Synopsis on signal processing papers of the 2002 yearbook on medical informatics

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1 Synopsis

Signal processing is generally refereed to as the technique to analyze time domain series acquired from a physical phenomenon, representing some physical time-varying magnitude. Signals can be of different nature: one-dimensional continuous signals (e.g. bioelectric signals, speech, etc); two-dimensional signals (images, etc); three-dimensional signals (video, etc). However, when we use the term signal we will tacitly refer here (and in many references) to one-dimensional signals. One-dimensional signals can also be continuous or discrete in time, the latest ones either from their nature or from discretization of a continuous signal, as is usually the case in biomedical signal analysis. These time-discrete one-dimensional signals have been subjected to the huge development of the information processing techniques in the last decades, and particularly signal processing techniques focused on obtaining the information of interest carried on the signal.

In biomedical system field, Electrocardiogram (ECG), Electroencephalogram (EEG), and to a lower extend Electromyogram (EMG) are those bioelectric signals with the broader history in signal processing development. The aim has always been to obtain relevant information to diagnose, evaluate, monitor, and/or follow-up the physiological system under study. Especial and separate attention has been conducted to voice signal. This is a pressure signal, further converted to electrical signal with a microphone transducer, and even been of biological origin, has been subject of many signal processing developments in the context of communications (speech recognition, synthesis, enhancement, etc). For the particular use of biomedical application synthesis is having a major role for speech impaired help. Also the transient evoked otoacoustic emissions (TEOAE) generated by the cochlea as response to acoustic stimuli are of interest for hearing impaired identification. The five selected papers for this 2002 yearbook in the signal processing area deal with EEG, ECG and TEOAE.

Even signal processing is a very useful technique in many biomedical applications, it should be remarked that most of the biological system diagnosis involved in the biomedical signals can be done, and in most cases largely outperformed, by more elaborate techniques like imaging, invasive test, etc. These techniques, even with better sensitivity and specificity, present two major drawbacks: the price paid by the patient or the public health system that made them prohibitive for massive screening, and the invasive aspect that results in highly uncomfortable procedures for the patient with collateral risks in some cases. These two reasons make still very challenging to push in signal processing techniques developments that improve actual levels of sensitivity/specificity in the related domain diagnosis. Both low cost and noninvasive technique are properties of signal processing. Recording equipment is nowadays within very accessible price ranges and processing is implemented in today's computers whose limitations are often procedural rather than computational. These two properties are very valuable in large populations screening and in pathologies associated with large prevalence as cardiac disorders in western countries.

In the last decades, signal processing researchers have developed linear time-discrete signal processing techniques, which today are well established. This linear processing allows accounting for most of the phenomena that can be modeled as linear, or whose real behavior is not far from being linear. Thus the signal can be filtered, to separate undesired components or those originated in a different biological subsystem from the one under study. The system structure that generates the signal can, in many cases, be estimated based on linear system identification techniques and from the estimated system parameters its clinically valuable indexes can be inferred. Examples of these processing can be spectral analysis in EEG for sleep analysis, ECG filtering to remove the EMG and baseline wander that essentially lies on different frequency bands, heart rate variability (HRV) analysis identifying the central nervous system influence on rhythm by evaluating the relative frequency band power content, etc.

In many cases linear techniques by themselves are not enough to extract the clinical information of interest. Then other ad hoc rules are introduced in the linear analysis for a particular purposes. Examples of these structures can be: threshold based QRS detectors that combine linear and non-linear techniques like squaring with threshold decision rules; fiducial point identification in ECG wave analysis with threshold based rules, arrhythmia analysis and beat type identification systems requires features extraction from linearly processes signal plus some classification criteria; high frequency indexes extraction to stratify post myocardial infarction patients at risk of sudden cardiac death (late potentials or intra-QRS potentials); ischemia detection and monitoring; otoacoustic emission detection, etc. Many of these ad hoc techniques can be studied from detection or estimation theory, and then the optimum rules can be estimated from the statistic of the problem.

