Guest Editorial

Multimodal Source Imaging: Basic Methods, Signal Processing Techniques, and Applications

MULTIMODAL source imaging is an emerging field in biomedical engineering. Its central goal is to combine different imaging modalities in a single model or data representation, such that the combination provides an enhanced insight into the underlying physiological organ, compared to each modality separately. It requires advanced signal acquisition and processing techniques and has applications in cognitive neuroscience, clinical neuroscience, and electrocardiology. Therefore, it belongs to the heart of biomedical engineering.

This issue of IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING contains a special section that is devoted to multimodal source imaging. The clinical importance of functional imaging of organs is today beyond discussion and many complementary imaging modalities have emerged. As data acquisition methods, signal processing techniques and computational power continue to develop, imaging modalities continue to evolve and improve. Gradually, it has become clear that a combination of different modalities is often essential to extract maximum information from the available data. One obvious example is EEG inverse modeling, where structural MRI is essential to derive accurate forward models and to provide an anatomical framework to visualize results. In this way, advanced EEG forward modeling requires knowledge of both image processing and numerical mathematics to address the computational issues of the forward problem in acceptable amount of time.

Most of the papers presented in this special section originate from contributions and topics presented at the 2nd International Conference on Basic and Clinical Multimodal Imaging (BaCI) that was held in Utrecht, The Netherlands, in September 2–5, 2015.

The contribution by Fiederer *et al.* provides a nice example of state-of-the-art finite-element method (FEM) modeling and signal analysis and presents an intriguing finding relevant for cognitive neuroscience that gum chewing can have an effect on cognition [1], [2]. In this study, a realistic FEM model was built for the simulation of extra- and intracranial potentials in a chewing epilepsy patient undergoing invasive seizure monitoring. Assuming current dipole generators in the masticatory muscles, they were able to show that the computed field strength in cortex can be high enough to allow for neuronal modulation effects, similar to those that have been observed in transcranial electrical stimulation. Simulated intracranial potentials had a similar topographical distribution as the EMG artifacts observed in the intracranial EEG.

The forward problem of the EEG, i.e., to accurately predict the recorded potential for a given source and given volume conductor continues to inspire scientist with innovative ideas. In [3], Nüßing *et al.*, a novel approach of the FEM is proposed, the unfitted discontinuous Galerkin (UDG) FEM. An important issue in FEM modeling is the creation of a 3-D mesh that is geometrically correct and that gives an adequate description of the interfaces where conductivity jumps quickly from one value to another. Particularly, when the object of interest contains thin layers with a deviating conductivity (such as the skull), this may lead to inaccurate predictions of the requested potential distribution. With the UDG-FEM, these problems are approached by assuming a regular mesh and invoking the concept of level set functions to describe compartment interfaces. This approach leads to simpler computational pipelines without compromising the accuracy.

Even though they can learn a lot from each other's methods, researchers form the fields of brain and heart modeling tend to dwell in separate communities. The BaCI meeting brings together researchers from the fields. A nice example of methodology that is of interest to both fields is the contribution by Potyagaylo *et al.* [4]. In this cardiac study, the authors compare the results of a FEM and a BEM volume conductor model for the same geometry. The main difference between these two models is that in the BEM model, the boundaries are described rather than the complete geometry, which greatly reduces the number of elements at the cost of not being able to include anisotropic conductivity. Their study showed that the resulting error by the BEM is small enough not to compromise the results.

An important parameter in volume conductor modeling is the conductivity of the tissues involved. Reports in the literature, of the values of these conductivities, show little consensus. Recently, a novel method is being developed to image the conductivity: Magnetoacoustic tomography with magnetic induction (MAT-MI) [5]. In this method, induced eddy currents generate acoustic vibrations that are recorded by transducers located around the object. In previous MAT-MI studies, the acoustic inhomogeneity of the object was ignored. Zhang *et al.* [6] introduce a novel MAT-MI algorithm that does include this inhomogeneity. The authors show that this improves the spatial resolution of the method, thus taking an important step toward practical application.

