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A software for recording and analysis of human tremor

M. Lauk [a,d,*], J. Timmer [a], C.H. Lücking [b], J. Honerkamp [a], G. Deuschl [c]

[a] *Zentrum für Datenanalyse und Modellbildung and Department of Physics, University of Freiburg, Eckerstr. 1, 79104 Freiburg, Germany*

[b] *Department of Neurology and Clinical Neurophysiology, University of Freiburg, Breisacher Str. 64, 79110 Freiburg, Germany*

[c] *Department of Neurology, University of Kiel, Niemannsweg 147, Kiel, Germany*

[d] *Center for BioDynamics, Boston University, 44 Cummington St., Boston, MA 02215, USA*

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Abstract

For many diseases various methods for the diagnosis and treatment monitoring are available. Presently, such methods are not established for an investigation of tremor diseases, although the different forms of tremor are common neurological symptoms and occur frequently in various neurological diseases and also other conditions. We developed an easy-to-use application for tremor-analysis and recording, running under MS-Windows, that allows us to investigate different forms of tremor by advanced mathematical methods of time series analysis. The application is also applicable for users who are not familiar with these kind of advanced data analysis methods. It provides tools for the diagnosis and treatment monitoring under laboratory conditions, based on previously developed and established methods of spectral and cross spectral analysis of tremor and electromyographic time series.

Keywords: Tremor; Time-series analysis; Electromyography; Electrophysiology; Spectral analysis; Cross-spectral analysis

1. Introduction

The electrophysiological analysis of human tremor has a long tradition. The earliest works on this field usually investigated electromyographies (EMG), recorded from different muscles and plotted using analog devices [1–3]. In the sixties, different techniques were used to measure the amplitude and frequency of tremor [4,5]. Spectral analysis was performed with analog computer devices. With the fast development of digital computers, one began to sample

* Corresponding author. Tel.: +49-761-2037710; fax: +49-761-2037700.

E-mail address: lauk@fdm.uni-freiburg.de (M. Lauk)

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the tremor records to analyze the data off-line mainly by the new developed methods of spectral and cross-spectral anal ysis of stochastic processes [6–12]. From this time, the tremor has been usually measured with piezoresistive accelerometers (ACC). In the following years researchers presented various different approaches to measuring and modeling tremors [13–24].

Despite these intensive works, until today, the electro-physiological analysis of tremor using advanced mathematical methods is reserved to specialized laboratories. Each group working in tremor research uses its own developed software and hardware. A software or tools for tremor analysis, also available for people who are not specialized on this field could help to improve diagnosis and treatment monitoring of tremor diseases in widespread areas of neurology, rehabilitation and pharmacology.

The needed mathematical methods, e.g. the theory of linear stochastic processes or linear time series analysis, have been well investigated [25–31]. Also the different proposed recording techniques, e.g. systems based on ACCs or lasers, have been well established and used in widespread areas of other sciences and in industry. The difficulties are rather the proper interpretations of results in terms of physiology and physics and the development of so-called 'data-driven' algorithms for special tasks like tremor analysis.

We developed a software for tremor recording and analysis (TRAS) that is useful for at least two different user groups. Firstly, people who want to analyze tremor records in a standardized daily clinical procedure, and secondly, users who work in the different fields of tremor research. The difference between the requirements of these two groups is the way they are working with an application: For the first group the software should provide the possibility to get the results of a tremor analysis by just 'pushing one or two buttons' on the desktop, whereas researchers usually need the possibility to modify configurations and parameters. We here describe how these two different concepts were realized in TRAS.

2. Background

TRAS was planned, written and tested together with clinical laboratories during the different stages of the development. Therefore, we could secure that our application is able to fulfill different criteria that would be necessary to build a software which will be accepted by clinical and laboratory staff.

This paper does not describe in detail any research work on both mathematical or clinical aspects of tremors. It was rather written to describe the implementation of new analysis methods, investigated and established in earlier clinical and methodological studies [23,24,32–42], in a highly integrated, actual software system.

As already mentioned in the introduction, the electrophysiological analysis of the different tremor-related disorders and diseases has up to now only been done by a few specialized laboratories. In addition to perform the mathematical calculations, TRAS is designed to provide solutions for the following problems:

- Data recording: What technique should be used, how long should the data-record be?
- Quality of recorded data: In some cases the data consists of different recording failures and artifacts that could lead to serious misinterpretations. Examples of such failures are trends or drifts reflecting voluntary movements or crossings of the maximum A/D range.
- Data analysis: Advanced mathematical methods in data analysis often need to choose some initial parameter settings requiring preliminary knowledge of the dynamics or assumptions on the underlying process for the data under investigation.
- Quantitative results should be given with confidence regions for a particular value to allow a comparison to well investigated populations of different groups (i.e. controls and patients with different tremor diseases).
- Interpreting qualitative results of spectral and cross spectral methods in terms of physics and physiology is a difficult task and must be assisted by the application.

A part of these issues are caused by the fact that the various forms of tremor cover a wide range of different possible dynamics. They range from linear stochastic processes for the physiological tremor (PT) to non-linear, almost deterministic processes for some pathological forms of tremor [32–34,36,37]. The amplitude often differs more than three magnitudes between a weak PT and some severe pathological tremors [34].