Further than measuring on the signal particular parameters of interest, it has also been addressed the problem of identifying hidden parameters that give relevant information for some diagnostic objective which are not evident from signal visual inspection or its automated measured descriptive parameters. This is often addressed by statistical signal processing refereed to data coming from documented patient's databases that should further be corroborated by prospective studies. The classification rules, typically to separate patient groups, can be linear (MANOVA)or non-linear like higher order classifiers or neural networks. In terms of patients screening and decision rules based on signal-extracted parameters, the neural networks non-linear classifiers have had a large development given better classification properties than linear rules and often with simpler algorithmic implications. This nonlinear interpolators are always based in the availability of appropriated training set were the network can be trained and posterior prospective studies.

In addition to the ad hoc non-linear rules introduced in many parts of the signal processing, the linear approximations itself are many times far from the reality of the biological system where very complex cross-systems influences take part. That implies that linear analysis of the system generated signals loses inside in the behavior of the system. Frequently, if we were able to study the non-linear relationships within the signal, in a way related to the non-linearity inherent in the system, we will be able to get closer insides to the physiological process than with just linear strategies. Non-linear signal processing is being developed and some indexes based on chaos studies, fractal dimension of signal etc, are being considered to extract useful information from signals that usually remains hidden in linear analysis. These indexes will potentially add strength in signal analysis if they are able to closely relate to the underlying mechanisms of the physiological system. Since these mechanisms are often unknown, and non-linear signal analysis can be performed in many ways with a less well-established framework than linear analysis, in my opinion more fundamental work is still required to assess the real impact of these techniques and to obtain the most suitable non-linear representation in each case. Examples of these non-linear approaches are the studies on heart rate variability carried on in the past decade, the symilarity index to predict sizures [4] in EEG analysis, etc.

The phenomenon behind biomedical signals is typically spatial and implies at least three orthogonal dimensions (signals) to be able to describe the phenomenon. In cardiac and brain multi-channel (leads) analysis recordings are well established. Time-space signal processing techniques have also been recently explored to diagnose brain or cardiac dysfunction. These techniques, to the scope of the author, have still room to pursue since they have not achieve the situation of maximum possible information that, from them, can be extracted.

The five selected papers for this section on signal processing deal with three types of biomedical signals: Electrocardiogram [1], otoacoustic emissions

[2], and Electroencephalogram [3, 4, 5].

The paper by Zigel et al. [1], presents a very important evaluation proposal for ECG data compression strategies. One of the main evaluation strategies of signal data compression is the use of mathematical distortion measures as percentile root mean square difference (PRD) which is a quadratic norm of the differences between original and reconstructed signal. Other alternatives have introduce linear norms. In any case this gives a general idea of the shape distance (measured sample by sample) between the signals. However the interest in the biomedical signal is not in the overall waveshape but in the clinical information carried on the signal. Then a reduced PRD, or its variations, does not guaranty the preservation of the clinical information. The introduced Weighted Diagnostic Distortion (WDD) index evaluates the difference between the clinical parameters measured in the original and the reconstructed signals (waves amplitudes, intervals duration, etc) and is much more suitable for the purpose of clinical diagnoses. It will be desirable that in future the data compression techniques measure their performance with these or related alternative indexes rather than mathematical ones. A mean opinion score (MOS) given by expert cardiologist in term of diagnosticability has been used to compare the WDD and the classical PRD. Not surprisingly the WDD correlated much better with the expert MOS corroborating the convenience to using this kind of WDD indexes to evaluate data compression algorithms. This approach is parallel to coders evaluation in speech processing where the overall waveshape is not of interest but the listener perception when listening to the reconstructed signal.

