

## Mini-Symposia Title:

Methodological and technical advances in fetal/newborn heart rate monitoring

### Mini-Symposia Organizer Name & Affiliation:

Maria G. Signorini - Politecnico di Milano, Italy

### Mini-Symposia Organizer Name & Affiliation:

Giovanni Magenes, University of Pavia, Italy

### Mini-Symposia Speaker Name & Affiliation 1:

Maristella Lucchini, Columbia University, NY, USA

### Mini-Symposia Speaker Name & Affiliation 2:

Philip Warrick, Perigen Inc., Canada

### Mini-Symposia Speaker Name & Affiliation 3:

Rik Vullings, Technical University Eindhoven, NL

### Mini-Symposia Speaker Name & Affiliation 4:

Maria G. Signorini, Politecnico di Milano, Italy

### Mini-Symposia Speaker Name & Affiliation 5:

Petar Djuric, Stony Brook University, USA

### Mini-Symposia Speaker Name & Affiliation 6:

Giovanni Magenes, University of Pavia, Italy

## Theme:

- 01. Biomedical Signal Processing
- 02. Biomedical Imaging and Image Processing
- 03. Micro/Nano-bioengineering; Cellular/Tissue Engineering & ...
- 04. Computational Systems & Synthetic Biology; Multiscale mode
- 05. Cardiovascular and Respiratory Systems Engineering
- 06. Neural and Rehabilitation Engineering
- 07. Biomedical Sensors and Wearable Systems
- 08. Biorobotics and Biomechanics
- 09. Therapeutic & Diagnostic Systems and Technologies
- 10. Biomedical & Health Informatics
- 11. Biomedical Engineering Education and Society
- 12. Translational Engineering for Healthcare Innovation and Commercialization

### Mini-Symposia Synopsis— Max 2000 Characters

Antepartum and neonatal heart rate monitoring represents one of the most informative techniques to assess the healthy development of the neural and cardiovascular systems in the first stages of life. Both methodological and technological innovations have been proposed in the last years, starting from non linear analysis of HR time series and going through wearable systems able to provide remote continuous monitoring of fetal/newborn heart rate. The minisymposium aims at discussing at first the clinical needs at the state of the art in the clinical practice (B. Fifer et al., Columbia University, USA). The second talk will focus on classical FHR feature detection (i.e., baseline, accelerations and deceleration detection) and fetal state estimation using machine learning techniques (P. Warrick, PeriGen Inc., Canada). Then, the most recent technological advances for non-invasive fetal ECG detection will be presented (Vullings & Mischi, Technical University of Eindhoven, Netherlands), and some innovative methods for extracting information from HR time series will be examined with the purpose of introducing them in the clinical routine (M.G. Signorini, Politecnico di Milano, Italy). The last talk will deal with Nonparametric Machine Learning methods, focused in particular on Bayesian methods that provide inference related to classification or prediction with as few assumptions about the data as possible (P. Djuric, Stony Brook University, USA). A general discussion among the presenters will close the symposium (chair G. Magenes, University of Pavia, Italy).

# Monitoring the Origins of Sleep Patterns and Autonomic Regulation

Speaker 1 Maristella Lucchini & William P. Fifer, Columbia University College of Physicians & Surgeons, New York, USA) PIN: 83450 & 83453.

## SHORT BIOGRAPHY

William Fifer, Columbia University, USA is the Chief of the Division of Developmental Neuroscience at the New York State Psychiatric Institute and the Associate Director of the Sackler Institute of Developmental Psychobiology at Columbia University Medical Center.

He and his team investigate the complex interplay of sleep physiology, patterns of brain activity, attention, and autonomic control and how they relate to risk for neurodevelopmental disorders. A major emphasis of his work is to determine how early life experiences, often associated with pre or perinatal exposures, shape the developing brain and later neurodevelopmental outcome. .

## SUMMARY OF THE TALK

Heart rate variability (HRV) monitoring is extensively used during pregnancy and labor to assess fetal wellbeing. Similarly, fetal and neonatal HR and HRV patterns can also provide a rich source of information on neuromaturation and subsequent developmental vulnerabilities. HRV has been widely employed as a non-invasive measure of autonomic nervous system (ANS) activity and control throughout the perinatal period. Assessment of early autonomic maturation is essential as the ANS is responsible for the regulation of multiple physiological systems crucial for survival and growth. Additionally, throughout the lifespan the ANS maintains a background level of functioning with connections to the brains' limbic structures that are involved in mood, memories, and emotional state regulation.

