Discussion of “Time-frequency Techniques in Biomedical Signal Analysis: A Tutorial Review of Similarities and Differences”

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With these comments on the paper “Time-frequency techniques in biomedical signal analysis: A tutorial review of similarities and differences”, written by Matthias Wacker and Herbert Witte [1], the journal wants to stimulate a broad discussion on methodological fundamentals of non-parametric time-frequency analysis techniques in biomedicine. An international group of experts have been invited by the editor of Methods to comment on this paper. Each of the invited commentaries forms one section of this paper.

1. Comment by C. Baumgartner

The human body is a complex biophysical system which continuously communicates biological information about (patho-)physiological mechanisms from basic cellular to systems level. This leads to a broad spectrum of biosignals. A profound understanding and knowledge about mechanisms of biosignal formation, which can be electric, magnetic, mechanic, acoustic etc., is crucial for using a proper sensor system to register biosignals, and, subsequently, selecting a reasonable signal processing strategy. Biomedical signal processing analyzes these measurements, which reflect diverse biophysical and physiological phenomena, relevant to determine the state of a patient’s health. These measurements can also be used to initiate an effective and efficient therapeutic management. In a critical care setting, real time signal processing is essential for enabling early diagnosis of acute diseases, such as myocardial infarction or stroke.

It is my great pleasure to comment on the review article entitled “Time-frequency techniques in biomedical signal analysis: a tutorial review of similarities and differences” written by Matthias Wacker and Herbert Witte [1]. This work presents and discusses methodological principles and properties of the most frequently used time-frequency representatives (i.e. approaches mapping a one-dimensional signal of time into a two-dimensional function of time and frequency), and their applicability to the interpretation of such complex non-stationary signals to advance the processing of biomedical information.

The combination of time- and frequency domain analyses shows a more informative picture of the temporal location of a biosignal’s spectral components. In this review the authors introduce a class of linear transforms such as the short-term Fourier transform (STFT), the Gabor transform (GT), the Hilbert transform (HT), the S-transform (ST), the continuous Morlet wavelet transform (CMWT), and the Wigner-Ville distribution (WVD) as an example of the class of quadratic time-frequency approaches, as well as signal adaptive approaches. The application of time-frequency methods is demonstrated by appropriate representations such as time-frequency distributions, spectrograms or scalograms in addition to instantaneous amplitude, frequency and phase measures. To demonstrate issues the authors selected human EEG/MEG signals of a neuroscience experiment with specific properties to elucidate pros and cons of the different methods. Therein, volunteers were stimulated by flicker stimuli and frequencies were adjusted to the individual’s frequency.

In biomedicine the wavelet transform has emerged as a powerful tool over recent years not only for the analysis of neurological signals like the EEG, but also for processing signal data in electrocardiology such as the ECG or experimental field potentials. The use of STFT for ECG analysis seems natural, but the major drawback is
that its time-frequency precision is not optimal. Wavelet transform, in turn, allows a time-frequency decomposition of the signal in a set of individual signal components compared to STFT, allowing a local scale-dependent spectral analysis of these features. In addition to EEG or ECG, wavelet transform analysis has been applied to a broad field of biomedical applications such as medical sounds, blood pressure and flow, respiration signals or molecular data like DNA or RNA sequences.

After careful experimental work, if researchers have signal data, containing unknown characteristics, the diversity of potential approaches and choices raises the question of how to choose the „best” signal-processing method. It is obvious that the choice deeply depends on the nature of signals to be analyzed, which, on the other hand, determines the relative performance of the selected method. Hence, prior knowledge of the signals and their time-frequency characteristics, as well as some degree of user expertise is needed to progress with this problem. This is a question that arises not only in traditional signal processing, but also in many fields of biomedical data analysis and mining. In general, it can be said that one needs to learn from many examples to develop progress and expertise in this field. Once a specific method has been selected, the parameterization of the variant types of time-frequency approaches, (e.g. parameters such as the window length which determines the degree of smoothing) including the graphical representation of results, is one of the most challenging steps of this process. As the authors correctly state “only when a signal’s time frequency characteritics strongly correspond with the frequency-(in)dependent time-frequency resolution of the analysis method, the application can be considered optimally”. This is a simple rule to approach an existing signal processing problem. There is no easy simple strategy to approach an existing signal processing problem. There is no easy simple strategy to approach an existing signal processing problem.

