Biomedical Engineering and Informatics Applications in Critical Care

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Informatics Director, Neurocritical Care
Columbia University Medical Center
Overview of Clinical Informatics and Why You Should be Interested in Critical Care.

History of Monitoring in Critical Care

Clinical Challenges: Data acquisition, analysis, visualization

Patient Monitoring Two-Way Translational Research
Biomedical Informatics in Perspective

Basic Research

Biomedical Informatics Methods, Techniques, and Theories

Bioinformatics ≠ Bioinformatics

Bioinformatics

Imaging Informatics

Clinical Informatics

Public Health Informatics

Applied Research And Practice

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Clinical informatics

Deals with biomedical information, data and knowledge:

• Storage
• Retrieval
• Optimal use for problem solving and decision making

...as applied to problems in clinical care.
More than 5 million Americans with life-threatening conditions are admitted to Intensive Care Units each year. Critical care saves lives but it is complex, error prone, and very expensive.
Critical Care is Error Prone

**Clinical Activity** | % of Errors*
---|---
Treatment and Procedure Errors | 74.8
Medication error | 61.4
Failure to follow protocol | 7.9
Prevention and Diagnostic Errors | 24.2
Failure to follow protocol | 10.8
Avoidable delays in diagnosis | 4.7
Monitoring and Reporting Errors | 19.9
Inadequate reporting / communication | 13.7
Inadequate monitoring system | 6.1

*More than one factor may be associated with a serious medical error, with the total exceeding 100%

“Critical care settings provide life-saving care for the sickest patients but are also associated with significant risks for adverse events and serious errors. It will be especially important to ‘engineer out’ slips and lapses, to improve the likelihood that treatment in the ICUs is implemented as intended.”

Critical Care is One of the Most Expensive Components of Health Care

- 1 out of 7 hospital dollars is spent in the ICU
- $65 billion dollars of Medicare’s costs
- Costs are rising because of the aging U.S. population.

Drivers of ICU Demand
Elderly Patients
US Population >65, Millions

Future Needs of Critical Care Medicine 1998

Focus on Electronic Health Record Adoption
Electronic health records (EHR), laboratory tests, imaging, and bedside monitors are important. However these data sets are not integrated to provide **interpretable and actionable information**.

Caregivers need to **understand the data** and its implications in order to make the best choices about treatment.

**IMEDES will transform medicine by enabling clinicians to provide proactive care before patients worsen instead of reacting to life-threatening events already in progress.**
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ICU Data Integration Today
Too Much Data. Not Enough Information.

- **Data Overload.** There are staggering amounts of data, beyond the capability of any person to absorb, integrate and act upon reliably.

- **Lack of Integration.** Device interoperability is limited.

- **Lack of Processing.** Basic statistical analyses are elusive. More sophisticated analyses and correlations are unavailable at the bedside.

- **Inability to Search.** It is difficult for data to be indexed, searched, and assembled to provide accurate information to treat patients, because the original context of the data is lost.

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“Computational Technology for Effective Health Care: Immediate Steps and Strategic Directions,” NRC, 2009
"The success of the NASA-led glass cockpit work is reflected in the total acceptance of electronic flight displays... **Safety and efficiency** of flight have been increased with improved pilot understanding of the airplane's situation relative to its environment. The cost of air travel is less than it would be with the old technology and more flights arrive on time.”
The Need for Improved Information
Applying Systems Engineering in the ICU to Reduce Errors

“A systems-integration approach that incorporates the fundamental building blocks of health care, from equipment and technology to clinical insight and workflow processes, is needed to take the next major leap in improving quality and safety.”

Mathews & Pronovost The Need for Systems Integration in Health Care JAMA 2011;305

In aviation, a systems engineering approach mitigated cognitive errors and reduced crashes 65%.

Wald, New York Times, October 1, 2007
The IMEDS™ Approach

• **Present** all information in readily interpretable form, much as a GPS receiver takes data from satellites and creates **situational awareness** to provide a map back to health for each patient
HOW THE HECK DID WE GET HERE?