The approach presented by Janušauskas et al. in [2] deals with the pass/fail separation problem for hearing impairment screening. The otoacoustic emissions are carefully analyzed both in time and frequency to design ad hoc linear processing detection strategies. Different time windows are taken from the elicited stimulus as function of the frequency bands under analysis according to the different lags, of the three different bands, reported for these emissions. The very poor signal to noise ratio of this signal is treated in the wavelet transform domain by clipping (time-varying linear operation) the coefficients under some selected threshold and thus just keeping those components of dominant energy at the averaged TEOAE. This operation is performed on two subaverage sets of TEOAE. If the obtained signal is not noise it should present correlation between the two subaverages. This correlation at three different wavelet scales are used to decide, with a threshold based rule, the pass/fail strategy. The received operating curves (ROC) evaluated on a very large subject database give for a sensitivity of 90% an increase in specificity from 68% (classical detection methods) to 90% which is a remarkable improvement. This paper corroborates that fine knowledge of the signal under study and their underlying mechanisms allow ad hoc signal processing refinement that results in further improvement. More elaborated decision rules or similarity measures from the two subaverages TEOAE will probably be the direction to pursue in this kind of studies.

The remaining three papers [3, 4, 5] deal with the EEG problem. This signal is more random in nature than ECG or TEOAE are. The mechanisms under the brain behavior are more complex and difficult the inference of valuable clinical decisions from the EEG, that represent a spatio-temporal summation of the total brain activity. This difficulty in obtaining information from the EEG is reduced when the objective is to locate areas of particularly intense activation like in epileptic patients or in evoked responses to a particular stimuli.

The paper by Zhukov et al. [3] presents a very interesting strategy to integrate most of the available developments in identifying source location when a single source is assumed and extends this technique to multifocal source location. The work assumes that the different focus are not correlated and then using Independent Component Analysis (ICA) it separate the EEG component related to each focus. Single focus techniques are then applied with the much reduced computational load and the more effective results in this simpler case of single-focus inverse problem in Electroencephalography. First it makes a noise reduction by applying principal component analysis and after using the ICA techniques it isolates every focus-related EEG component. Since the inverse EEG source location is an ill-posed problem there is not guaranty that the solution is correct due to the solutions multiplicity. In simulations the work reports precision in locating the focus between 2 and 5 mm.

The work presented by le van Quyen et al. [4]

deals with well in advance prediction of epileptic seizure. This will be especially useful in uncontrolled epilepsy patients allowing to apply preventive measures and improve quality of life. The rational behind the work is to compare, from the non-linear point of view, time windows of scalp-EEG signals from a reference period and a running window recording. Since the recordings are highly noisy, many non-linear techniques fail due to the noise influence. In this work a similarity index based on zero crossing of the signal that makes the noise influence very limited is used. A threshold based rule is then used to decide when the time window under analysis is different from the reference one. In a set of 23 patients with temporal-lobe epilepsy (TLE) the anticipation of the seizures was 416 s (SD 356) suggesting that the preictal state is a process which largely varies within individual patients. Details about the non-linear technique are refereed to the appendix in www.thelancet.com. The finding that similar results can be obtained from the scalp-EEG and from intracraneal recordings is both surprising and challenging. Surprising because the scalp-EEG is an attenuated and blurred version of the intracraneal activity and challenging because the convenience in practical clinical implications.

The last work in this section by Gonzalez Andino et al. [5] deals also with EEG signal analysis. They try to infer neurophysiological activation with measures of signal complexity. They assume that signals with low complexity belong to organized sources and signals with high complexity belong to unorganized sources and represent noise or unstructured activation. In this work the time-frequency representation of the signal is performed and in the time-frequency plane the Renyi entropy throughout the Renyi number is computed. This number gives an estimation of the degree of ordering in the signal. If the signal is organized in the time frequency plane with well defined elementary function then the degree of complexity will be low, when not elementary function can be identified at the frequency plane the Renyi number will be low representing higher degree of complexity and then no relation with a synchronized activity. This technique allows to have cerebral maps of activation areas according to the Renyi number at each lead. This approach in addition does not require strong assumptions about noise statistics and then is less restricted than other techniques with same objective.

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