Finally, a comfortable graphical and interactive user-interface with support for mouse, menus, icons and buttons provides a user-friendly, common interface which gives potentially any person the possibility to work with it.

3. Design considerations

The application uses a multi-document-interface (MDI). Thus, the user can work with it in the same way he is used to working with common applications, e.g. word processing programs. A further advantage of this strategy is the possibility to compare different records and results directly on the screen. The only restriction is the amount of available system resources.

TRAS was developed in C and C++. We separated strictly numerical parts and parts containing the interface sources and I/O routines. All numerical parts were developed in standard C without using any object-orientated programming feature. The other parts of the software providing the user interface and different kinds of I/O, e.g. menus, dialog-boxes, graphics displays and printouts, were realized in a few C++ classes, based on Borland's Object-Windows, which is a C++ class library for the development of Windows applications [43]. This strict separation between numerical and system dependent elements provides an easy portability of the software to other platforms and also other programming languages. Furthermore, all string resources like menus, titles, error messages and letterings reside in separate resource files, which allows us to easily create new language versions. Presently, English and German versions are available, running under Microsoft's Windows 3.1 (1), Windows 95, Windows 98, Windows NT 3.51 and NT 4.0.

Each data record, i.e. each stored data file, is coupled with a MDI-child window, in the following referred as the main window (MW). This window is based on a class that is responsible for the parameter settings, all analytic operations and storage and export of data. In the first instance, this main class represents an abstract, virtual class that can perform all operations on a single data-channel. Further instances of the main class, derived from the first instance, realize multi channel classes, i.e. classes which inherit all functionality of the main class but handle in addition multiple, simultaneously recorded channels. All graphs of the different analysis results reside in their own MDI-child classes and are independent of the main class. If the user requests the graph, the main class transfers the corresponding data to the graphics class, i.e. the graphics window. Fig. 1 displays schematically the basic structures of TRAS.

The main advantages of this concept are: (1) It allows us to easily modify existing and to create new instances of multi channel classes due to its modular structure. (2) Further data analysis methods and graphics classes can be added in the future without any modification of the existing classes. (3) Since each graphically displayed result is independent from other windows, one can compare results originating from calculations with different parameter settings simultaneously on the screen. This is often wanted in research applications.

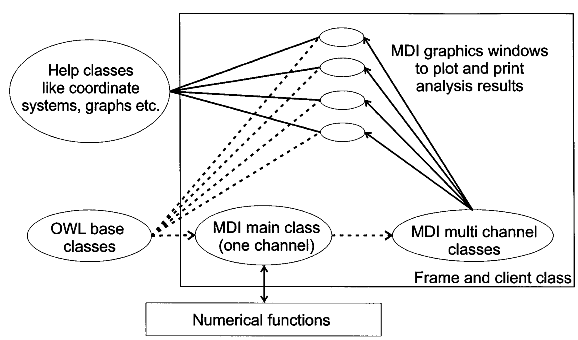

Fig. 1. Schematic display of the basic structure of the application. Dashed lines symbolize inheritance, solid lines simple I/O in the sense of function calls and the 'use' of other classes. For sake of clarity the recording MDI child which interacts with the multi channel MDI window is not shown. All numerical parts are realized in standard C and do not use OOP-features.

Table 1
Available analysis methods and performance of the calculations (including the respective statistics as described in the text) on a standard Pentium 133 MHz personal computer. The operating system is Microsoft's Windows NT 4.0, the computer has 32 MB of RAM

Method	Analyzed series	Time (s)
Heuristic data test	All six channels	0.4
Spectral estimation	Six channels, constant estimator	2.0
(Including statistics)	Six channels, variable estimator	3.0
Autocorrelation	One channel	0.6
Cross-correlation	Two channels	0.7
Cross-spectrum, coherency and phase	Two channels	0.4
Overview-plot (see text)	Two channels	0.9

3.1. General I/O concepts

All diagrams and graphics are implemented as objects which receive the corresponding data from only one channel to plot them automatically in a defined rectangular region on an arbitrary device context. Therefore, all graphics displaying results of multiple channels in one plot are highly modular and can also be easily extended to plot them on other devices as the so far implemented screen- and printer-outputs.

TRAS provides the possibility to export all kinds of analysis results in an ASCII format. To our experience this is helpful or even needed, especially for research applications. Beside the graphs offered by TRAS itself, users can create arbitrarily styled presentation graphics using results calculated by TRAS.

Note that TRAS does not store any result in own data formats and does not read any files containing results. The calculation of results from raw-data takes a maximum of about 0.5 s for each channel on a standard Pentium 133 MHz PC (see also Table 1). Therefore, a storage and re-read of analysis results beside the provided ASCII export is not necessary. In addition, an advantage of this strategy is that changes in future releases will only affect the raw data files.

4. System description

4.1. Recording technique

Different approaches for tremor measurement have been proposed [5,19,22–24,44,45]. We recommend to measure tremor with ACCs since: (1) The 'natural' high-pass filter effect of the ACCs reduce significantly the slow drifts which are often present due to voluntary movements [19]. (2) ACCs are able to measure accurately over a wide range of amplitudes from less than 1 mm/s^2 to a few m/s^2. This is important to cover all types of tremor with the same measurement system.