- LOST
- CONFUSED
- UNSURE
- UNCLEAR
- PERPLEXED
- DISORIENTED
- BEWILDERED
Reactive Medicine: Phases of Monitoring

• Phase 1: Clinical neuromonitoring
  • 1960-1980
  • React to clinical events paired with clinical treatment protocol followed blindly.
Clinical examination
Backbone of neurological diagnosis and crucial in the acute brain injury assessment but clear limitations

**ASSESSMENT OF COMA AND IMPAIRED CONSCIOUSNESS**
A Practical Scale
Graham Teasdale, Bryan Jennett
University Department of Neurosurgery, Institute of Neurological Sciences, Glasgow G51 4TF
THE LANCET, JULY 13, 1974

<table>
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<tr>
<th>EYE OPENING</th>
<th>Spontaneous To speech To pain None</th>
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<tr>
<td>BEST VERBAL RESPONSE</td>
<td>Orientated Confused Inappropriate Incomprehensible None</td>
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<tr>
<td>BEST MOTOR RESPONSE</td>
<td>Obeying Localising Flexing Extending None</td>
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Purpose: facilitate rapid communication between first responders and specialized brain injury units to triage TBI patients

**Problems:**
- Recording the best responses only
- Developed on TBI patients only
- Variability between experienced vs. inexperienced users *Rowley Lancet 1991*
- Variable predictive accuracy for outcome *Balestreri JNNP 2004*

**Validation of a New Coma Scale: The FOUR Score**
Eelco F. M. Wijdicks, MD,1 William R. Bamlet, MS,2 Roby V. Maramattom, MD,3 Edward M. Manno, MD,3 and Robyn L. McClelland, PhD2
Ann Neurol 2005;58:585–593

- Good Kappa btw different MDs, RNs vs. MDs,
- Validated in Neuro ICU, ER, MICU
- Prognosticates mortality and functional outcome in mixed ICU populations
Sternal Rub
Intracranial Mass Effect
Reactive Medicine: Phases Neuromonitoring

- Phase 1: Clinical neuromonitoring
  - 1960-1980
  - React to clinical events
- Phase 2: Physiological neuromonitoring
  - 1980-2000
  - React to pathophysiological events
Stable patient - fly by sight
Critically ill patient - fly by gauges
Monitoring in the ICU

- **CV**: ECG, MAP, CVP, PAD, CO, Echo, troponin
- **Pulmonary**: O$_2$ sat, ABGs, CXR
- **ID**: Cultures, WBC, Temperature
- **Renal**: Fluid balance, lytes
- **Nutrition**: REE, VO2, Nitrogen balance
- **Heme**: CBC, coagulation cascade
- **Neuro**: Exam, ICP, EEG, neuroimaging
Parenchymal Micosensor
Ventricular catheter
Epidural Monitor
Richmond Bolt
Invasive neuromonitoring: What’s the Rationale?

CBF, pbtO₂, pbCO₂, pH, brain temp
Microdialysis

ICP/CPP

cEEG

SjvO₂

TCD
Many questions can be addressed

- Did the fuel arrive?
  - CBF monitoring
  - LICOX (P_{btO_2})
  - CMA (brain glucose)

- Was it enough fuel?
  - Cerebral Microdialysis
    - Lactate, pyruvate, Lactate / Pyruvate ratio changes
    - Glutamate changes
    - Glycerol

- Are there demand / metabolism changes?
  - P_{btO_2} and brain glucose changes in accordance to lactate and pyruvate moving up or down together

- Is the neuronal activity healthy?
  - EEG / qEEG
this is inadequate
Relationships are *not* linear
High Dimensionality in Physiology
Clinicians may be confronted with 200 related variables, yet human beings can only determine the relationship between two variables unassisted.
Too Much Data. Not Enough Information.

Lack of Integration. Clinicians are forced to do this in their heads.

Lack of Processing. Basic statistical analyses are elusive. More sophisticated analyses are unavailable at the bedside. Once again, done in their heads.

Inability to Search. It is difficult for data to be indexed, searched, and assembled to provide accurate information to treat patients, because the original context of the data is lost.

“Computational Technology for Effective Health Care: Immediate Steps and Strategic Directions,” NRC, 2009
None of this data is processed

Some monitors display raw trends but even basic analyses (mean, median, standard deviations) are nearly impossible to perform. Standard biostatistical methods are not sufficient.
Conceptually, analysis has been restricted to **linear** and **univariate** statistical models. Alarm limits are based on arbitrary thresholds without regard for dynamic interactions between variables.