2. Comment by K. J. Blinowska

In their manuscript Wacker and Witte [1] conclude that, among time-frequency techniques, Matching Pursuit (MP) method is preferred, since it provides an appropriate time-frequency resolution for all frequencies, while simultaneously reducing cross-terms. In this context it is worth mentioning other favorable features of MP underlined e.g.: in [2, 3]. (In [3] different time-frequency methods are described and compared.) MP is the first signal-processing algorithm, which adopts the window length to the local features of the analyzed time series. The MP method allows description by one formalism periodic and transient structures of the signal. Moreover these structures are described parametrically by means of: frequency, time occurrence, time span, amplitude and phase. This kind of description is compatible with the traditional visual analysis of signals. After the MP decomposition of the signal it is possible to extract desired structure e.g.: epileptic spike or sleep spindle according to its clinical definition. These features of MP allowed for explicit parametrization of sleep EEG transients [4, 5], exhaustive description of micro- and macrostructure of sleep and finally led to the construction of automatic system for sleep staging [6], fully compatible with the classic criteria and providing high concordance with the visual analysis. Multichannel MP by extracting particular structures of the signal helped to improve the inverse problem solutions for sleep spindle, epileptic focus localization [7, 8].

In the Wacker and Witte paper the authors put emphasis on the fact that the t-f approaches work best, if the functions used for construction of t-f distribution match the signal components present in the signal. Gabor functions usually applied in MP match a large repertoire of transients in the biomedical signals and additionally they provide the highest t-f resolution. However, some signals contain highly asymmetric components, which are poorly described by Gabor functions. This is a case especially for acoustic signals e.g. otoacoustic emissions (OAE), speech, music.

The fact that Gabor functions give inadequate representation of asymmetric signals is illustrated in Figure 1. Four Gabor atoms are needed to describe simulated asymmetric function. Additionally the energy of the signal appears before the signal onset. In order to account for the presence of asymmetric waveforms, quite prominent in OAE signals, a dictionary consisting of asymmetric functions was proposed [9].

Each of these functions is composed of two parts: the ascending part is based on a Gabor function, and the descending part on exponentially decaying sinusoid. Such waveform could be described by the formula:

\[
\Lambda (\mu, \omega, T_m) = \exp \left( -\frac{(t-\mu)^2}{2\sigma^2} \right) \quad ; \quad t \leq T_m \\
N \cdot \exp (-\alpha \cdot (t-t_m)) \quad ; \quad t > T_m
\]

where \( \alpha = \frac{T_m - \mu}{\sigma^2} \) and \( T_m = \frac{\mu + T_m}{2} \).

Additional parameter \( T_m > \mu \) controls the asymmetry of the atom. \( T_m \) describes the point where the Gaussian envelope changes into exponent. \( N \) is normalization constant. The function obtained in this way is continuous up to first order derivative. The waveforms described by the above formula could have different rise and fall times for the same frequency. The envelope of such atom is:

\[
\Omega (\mu, \omega, T_m) = \\
\exp \left( -\frac{(t-\mu)^2}{2\sigma^2} \right) \quad ; \quad t \leq T_m \\
N \cdot \exp (-\alpha \cdot (t-t_m)) \quad ; \quad t > T_m
\]
Figure 1
Top: simulated signal. A1 – WVD distribution of the signal approximated by asymmetric function (Eq. 1), B1 – WVD of the function approximated by Gabor dictionary, C1 – amplitude-t-f representation of the signal approximated by asymmetric function, D1 – amplitude-t-f representation of the signal approximated by Gabor dictionary. Lower part of the figure – corresponding amplitude envelopes.
WVD is not an optimal choice to represent the asymmetric functions in t-f space, since for asymmetric functions squaring procedure leads to the appearance of cross terms (Figure 1, A1). Additionally the maximum of energy in the t-f map is shifted in relation to the maximum of amplitude.

