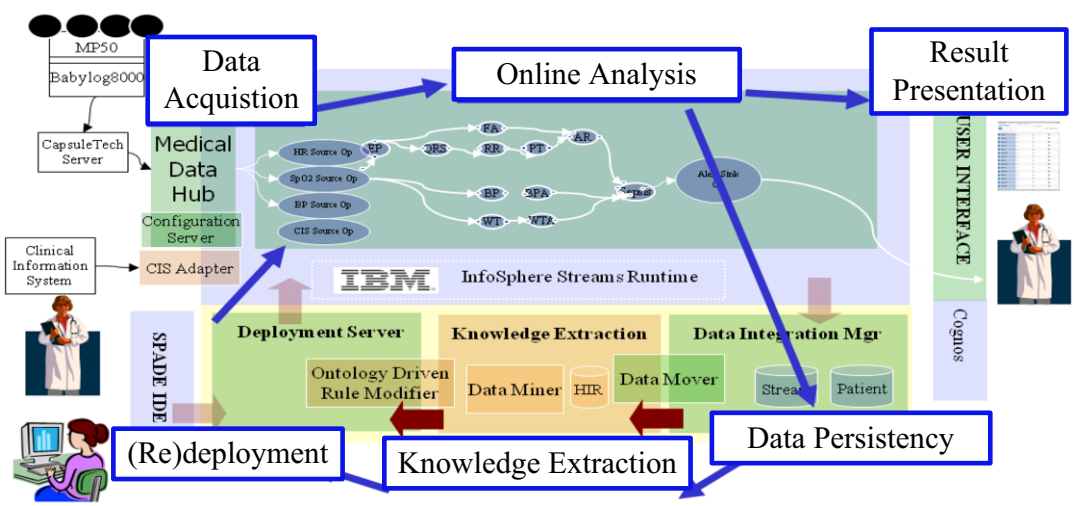


*Figure 1- Artemis Platform* [7]

The Phillips Intellivue MP70 monitors are in use within the NICU at The Hospital for Sick Children. The *CapsuleTech* [11] device was used as part of the Artemis Data Acquisition component to obtain data directly from the Philips Intellivue MP70 monitors. The Ethernet port on these devices was in use to support the Philips central monitoring solution and hence the serial ports on these devices were used for this research. Serial to Ethernet conversion was performed at the bedside using either the CapsuleTech bedside Ethernet convertor or other serial to Ethernet converter boxes. The data was then transmitted through wired connection through the hospital network to the Artemis platform. An alternate unique identifier for patient id was used to tag the data as it was transmitted to the Online Analysis to support the privacy and confidentiality of personal health information.

***Online Health Analytics***

An algorithm was designed through extensive collaboration by all the co-authors. It utilised information from published research on ECG physiological stream behaviours representing potential early onset indicators for LONS. However, given our ability to perform multi-stream analysis in real-time, we included additional clinical insight from a neonatologist (AJ) for potential early onset indicators from other physiological streams. The algorithm was then developed for deployment within the online health analytics environment utilising the initial programming language for InfoSphere Streams version 1, namely, the Stream Processing Application Declarative Engine (SPADE).

A number of stream features were derived in real-time and then analysed to determine a LONS onset score. The levels of the LONS onset score were defined as follows:

- Level 0: No specified features present.
- Level 1: Presence of features reporting reduced heart rate variability (HRV), or bradycardia, or a significant downward drift of heart rate.
- Level 2: Presence of level 1 features plus the presence of a respiratory pause as determined by fall in respiratory rate below the defined threshold.
- Level 3: Presence of level 2 features plus a blood oxygen desaturation threshold breach or a significant downward drift of blood oxygen desaturation.
- Level 4: Presence of level 3 features plus a blood pressure threshold breach on any of the readings or a significant downward drift of any of the blood pressure readings.

Note that level 4 would only be attained at times when the blood pressure data was streamed in real-time.

## Results

LONS onset score profiling for each enrolled patient was calculated each second. In this work we present a user interface design demonstrating how that LONS onset score can be presented on an ongoing basis as an hourly summary. An example of this is presented in Figure 2 for a patient who was suspected of having infection throughout the day on July 1. Due to the device sampling variability for the data provided at 1Hz, the number of values report per hour can be slightly less than the expected 3600 readings per hour. For example, some signal loss was experienced in some hours due to bedside interventions requiring changes in lead placement.

The graph highlights the increasing frequency LONS onset higher value scores as present on June 30 with further increasing LONS onset scores through the early hours of July 1 prior to clinical suspicion of infection. Colour gradient from blue to yellow to red enables the representation of severity without the usual pitfall of user interface traffic light reporting, which does not support the needs of those who are colour blind.

The LONS onset score demonstrates the added value of the multi-stream analytics as compared to other research focused solely on the analysis of ECG as the presence of pathophysiological behaviours on multiple streams are shown.

## Discussion

In earlier research, we have demonstrated the potential for multi-stream analytics approaches using another algorithm within the Artemis platform to distinguish potential false positives for LONS through the dual feature analysis of HRV and respiratory rate variability (RRV) [12]. These false positives were able to be classified out of a LONS model through their association with the presence of certain drugs. While our initial hypothesis for this research was to model the risk of LONS, our multi-dimensional approach has enabled us to present early research outcomes for a multi-condition/multi-health state approach for online clinical decision support over time. Using this technique, multi-risk scores can run concurrently, and their potential presence can be modeled concurrently in real-time.