**Electronic Order Set**

Notify physician:

- HR < 60 or > 125 bpm
- SBP < 90 or > 180 mm Hg
- Respiration < 10 or > 30 per minute
- Pulse oximetry < 90% SaO\textsubscript{2}
- Temperature < 35.0 or > 38.8°C Celsius
- Urine Output < 50 mL per hour
- Blood Glucose < 60 or > 130 mg/dL
- Cardiac Index < 2 L/min/m\textsuperscript{2}
Analytic Monitoring: The Future
Identification of complex metabolic states in critically injured patients using bioinformatic cluster analysis

Mitchell J Cohen, Adam D Grossman, Diane Morabito, M Margaret Knudson, Atul J Butte and Geoffrey T Manley

Abstract

Introduction: Advances in technology have made extensive monitoring of patient physiology the standard of care in intensive care units (ICUs). While many systems exist to compile these data, there has been no systematic multivariate analysis and categorization across patient physiological data. The sheer volume and complexity of these data make pattern recognition or identification of patient state difficult. Hierarchical cluster analysis allows visualization of high dimensional data and enables pattern recognition and identification of physiologic patient states. We hypothesized that processing of multivariate data using hierarchical clustering techniques would allow identification of otherwise hidden patient physiologic patterns that would be predictive of outcome.

Methods: Multivariate physiologic and ventilator data were collected continuously using a multimodal bioinformatics system in the surgical ICU at San Francisco General Hospital. These data were incorporated with non-continuous data and stored on a server in the ICU. A hierarchical clustering algorithm grouped each minute of data into 1 of 10 clusters. Clusters were correlated with outcome measures including incidence of infection, multiple organ failure (MOF), and mortality.

Results: We identified 10 clusters, which we defined as distinct patient states. While patients transitioned between states, they spent significant amounts of time in each. Clusters were enriched for our outcome measures: 2 of the 10 states were enriched for infection, 6 of 10 were enriched for MOF, and 3 of 10 were enriched for death. Further analysis of correlations between pairs of variables within each cluster reveals significant differences in physiology between clusters.

Conclusions: Here we show for the first time the feasibility of clustering physiological measurements to identify clinically relevant patient states after trauma. These results demonstrate that hierarchical clustering techniques can be useful for visualizing complex multivariate data and may provide new insights for the care of critically injured patients.
Hierarchical Cluster Analysis

Development of “Patient States” based on complex multivariate relationships of changing physiology not otherwise discernable to clinician.

Courtesy of J. Claude Hemphill, MD
Identification of complex metabolic states in critically injured patients using bioinformatic cluster analysis
Identification of complex metabolic states in critically injured patients using bioinformatic cluster analysis

- Probability of death = 0.13
- Probability of death = 0.025

Time (minutes from start of data collection)
Mortality Reduction by Heart Rate Characteristic Monitoring in Very Low Birth Weight Neonates: A Randomized Trial

Joseph Randall Moorman, MD, Waldemar A. Carlo, MD, John Kattwinkel, MD, Robert L. Schelonka, MD,* Peter J. Porcelli, MD, Christina T. Navarrete, MD, Eduardo Bancalari, MD, Judy L. Aschner, MD, Marshall Whit Walker, MD, Jose A. Perez, MD, Charles Palmer, MD, George J. Stuckenborg, PhD, Douglas E. Lake, PhD, and Thomas Michael O'Shea, MD
Analytic Monitoring: The Future

No Clinical Symptoms

Prediction

Analytic Monitoring

Physiologic Monitoring

Clinical Monitoring

Clinical Symptoms

Complication Time

Crashing Patient

Nothing
I’m not telling you it is going to be easy,

I’m telling you it’s going to be worth it.
Physiologic Monitoring in the 1970’s
Physiologic Monitoring today
Analytic Monitoring today
Despite the growth of critical care and development of monitoring technology, the basic information technology architecture remains primitive.
Even just acquiring data is hard

**Proprietary limitations** from industry, glaring absence of standard **data formatting**, and lack of **interoperability** make seamless data acquisition and data integration nearly impossible.
**Interoperability:**

Ability of two or more systems or components to exchange information and to use the information that has been exchanged.