In order to counteract to this unfortunate properties of WVD the representation in time-frequency-amplitude space was proposed in [9]. The idea is based on calculation of dot product between scaled to 1 modulus of Fourier transform of an atom and a vector describing its sampled envelope \( P(t) \). In this way, we get the amplitude representation of an atom in t-f space \( A(\omega, t) \), given by the expression:

\[
A(\omega, t) = Z^T(\omega) \cdot P(t)
\]

\[
Z^T(\omega) = \frac{FT(\Lambda)}{\max(FT(\Lambda))}
\]

(2)

\[
P(t) = \left< R^T F, \Lambda, \right> \cdot \Omega(\mu, \sigma, T_m)
\]

Where \( \Lambda_j \) is the winner atom (chosen from dictionary) and \( \left< R^T F, \Lambda, \right> \) is this atom amplitude. \( Z^T(\omega) \) is moanus of Fourier transform of an atom scaled to 1, and \( P(t) \) the atom’s envelope. The t-f representation of the decomposed signal is a sum of distributions given by Equation 2.

The properties of the amplitude representation versus VWD are illustrated in Figure 1. One can see that by the application of enriched dictionary (encompassing Gabor and asymmetric functions) and t-f-amplitude representation the asymmetric function is best described: the representation is sparse, the maximum of distribution coincides with a maximum of the amplitude, the cross-terms and pre-echo effect are eliminated. The amplitude representation, especially in case of biomedical signals is more intuitive and more meaningful, since it allows a relatively fast and automatic broadband modeling of time-frequency atoms, each of them could be easily interpreted. The resulting bump models represent the most prominent oscillatory activity in the signals which may correspond to various physical or biological phenomena, e.g., oscillatory events in EEG and other brain signals [12, 13].

3.2 Space-Time-Frequency (STF) Representation and Multiway Analysis of Biomedical Data Using Tensor Decompositions

In many biomedical signal processing tasks/problems, data are recorded by many electrodes (sensors) and represented as multiple time series or set of images (neuroimages). Such kind data occurs in the analysis of electroencephalography (EEG) and magnetoencephalography (MEG), and can be naturally represented in the time-frequency domain by tensors (multiway arrays – which are generalizations of matrices and vectors) [10]. The order of a tensor is the number of modes, also known as ways or dimensions (e.g., space, time, frequency, subjects, trials, groups, conditions, wavelets, dictionaries). In the simplest scenario for multichannel signals a 3rd order tensor has three natural modes: space x time x frequency. For multiple trials and multiple subjects, the biomedical data data sets can be naturally represented by higher order tensors: e.g., 5th-order tensor: space x time x frequency. For multiple trials and multiple subjects, the biomedical data data sets can be naturally represented by higher order tensors: e.g., 5th-order tensor: space x time x frequency.
From time-frequency analysis perspective, tensor decompositions are very attractive, even for single channel, because they simultaneously take into account temporal and spectral information and variability and/or consistency of TFRs along trials and/or subjects. Furthermore, they provide links among various latent variables (e.g., temporal, spectral and spatial components) often with physical or physiological meaning and interpretations [10]. In fact, tensor decompositions are emerging techniques for data fusion, dimensionality reduction, feature extraction, classification, pattern recognition, multiway clustering, sparse representation and coding, and nonlinear blind source separation (MBSS). The multi-way analysis (tensor factorizations and decompositions) is a quite natural choice, for instance, in EEG/MEG studies as it provides convenient multichannel and multi-subject space-time-frequency sparse representations, artifacts rejection, feature extraction, multi-way clustering and coherence tracking [10,11].

