

**Editorial**

Proceedings from the Montebello Round Table Discussion. Second annual conference on Complexity and Variability discusses research that brings innovation to the bedside

1. Introduction

September 28–October 1 2010. Montebello, Quebec: Scientists, mathematicians, and physicians from across Canada, United States, and France were invited to participate in the second round table discussion on *Complexity and Variability at the Bedside* to present research, discuss, methodology, and promote applications of “variability analysis”—a novel method for continuous monitoring of variations in physiological systems at the bedside of patients. Recent advancements in research and technology of variability analysis may significantly improve the care provided to patients afflicted with acute and critical illness. Using mathematical models to analyze data harvested from heart, respiratory, and brain monitors at the bedside of adults and children, preliminary findings show that doctors in intensive care units (ICUs) and acute ambulatory clinics can better determine severity of certain diseases, such as trauma and asthma, and may even predict the onset of illness, such as septic shock. It has been reported that sepsis, a systemic inflammatory response to an infection, strikes an estimated 750 000 adults in the United States annually, with 215 000 deaths per year. It costs the US health care system an average of \$20 000 to \$30 000 per case to treat patients. Severe sepsis remains a major killer in critically ill patients despite advances in systemic therapy. However, the answer to battling sepsis in the ICUs may rely on applications of complex systems science and monitoring of variability analysis in physiological systems of patients.

2. Complexity and variability

Over the last decade, the science of analyzing biological signals has improved with development of advanced computational methods and better understanding of mathematical techniques to measure variations in physiological rhythms associated with disease. Under disease states, a human body

exhibits systemic variations in physiological rhythms that are remarkably different from a healthy state. If we consider human bodies as biological systems composed of multiple interacting organ systems with biological and chemical feedback loops, then, in a state of illness, we may not adequately analyze its malfunction by breaking the system down into its component parts and considering each in isolation.

“Complex systems” science provides a theoretical framework for evaluating and analyzing biological systems. Complexity science studies how relationships between parts give rise to collective behaviors. Complex systems exhibit global properties distinct from properties of individual components. When a complex biological system breaks apart, the systemic properties disappear, whereas the properties of individual components may be maintained. Analytical methods in complexity science identify and measure global, systemic patterns that reflect behavior instead of a singular, distinguishing marker. Complexity science computational and mathematical tools are based on a range of disciplines including and not limited to chaos theory, nonlinear dynamics, statistics, and computational theory. Applying complexity-based analytical methods to medicine has advantages in offering a means to analyze a holistic multivariate or time-varying data.

“Variability”—described as analysis of patterns of change in complex systems over time—is performed on a series of data collected continuously or semicontinuously over time. Continuous variability analysis, namely, real-time multiparameter characterization of the degree and character of the fluctuations of physiologic parameters, offers an opportunity to track the underlying dynamics of complex systems over time. Patterns of variation over time contain valuable information about the state of the overall system that provides an important means for physicians to treat their patients. The technology of variability analysis is particularly valuable in the ICU, where patients are critically ill and numerous physiologic parameters are routinely

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measured continuously. Working with the belief that human physiology comprises a complex system, whereas variability analysis of organ systems using mathematical models may describe systemic host response to infection or injury, it is imperative to bring the science of complex systems to the bedside of patients.

3. Complexity and Variability at the Bedside conference series

The *Complexity and Variability at the Bedside* conference series aims to bring together scientists, mathematicians, and clinicians to present their current work and discuss theory, methodology, and clinical applications of complexity and variability science. The talks presented at the conference series promote interest among young researchers and generate novel research topics to conduct new investigations in complexity and variability science that may ultimately result in clinically useful applications. This conference series allows the opportunity for experts to share ideas and their experience with other investigators who are conducting clinical trials.

Montebello Round Table Discussion was the second conference on *Complexity and Variability at the Bedside* held in Canada since its inaugural event in August of 2009 at Wakefield, Quebec. This year, the 3-day conference attracted a larger number of participants with a total of 26 invited speakers of which 11 were speaking at this conference series for the first time. Also, this year, there was a greater participation of invited speakers from international countries, including the United States and France. Invitations were also open to graduate students from academic institutions with opportunities provided for travel reimbursement. With a greater presence of researchers from academic institutions and industrial organizations, including Philips Healthcare, IBM T.J. Watson Research Center, and Therapeutic Monitoring Systems Inc., the discussions pertaining to complexity and variability analysis were more in-depth, and a significant number of opportunities existed to collaborate on new research projects.

The Montebello Round Table organizing committee is thankful for the support from its session chairs who directed and maintained the focus of the talks— Dr Andrew J.E. Seely, Dr Peter Macklem, Dr Thomas Similowski, Dr Adam Seiver, Dr Timothy G. Buchman, Dr Andriy Batchisky, Dr Randall Moorman, and Dr John Morris. The organizing committee would also like to thank Dr Stuart Kauffman for giving the keynote address and for engaging in the discussions. Montebello Round Table Discussion was supported in kind through grants funded by the Centre of Mathematical Medicine at Fields Institute and Canadian Institute for Health Research, and sponsored by the Division of Thoracic Surgery, the Ottawa Hospital, and industrial partnership with Therapeutic Monitoring Systems (www.therapeuticmonitoring.com).

To read more about the *Complexity and Variability at the Bedside* conference series, or to review abstracts and presentations, please visit our Web site at <http://sites.google.com/site/wonderfulwakefieldwiki>. For more information on *Complexity and Variability at the Bedside* conference series, please contact the coordinator for the series Zeb Khan at montebelloroundtable@gmail.com.

In these conference proceedings, the abstracts appear in the order in which they were presented. The topics encompass areas of theory, methodology, and clinical applications pertaining to complexity and variability analysis over the following 8 sessions: (1) history of clinical applications of complexity science, (2) characteristics of life, (3) clinical insights from complexity science, (4) complexity and pathophysiology of disease, (5) clinical applications of complexity science, (6) clinical implications of nonlinear dynamics, (7) origins and etiology of complex variability, and (8) clinical applications of variability analysis. All authors were asked to submit an abstract summarizing their presentation at the Montebello Roundtable Discussion. The format requested was simply to keep the length to a limit of 1 page.

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