**Semantic interoperability:**

Shared Data types, Terminology ("ontology"), Coding

**Functional interoperability:**

Shared Architectures, Methods, Frameworks
Semantic Interoperability
Data Coming Out of the Box

- Institute of Electrical and Electronics Engineers (IEEE)
  - Data & waveforms
- Health Level 7 (HL7)
  - v2 waveforms
  - v2 data
  - v3 data
  - CDA data
- Comité Européen de Normalisation (CEN)
  - Technical Committee 251
  - Open EHR / 13606 data
  - ECG files
  - Sleep-lab files
- International Organization for Standardization (ISO)
  - Data & waveforms
  - ‘Lab’ data
- National Electrical Manufacturers Association (NEMA)
  - DICOM
  - Cathlab waveforms
Semantic Interoperability
Data Coming Out of the Box
Third Party (Software) Solutions

- **Bedmaster** ([www.Excel-Medical.com](http://www.Excel-Medical.com))
  - Comprehensive acquisition and storage system for trend and waveform data, designed around GE/Marquette monitors. Working on future support for Philips Intellivue monitors.

- **RugLoop** ([www.Demed.be](http://www.Demed.be))
  - Designed as data acquisition system for OR. Captures waveform data from multiple monitors, including Philips Intellivue, and trend data from many other monitors (GE/Marquette, Philips, HP/Agilent/Philips, Siemens, Draeger, Apsect, …)

- **Dataplore/Trendface** ([www.ixellence.com](http://www.ixellence.com))
  - Support for trends and waveforms from the new and old Philips monitors

- **Mobius** ([www.integra-ls.com](http://www.integra-ls.com))
  - Provides waveform and trend data from new and old Philips monitors, support for various other monitors including their Licox brain tissue oxygen and Camino ICP monitors.

- **ICUPilot** ([www.microdialysis.se](http://www.microdialysis.se))
  - Trends only, with interfaces to many different monitors
None of this data is processed

Some monitors display raw trends but even basic analyses (mean, median, standard deviations) are nearly impossible to perform.
Critical Care Bioinformatics
Suite of Complex Systems Analysis Tools

There is no universal equation for “complex systems”. There is no single tool.

We need high resolution data acquisition and a suite of tools for physiologic signal processing and analysis, using both classical techniques and novel methods based on statistical physics and nonlinear dynamics.
Critical Care Bioinformatics
Suite of Complex Systems Analysis Tools

- **Distributional Variance**
  - Mean
  - Standard Deviation
  - Coefficient of Variation
  - Shannon Entropy

- **Linear Properties**
  - Autocorrelation
  - Multiorder Histograms
  - Hierarchical Clustering
  - Poincaré Analysis
  - Frequency Analysis

- **Nonlinear Properties**
  - Multiorder Histograms
  - Poincaré Analysis
  - Surrogate Comparisons
  - Mutual Information
  - Sample Entropy

- **Attractor Properties**
  - Correlation Dimension
  - Lyapunov Exponent
  - Visual Reconstruction
  - Surrogate Comparisons
  - Mutual Information
  - Sample Entropy
  - Approximate Entropy

- **Predictability**
  - Mutual Information
  - Sample Entropy
  - Approximate Entropy

Networked to facilitate collaboration

Synchronize

Integrate

Process

Present

Data Synchronization and Alignment

Data Conditioning

Data Correlation (Information)

Physiological Models

Treatment Decision Support

Diagnosis Support

Unified Display

“Omic” Data

- Genomics
- Proteomics
- Metabolomics
- Glycomics’

Phenotypic Data

- Present Illness
- Past history
- Medications
- Physician Exam
- Nursing notes
- Lab data
- Cultures
- Imaging data

Physiologic Data

- BP, HR, RR
- Temperature
- O2 Saturation
- ICP, CPP
- CBF
- Brain Tissue PO2
- Microdialysis
- Continuous EEG

Present Illness

Past history

Medications

Physician Exam

Nursing notes

Lab data

Cultures

Imaging data

BP, HR, RR

Temperature

O2 Saturation

ICP, CPP

CBF

Brain Tissue PO2

Microdialysis

Continuous EEG
Nonconvulsive Seizures after Subarachnoid Hemorrhage: Multimodal Detection and Outcomes