High-frequency oscillations (HFOs, 80-500 Hz) in the intracranial EEG have been newly found as biomarkers for epileptogenic tissue [7]. The identification of HFOs is mainly done by visual review, which is time consuming. There is lack of a tool that allows an objective detection and classification scheme that clinicians can agree upon. The paper by Roehri *et al.* proposes a framework based on an advanced time-frequency analysis that could provide such a tool [8]. In this simulation study, they used the continuous-wavelet transform and evaluated different prewhitening strategies that lead to a different performance in terms of distinguishing various types and mixtures of HFO events in the presence of real background activity obtained from patient data. The optimal prewhitened time-frequency decomposition they propose hold promise as a uniform representation for which automatic HFO detectors can be developed. The

Manuscript received October 12, 2016; revised October 19, 2016; accepted October 19, 2016.
Digital Object Identifier 10.1109/TBME.2016.2620154

availability of such detectors could have a significant impact on the yield of intracranial EEG data in the presurgical evaluation of patients for epilepsy surgery.

So far the use of HFO's has mainly been restricted to intracranial recordings, because of the low-signal-to-noise ratio of HFO's in the surface EEG. Recently, it has been shown that there exists a cross-frequency coupling between low-frequency phase and high-frequency amplitude [9]. Based on this observation, Li *et al.* propose a method to combine the high-frequency amplitude and the low-frequency phase in ictal surface EEG recordings in order to locate the epileptic zone from ictal EEG recordings [10]. They show promising results, both in a model and in a patient study, demonstrating that it is possible to locate the epileptic zone with a signal-to-noise ratio as low as 0.4.

Most methods to locate the epileptic zone rely on recordings that display activity that is clearly related to epilepsy (ictal activity or interical spikes). The contribution by Coito *et al.* shows that the location of the epileptic region can also be inferred from deviations in the direction of functional connectivity [11]. They used high-density resting-state EEG recordings to estimate the source activity in 82 brain regions in 20 controls and 40 temporal lobe epilepsy patients. Subsequently, multivariate Granger-causal modeling was applied to determine the strength of connectivity between these regions in both directions. In the patient group, the outflow from the default-mode network was significantly less than in the controls for regions that are known to be involved in temporal lobe epilepsy.

The brain acts as a huge network of electrophysiological sources that mutually exchange information that can be modeled as nonlinear transformations of time series that constitute the EEG. Transformed to the frequency domain, these nonlinear transformations manifest themselves as (sub-)harmonic coherencies. With this underlying idea, Yang *et al.* [12] present a novel data analysis framework to characterize these interactions. These authors evaluate their methods using the EEG data of healthy subjects of whom the proprioceptive system is activated though a specific motor control task.

Simultaneous EEG-fMRI has evolved over the past decade as a true multimodal imaging approach with applications both in the neurosciences and in the clinical domain, especially in epilepsy [13]. The study of Hermans *et al*. addresses one of the challenges that the simultaneous recording of these modalities poses: the artifacts in the EEG that can arise due to physiological or spontaneous small movements in magnetic field of the scanner and that can be misinterpreted as relevant (pathological) signal [14]. In their paper, they analyze the performance of two new approaches, based on additional current loops added to the EEG cap and based on a novel cap with an insulated layer containing a reference electrode for each EEG electrode. They find that the new approaches do not outperform traditional signal postprocessing methods in the case of small pulsations caused by the heartbeat. Spontaneous subtle movements, however, are corrected by both hardware-based methods, whereas they remain as artifacts in the signal using the traditional methods. For application in epilepsy, this would imply an increased sensitivity of EEG-fMRI for localizing the sources of pathological activity.

