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Synopsis

Signal Processing

Signal processing is generally referred 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 are such either by nature or by 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 of the last decades, particularly to signal processing techniques focusing on obtaining the information of interest carried by the signal.

In the biomedical system field, Electrocardiogram (ECG), Electroencephalogram (EEG), and to a lower extent Electromyogram (EMG) bioelectric signals possess a 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. Special and separate attention has been given to the voice signal. This pressure signal, converted to electrical signal by a microphone transducer and of biological origin, has been the subject of many signal processing developments in the context of communication (speech recognition, synthesis, enhancement, etc). In the particular use of biomedical application synthesis is playing a major role in helping the speech impaired. 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 the signal processing section of the 2002 Yearbook deal with EEG, ECG and TEOAE.

Signal processing is a very useful technique in many biomedical applications. Therefore, it should be restated that most biological system diagnosis involving biomedical signals can be done, and in most cases largely outperformed, by more elaborate techniques, such as imaging, invasive test, etc.. These techniques, even with their better sensitivity and specificity, present two major drawbacks: the price paid by the patient or the public health system, which has made them prohibitive for massive screening, and the invasive aspect, resulting in highly uncomfortable procedures for the patient with collateral risks in some cases. These two reasons still make it very challenging to push signal processing techniques developments that improve actual levels of sensitivity/specificity in the related domain diagnosis. Both low cost and non-invasive techniques are important aspects of signal processing. Recording equipment today is within very acceptable price ranges, and processing has been implemented in computers today. Limitations of the computers are often procedural rather than computational. These two properties are very valuable in screening large populations and in pathologies associated with large prevalence, such as cardiac disorders in western countries.

In the last decades, signal processing researchers have developed well-established linear time-discrete signal processing techniques. 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 biological subsystem other than the one under study. The system parameters that generate the signal can, in many cases, be estimated based on linear system identification techniques. From these system parameters, clinically valuable indices can be inferred. Examples are 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 to identify the influence the central nervous system has on rhythm by evaluating the relative frequency band power content, etc..

In many cases, linear techniques alone are not enough to extract clinically relevant information. Therefore, other ad hoc rules are introduced to the linear analysis, depending on its purpose. Examples of these structures are: threshold based QRS detectors to combine linear and non-linear techniques (such as squaring with threshold decision rules), fiducial point identification in ECG wave analysis with threshold based rules, arrhythmia analysis and beat type identification systems (requiring feature extraction from linearly processed signals plus some classification criteria), high frequency indices 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. Many of these ad hoc techniques can be studied using detection or estimation theory, after which the optimum rules can be estimated from the statistics of the problem.

Beside measuring particular signal parameters, the problem of identifying hidden parameters has also been addressed. These parameters give relevant information for some diagnostic objective that is not apparent in signal visual inspection or its automated, measured descriptive parameters. This is often addressed by statistical signal processing in reference to data from documented patient databases and should be investigated further by prospective studies. The classification rules, typically used to separate patient groups, can be linear (MANOVA) or non-linear, such as higher order classifiers or neural networks. In terms of patient screening and decision rules based on signal-extracted parameters, neural network non-linear classifiers have developed greatly. They possess better classification properties than linear rules and often involve simpler algorithmic implications. These nonlinear interpolators are always based on the availability of an appropriate training set with which the network can be trained and further studies conducted.

In addition to the ad hoc non-linear rules introduced in many parts of signal processing, linear approximations are often far from the reality of biological systems, in which very complex cross-systems influences take part. This implies that linear analysis of the signals generated by the system gets lost within 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 gain better insight into the physiological processes than by just using linear strategies. Non-linear signal processing is under development and some indices 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 indices will add strength to signal analysis if they are able to relate closely to the underlying physiological mechanisms of the 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 out in the past decade, and the similarity index to predict seizures [4] in EEG analysis.

The phenomenon behind biomedical signals is typically spatial and requires at least three orthogonal dimensions (signals) to describe it. Analysis recordings are well established in cardiac and brain multi-channel (leads). Time-space signal processing techniques have also recently been explored to diagnose brain and cardiac dysfunction. These techniques, within the scope of the author, still have room to grow, since they have not achieved maximum possible information extraction.

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], proposes very important ECG data compression evaluation 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 introduced linear norms. In any case, this gives a general idea of the shape distance (measured sample by sample) between the signals. However, interest in the biomedical signal is not in the overall waveshape, but in the clinical information carried by the signal. 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 in the future for data compression techniques to measure their performance with these or related alternative indices rather than mathematical ones. A mean opinion score (MOS) given by expert cardiologists in terms 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 of using this kind of WDD index to evaluate data compression algorithms. This approach is parallel to coders evaluations in speech processing. Here, the overall waveshape is not of interest, but the perception of the listener when listening to the reconstructed signal.

The approach presented by Janušaukas 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 functions 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 is used to decide the pass/fail strategy using a threshold based rule. For a sensitivity of 90%, the received operating curves (ROC) evaluated on a very large subject database allow 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 its underlying mechanisms allow ad hoc signal processing refinement which results in further improvement. More elaborated decision rules or similarity measures from the two subaverages TEOAE will probably be the direction to pursue in these 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. The mechanisms of brain behavior are more complex and make the inference of valuable clinical decisions from the EEG more difficult. The EEG represents a spatio-temporal summation of the total brain activity. The difficulty in obtaining information from the EEG is reduced when the objective is to locate areas of particularly intense activation as 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 (if a single source is assumed) and extends this technique to multifocal source location. The work assumes that the different focuses are not correlated. By using Independent Component Analysis (ICA), it separates the EEG component related to each focus. Single focus techniques are then applied. The computational load is greatly reduced and more effective results in this simpler case of the single-focus inverse problem in Electroencephalography are achieved. First, it achieves noise reduction by applying principal component analysis. 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 no guarantee that the solution is correct, due to the solution's multiplicity. In simulations, the work reports precision in locating the focuses 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 application of preventive measures and improvement of quality of life. The rational behind the work is to compare, from the non-linear point of view, scalp-EEG signals time windows 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 which 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 referred to the appendix in www.thelancet.com. The finding that similar results can be obtained from the scalp-EEG and from intracranial recordings is both surprising and challenging. Surprising, because the scalp-EEG is an attenuated and blurred version of the intracranial activity and challenging, because of the convenience in practical clinical implications.

The work by Gonzalez Andino et al. [5] also deals with EEG signal analysis. They try to infer neurophysiological activation with measures of signal complexity. They assume that signals of low complexity belong to organized sources, and signals of 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 estimate of the degree of ordering in the signal. If the signal is organized with well defined elementary function in the time frequency plane, the degree of complexity will be low. If no elementary function can be identified at the frequency plane, the Renyi number will be low representing a higher degree of complexity and no relation with synchronized activity. This technique allows 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 is less restricted than other techniques with the same objective.

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