Six channels are measured for a standard tremor analysis, three per side of the body. In this standard measurements, two ACCs, attached to the left and right belly of the hand, and four EMG, measured over the Flexor and Extensor carpi ulnaris of each body side, are recorded simultaneously.

Beside this standard configuration, an arbitrary channel configuration can be chosen. This is done with an interactive dialog-box displayed in Fig. 2. Along with a description and a short abbreviation which is displayed for each channel in graphs and print-outs, there are check-boxes to indicate whether the channel will be digitally full-wave rectified [19,46] or filtered or not. Furthermore, one can choose if the channels 1 and 4 are ACCs or EMGs. TRAS excludes senseless configurations, e.g. a full-wave rectified ACC channel.

The digital EMG-filters are high-pass filters which act in the Fourier space [47,48]. They could be used to cut off signals lower than 60 Hz in un-rectified EMGs to eliminate slow movement-artifacts. General aspects concerning EMG recordings can be found in [19,46,49].

The use of digital filters and digitally full-wave rectified EMGs depends on the hard-ware and can not be dictated by the software. Therefore, it is also the user's responsibility to have an adequate anti-aliasing filter. This can not be done by the software. Nevertheless, the complete channel configuration can be saved interactively in configuration files together with later discussed parameters to prevent inexperienced users from erroneous decisions.

TRAS uses a Keithley DAS 1602 A/D converter. This relatively inexpensive 12 bit A/D converter covers all needed features. Since Windows is far away from being a system that can be used for real-time routines, we realized the real time A/D sampling with direct memory access (DMA) by a cycling DMA buffer which is accessible under Windows. The timing during the sampling process is done by the A/D hardware.

The success of such a routine depends on the system's and the graphics' speed. With a standard Pentium 133 MHz PC sampling frequencies over 15 kHz per channel are reached; this is far away from the sampling intervals needed to record ACC and EMG data. Tremor records are usually done with 1 kHz or even below 300 Hz if the EMGs are rectified by analog devices. Nevertheless, TRAS also checks during the recording procedure if an overrun of the cycling DMA buffer occurred.

During the recordings, the six channels are displayed in real-time consecutively with different colors. The recording window provides different buttons to start and stop the recording session.

We included the possibility to call an arbitrary external recording software by indicating the name and parameters of the external recording program in the initialization file of TRAS. In this case the external software is responsible to store the data in a format that can be read by TRAS.

4.2. Testing the quality of data

TRAS provides a heuristic test to check tremor time series for different recording failures and artifacts. Some kinds of tremor differ up to three magnitudes in amplitude which renders it sometimes difficult to chose the correct amplification for EMGs and ACCs. The first test shows an error if either the total variance is too small, i.e. the digitized series covers only 1/100 or less of the maximum A/D range, or the variance is too high, i.e. the series reaches at least once the maximum A/D range of 0 resp. 4095 (12 Bit).

The second test is a heuristic test for stationarity of the mean. Due to voluntary movements during a trial it sometimes occurs that the mean of a series shows slowly varying trends over more than 20 tremor periods (partially caused by the bridge amplifiers used for the ACCs). An error is signaled whenever the mean of the series fluctuates between two or more of 20 period pieces more than the standard deviation of the whole data set.

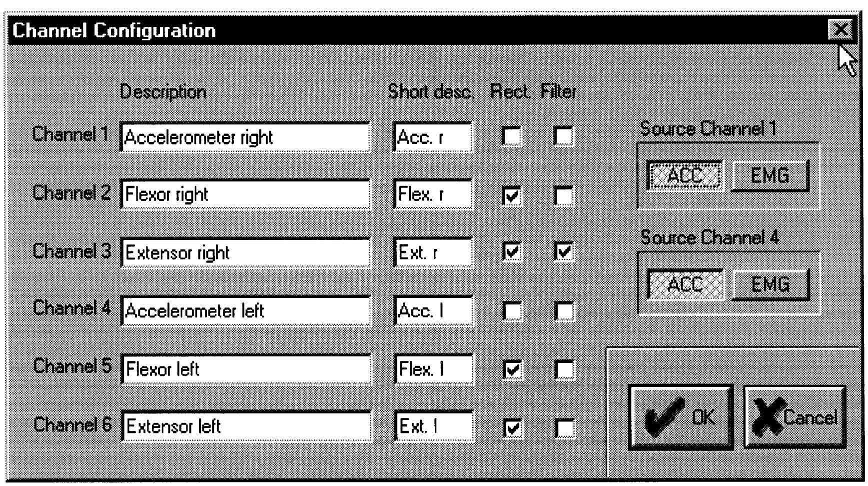

Fig. 2. Screen shot of the channel configuration dialog-box. Channels 1 and 4 can be used as ACC or EMG channels, the other four channels for EMGs only. If the field 'filter' is checked, the corresponding channel is digitally high-pass filtered to avoid movement artifacts in the EMG. If the button 'Rect.' is checked, the corresponding channel is digitally rectified. The program avoids senseless combinations like, e.g. rectifying an ACC signal.