Jan Claassen, MD, PhD,1,2,3 Adler Perotte, MD,4 David Albers, PhD,4
Samantha Kleinberg, PhD,4 J. Michael Schmidt, PhD,1 Bin Tu, MD,2
Neeraj Badjatia, MD,1,3 Hector Lantigua, MD,1 Lawrence J. Hirsch, MD,2
Stephan A. Mayer, MD,1,3 E. Sander Connolly, MD,3 and George Hripcsak, MD4

Objective: Seizures have been implicated as a cause of secondary brain injury, but the systemic and cerebral physiologic effects of seizures after acute brain injury are poorly understood.

Methods: We analyzed intracortical electroencephalographic (EEG) and multimodality physiological recordings in 48 comatose subarachnoid hemorrhage patients to better characterize the physiological response to seizures after acute brain injury.

Results: Intracortical seizures were seen in 38% of patients, and 8% had surface seizures. Intracortical seizures were accompanied by elevated heart rate (p = 0.001), blood pressure (p < 0.001), and respiratory rate (p < 0.001). There were trends for rising cerebral perfusion pressure (p = 0.03) and intracranial pressure (p = 0.06) seen after seizure onset. Intracortical seizure-associated increases in global brain metabolism, partial brain tissue oxygenation, and regional cerebral blood flow (rCBF) did not reach significance, but a trend for a pronounced delayed rCBF rise was seen for surface seizures (p = 0.08). Functional outcome was very poor for patients with severe background attenuation without seizures and best for those without severe attenuation or seizures (77% vs 0% dead or severely disabled, respectively). Outcome was intermediate for those with seizures independent of the background EEG and worse for those with intracortical only seizures when compared to those with intracortical and scalp seizures (50% and 25% death or severe disability, respectively).

Interpretation: We replicated in humans complex physiologic processes associated with seizures after acute brain injury previously described in laboratory experiments and illustrated differences such as the delayed increase in rCBF. These real world physiologic observations may permit more successful translation of laboratory research to the bedside.

ANN NEUROL 2013;74:53–64
Each minute of EEG was classified after visual inspection by a blinded experienced electroencephalographer as ictal, ictal-interictal continuum or nonictal.

Two key problems in working with high resolution data:
- Data was acquired then converted by a human as opposed to computer into clinical information.
- Data reduction from 200 Hz to 1 minute resolution.

New onset seizures were defined as lasting at least 5 minutes and preceded by 30 minutes without any seizure activity and then combined with physiological data.
- Series of SQL queries to automatically identify new onset seizures meeting both criteria
- Then linking physiological data stored in a different database by the defined time window.

Physiologic signals were preprocessed through several steps of filtration and missing data were extrapolated.

Significance was assessed by constructing a permutation test where investigators resampled by patient and evaluated a Monte Carlo estimate of the significance level.
Nonconvulsive Seizures after Subarachnoid Hemorrhage: Multimodal Detection and Outcomes

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FIGURE 2: Grouped data of physiologic changes associated with the onset of intracortical seizures. Spectrograms (upper 3 panels), displayed as relative changes on a group level, demonstrate increases in electroencephalographic (EEG) power predominantly in the 2 to 5 Hz frequency range, first seen in the minidepth EEG recording (third panel from top), followed by contralateral (top panel) and ipsilateral scalp (second panel from top) recordings. Spectrograms reveal clear changes in EEG power recorded from the minidepth as well as the scalp, which precedes the seizure onset determined by visual inspection of raw EEG tracings (indicated as 0 on the x-axis and by the vertical red line). Regarding physiological recordings, timing of increases in cardiovascular (heart rate, mean arterial pressure) and respiratory (respiratory rate, minute ventilation [not shown]) parameters coincides with detection of first intracortical spectral power changes, whereas rising intracranial pressure is only detected later, when seizures become recognizable on inspection of the raw EEG. Global brain metabolism increases sharply for a short time, as suggested by the transient drop in jugular bulb oxygenation (approximately 2 minutes after seizure onset). This lasts for several minutes followed by gradual return to preseizure baseline global metabolism (approximately 8 minutes after seizure onset). There is a small drop in partial brain tissue oxygenation starting 5 minutes after seizure onset. Whereas cerebral perfusion pressure rises with increase in mean arterial pressure at the time the first spectrogram changes are recognizable on the minidepth recording, there is a very delayed increase in regional cerebral blood flow, seen starting about 10 minutes after seizure onset. Physiology graphs are displayed as means (blue lines) with 1 standard error of the mean (shaded areas).
Nonconvulsive Seizures after Subarachnoid Hemorrhage: Multimodal Detection and Outcomes

