Bridging the gap between the development of advanced biomedical signal processing tools and clinical practice

2015 Physiol. Meas. 36 627

(http://iopscience.iop.org/0967-3334/36/4/627)

IOP Publishing | Institute of Physics and Engineering in Medicine Physiological Measurement

Physiol. Meas. 36 (2015) 627–631 doi:10.1088/0967-3334/36/4/627

Preface

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In the last twenty years the field of the biomedical signal processing has known an upsurge, as witnessed by the progressively increasing number of peer-review international journals and sessions in biomedical meetings. Topics that twenty years ago were confined to restricted communities of theoretic researchers and primarily addressed in specific fields of the science such as causal inference, information coding, graph theory, symbolic dynamics and complexity analysis, are now becoming the hot matter of special issues of international biomedical journals and invited sessions in biomedical conferences around the world (Merletti and Farina 2008, Laguna and Sornmo 2009, Porta *et al* 2009, Olbrich *et al* 2011, Fang *et al* 2011, Wessel *et al* 2011, Faes *et al* 2012, Porta and Faes 2013, Micera and Akay 2013, Clifford *et al* 2014, Gruzelier *et al* 2014, Porta *et al* 2015). The rapid dissemination of results, tools and datasets, enabled by web-based facilities, journals with flexible copyright policies, open access repositories and free-downloadable computer programs, has been enlarging the possibility of applications of advanced signal processing techniques to the biomedical field at a faster than ever rate. Despite these flourishing advances, studies proving the clinical utility of most of the proposed advanced signal processing techniques are still lacking. The main reason for this lack of transfer from theory to clinics is the absence of any, really relevant, arena in which people expert in biomedical signal processing can meet personally, or virtually, people who know the physio-pathology underpinning a given syndrome and have access to a large community of individuals affected by the considered disease. The main meetings featuring biomedical signal processing among their themes fail to attract the interest of clinicians and vice versa, big clinical meetings are rarely interested in having technical sessions devoted to biomedical signal processing. Nowadays, at best, the most active groups of research in the biomedical field who are trying to combine expertise in signal processing, physio-pathology and clinics, have only partially accomplished the process. Usually, one, or more, of the following conditions limits their action: i) the comprehensive expertise in biomedical signal processing, especially in consideration of its recent explosion; ii) the access to really big databases built by large groups of individuals and reliably categorized according to strict enrolling criteria; iii) the knowledge of the physiological mechanisms that can be involved in, or govern a specific pathology; iv) the possibility to carry out ad-hoc experiments specifically validating new ideas and/or tools; v) the chance to participate to clinical trials. Sharing databases to stimulate competition among groups over a common issue and providing open access signal processing tools may help in disseminating methodology, ranking methods, testing software and indicating relevant challenges, but it cannot ensure the penetration of new techniques, procedures and ideas into the clinical practice.

The present issue of *Physiological Measurement* aims at stressing the necessity of bridging the gap between biomedical signals processing and clinical applications via a series of contributions intended to show the practical value of advanced biomedical signal processing techniques in preclinical and clinical contexts. The issue follows the 8th conference of the European Study Group on Cardiovascular Oscillations (ESGCO) which was held in the beauty of the Dolomites Mountains in Fai della Paganella, Trento, Italy, on May 25–28, 2014. The 8th ESGCO meeting was the last event in a series of meetings organized by the ESGCO community which started in Cardiff, Wales, in 2000 and then, took place in Siena, Italy, in 2002, Leuven, Belgium, in 2004, Jena, Germany, in 2006, Parma, Italy, in 2008, Berlin, Germany, in 2010 and Kazimierz Dolny, Poland, in 2012. The main aim of the ESGCO meetings is to create an interdisciplinary arena in which biophysicists, bioengineers, mathematicians, computer scientists, biologists, physiologists, physicians and clinicians can discuss physiological states and transitions, regulatory mechanisms and their interrelations and clinical implications of cardiovascular and cerebrovascular oscillations in all their forms, in the spirit of favoring the transfer from methodology to clinical applications. The 8th ESGCO meeting was specifically focused on full multivariate applications and methods, with the aim of quantifying the interactions among subunits of a given physiological system (e.g. the cardiovascular system) and more ambitiously, of describing the relations among physiological systems whose links are traditionally less explored (e.g. the heart-brain interactions). Following a well-established tradition of the ESGCO meetings (Voss and Hoyer 2006, Di Rienzo and Porta 2009, Porta *et al* 2009, Wessel and van Leeuwen 2012, Porta and Zebrowski 2013) a scientific committee, formed by participants of the conference with high international reputations, selected from all contributions presented at the meeting a subset for submission to this issue. The selection was made according to the originality of the study, relevance of the topic, foreseen impact on future research, quality of the experimental data, study design and presentation during the meeting. The papers collected in this issue, resulting from the aforementioned process of selection and the subsequent standard peer-review procedure made by the journal, accurately demonstrate the variety of themes highlighted at the meeting, the diversity of the presented signal processing approaches, the relevance of the proposed applications, the originality of the topics and the level of scrutiny devoted to methodology even when this is traditional and widely utilized.