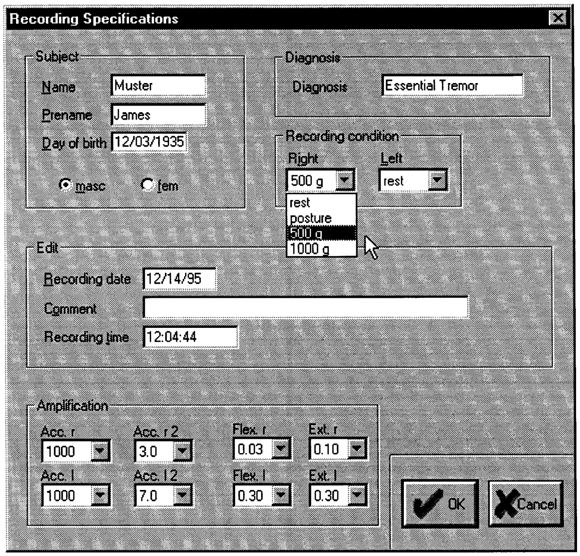

Fig. 3. Screen shot of the dialog box to enter recording informations and personal data for the recorded person. With the use of newer hardware, the explicit input of the amplification factors is obsolete, since they are transferred automatically to the program via the A/D converter or the parallel port (depending on the amplification system used).

The test is performed by pushing a button on the desktop. If the algorithm detects one or more of the described errors, a warning message with detailed informations on the error is displayed.

4.3. Storage and display of data

The data are stored as 2 Byte binary integer values, each channel in one block of size 2 N, where N denotes the number of data-points. All further informations like the channel configuration, amplification factors and the subject's personal data are stored in a file header of size 4 kByte. Fig. 3 displays the dialog box to enter the informations on the investigated person, amplification factors and individual measurement specifications which are stored in the file header along with the channel configuration.

TRAS provides a multi-channel data scroller that displays multiple channels of recorded raw data in one horizontally scrollable window. The scroller provides different zoom factors and the possibility to print a previously by click-and-drag chosen part of the data as a polygraphy. The chosen region can also be exported in ASCII. The scroller is realized with an object that reads raw data and displays them automatically in a defined rectangular region on an arbitrary given device context. The scroller is therefore highly modular and just consist of i times the raw-data graphics object whereas i is the number of channels displayed.

4.4. Spectral methods

In this section we discuss univariate spectral analysis methods. Since all multiple channel calculations and plots are based on one-channel classes and then expanded to multiple-channel objects as explained in Section 3, all further described concepts and results are only explained for one single channel. To overcome leakage [27], the data can be optionally tapered by a Bartlett-Window before performing spectral and cross-spectral analyses.

Although discrete Fourier transformations (FT) are defined on any number of data points, conventional Fast Fourier transformations (FFT) are restricted to numbers $N = 2^j$ where j is an integer [48]. Often the data series is filled up with zeros to reach the next number that can be written as $N = 2^j$. Unfortunately, this operation seriously modifies the statistics of the periodogram and the estimated spectrum [27]. Therefore, we use an algorithm which handles all numbers N and is as fast as the FFT for numbers that can be written as $N = 2^{j_1}\, 3^{j_2}\, 5^{j_3}$, where the j_k are integers [48,50]. Especially for the estimation of auto- and cross-correlation functions by FFTs this is needed. For these calculations one can not fill a series with zeros up to the next possible number $N = 2^j$ and therefore would have to cut the series to reach the next possible lower $N = 2^{j-1}$.

After calculating the FT of a series, the spectra are estimated by a direct spectral estimation procedure [24,26–29] that was designed especially for this purpose. A detailed description of the estimation procedure used is given in [24]. Briefly, the periodogram is convolved with a triangular window of a variable width. The window width is determined automatically based on the broadness of the highest peak found in a preliminary estimation. This routine leads to good results for low amplitude physiological tremors as well as for high amplitude, almost deterministic spectra of data recorded from severe pathological forms of tremor [24], without asking the user for special parameter settings or a kind of 'a priori' knowledge of the underlying dynamics. A discussion concerning the accuracy of this estimation procedure compared with conventional estimations is also given in [24].

Based on the confidence levels of the spectral estimate [24,26,27], TRAS searches automatically for significant peaks in each of the spectra, as described in detail in [24]. In addition, confidence intervals for peak frequencies are calculated by a bootstrap method [35,38]. The accuracy for the frequency estimation has shown to be sufficiently high. It also depends on the broadness of the peaks. 95% confidence intervals range from about 1 Hz for broad peaks of a physiological tremor down to only 0.1 Hz (three bins) for severe pathological tremors [35,38].

For each series a Kolmogorov–Smirnov-test [24,30,48] is performed to test against the null-hypothesis that the series is consistent with white noise.