Jan Claassen, MD, PhD, Adler Perotte, MD, David Albers, PhD, Samantha Kleinberg, PhD, J. Michael Schmidt, PhD, Bin Tu, MD, Neeraj Badjatia, MD, Hector Lantigua, MD, Lawrence J. Hirsch, MD, Stephan A. Mayer, MD, E. Sander Connolly, MD, and George Hripcsak, MD

FIGURE 6: Model illustrating the relationship between acute brain injury complicated by seizures and secondary brain injury accounting for findings made in the current study. Physiologic observations supported by significant changes or trends are indicated by white boxes. Observations made in isolated cases or by visualization of grouped graphs but that were not found to be significant are kept in gray boxes. EEG = electroencephalogram; $S_{v}O_{2}$ = jugular venous oxygen saturation.
• Example of bedside-to-bench translational research
• Study was truly a multidisciplinary effort:
  – Department of Neurology, Division of Critical Care Neurology
  – Department of Neurology, Comprehensive Epilepsy Center
  – Department of Neurosurgery
  – Department of Biomedical Informatics.
• Required considerable clinical, data management, and analysis expertise.
• BUT, no clear pathway back to the bedside.
  – Relies on a human to classify seizures
  – No clinical system to send real-time analysis results back to the bedside

Nonconvulsive Seizures after Subarachnoid Hemorrhage: Multimodal Detection and Outcomes
The bedside monitor displays present state, reached from many trajectories.

To predict future trajectory, we have looked backwards to identify trend.

What we really want to know is if patient will move from condition 1 (good) to 2 (bad).

With “velocity” (“speed” and “direction” at which patient is moving) and probability density “space”, we can forecast trajectory.
JCP Jc Penney Co Inc  46.21  -1.51  -3.16%
D: 07/13/2007  O:74.36  H:75.64  L:73.86  C:75.20  R:1.78  Y:53.2545
Video
**Intracranial pressure management**

- **Goal**: to determine an ‘ideal’ target for cerebral perfusion pressure that will maintain adequate perfusion of the brain.
- **Challenges**:
  1. Difficult to understand patient monitoring data without visualization due to multidimensional nature of physiology.
  2. For example the relationship between cerebral perfusion pressure (CPP) and brain oxygen tension is dependent on end tidal CO$_2$ concentrations.
  3. Notice that when end tidal CO$_2$ is below 30 the patient appears to regulate cerebral blood flow properly when CPP is greater than 80 mmHg (normal), but when end tidal CO$_2$ is above 30 brain oxygen tension increases as cerebral perfusion pressure increases (abnormal).
Cerebral Autoregulation after Acute Brain Injury

Graph showing the relationship between CBF (ml/100 g/min), ICP (mm Hg), CPP (mm Hg), and vascular caliber. The graph illustrates the vasodilatory and vasoconstrictory cascades, passive collapse, zone of normal autoregulation, and autoregulation breakthrough zone.
PRx based optimal CPP

- Validated in various disease conditions

Effects of cerebrovascular pressure reactivity-guided optimization of cerebral perfusion pressure on brain tissue oxygenation after traumatic brain injury

“Optimal Cerebral Perfusion Pressure” in Poor Grade Patients After Subarachnoid Hemorrhage

Philippe Bijlenga · Marek Czosnyka · Karol P. Budajski · Martin Soehle · John D. Pickard · Peter J. Kirkpatrick · Peter Smielewski

![Graphs showing PRx and CPP values across different conditions](image-url)

(Crit Care Med 2010;)

Video
**Study/Product Aim(s)**

- Develop interactive visualization to support earlier prediction of conditions that require integration across multiple dimensions and detection of subtle trends. Propose initial use cases of sepsis and acute brain injury.
- Transform the underlying physiological processes (learned in school and through years of training) into an intuitive display, where current and future patient state can be instantly integrated into the decision process.
- Perform an experiment with experienced clinicians to quantitatively evaluate the benefits of the visualization technique against current methods in faster detection of emerging events.