3.3 Are Several Heads Better than One? – Set of TFRs

The key issue in the STF representation of tensor data is choice of a suitable TFR or frequency transform and the selection of optimal or close to optimal corresponding parameters. The paper of Wacker and Witte provides insightful information as to how to make such selections. This allows researchers to choose suitable time-frequency representation to perform tensorization of multichannel data on basis of a priori information about underlying signals. However, in some scenarios such a priori information is quite limited or not available and signals are highly non-stationary. Such cases occur, for example, in the mentioned in the paper BCI, and also in Neurofeedback implemented online or in the early prediction of Alzheimer disease [10–13]. In such a scenario, we can apply two or more time-frequency representations or optionally the same frequency transform but with two or more different parameter settings, in order to extract the most significant information. In other words, different frequency transforms (or different mother wavelets) allow us to obtain different sparse representations with various sparsity profiles and some complimentary information. In the simplest scenario for a single channel signal we can generate several (at least two) spectrograms and/or scalograms or TFD with different wavelets and next organize (collect) them as frontal slices of a 3rd-order tensor: time x frequency x TFR or time x frequency x wavelets. For multichannel signals we can generate a block of at least 2 tensors (referred here as „2-head” tensors) [10,14], which can be concatenated as a single data tensor: space x time x frequency x TFR x trial. In other words, we propose here to use multi-block („multi-head”) tensor analysis by exploiting more than one TFR and/or more than one mother wavelet to analyze hidden time-frequency structures in a stream of multidimensional non-stationary data [10, 14]. In fact, in multi-way analysis or tensor decompositions we may consider several TF techniques discussed in this paper [1]. By exploiting various TFRs, possibly with suitably selected different parameter settings for the same data, we may improve the classification accuracy of BCI due to additional (partially redundant) information. We extensively analyzed such approaches, e.g., for motor-imagery BCI by applying different complex Morlet (Gabor) wavelets for EEG data sets with 62 channels [11]. For such datasets, for example, we selected different complex Morlet wavelets with two different bandwidth frequency parameters \( f_b = 1 \text{ Hz} \) and \( f_b = 6 \text{ Hz} \), but the same center frequency \( f_c = 1 \text{ Hz} \) (using MATLAB notation we used CMOR1-1 and CMOR6-1 wavelets).

For each mother wavelet we constructed a 4th-order tensor: 62-channels x 23-frequency bins x 50-time frames x 120-trials for both training and test EEG data. The block of training tensor data can be concatenated as the 5th order tensor: 62-channels x 23-frequency bins x 50-time frames x 2-wavelets x 120-trials. Performing tensor decomposition for such data tensor, we achieved considerable improvement in performance of motor-imagery BCI in comparison to the standard approaches [11]. A multi wavelets or multi-scale dictionaries (with different set parameters) can relax (alleviate) the problem of time frequency resolution and allows us to capture the different intrinsic TF characteristics of a set of signals. In other words, using a set of wavelets/dictionaries would allow us to represent the data in a more efficient way, i.e. sparse manner with different sparsity profile.

In summary, the recent advances in neuroimage technologies (high density array EEG/MEG, fMRI, DTI, NIRS) have generated massive amounts of brain data exhibiting high dimensionality, multiple modality and multiple couplings, functional connectivity. By virtue of their multi-way nature, tensors provide a powerful and promising tools for TF analysis and fusion of such massive data together with a mathematical backbone for the discovery of underlying hidden complex (space-time-frequency) data structures [10, 11]. Of course, the topics and approaches briefly mentioned in our comments were out of the scope of the paper of Wacker and Witte [1]. However, we would like to emphasize the challenges and perspective of such kind of research in time-frequency analysis, especially for multidimensional, multimodal biomedical data, which probably deserves a complementary review/tutorial paper in the near future.

I congratulate the authors for a stimulating and insightful article. I share the authors’ enthusiasm for this area of research, and appreciate their aim of building a straightforward and efficient time-frequency analysis.

4. Comment by H. Dickhaus

The tutorial review by Wacker and Witte [1] demonstrates in a comprehensive, quantitative way the strengths and weaknesses of the most important and most frequently applied non-parametric time frequency representations (TFR) in respect to different signal properties. Starting from simple linear approaches they develop and derive an analytical framework that ranges from Gabor and Hilbert transforms to signal adaptive extensions. A collection of typical simulated test data with specific characteristics and some recordings from neuroscience illustrate the underlying formal description and motivate the reasons
that lead into methodological advancements.

Indeed time frequency analysis puts its focus on an essential property of many phenomena observed and recorded in medicine and biology. Independent of their physical origin and meaning, oscillations, modulated waveforms, repetitive patterns, bursts and other type of rhythms are identified as so called bio signals. They contain information about physiological processes which are controlled and modulated by time-varying frequency-dependent variables to provide and control important vital functions on different scales. Respiration, cardiovascular variables like heart rate or blood pressure, neuronal information processing, cellular signal transduction, cell division respectively amitosis, and metabolism, they all exhibit such characteristic frequency patterns. For interpretation of physiological interrelations and their dependencies as well as their dysfunctions and abnormalities, the knowledge about time frequency characteristics of these signals and parameters provides a useful window that permits a deeper look into these processes and helps to better understand the underlying mechanisms.