By pushing a button on the desktop, TRAS calculates the spectrum for each channel of a recording and displays them in a window that can be printed along with the patient's data and a table with all quantitative results including confidence regions. Significant peaks are indicated by vertical lines. The calculation time for a standard six-channel record, consisting of six series with 30 000 points each, is about 3 s on a standard Pentium 133 MHz system. Fig. 4 displays an example for the estimated spectra of a six-channel hand tremor recording of a patient suffering from an unilateral Parkinsonian tremor. On the unaffected left side, the tremor shows the typical characteristic of a physiological tremor. A single broad peak in the ACC spectrum and weak synchronizations in the EMG spectra appearing at higher frequencies as the ACC peak. On the affected right side, one can see a sharp peak with its higher harmonics in the ACC and EMG spectra at the same frequency, which is the typical picture for a Parkinsonian tremor.

Beside this standard estimation procedure there exists the option to choose different spectral estimators. Furthermore, users can modify all necessary parameters as the displayed frequency range, confidence levels, width of the spectral estimator and the tapering. This can be done conveniently by interactive dialog boxes and can also be stored in the above mentioned configuration files for later use.

Quantitative and qualitative values obtained with the spectral estimation methods can be compared to the results from a control population (approximately 240 subjects) and patients with different common and also uncommon tremor diseases (over 1000 subjects). These recordings have been done by the Departments of Neurology at the Universities in Freiburg and Kiel, Germany, during the last 5 years.

4.4.1. Autocorrelation function

Autocorrelation functions (ACF) are estimated using the FT. We use the 'biased' estimator [29], since the ACF of tremor time series decays fast enough with increasing time lags. In tremor recordings the sometimes present asymmetric decay of the ACF is of interest for the differential diagnosis of pathological tremors [33,34]. A value representing the difference between the first two local maxima of the magnitude of the ACF is calculated as described in [33,34]. A plot of the ACF can also be printed and exported in an ASCII-file.

4.5. Cross-spectral methods

In this section we give a brief overview on multivariate methods provided by TRAS. The spectral estimation procedures are the same as described for the univariate case without the variable window width in the direct estimation procedure. Confidence intervals and general aspects of the used estimators are discussed in [26–29]. Special aspects of the multivariate methods with respect to tremor time series are given in [36].

All multivariate methods are applicable to pairs of channels. The user chooses the first channel to be analyzed in the main window. After selecting a cross spectral method from the menu or by pushing the corresponding button, a dialog box for choosing the second channel to be analyzed from the list of the other available channels is coming up. Again, all results are displayed in separate, independent MDI child windows and, therefore, easily comparable with respect to different parameter settings and/or different trials. All results discussed in this section can be printed out and exported in ASCII-files.

4.5.1. Cross-correlation function

The cross-correlation function (CCF) is estimated using the FT. Similarly to the ACF, the CCF is displayed with the confidence interval for the test against the hypothesis of zero correlation [27,36]. Note, that these confidence levels are only valid if at least one of the two series under investigation has a flat spectrum, i.e. is consistent with white noise [26,36,42]. Although there exists a filter method to obtain series with a flat spectrum, the so called 'prewhitening' [26], we recommend to do the test on significant correlations in the frequency domain using the coherency spectrum.

In general, CCF's are difficult to interpret [36]. Their use to investigate tremor records in a standardized manner is limited. One example for the use of CCFs in tremor analysis is the detection of EMG crosstalk [51]. Since crosstalk is an instantaneous effect, the CCF between two unrectified