Fetal HRV serves as a practical and non-invasive index for the etiology and assessment of a wide range of clinical conditions. These measures have also been implemented for research into the impact of maternal clinical disorders, exposures, or other environmental challenges during gestation such as maternal depression, stress and substance use [1]. HRV measures vary significantly by fetal behavioral state [2], therefore accounting for state is imperative for the meaningful biomarkers and identification of potential developmental abnormalities.

Postnatally the infant's ability to regulate physiological, psychological and behavioral states in response to environmental and psychosocial challenges. Departure from normal physiological trajectories of ANS perinatal development has been associated with pathological conditions such as IUGR, congenital heart disease and neurodevelopmental disorders [3,4].

Furthermore, maturation in utero may be highly susceptible to maternal physical and psychosocial health,

as well as genetic and epigenetic influences tied to the intrauterine environment. This can shape the long-term health through adulthood, the focus of an extensive literature on the developmental origins of health and disease (DOHaD). For example changes in fetal autonomic regulation are associated with prenatal exposure to maternal stress and anxiety [5]. Interestingly, the impact of these early exposures on the HPA axis extends not only into childhood and adolescence, but across the entire lifespan [6].

Monitoring fetal HRV also allows the investigation of early sleep patterns. The emergence of sleep states relies on a strong integration between fetal movement and fetal HRV. Spontaneous fetal movements can be identified from 7 weeks' gestation. A rhythmic cycling or alternating periods of activity and quiescence can be recognized by 23 weeks, alternation of rapid eye movement periods is distinguishable between 28 and 31 weeks, and the rapid eye movement (REM) state begins to coalesce in late pregnancy with regular sleep cycling continuing to develop throughout the perinatal period. Sleep maturation is not only a marker of integration of developing physiological systems, but also lays the foundation for sleep dependent regulatory processes including growth, immune function, attention and memory and emotional regulation. Now with recent technological advancements, HR and HRV monitoring is inexpensive, practical in multiple settings and minimally invasive, opening a window of opportunity timely risk stratification and early intervention.

## REFERENCES

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# Intrapartum CTG features and fetal state estimation

Speaker 2 Philip A. Warrick (PeriGen Inc., Canada) PIN:15550

## SHORT BIOGRAPHY

Philip Warrick, PeriGen, Canada Dr. Philip A. Warrick obtained a B.A.Sc. (Electrical Engineering) from the University of Waterloo (Waterloo, Canada), and a M.Eng. (Electrical Engineering) and Ph.D. (Biomedical Engineering) from McGill University (Montreal, Canada).

His research interests lie in the fields of systems modelling, statistical signal processing, machine learning (including deep learning), decision support systems, obstetrics and cardiology.

His interest in novel intra-partum signal modelling and associated diagnostic tools has exposed areas of improvement for current clinical data acquisition (ultrasound for fetal heart rate and tocography for maternal uterine pressure) that new sensor research and technology has begun to address by providing surface electrode acquisition of both fetal ECG and maternal uterine pressure as electrohysterography (EHG).

These developments facilitate research into higher quality models, in terms of signal-to-noise ratio and information extraction, to improve intrapartum diagnosis of the fetal state.

Many aspects of fetal heart rate interpretation share commonality with other biomedical signals, especially with other currently challenging issues in cardiology. He has directed successful projects involving fetal ECG detection from abdominal sensors, adult electrocardiogram (ECG), phonocardiogram classification for early diagnosis of arrhythmias and arousal detection from polysomnography.

## SUMMARY OF THE TALK

“Intrapartum CTG features and fetal state estimation”

The talk will focus on classical FHR feature detection (i.e., baseline, accelerations and deceleration detection) and fetal state estimation using machine learning techniques (P. Warrick, PeriGen Inc., Canada).

Then, the most recent technological advances for non-invasive fetal ECG detection will be presented (Vullings & Mischi, Technical University of Eindhoven, Netherlands), and some innovative methods for extracting information from HR time series will be examined with the purpose of introducing them in the clinical routine (M.G. Signorini, Politecnico di Milano, Italy). The last talk will deal with Nonparametric Machine Learning methods, focused in particular on Bayesian methods that

provide inference related to classification or prediction with as few assumptions about the data as possible (P. Djuric, Stony Brook University, USA). A general discussion among the presenters will close the symposium (chair G. Magenes, University of Pavia, Italy).

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# Non-invasive fetal electrocardiography: towards diagnostic quality

Speaker 3      Rik Vullings & Massimo Mischi, Technical University Eindhoven, NL

## SHORT BIOGRAPHY

Rik Vullings received the M.Sc. (Applied Physics) and PhD (Electrical Engineering) degrees from the Eindhoven University of Technology in 2005 and 2010, respectively. During his M.Sc. he worked on monitoring of the uterine activity and fetal heart activity during pregnancy. During his PhD he only focused on the fetal heart activity in terms of non-invasive electrophysiological monitoring of fetal heart rate and fetal electrocardiogram. After completion of his PhD, he stayed at Eindhoven University of Technology (TU/e) as Postdoctoral researcher and currently, after having received a Veni grant in 2012, is part-time member of the permanent staff of the Signal Processing Systems group (Electrical Engineering department) as Assistant Professor. In this capacity, he supervises 10 PhD students, half of which are working on pregnancy monitoring.