**Approach and Military Relevance**

Earlier detection of emerging events such as intracranial hypertension in severe brain injury and sepsis are critical and important problems for military medicine.

**Timeline and Cost**

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<td>Data Collection and Integration</td>
<td>Columbia</td>
<td>6 months</td>
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<td>Interactive visualization (Working interactive visualization with data)</td>
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<tr>
<td>Experiment (Conduct, Analyze, Publish)</td>
<td>Combined</td>
<td>3 months</td>
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<td>Estimated Budget ($260K)</td>
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<td>$65K</td>
<td>$125k</td>
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**Projected Goals/Milestones**

**Month 3 Goal** — Visualization prototype development complete
- After 3 months, we will have a prototype of the system that will be ready for development.
- Prototype development includes conducting a cognitive work analysis and multiple iterations of the visualization.

**Month 9 Goal** — Data integration and Interactive Visualization
- The backend system with actual historical data will be connected with the interactive visual interface
- A working interactive visual interface will be complete and ready for demonstration

**Month 12 Goal** — Experiment
- An experiment will be conducted with clinical staff to quantitatively validate the effectiveness of the visualization over current methods.
- A final report on the results of the study will be delivered.
Sepsis Identification

Goal: To help clinicians identify patients that are in early stages of sepsis

Challenges:
1. Well-defined criteria to recognize if a patient is in septic shock. Generally, if two or more criteria are met, there is a suspected infection.
   1. temperature $>38^\circ$C or lower than $36^\circ$C;
   2. heart rate $>90$ beats/min;
   3. respiratory rate $>20$ breaths/min; and
   4. white blood cell count $>12,000/mm^3$ or $<4,000/mm^3$ which more than 10% immature forms.
2. Monitor 6 variables (4 SIRS criteria, and 2 additional):
   1. temperature
   2. heart rate;
   3. respiratory rate
   4. white blood cell count
   5. heart rate variability
   6. blood pressure
Sepsis Identification

Challenges (cont):

1. The challenge is that once these criteria are met, it is often the case that the patient is severely ill.

2. It is possible that we can help to detect the early emergence of SIRS through supporting clinicians in seeing early trends in SIRS-related variables.

3. Clinicians need help seeing subtle trending of multiple variables at one time.

4. For clinicians, the challenge is the monitoring for these slight trends in multiple variables are multifaceted:
   1. Monitoring for the emergence semi-rare events with weak evidence is challenging.
   2. The variables that the clinicians are monitoring are not all located in the same place.
   3. It is easy to see many of the variables on the patient monitor (HR, RR, Temp), however that monitor only provides the last 10 seconds of data. Longer trends are not shown here.
   4. Rate of change of individual variables is not easily found
   5. Rate of change of multiple variables requires integration in the clinician or nurses head.
Sepsis Identification

Solution

Individual Variables
1. Present all 6 variables in a single location
2. Present longer trends of all variables
3. Show their individual values at time steps of 15-minutes.
4. Color code the individual values to indicate how close they are to normal or alarm stages

Integrated Display
1. The goal is to detect slight trending of the 6 variables over time.
2. Present the 6-variables in a spider-plot.
3. Normalize the variables so that the larger the circle the higher the likelihood that SIRS trends are being observed.
4. The x-axis is time in 15-minute intervals
5. The y-axis is likelihood of SIRS.
6. Redundant coding for position on the y-axis and size of the circle.
7. Color of the circle as a whole could be used to indicate rate of change. This could be redundant to the jump along the y-axis between two time points.
8. POSSIBLE: We could color code individual dots on the circle to indicate how close the individual values are to alarm state.
Design concerns:
1. The presentation of the individual variables and numbers would not reduce clinician cognitive load.
2. Clinicians would have to trend many hours of data to determine if changes were occurring.
3. We wanted to maximize the ability to make single comparison between the current status and past status.
Small plots, from each observation between 1st and latest. Could be circles too if small version of spider is too small.