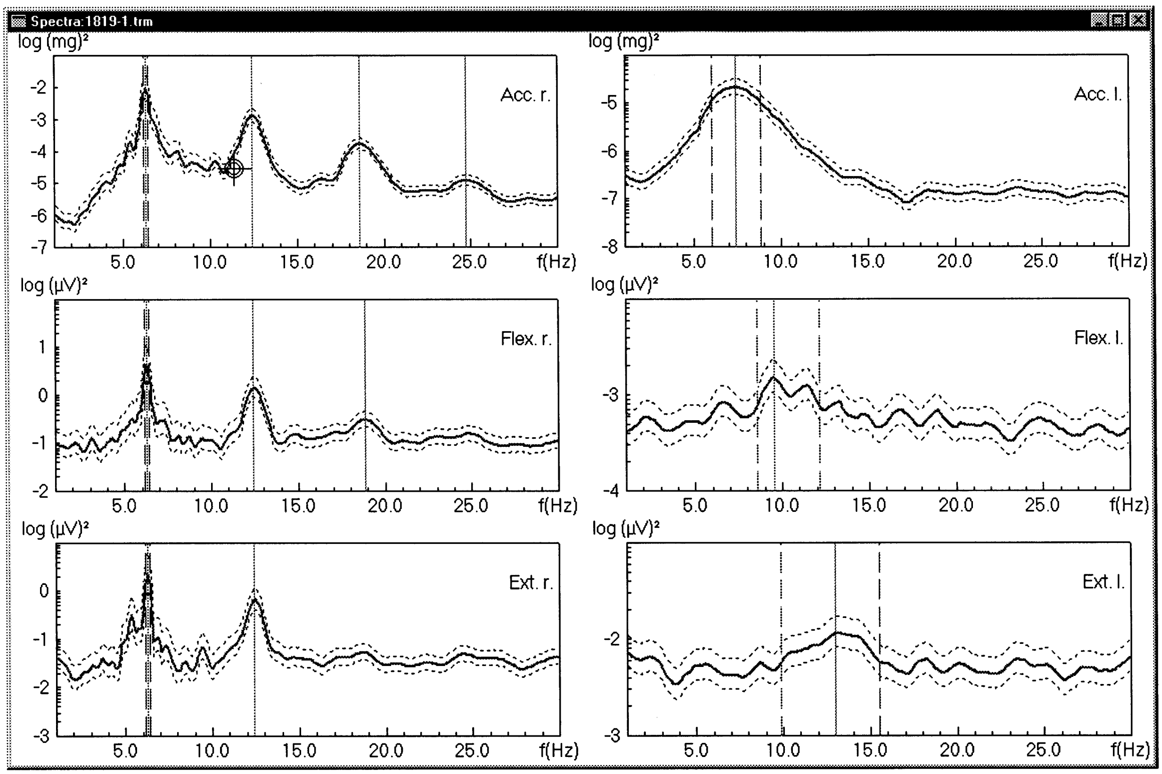

Fig. 4. The MDI child window containing the estimated spectra of all six channels. The displayed example is a hand tremor of a patient with Parkinson's disease (from the upper right edge to the lower left: ACC-spectrum right side, ACC left side, EMG-spectrum of the Flexor carpi ulnaris (Flex) right side, Flex left side, EMG-spectrum of the Extensor carpi ulnaris (Ext) right side, Ext left side). Each plot contains the estimated spectrum (thick solid line) and the upper and lower confidence intervals (dashed lines). The vertical straight solid lines mark the significant peaks detected by the algorithm and the vertical dashed lines represent the peak width, which is determined by the frequencies where the power is half the maximum value at the peak. The sum over the power of this 'half value with' is a good and also robust measure for the tremor power. This display can be printed out. The print-out also contains the numerical values. In the program, numerical values appear in the main-window (see Fig. 6).

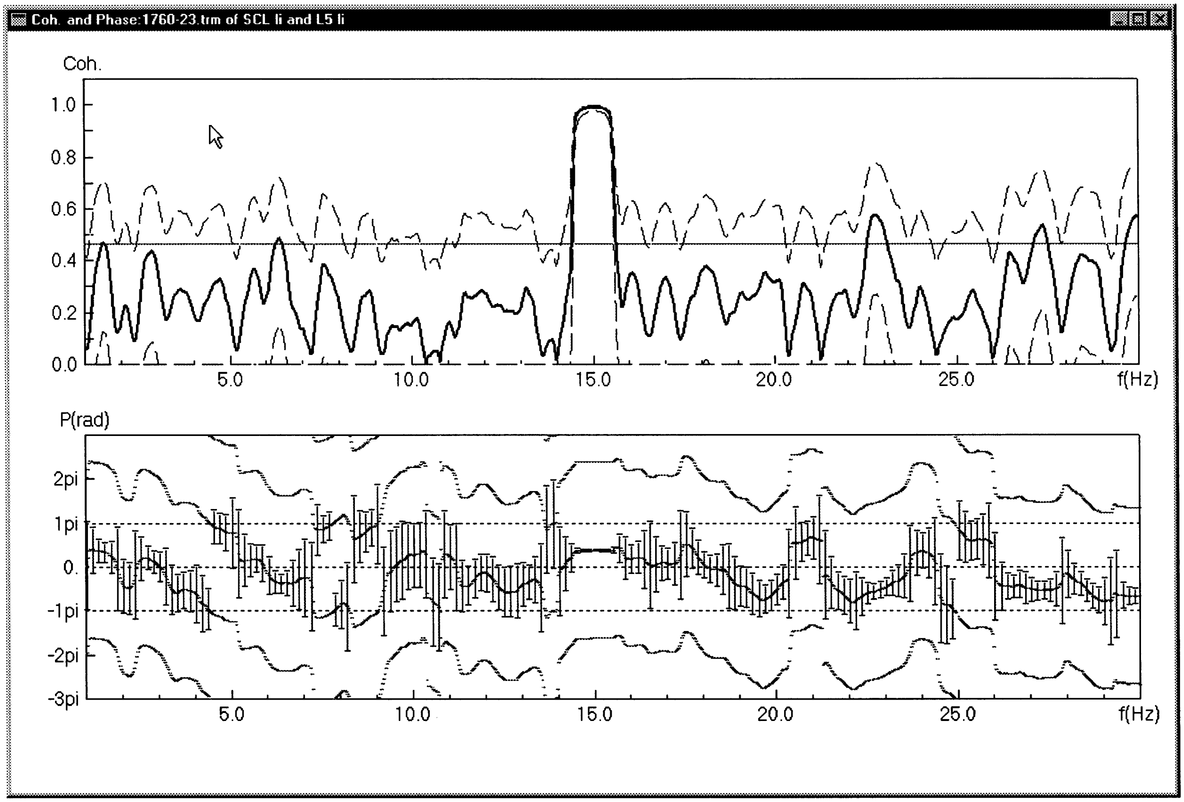

Fig. 5. Coherency and phase between two EMGs of an orthostatic tremor (OT) in the corresponding MDI child window. The upper plot shows the coherency which is very high in a range around 15 Hz. This is a typical scenario for an OT, indicating that the two EMGs measured are driven by the same sources or that there is some crossing of the signal transmitting pathways. The horizontal straight line corresponds to the level of significance (95%) for a test against the hypothesis of zero coherency. The lower plot shows the phase spectrum, plotted 2π periodically. The error bars are plotted on each fifth point. The error in the phase spectrum depends on the coherency, i.e. large errors in regions where the coherency is low and vice versa. Again, corresponding numerical values are displayed only in the main window and on the print-out.