The most interesting and relevant property of TFR approaches for practical issues on signal analysis and interpretation is without any doubt the effective simultaneous time and frequency resolution for different phenomena. However, optimizing this issue is principally limited by the Heisenberg uncertainty which inevitably links both independent variables time and frequency. For this reason all procedures – no matter whether sophisticated or straightforward – have to be discussed under the heading of the "no free lunch theorem". That means for a specific application – regardless in which field the phenomenon is recorded – maximal resolution of one variable implies a corresponding reduction for the other and vice versa or respectively may in some cases produce so-called cross or interference terms for quadratic methods as the Wigner Ville distribution.

To speak with the authors’ words "there is always a tradeoff between the extent of interference and the number of good properties" or equivalently "interferences are the price to be paid for good time and frequency resolution".

Because of the conflicting constraints of time and frequency resolution one has to identify and be aware of the most relevant property for the expected results in the context of a specific question. Moreover, is it desirable to include as much prior knowledge as available about the signal’s temporal characteristics, e.g. with respect to stationarity or transients. The authors are perfectly correct in emphasizing these fundamental facts, and their examples clearly demonstrate that only a priori knowledge about the experimental situation and the basic signal properties allow an optimal selection of analysis methods from a variety of adapted linear or quadratic TFR methods.

Although these explanations and remarks are important to make aware and worth to point out, time frequency methods are well-known and have been published throughout the last 20 years of the last century on different academic levels in mathematics, physics, speech processing, acoustics and electrical and communications engineering. It appears appropriate to give credit to the contributions of pioneers in this field: G. F. Boudreaux-Bartels [15, 16], L. Cohen [17], P. Flandrin [18, 19], F. Hlawatsch [16], N. E. Huang [20, 21], S. G. Mallat [22, 23], O. Rioul [24], W. J. Williams [25] who published their basic ideas on TFR methods mostly in technical and engineering oriented journals. One very instructive figure that goes back to Hlawatsch and Boudreaux-Bartels [16], demonstrating the different time and frequency resolution for linear TFR methods deserves explicit reference: Figure 2 illustrates the situation with respect to mutual dependence of frequency and time resolution for the Short-time Fourier-transform (left) and the Wavelet-transform (right) very intuitively.

A huge number of papers focusing on different biomedical applications as well as reviews and other substantial papers appeared mainly in the 90ties of the last century [26, 27]. They stimulated some new ideas complementing and advancing the TFR methods to applications which demand for signal-adaptive methods as the Hilbert Huang Transform [20, 21] and the Matched Gabor Transform [28]. In particular the latter one which depends on a dictionary of Gabor atoms was developed and demonstrated with good success by the authors of this review. Both approaches expanded significantly the bandwidth of useful problem solutions.

It is the merit of this tutorial review to update and refresh the classical collection of TFR methods for biological applications and to illustrate the underlying concepts in quantitative terms. It improves the understanding of these methods when the authors demonstrate that only smoothing is necessary to provide a passage from the Wigner Ville Distribution to the spectrogram or that different linear transforms are equivalent when specific kernel functions are provided. Moreover such condensed presentation focusing on methodic traps and misconceptions or optional mistakes is highly appreciated in the community, in particular for researchers who are not so
familiar with the formal background of these tools.

Independent from the importance TFR methods have for typical one dimensional signal analysis applications, these methods can be easily expanded to higher-dimen-
sional applications as for example time dependent 2D or 3D image sequences or videos [29,30]. From this general point of view the presented review with its sum-
marized remarks is ideally suited to pro-
vide young researchers and interested stu-
dents without too much ballast with an in-
tuitive understanding for different meth-
ods and approaches on nonparametric time frequency analysis techniques in medicine and biology. Therefore this paper is highly recommendable to serve as an easy to follow tutorial for adequate problem solutions based on a correct methodi-
cal framework.

5. Comment by P. J. Durka

Time-frequency analysis is quite a broad field, nowadays encompassing a significant part of the mathematical methods used in biomedical signal processing. In spite of this, the review by Matthias Wacker and Herbert Witte [1] addresses the major is-
issues within an elegantly uniform mathemat-
ical framework, which places it above the popular "phone directory" approach. Nevertheless, it's probably impossible to address all the current issues in such an ambitious way in a single article, which leaves some space for constructive com-
ments.

