Short-term Cardiovascular-Respiratory Control Mechanisms

The American Institute of Mathematics

The following compilation of participant contributions is only intended as a lead-in to the ARCC workshop "Short-term Cardiovascular-Respiratory Control Mechanisms." This material is not for public distribution.

Corrections and new material are welcomed and can be sent to `workshops@aimath.org`

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Chapter A: Participant Contributions

A.1 Batzel, Jerry

Primary interest 1: My primary modeling efforts derive from my interest to understand how the various cardiovascular and respiratory control (CVRC) mechanisms interact.

Primary interest 2: A further fundamental interest is in model validation and in particular application of such CVRC models to the clinical setting. Applying such models faces key hurdles due to the significant number of parameters involved together with the clinical constraint of generally non-invasive patient testing which generates a restrictive set of data from which parameters can be estimated. This together with the inter-individual variation in a physiological system's inventory of control responses adds further complication to model application for diagnosis and treatment design.

Specific interests:
a) Understanding the interaction between the cardiopulmonary and arterial baroreflex pathways
b) Sleep related instability of the respiratory control system.

Suggested topics:

- What can heart rate variability tell us about various aspects of autonomic (AF) function and how solid are the inferences and interpretations drawn from HRV data?
- How well mapped out are the quantitative interactions of the cardiopulmonary and arterial baroreflex loops?
- How well understood are the interactions of global autonomic control effects, local metabolic control, and autoregulatory effects in local vascular control of blood flow and to what level of detail are these interactions understood ?

A.2 Fink, Martin

General interest: Modeling of physiological systems on various levels – from the cardiac cell to the whole cardiovascular-respiratory system.

Specific interest: Investigating the variability of short-term control mechanisms between individuals. Interaction between arterial and pulmonary baroreceptors.

Suggested topics:

- Do we agree on what the short-term control mechanisms are and how they interact? For instance, does the arterial baroreflex play a role during low LBNP or HUT?
- How can we cope with the variability between individuals?
- Which set of (clinically measurable) variables contains enough information to indicate problems early on in intensive care or during dialysis?
- What are the various possibilities to include the control mechanisms into the models? What is going to be the way forward?

A.3 Fitzpatrick, Ben

In this talk, we will examine the different types of variability inherent in quantitative physiological analyses. Of particular interest are problems involving dynamic models and

temporal data. We will apply the powerful and flexible Bayesian framework of statistics to help understand not only measurement error but also variability among individuals when experiments involve sampling from different individuals. We will study the interplay between the dynamic physiological model and the statistical model of the parameter space.

Finally, some suggestions for problems of treatment optimization in the presence of uncertainty will be discussed.

A.4 Furlan, Raffaello

Relationships among different cardiovascular parameters (RR interval, arterial pressure, central venous pressure), respiration and direct recording of post-ganglionic neural sympathetic discharge activity (MSNA) in physiological conditions (recumbent position, orthostasis and light physical exercise) and in pathophysiology (neurally mediated syncope, chronic orthostatic intolerance, ulcerative colitis, fibromyalgia and Parkinsons disease).

Evaluation of arterial and cardiopulmonary baroreflex function in the time and frequency domains

My group is also dealing with: Modelling of Autonomic Nervous System using univariate and multivariate techniques, analysis of complexity and causality. Non-linear methodology such as entropy, predictability and symbolic dynamics applied to bivariate processes.

A.5 Gray, Genetha

Modeling and simulation have become increasingly important in all areas of science and engineering. I am very interested in the process of developing mathematical models. In particular, what parts of the model are more correct? What parts are estimates? Why are the estimates included? Is it because of lack of information? Or is it lack mathematical tools? In studying cardiovascular-respiratory mechanisms, this is particularly fascinating. There are elements that resemble well-known mechanical models. But, there are also aspects that are unknown or hard to describe because of the complexities of the human body. I am interested in studying models and trying to quantify the uncertainty in them. It would be interesting to answer some what if questions.. what if we could improve this aspect of the model? Would that really improve the information we were able to obtain? Or is it now too complicated or have we introduced too many new uncertainties? I am also interested in the inherent parameters of a model. These parameters often represent something complicated but for simplicity have been boiled down to a number. How can we use optimization techniques to calibrate these parameters? More generally, I think this is an interesting way to approach the questions of what studying numerical models can teach us. In medicine, it always has to translate to the person, but how can we best do this?

Models in biology are of particular interest to me. I have taken a decent amount of biology and physiology (for a mathematician!) and have always had a deep interest in how the two work together. Recently, I have not had the opportunity to apply any of my mathematical skills to biology or medicine related problems. I hope that this conference gives me a new opportunity to do that!

A.6 Heldt, Thomas

My research interests revolve around modeling of physiological systems in general. I am interested in modeling, model analysis and reduction, parameter estimation and identification as applied to clincial problems such as monitoring of patients in intensive care and

understanding of post-spaceflight orthostatic intolerance. Of particular interest to me for the workshop (and beyond) is the analysis and reduction of large-scale physiological models (Guyton, for example) to allow for identification of model parameters from experimental data. Furthermore, I am interested in learning more about autonomic and non-autonomic control beyond the arterial and cardiopulmonary baroreflex loops.

A.7 Hu, Kun

Primary interest 1: The underlying mechanism responsible for the temporal organizations in the physiological fluctuations.

Primary interest 2: Contributions of circadian pacemaker and daily activity to 24-hour daily rhythms of the adverse cardiovascular events.

Specific interest: Cardiovascular responses to behaviors and cerebral autoregulation at different circadian time and its alteration under pathologic conditions.