The contributions presented in this issue suggest the power of advanced signal processing techniques in addressing clinical problems such as assessing the outcome of a treatment, tracing the effect of drug administration, improving diagnosis, prognosis and therapy, stratifying the risk, identifying a pathological state or an impaired function, predicting the development of a disease based on its early signs, tracking the progression of a chronic syndrome, measuring the severity of a disease, differentiating pathologies, distinguishing physiological conditions, ranking widely utilized medical procedures, and quantifying the response to a given stimulus. Indeed, Loncar-Turukalo *et al* (2015) find that the analysis of cardiovascular variability is helpful to detect and monitor the cardiotoxic effects of a chemiotherapeutic agent such as doxorubicin in rats; Fischer *et al* (2015) suggest that markers extracted from the variability of an interval reflecting the entire duration of the ventricular depolarization and repolarization processes, such as the QT interval from the surface ECG, can improve risk stratification in patients suffering from dilated cardiomyopathy; Pinna *et al* (2015) review the literature supporting the claim that methods for cardiac baroreflex sensitivity assessment derived from spontaneous heart period and systolic arterial pressure variations provide valuable information for the clinical management of patients with cardiovascular disease; Rivolta *et al* (2015) trace over time the effects of the moxifloxacin or sotalol administration on the ventricular repolarization heterogeneity, as estimated from a recently developed index computable from 24 h Holter recordings; Guzzetti *et al* (2015) propose univariate and bivariate analyses based on symbolic dynamics to rank different general anesthesia procedures according to their ability to preserve cardiovascular control;

Runge *et al* (2015) exploit an information-theoretic approach for the estimation of the coupling delay and strength to describe the dynamical interactions in the cardiovascular system and to distinguish healthy pregnant women from those suffering from pre-eclampsia; Dalla Vecchia *et al* (2015) utilize cardiovascular control indexes derived from spontaneous heart period and systolic arterial pressure variability series to describe the autonomic function of amyotrophic lateral sclerosis patients and suggest their use to improve prognosis; Varon *et al* (2015) find that markers of cardiorespiratory interactions computed via information decomposition tools can separate control children from those suffering from temporal lobe or absence epilepsy during interictal periods; Barbic *et al* (2015) characterize the sympathetic arm of the baroreflex, i.e. the reflex responding to modifications of arterial pressure with changes of sympathetic nerve activity directed to muscles, in humans during head-up tilt and successive orthostatic syncope evoked by the application of lower body negative pressure; Rickards *et al* (2015) estimate the coupling between arterial pressure, cerebral blood velocity and cerebral tissue oxygenation in experimental conditions enhancing spontaneous hemodynamic variability or periodically disturbing arterial pressure control; Schiatti *et al* (2015) propose improved Granger causality measures and use them to investigate cardiovascular and cerebrovascular directed interactions in patients with a history of recurrent syncope during head-up tilt test prolonged until the development of pre-syncope symptoms; Porta *et al* (2015) delineate the limits of permutation entropy as a marker of the complexity of the cardiac control by assessing the heart period variability response to a pharmacological stimulus abolishing the vagally-mediated modifications of heart rate; Elstad and Walløe (2015) show that time and frequency domain indexes derived from stroke volume variability assessed during spontaneous breathing can detect the central hypovolemic condition evoked by lower body negative pressure; Cysarz *et al* (2015) prove the effectiveness of symbolic indexes in tracking the changes of the autonomic control induced by pharmacological challenges in humans, regardless of the strategy of symbolization; Faes *et al* (2015) quantify the causal interactions between time series of cardiac vagal autonomic activity, as derived from ECG signal, and brain waves activities, as derived from EEG, in healthy subjects during sleep; and Rapin *et al* (2015) present a new technology for cooperative dry-electrode sensors for multi-lead biopotential and bioimpedance monitoring and show their functioning in the context of the recording of the cardiac electrical activity.

We hope that the contributions presented in this issue can stimulate both people interested in the development of signal processing techniques, who are usually more focused on testing new methodologies and technologies, but less prone to apply them over large databases and to check their performance in comparison with more standard tools and people interested in clinics, who are usually more focused on the management of a disease, but less prone to test new paradigms and tools, especially if those already in use are believed to provide sufficient results, to cross the borders of their fields of competence and create a multidisciplinary arena able to bridge the gap between the development of advanced signal processing tools and clinical practice.

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