EMGs affected by crosstalk shows a sharp, non-continuous 'peak' at the time lag zero allowing the detection of crosstalk.

4.5.2. Coherence and phase spectra

The normalized magnitude resp. the phase of the cross-spectrum is defined as the coherency resp. the phase spectrum [26]. The coherency can be interpreted as measure of linear predictability [36,42]. Phase and coherency spectra are useful to investigate tremor origins as well as their mechanisms. Various clinical and methodological aspects of coherency and phase estimates in physiological as well as pathological tremors are discussed in [37,39,40,42].

TRAS estimates the cross-spectrum and the coherency and phase spectra. The coherency and the phase are displayed in a new MDI-child window together with confidence regions and error bars (see Fig. 5 for an example). Phase spectra are plotted 2π periodically to simplify the detection of particular functional dependencies over a certain frequency range, e.g. a straight line in case of a time delay between the two series under investigation [29]. Furthermore, TRAS provides a test against the hypothesis of zero coherency, as described in detail in [27,36].

The particular interpretation of phase spectra requires strong assumptions on the underlying dynamics of the analyzed series [36,37,52,53]. An automated procedure for the interpretation of phase spectra is not available so far, but it is planned to be realized in future releases.

One simple example where a simple interpretation is possible is the above mentioned time delay. If one series lags or leads the other one, the phase spectrum is just a straight line whose gradient is proportional to the time delay [54,55]. To our experience, this simple situation is rather the exception than the rule in tremor recordings. For example, the phase spectrum between antagonistic muscles is relatively easy to interpret [22], if the investigator is interested in knowing whether the flexor-extensor timing is co-contracting or alternating (or something between them). Unfortunately, the situation is often much more complex.

Again, all parameters needed for this kind of analysis can be modified in interactive dialog-boxes.

Finally, TRAS provides an 'overview' plot of two channels containing the ACFs, CCF, auto-spectra and cross-spectra, the coherency and the phase-spectrum to give an overview of the dynamics of the series at a glance.

5. Status report

Our software shows that it is possible to integrate advanced mathematical methods in an easy-to-use application. In the meantime, our application is accepted among clinical staff and medical doctors as a convenient, powerful and fast but also secure tool. It has been used for daily clinical routine as well as research purposes in three different European hospitals. More than 10 000 tremor data-sets were recorded and analyzed during the last 5 years using TRAS.

A functional test of the application and measurement system as it is done with various other engineering products is difficult to perform, since there is no established tremor recording and measurement system for a comparison available. So the only way to test the reliability are the findings of experienced medical doctors, a mathematical investigation of the estimators by analytical calculations or simulations [24,35,36,38] and repeated measurements. Repeated measurements of physiological and enhanced physiological tremors showed a very high reproducibility over periods of more than 3 years in power and frequency, if the laboratory conditions have not been varied. Pathological tremors often differ in their power in repeated recordings, due to their medication, disease duration or due to the mental state of the patients. However, tremor frequency is also for pathological tremors a highly reproducible and reliable value.

The reliability of phase measurements between extensor and flexor muscles was also studied. Repeated recordings led us to the conclusion, that the phase between antagonistic muscles in essential as well as parkinsonian tremor might depend on the position of the limb under consideration. Coherency values did not change significantly between repeated recordings, taking into account the confidence intervals of the estimations.

Fig. 6 displays a screen-shot over the whole application frame window to give an impression of the design of our software.

Table 1 summarizes the analysis methods provided by TRAS and the time they consume on a standard Pentium 133 MHz personal computer running under Microsoft's Windows NT 4.0 (32 MB of RAM). The test data-set consists of 30 000 points each channel, sampled at 1 kHz.

6. Lessons learned

We always tried to work as close as possible with the future users, i.e. medical doctors and their laboratory assistants. This was one of the most important issues in developing such an application. Based on the results of the clinical tests and suggestions of clinical staff or complaints of the users, we are permanently modifying the application to improve its performance and user acceptance. Furthermore, we implemented (and still implement) newly established analysis methods as fast as possible and adopt new results from different fields of tremor research. Due to the modular structure of our application this could be done without substantially modifying source codes of the existing application.

The concept to develop specialized software for particular tasks might seem to be expensive and time-consuming. On the other hand, it is the only way to provide applications which are accepted by those who are not familiar with the used mathematical methods and/or algorithms. Other software packages which basically provide tools for time series analysis are available. But usually they require fully-fledged staff, which is too expensive for a daily clinical routine. Secondly, numerous mathematical methods can not be applied 'naively' to arbitrary data. It is often essential to modify existing concepts to treat a special problem, which could not be provided by an analysis package like Matlab.