Suggested topics:

What can the fluctuations in the heart beat intervals provide information related to the underlying mechanism of cardiac control?

How can we reliably estimate baroreflex sensitivity based on short-term variations of blood pressure and beat-to-beat intervals?

How can we explore the regulation of cerebral blood flow based on the spontaneous fluctuations of arterial blood pressure and cerebral blood flow velocity? How are cerebral autoregulation and cardiac control influenced by the circadian pacemaker?

A.8 Karemaker, John

I have been active in the field of model development starting at baroreflex physiology, blood pressure control to explain blood pressure - and heart rate variability (project with RW DeBoer). Furthermore I have been active in respiratory control in particular related to sleep apnea, again in modeling and physiological experimentation (project with JG van den Aardweg). My latest projects were related to gravitation and circulatory control (projects with J. Gisolf and K.van Heusden). Presently I work on a new project with G.Wallin and M.Joyner in model development to explain relations between sympathetic nerve activity and the physiological parameters that drive it on the one hand and the effects on the circulation on the other.

I think I may contribute to the meeting by my expertise and I hope to find help for my newest project. In particular the (modeling of) respiratory and cardiovascular control mechanism and their interaction, and the way to make physiological sense of various types of "noise" that are used in models to incorporate the observed variability in actual recordings.

A.9 Khoo, Michael

I am most interested in the development of models that enable the successful prediction of the major oscillatory bands of blood pressure variability observed in humans under conditions of health and disease. The approaches include:

(a)large-scale "structured" models in which there is some degree of isomorphism between the model components and the physiological entities that they are supposed to represent; and

(b) "minimal" models, the parameters of which can be estimated from measurements obtained from each individual subject.

The latter can be useful in allowing clinical assessments of patients or for detecting changes in the underlying system. My current work focusses on the impact of sleep-disordered breathing on cardiovascular autonomic control.

A.10 Ma, Yanyuan

I encounter inverse problems in my research in statistics, particularly in latent variable models. I would like to take the opportunity of the workshop to discuss new numerical procedures/methods available in solving type I integral equations that arising from these problems, and on handling tuning parameters, as well as analysing their effects.

Another issue frequently enountered in statistics is the model validity issue or model selection. It will be interesting to see what view points do the mathematicians hold on this issue, and what kind of criteria are used in this community to assess modeling issues. I believe a combined effort of mathematicians and statisticians could lead to a new approach in model selection methods.

I would also like to use this opportunity to get exposed to new research topics in this area.

A.11 Ottesen, Johnny

My interest is mathematical modeling in general and specific in physiology, where most of my research has been related to modeling parts or the overall cardiovascular system and its control mechanisms.

Especially I am committed to questions such as how can mathematical modeling contribute? What kind of knowledge and insight is gained? Are there non-trivial ways from which we can benefit from modeling? Can mathematical model make otherwise inaccessible parts accessible? Which factors have influences the development of the various models? Which alternatives do we have to a particular model? How reliable are various models? How are parameter estimation and model validation coupled? How can models be used for defining new concepts and clinical measurements and investigations?

A.12 Panerai, Ronney

General interests: Modeling and system identification of physiological regulatory mechanisms.

Specific interests: Regulation of cerebral blood flow, short-term regulation of arterial blood pressure. Multivariate modeling. Clinical applications.

Suggested topics for discussion: Modeling, system identification and clinical applications of time-varying physiological systems. Which modeling or system idenfication approaches are more efficient and robust? How do we apply the classical concept of 'reproducibility' in this context? How to establish limits of normality with a view towards clinical applications?

A.13 Verghese, George

My background is in control theory and signal processing. I am currently a co-PI on an NIH project devoted to integrating data, models and reasoning in patient monitoring for critical care. Our particular focus is cardiovascular dynamics, and my group is examining how

to use static and dynamic models from physiology to correlate the multiple data streams collected in the ICU. Our efforts include signal analysis, model development (to adapt detailed dynamic models to a level of complexity commensurate with the time scales of interest and the quality of the available data), identification, application of Bayesian networks to combine numerical and qualitative information, improved alarm generation, and explorations of more effective data displays. I would be very interested in learning from others at the workshop, and getting involved in modeling and analysis efforts that may emerge from the workshop.

A.14 Wu, Hulin

I have backgrounds in Control Engineering (MS) and Statistics (Ph.D.). I am interested in modeling HIV and influenza virus dynamics using both mathematical models and statistical methods. In particular, I am interested in identifying dynamic parameters in dynamics models (differential equation models) based on experimental data. I really like to see more collaboration and interactions between mathematicians and statisticians as well as experimental scientists. Currently my research group includes biomathematicians, physicists, computer scientists, software developers and statisticians with a total of 15 researchers who are actively interacting with experimental scientistis and clinical investigators to tackle complicated biomedical problems. I will share my experience how to lead an interdisciplinary team of quantitative researchers to work on a biomedical project by collaborating with biomedical investigators. I am also interested in learning from others on how to use mathematical and engineering tools to model biomedical process.

A.15 Zhao, Peng

My backgrounds are Control Engineering (BS, MS) and Medical Image Processing (PhD). The aims of current projects are to access cerebral vasoregulation in elderly patients with stroke or diabetes using transcranial Doppler ultrasound (TCD) and magnetic resonance imaging (MRI). Through this workshop, I hope to:

-Gain a better understanding of the theory, techniques, analysis tools and clinical applications of CardioVascular-Respiratory Control Mechanisms (CVRC).

-Discuss our current research work with the related CVRC problems, discuss the potential and validation to employ more signal/image processing techniques into CVRC.

-Understand the potential of new techniques in the field of CVRC.