Our clinical validation results for this LONS Risk Score across the enrolled patients within the larger prospective cohort study is the subject of other publications. As each hour is plotted in real-time on a continuous basis, we demonstrate the ease with which changing clinical state is modeled and represented.

While biomarkers for the detection of LONS are encouraging, the resultant information is slower on its arrival to clinicians, and these tests introduce additional costs. Artemis offers real-time surveillance with immediate and instantaneous alerting at minimal additional costs from an operational standpoint.

## Conclusion

This paper has presented initial results of the application of our multi-stream online analytics approach to condition onset detection of late onset neonatal sepsis (LONS). We present a multi-stream, multi-feature risk scoring approach to model patient state over time and demonstrate an approach for the graphical user interface for that patient state for clinical decision support.

The graphical user interface will be the subject of a future user interface study assessing usability and functionality of the method of presentation of the LONS risk score.

The Artemis platform is being utilised in our research on neonatal spells [13, 14]. In that research, we are utilising the information from the Clinical Information System such as gestational age and gender to adjust the thresholds used in real-time by the algorithms and will be profiling spell behavior in real-time.

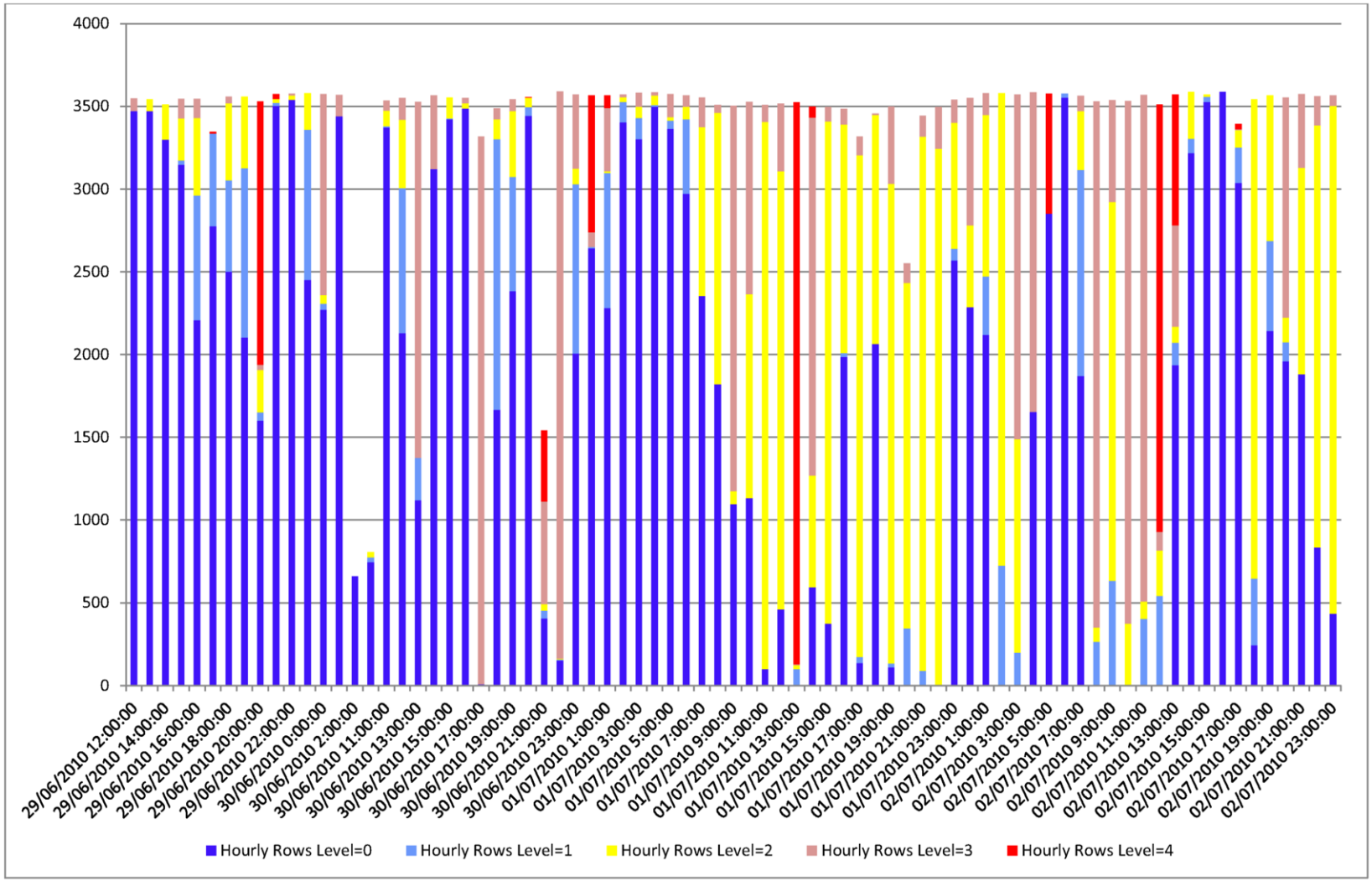


*Figure 2- LONS Onset Score Hourly summary distribution for one patient who developed LONS*

We are currently progressing research on the response of the newborn infant to nociceptive events. We have previously correlated and profiled physiological response, as collected by Artemis, to a range of bedside routine care and nociceptive events [15] as captured on paper and through an iPod touch application [16, 17] by nursing staff. We are currently integrating those algorithms together with our continuing research on pain and spells to better classify in real-time physiological response relating to infection, drugs, spells, and pain.

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