The conclusion of this review seems to favor the matching pursuit (MP) ap-
proach – however, explicit parametriza-
tion of signal structures by MP was not listed among its advantages. Estimates of the time-frequency density of signals energy, obtained as weighted sums of the WVD of the selected g_n are indeed robust and in most cases relatively free of cross-terms. They are also appealing visually, but look-
ing only at this quadratic time-frequency map we loose all the beauty and sparseness of the linear approximation given by Equation 46 from [1]. Explicit parameter-
ization of the signal's structures should be viewed as directly offering the information, which in previous approaches was obtained in a series of steps relying on more or less arbitrary choices of parameters.

We can also explore the extra compat-
bility of the MP's time-frequency descrip-
tion with the vocabulary used by human experts in a large part of traditional, visual analysis of EEG. For example, using only the standard definition of sleep spindles, basically unchanged since 1968 [34], we can implement their detailed and auto-
matic detection and description as a simple filter on the set of parameters of the Gabor functions fitted to the EEG by MP pro-
cedure [33]. Overall, MP can be viewed as at least partial unification of desired fea-
tures found in most of the time-frequency methods of biomedical signal analysis [32].

Another issue worth mentioning here is the multivariate MP decomposition. Contrary to the relatively well-defined monovariable case, the term "multivariate matching pursuit" (MMP) can refer to one of several, significantly different, ap-
proaches. By varying the multivariate structure of the dictionary – that is, which parameters of the time-frequency atoms are allowed to vary across the analyzed epochs – we obtain different versions of the algorithm. Detailed discussion of some of these cases can be found in [33].

As for the applications of MMP, the most natural one seems to be the parame-
terization of relevant structures in multi-
channel EEG/MEG data, as a preprocess-
ing for the inverse solutions. Spatial local-
ization of sources is the Holy Grail of con-
temporary EEG/MEG analysis, and prop-
erly applied MMP preprocessing seems to improve its robustness and sensitivity by at least an order of magnitude [7].

Contrary to e.g. [37], the approach to MMP algorithm proposed in [33] is sepa-
rated from the physical constrains that would stem from taking into account the final aim of the parameterization. This allows to use the algorithm (code), that was designed and tested e.g. for parameteriza-
tion of similar EEG structures in subse-
quent channels, for a completely different task, like for example decomposing subse-
quent trials of event-related fields [36]. MMP could be also applied as another esti-
mate of the phase-locking index (PLI) mentioned in the Review – by fitting func-
tions with the same frequency, time posi-
tion and width, but potentially different phases (and, of course, amplitudes) to the subsequent epochs (realizations). Such a multivariate parameterization would di-
rectly give the variation of the phase with naturally reduced noise, as computed only in the time-frequency regions where the signal's energy is present.

Finally, Reproducible Research is the key to assess the real-world value of ad-
vanced signal processing methods like MP. If we publish only "advertisements of scholarship" [31], different algorithms will be tested on different, ridiculously small, datasets. Following the ideas of [35], we created SVAROG (Signal Viewer, Analyzer and Recorder on GPL) – a project started at the University of Warsaw to allow for an open evaluation of the advanced signal processing methods by the actual target users, not only engineers. Recent version of Svarog, with user-friendly interface allow-
ing to decompose by MMP mouse-selected data epochs, can be freely downloaded from http://braintech.pl/svarog.

6. Comment by P. V. E. McClintock and A. Stefanovska

In commenting on the review by Wacker and Witte [1], we would like to applaud the authors' emphasis on the importance of being able to treat signals with time-vary-
ing properties: this feature is universal in time series derived from measurements on living systems. From a physics perspective, life always corresponds to a thermody-
namically open system, for which energy and matter are being exchanged freely with the environment. Consequently, the oscil-
latory processes associated with life have natural frequencies and amplitudes that are continuously modulated by external in-
fluences. From the perspective of mathe-
matics, they are non-autonomous oscil-
lators and must be treated as such.