Navigation tabs

Change views here (or on the left tab). De-activated until multiple views available.

Color between the early and late view is based on sepsis risk.

Can change between line graph and spider plot.

Earliest view: connect the 1st (earlier) and 2nd (later) views on the spider plot and the line (or table) view.

Zoomable: last hr from present, last 24 hr, etc.

Green rectangle: current patient average (1 stdev?) over the last 24 hrs.

Also lists #s for top and bottom of range.

Circles are each observation from the data file.

Color on line indicates observation over 24 hr range. If 2 observations are over, the line between the dots are red.

Time guide could be similar to google finance. Low-level metrics and small guides under the time could go up under the plots.

Tooltip line has #s available for all variable observations.

Note: the rest of the variables will have the same line plot.
Identifying Priority Patients

Goal: Identify patient state changes and identifying patients that need clinician attention

Challenges:
1. Clinicians may be confronted by more than 200 variables for critically-ill patients.
2. In contrast people are not able to judge the degree of relatedness between more than two variables.
3. The most difficult task for clinicians is not determining which patients are doing poorly – this is usually self-evident – it is determining which patients are changing and require intervention.
4. We hypothesize that an interactive visualization can be designed to support clinicians in more quickly recognizing changes to patient state, situation awareness, and faster ability to pinpoint emerging situations.

Solution:
1. To apply a multivariate temporal analysis technique, specifically empirical orthogonal functions, to patient monitoring data.
2. This analysis will identify the sources of variance in patient data and what physiological parameters vary together.
Outlier Removal
1. Physiological data collected in the Neurological ICU is not collected in a controlled environment.
2. Frequent outliers represent spurious data from the perspective of patient care.
3. For example, catheters measuring body temperature are often removed prior to the termination of data collection.
4. Have temperature readings from in the body and room temperature.

Solution
1. We have implemented a variational Bayesian mixture model for the detection and removal of such spurious states – the results of which applied to the same variable (temperature) can be seen in the figure below.

Unfiltered versus Filtered Temperature Values
Identifying Priority Patients
Update and Challenges

Missing Data
1. Empirical orthogonal function (EOF) can help visualize the patient's state over time and identify points of significant change.
2. Physiological variables are not always recorded at all times.
3. We had to address the issue of missingness.

Solution
1. We experimented with several approaches.
2. The combination of outlier removal as described above and constant interpolation was determined to be the most accurate approach.
3. Displayed is the application of this method showing a period of significant change when temperature is one of the variables involved in the change.
Identifying Priority Patients
Update and Challenges

Method 1 to assess change
1. EOFs that account for the most variance for each time period
2. Choose the top K EOFs and create a set from the variables that are significant contributors to those EOFs.
3. Evaluate the Jaccard Index and establish a threshold for alerting significant changes across time periods.

Method 2 to assess change
...for a given patient
...for a set of time bins prior to the current time bin
1. Build a multivariate normal or multivariate t distribution.
2. Evaluate the likelihood that a significant change has occurred in the current time bin (negative logarithmic scale, inverted likelihood scale)
3. Alerts can be designed sudden changes in state.

EOF analysis (above) and Temperature (below) corresponding to variable 'TMP-2'
YOU'VE HELD YOUR CELL PHONE SO MUCH THAT YOUR HAND HAS GROWN AROUND IT. YOU'LL NEED SURGERY TO REMOVE IT.

YOU MEAN THERE'S NO APP FOR THAT???
Reactive medicine is obsolete

- Treat physiologic states before thresholds broken
- Treat complications before clinical symptoms observed
- Evaluate effectiveness of treatment interventions
- Identify patient specific physiologic targets
- Identify physiologic states (healthy or not)
- Identify secondary complications before they cause damage
- Establish early intervention is beneficial (Key Step)
- Provide better prognostic information

Must be able to acquire all the data into single integrated system

Use informatics based suite of translational tools to Analyze data

- Enable clinicians to interrogate and model complex clinical data in relationship to clinical events and outcome.
- Models must be able to be evaluated in live ICU environments using clinical protocols.

Present information to clinicians to help decision making