The quality of the measurements, and, therefore, the reliability of the system, always depends on the quality of the data. In other words, the persons doing the data recordings should be familiar with the above mentioned movement artifacts, the EMG and ACC amplifiers, electrode settings and effects of analog filtering. However, this is also the case for a standard EMG or EEG analysis system, and Neurologists usually already know to work with such systems.

It barely occurs that it is not possible to get reliable recordings for a postural setting, i.e. with the hands outstretched, when recording patients with other very severe movement disorders. However, a measurement at rest is always possible. To

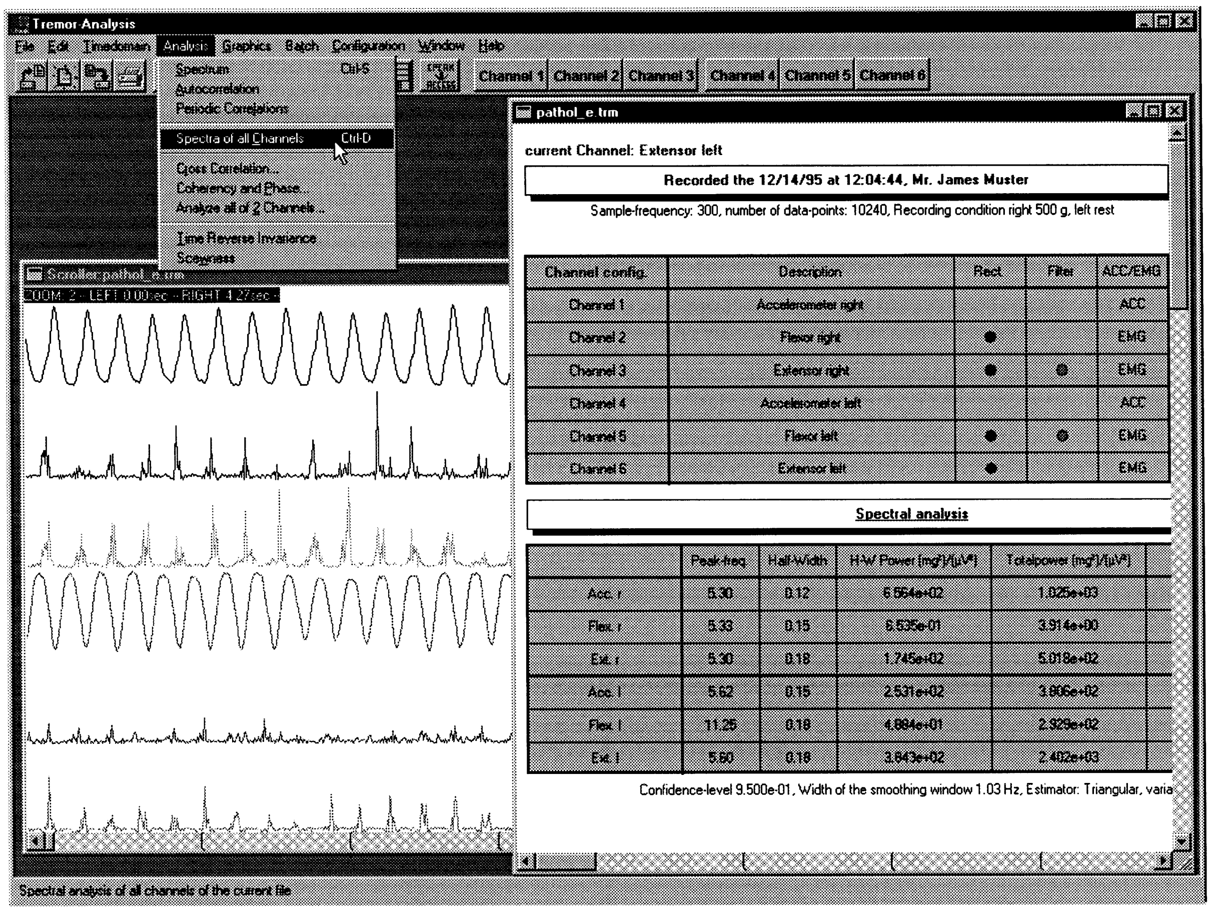

Fig. 6. Screen-shot of the application. On top is the main window that is linked to the data file. Also displayed is the six-channel-scroller (lower left window).

our experience, the system can be used without difficulties by non-technical staff knowing to handle other standard methods in Neurology like EMG or EEG without any technical assistance.

It is clear that the clinical and physiological interpretations of the results of more complex analyses like the coherency and phase spectra depend on the amount of experience an investigator has. Together with clinical staff we are currently working on different approaches to improve the presentation of results and to develop more easy-to-interpret values or graphs that can be calculated from the data.

Besides its application in tremor research and clinical routine, TRAS has been recently used successfully to study Doppler signals and other cardio-vascular time series, motion analysis time series, arbitrary EMG and EEG data and the postural control system. It was obvious that there is a lack of easy-to-use software for analyzing electro-physiological time series in the framework of linear stochastic processes.

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