The authors have provided a systematic review of the main methods currently available for time-frequency analysis of biomedical signals. The continuous wavelet transform has indeed been the main work-
horse for the analysis of such time-series, ever since it was introduced for the study of oscillatory processes in e.g. heart rate variability [38, 39] and blood flow [40]; and the other methods reviewed [1] certainly have their merits. We would like to point out, however, that there are additional approaches of which the reader should also be aware. We describe some of them below, but first we expand slightly on the physiological and medical applications of the continuous wavelet transform, complementing the mainly EEG-related discussion of [1] by mentioning some applications to signals derived from the cardiovascular system.

Multiresolution wavelet analysis was reported to discriminate between healthy subjects and those with cardiac pathology [41]; the continuous wavelet transform, using the Morlet mother wavelet, enabled the extraction of characteristic frequencies in blood flow [42], and their association with particular physiological processes [43]. The wavelet transform has been used e.g. as a filter for de-noising single events [44] and to reveal endothelial dysfunction in diabetes mellitus [45], post-acute myocardial infarction [46], congestive heart failure [47], hypertension [48], and ageing [49, 50]. Its great advantage lies in the possibility of logarithmic frequency resolution, enabling a very wide range of frequencies to be encompassed, a feature that is often essential in the analysis of physiological time series. The synchrosqueezed wavelet transform [51] has brought some additional advantages, being especially useful for phase detection [52].

In dealing with time series from systems whose frequencies and amplitudes vary in time, several distinct, often coexisting problems must be overcome: i) To identify basic oscillatory components, despite the time-variations; ii) to discriminate between oscillatory components that may have nearby characteristic frequencies which, with noise and time-variability, may pose a very difficult problem; iii) furthermore, there may be a mixture of harmonics and basic components, all with nearby frequencies to be distinguished. Where there are several oscillatory components, it may be useful to investigate the interactions that occur between the underlying physiological processes by studying measures of e.g. synchronization, coherence, phase coherence, bispectral density, couplings, coupling functions, and direction of coupling. We will enlarge briefly on these methods.

Ambiguities can arise in the analysis of signals containing oscillatory contributions at different frequencies, as commonly occur in physiological applications. Because of inherent nonlinearities, higher harmonics will be present in addition to basic frequencies, and an observed component may either be due to a real oscillatory process at that frequency or may just represent a harmonic of another lower-frequency process. The distinction can be especially hard to draw when several time-variable frequencies are present, combined with random noise, but a method [53] based on mutual information combined with surrogate testing [54] enables the question to be settled in most cases.

As indicated in [1], wavelet phase coherence analysis [55–57] can be used to establish whether there is a relationship between the oscillatory processes giving rise to two complex signals, even where there is time variability and noise. Time-localised wavelet phase coherence has been applied to test [57] the possible influence of arterial blood pressure on intracranial pressure (ICP) in intensive care, related to the preservation or otherwise of ICP auto-regulation.

Synchronization analysis [58] provides another method that is robust in the face of time-varying frequencies in the presence of noise. It has been applied to investigate the cardio-respiratory interaction by many authors. Where bivariate data are being analysed, it is quite possible for both frequencies to vary together with time, mutually locked at a particular synchronization ratio (which in general is not 1:1). Alternatively, the ratio may evolve discontinuously with time e.g. during the induction of, or awakening from, anaesthesia [59], or during exercise [60]. The ratio can be found either by plotting a synchrogram [58] or by the calculation of synchronization indices [61].

Where two oscillatory processes are tending to synchronise, thus demonstrating an underlying interaction, it is interesting to ask which process is dominant, i.e. which oscillator is mainly the driver and which of them is adjusting its frequency and amplitude mainly on account of being driven? This directionality of interaction can be established either by an analysis of phase dynamics [62], by the use of information theory [63], or by wavelet-based bispectral analysis [64]. For example, evaluation of coupling strengths showed causal interaction between the phases of respiration and δ-waves in the EEG and how it changes in anaesthesia [65]. Arguably, however, the most complete way of describing the interaction between two oscillatory processes, based on measurements of their time series, is by calculation of their coupling functions [66]. Bayesian inference enables coupling functions to be followed efficiently as they change with time in the presence of noise, as demonstrated by application of this method to study the cardio-respiratory interaction as a function of time [67, 68].