In 2009, he co-founded Nemo Healthcare and currently, next to his position at TU/e, he works as Chief Scientific Officer at Nemo Healthcare, leading the team responsible for the development of signal processing and signal interpretation methods. His research interests include biomedical signal processing and modelling, machine learning – including deep neural networks and pattern recognition, with a special interest in pregnancy monitoring. He has (co)authored 9 patents and/or patent applications and more than 40 peer-reviewed journal papers, mainly about pregnancy monitoring.

## SUMMARY OF THE TALK

“Non-invasive fetal electrocardiography: towards diagnostic quality”

Non-invasive electrophysiological recordings have the potential to replace conventional fetal monitoring technologies for providing a reliable cardiotocogram. They combine the unobtrusiveness of currently used Doppler ultrasound technology, with the reliability of fetal scalp electrode recordings. Unfortunately, up till now the use of non-invasive electrophysiology is impeded by the poor quality of the recorded signals. Novel probabilistic signal processing techniques [1], combined with advances in deep neural networks [2] can significantly improve the quality of the signals and enable reliable detection of fetal heart rate patterns. Moreover, these methods can also provide the fetal electrocardiogram [3] which has the potential to compliment the cardiotocogram towards a more accurate assessment of fetal well-being.

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# Clinical perspectives of innovative methods for extracting information from FHR time series.

Speaker 4      Maria G. Signorini,

Dept of Electronics, Information and Bioengineering DEIB, Politecnico di Milano, Italy

## SHORT BIOGRAPHY

Maria G. Signorini is Associate Professor at the Department of Electronic, Information and Bioengineering, Politecnico di Milano

Her main research field is focused on improving healthcare paths and medical devices by introducing both new methodological approaches and technological solutions based on biomedical signal processing. She developed application of nonlinear analysis to biomedical time series. Her activity is devoted to fetal heart rate monitoring through analysis and classification by data analytics and machine learning techniques.

She developed multiparameter approaches integrating linear and nonlinear parameters towards the prediction of risk in antepartum fetal monitoring, premature babies, dialysis patients and others cardiovascular diseases.

Research results have been translated into technological solutions with modification of existing biomedical devices (Cardiotocography, Dialysis) or design of new instrumentation (wearable fetal HR monitoring).

## SUMMARY OF THE TALK

“Clinical perspectives of innovative methods for extracting information from FHR time series.”

The quantitative analyses of antepartum, intrapartum and early life heart rate variability (HRV) reliably contribute to noninvasive assessment of fetal and neonatal development throughout pregnancy and infancy.

HRV analysis provides indications about the synergic effect of autonomic nervous system (ANS) on the regulation of heartbeat dynamics in various conditions [1], [2]. Since the 1980s, Cardiotocography (CTG) is the most diffused technique to monitor fetal well-being during pregnancy. Indices in time and frequency domains represent the first adopted approaches for the quantification of FHR variability in pathophysiological conditions (quiet, activity, fetal hypoxia, acidemia, intrauterine growth restriction (IUGR), diabetes [1]).

Description and characterization of these FHR features are in [1], [3].

Frequency domain analysis allows to decompose signal power in frequency components which are an indirect measure of ANS modulation.

A further advancement is represented by nonlinear methods which have been introduced in recent years.

Measures of complexity as Approximate Entropy (ApEn) and Sample Entropy (SampEn) have been successfully employed for the quantification of fetal

distress before and during labor as well as in premature newborns.

In the context of early Intra Uterine Growth Retardation (IUGR) detection, Lempel Ziv Complexity (LZC) has been used in multivariate frameworks.

Lastly, Phase Rectified Signal Averaging (PRSA) and derived parameters such as average Acceleration and Deceleration Capacities (AC and DC) achieved higher performances in detecting several adverse fetal conditions if compared to traditional approaches [4,6]

The main drawbacks of the current CTG practice rely on its intermittent use throughout pregnancy and its feasibility in the clinical environment only.

The advent of wearable devices with unconventional monitoring solutions, has contributed to a FHR monitoring able to derive profile of FHR maturation as a function of gestational age, fetal sex, exposures, maternal conditions, and various factors contributing to fetal wellbeing in the pregnancy period [3].