Another paper on EEG-fMRI technology, by LeVan *et al.* [15] is aimed at the correction of *gradient* artefacts in the EEG from a moving subject. Contrary to [14], no extra EEG channels are needed. Two novel methods are proposed, one based on the estimation of artefactual templates built from fitting artefact templates, modulated by slowly varying splines and the other method incorporates additional head motion information recorded from a Moire phase tracking device. Both methods appear to be an improvement of existing methods.

Together, these papers demonstrate that multimodal source imaging has become a very active field of biomedical engineering over the last decade. The combination of state-of-the-art recording techniques, basic applied physics and mathematics, and advanced signal processing has allowed applications that would have been difficult to imagine 20 years ago. These techniques and applications are reflected in the contributions to this special issue, to which also BaCI attendents were proposed to submit their work.

References

[1] L. D. J. Fiederer *et al.*, "Electrical stimulation of the human cerebral cortex by extracranial muscle activity: Effect quantification with intracranial EEG and FEM simulations," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2552–2563.

[2] A. Smith, "Effects of chewing gum on cognitive function, mood and physiology in stressed and non-stressed volunteers," *Nutrational Neurosci.*, vol. 13, no. 1, pp. 7–16, 2010.

[3] A. Nüßing *et al.*, "The unfitted discontinuous Galerkin method for solving the EEG forward problem," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2564–2575.

[4] D. Potyagaylo *et al.*, "Influence of modeling errors on the initial estimate for nonlinear myocardial activation times imaging calculated with fastest route algorithm," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2576–2584.

[5] Y. Xu and B. He, "Magnetoacoustic tomography with magnetic induction (MAT-MI)," *Phys. Med. Biol.*, vol. 50, pp. 5175–5187, 2005.

[6] W. Zhang *et al.*, "Image reconstruction in magnetoacoustic tomography with magnetic induction (MAT-MI) with variable sound speeds," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2585–2594.

[7] M. Zijlmans *et al.*, "High frequency oscillations as a new biomarker in epilepsy," *Ann. Neurol.*, vol. 71, no. 2, pp. 169–178, 2012.

[8] N. Roehri *et al.*, "Time-frequency strategies for increasing high frequency detectability in intracerebral EEG," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2595–2606.

[9] U. Friese *et al.*, "Successful memory encoding is associated with increased cross-frequency coupling between frontal theta and posterior gamma oscillations in human scalp-recorded EEG," *NeuroImage*, vol. 66, pp. 642–647, 2013.

[10] C. Li *et al.*, "Epileptogenic source imaging using cross frequency coupled signals from scalp EEG," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2607–2618.

[11] A. Coito *et al.*, "Directed functional brain connectivity based on EEG source imaging: methodology and application to temporal lobe epilepsy," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2619–2628.

[12] Y. Yang *et al.*, "A generalized coherence framework for detecting and characterizing nonlinear interactions in the nervous system," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2629–2637.

[13] T. Murta *et al.*, "Electrophysiological correlates of the BOLD signal for EEG-informed fMRI," *Hum. Brain Mapping*, vol. 36, no. 1, pp. 381–414, 2015.

[14] K. Hermans *et al.*, "Effectiveness of reference signal based methods for removal of EEG artifacts due to subte movements during fMRI scanning," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2638–2646.

[15] P. LeVan *et al.*, "EEG-fMRI gradient artifact correction by multiple motion-related templates," *IEEE Trans. Biomed. Eng.*, vol. 63 no. 12 pp. 2647–2653.

GEERTJAN HUISKAMP, *Guest Editor*
Department of Neurology and Neurosurgery
Brain Center Rudolf Magnus
University Medical Center Utrecht
Utrecht, The Netherlands
e-mail: ghuiskam@umcutrecht.nl

T. F. OOSTENDORP, *Guest Editor*
Donders Institute for Brain, Cognition and Behavior
Radboud University Medical Center
Nijmegen, the Netherlands

J. C. DE MUNCK, *Guest Editor*
Department of Physics and Medical Technology
VU University Medical Center
Amsterdam, The Netherlands