In conclusion, we agree with Wacker and Witte [1] that the use of time-frequency methods is virtually mandatory for the meaningful analysis of biomedical time series. It is a rapidly evolving area of scientific endeavour, with a steady stream of new methods being proposed and validated.

7. Comment by G. Pfurtscheller

Biomedical signals cover a broad range from infraslow (0.01–0.1 Hz or even less) to ultrafast (up to several hundreds of hertz) frequencies. Many of these signals are non-stationary and display a local or global non-linearity.

The dynamic spectral power estimation (dynamic spectra) is the most frequently used method to calculate the mean power spectral density as function of time and frequency but, there exists also a great number of other powerful methods suitable for time-frequency analysis. The choice of the most appropriate method for a specific application is very important therefore. The instant paper gives not only an excellent overview about the different linear and quadratic transformations and decomposition methods but discusses also the specific conditions of their appropriate

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use and the selections of the optimal filters and kernels. The brilliant quality of the figures and videos makes it easier to understand the underlying mathematical equations and the problems introduced also for scientists not so familiar with the biomedical signal processing methods.

The AAs take the credit not only for the comparison of the different standard time-frequency transform methods but also for the discussion of not frequently used methods as e.g. the matching pursuit (MP) decomposition and the empirical mode decomposition (EMD). Of interest is the discussion about pros and cons of the EMD and on the combination of Hilbert transform (HT) and EMD known as Hilbert-Huang transform (HHT). The HT is a linear transform not appropriate to study non-linear signals, but the combination of both has been proposed as non-linear analyzing method.

Of increasing interest is the fine structure of low frequency spectra of blood pressure, heart rate and other hemodynamic signals below 0.1 Hz. Components in this frequency band display slow fluctuations and it would be important to know the best method to study small frequency changes even in the case of non-linearity. What is perhaps missing in this respect is the direct comparison of the short-term Fourier transform and Wigner-Ville distribution with the autoregressive (AR) methods of different model order (an excellent overview about multivariable AR models was published by the AAs recently).

8. Comment by S. Tong

Biomedical signals are intrinsically non-stationary or time-variant, particularly during the pathological conditions. Although time-frequency analyses have been the major techniques for describing the non-stationarity in the signals, most researchers empirically select a method without theoretical comparison, e.g. which method is superior for the signal to be processed. Wacker and Witte systematically reviewed the most currently used time-frequency techniques in three threads, 1) the linear methods, e.g. short-time Fourier transform (STFT), Gabor transform(GT) and S-transform(ST) and continuous Morlet-wavelet transform (CMWT), 2) nonlinear method, e.g. Wigner-Ville distribution(WVD), and 3) hybrid method that combines linear (GT) and nonlinear (WVD) method, or signal-adaptive method. This review targeted the similarities and the differences among these time-frequency techniques in analyzing the biomedical signal and their drawbacks as well. Wacker and Witte provided detail mathematical fundamentals for different time-frequency analysis methods. Based on these theoretical analysis, they recommended a guide for selecting the method when analyzing a particular biomedical signal. It was concluded in the end that the selection of the method was dependent on the signal characteristics, which is still not a ready-to-use recommendation, however, the paper did provide several critical considerations for selecting the “optimal” method, i.e. the time-frequency resolution. High time- or frequency resolution is always at the price of interference (cross) items, which is critical for analyzing the signal with multi-rhythmic oscillations.

Matching pursuit (MP) method though has been given many credits for optimal time-frequency resolution and reduction of interference items in time-frequency distribution automatically [69, 70], nevertheless, theoretically MP is based on the decomposition with a atom dictionary, which therefore introduces discrete-position related bias. Randomly perturbed dictionaries could solve this problem. Most literature have shown that MP was superior in detecting the local transient events [69, 70], however, we should keep in mind that such an “atom-based” decomposition is still a sub-optimal solution due to the “greedy” interactive algorithm.

On conclusion, in practice of time-variant biomedical signal processing, it is recommended to understand the characteristics of the signal itself before we select an appropriate time-frequency analysis method. In addition, the aims of the research could also influence the selection of the methods. Another issue that related to time-frequency analysis, though not within the scope of this paper, is how to quantify and compare the time-frequency distributions of different signals, which is of particularly interesting in practical biomedical signal processing [71].

References


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