The expected outcome is a more comprehensive and data-driven monitoring of fetal and neonatal wellbeing able to incorporate heterogenous data to achieve a prompt intervention in the context of adverse fetal and maternal conditions.

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# Nonparametric machine learning methods for fetal monitoring

Speaker 5      Petar Djuric, Stony Brook University, USA

## SHORT BIOGRAPHY

Petar M. Djurić received the B.S. and M.S. degrees in electrical engineering from the University of Belgrade, Belgrade, Yugoslavia, respectively, and the Ph.D. degree in electrical engineering from the University of Rhode Island, Kingston, RI, USA. He is a SUNY Distinguished Professor and currently a Chair of the Department of Electrical and Computer Engineering, Stony Brook University, Stony Brook, NY, USA.

His research has been in the area of signal and information processing with primary interests in the theory of signal modeling, detection, and estimation; Monte Carlo-based methods; signal and information processing over networks; machine learning; RFID and the IoT. Recently, his research has been applied to problems related to machine learning methods for intrapartum fetal monitoring. He has been invited to lecture at many universities in the United States and overseas.

Prof. Djurić was a recipient of the IEEE Signal Processing Magazine Best Paper Award in 2007 and the EURASIP Technical Achievement Award in 2012. In 2008, he was the Chair of Excellence of Universidad Carlos III de Madrid-Banco de Santander. From 2008 to 2009, he was a Distinguished Lecturer of the IEEE Signal Processing Society. He has been on numerous committees of the IEEE Signal Processing Society and of many professional conferences and workshops. He was Editor-in-Chief of the IEEE Transactions on Signal and Information Processing over Networks. Prof. Djurić is a Fellow of IEEE and EURASIP..

## SUMMARY OF THE TALK

“Nonparametric machine learning methods for fetal monitoring”

We address the processing of fetal heart rate (FHR) and uterine activity (UA) signals during labor with the objective of providing assistance to clinicians in making better decisions about interventions for preventing adverse outcomes.

We employ Bayesian nonparametric methods that include Dirichlet process mixture models, Gaussian processes, and deep Gaussian processes.

We apply these methods for dynamic classification of FHR/UA signals, for estimating missing samples, and for making inference about the interactions between the FHR and UA signals.

The methods use minimal assumptions and provide results that can readily be interpreted. We compare the performance of our approaches with that of other modern methods

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# Critical review and future trends of Fetal Heart Rate analysis

Speaker 6

Giovanni Magenes, University of Pavia, Italy

## SHORT BIOGRAPHY

Giovanni Magenes (M'90, S'2018) is currently Full Professor of Biomedical Signal and Image Processing at the Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Italy, where he is also the Director of the Centre for Health Technologies (CHT). He received the Ph.D. degree in Biomedical Engineering from the Politecnico di Milano, Milano, Italy, in 1987. His research interests include soft computing methods in biomedical applications, biomedical signal and image processing, hybrid tissues, and wearable devices. He has been involved in various European research projects in the field of ICT with applications to the biomedical domain. Since the '90ies he focused his attention on the prenatal monitoring for the assessment of fetal well being, both with novel technological and methodological approaches. In this field he was a scientific consultant of Hewlett Packard Italy –Medical Division for the design of a new CTG software [1]. In collaboration with M.G. Signorini he developed new methods for Fetal Heart Rate analysis [2,3], for the classification of CTG recordings [4] and a telemedicine wearable system for Fetal ECG [5]. He was a Visiting Researcher at the Institut Nationale de la Santé et Recherche Medicale, Lyon, France and a Visiting Professor at the Faculté des Sciences, Université de la Méditerranée, Luminy, France.

## SUMMARY OF THE TALK

“Critical review and future trends of Fetal Heart Rate analysis”

The development of a human being starting from the fetal condition during pregnancy can be monitored by means of the Heart Rate Variability (HRV) signal, usually collected through CTG exams. A critical review and a discussion of the traditional approaches in reading and analyzing CTG tracings will be done by all participants to the minisymposium. Classical time domain, frequency domain and non-linear parameters of Fetal Heart Rate (FHR) time series will be considered in the discussion, with the relevant physiological meanings. A particular

attention will be devoted to multivariate classification methods and to machine learning approaches for the identification of fetal/newborn pathologies [6].

However, most methodological tools for HRV analysis, although considering different ranges in the various gestational ages, basically make a static “snapshot” of the fetal heart control at a certain moment. This concluding discussion aims at proposing a novel approach, by considering the fetus as a time varying system and the changes of fetal HRV indices as the dynamic response of this system during the evolution of pregnancy. In this view, longitudinal fetal monitoring can be suggested in the clinical practice, to enhance the diagnostic capability of HRV analysis [7].

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