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Quantitative analysis of tremor time series

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Abstract

Spectral analysis is applied to tremor time series in basic research and treatment monitoring. The estimation of the spectra from the data is usually done by averaging the squared modulus of the Fourier transform of segments of the data. We discuss drawbacks of this method and propose an alternative procedure to estimate the spectra adaptively based on the data. Thus, the method can be applied to all types of tremor. Applying the theory of spectral estimation, we propose a method to decide whether a spectrum exhibits multiple significant peaks and discuss different approaches to determine the amplitude of the tremor from the spectrum.

Keywords: Tremor measurement; Fourier analysis

1. Introduction

In mathematical terms tremor can be described as an oscillating time series. Thus, for obvious reasons these time series are often transformed into the frequency domain (Wade et al., 1982; Calzetti et al., 1987; Cleeves and Findley, 1987; Findley and Koller, 1987; Elble and Koller, 1990; Gresty and Buckwell, 1990) by applying the Fourier transform (FT). Moreover, a measure of the tremor amplitude is obtainable by squaring the absolute values of the Fourier transform for every frequency. A proper methodological approach to this problem involves critical steps based on a complicated mathematical background to get reliable results both for the frequency and amplitude information of tremor. Thus, a reliable mathematical approach to this problem is not only necessary for the valid measurement of tremor amplitudes and frequencies in the setting of treatment studies but also for physiologic experiments involving this type of measurement.

In this paper, we discuss drawbacks of the available method to estimate the spectrum of tremor time series and propose an alternative procedure. This method allows automatic estimation of the spectra of the whole variety of possible tremors. Furthermore, we suggest a method to decide whether a spectrum exhibits significant peaks at different frequencies and discuss different ways to determine the tremor amplitude from the spectrum.

2. Methods

The detailed procedure to record tremor time series has been published elsewhere (Deuschl et al., 1991; for general aspects of tremor recording, see Stein and Lee, 1981; Elble and Koller, 1990). Briefly, the subjects are sitting in a comfortable chair with the arms supported and the hands outstretched. Accelerometers are attached to the dorsum of the hand at a distance of 9 cm distal to the ulnar epicondylus. The EMG of the flexor and extensor muscles are recorded with surface electrodes fixed over the belly of the extensor carpi ulnaris muscle and the flexor carpi ulnaris muscle, respectively. After appropriate filtering, all signals are digitized at 300 Hz with a resolution of 12 bit and stored in a computer. Each tremor record consists of 10240 data points corresponding to a time period of approximately 35 s. Here, we report on accelerometer data. The method can also be applied to rectified EMG data (Elble and Koller, 1990).

Fourier analysis is performed off-line according to the procedures described below.

The spectra are displayed on a logarithmic power scale

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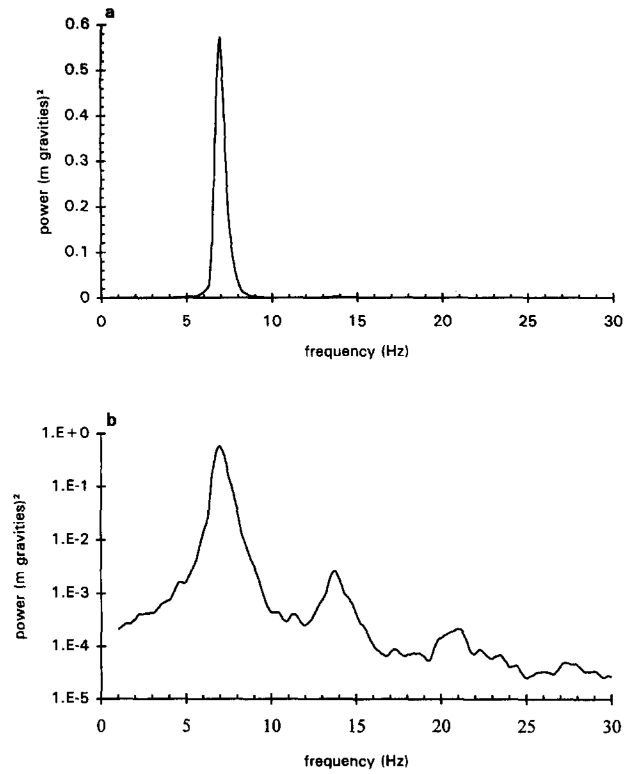

Fig. 1. Tremor spectrum of a patient with essential tremor displayed with a linear power axis in (a) and with a logarithmic axis in (b). It is evident that the logarithmic scaling shows relevant low-power higher harmonics and should therefore be preferred for display of tremor power spectra.

ordinate, as with linear scaling relevant information about smaller peaks will be lost. Fig. 1 shows a typical example of a spectrum from a subject with small amplitude essential tremor showing higher harmonics when displayed with logarithmic power axis which are suppressed with linear scaling.

3. Fourier transform: the basis of tremor quantification

As tremor is a rhythmic oscillation a conventional way to quantify such a series $x(t)$ is to transform it into the frequency domain by applying the FT

$$FT(f_k) = \frac{1}{\sqrt{N}} \sum_{t=0}^{N-1} \exp(2\pi i f_k t) x(t), \quad (1)$$

$$f_k = \frac{k}{N\Delta t}, \; k = -\frac{N}{2}, \ldots, \frac{N}{2}$$

where N is the number of data points, Δt the sampling interval and f_k the discrete frequency for each k.

The squared FT, the periodogram, $P(f_k)$ encodes the amplitude information as the spectral power. For reasons of symmetry, the periodogram is only computed for positive frequencies. It is multiplied by a factor of two to include the spectral power of the negative frequencies (Press et al., 1993) and is normalized by N:

$$P(f_k) = \frac{2}{N} |FT(f_k)|^2 \quad (2)$$

and, therefore, $P(f_k)$ represents the spectral power of the time series for every frequency bin.

It is well known that the periodogram is not a consistent estimator for the spectrum of the process, because its variance does not decrease with increasing N. The estimation of the spectrum is usually performed by averaging the squared modulus of the Fourier transform of segments of the data (Gresty and Buckwell, 1990; Bain et al., 1993a) or by smoothing the periodogram of the whole data set (Stiles, 1976; Elble, 1986). Both methods lead to an asymptotically correct estimate of the spectrum. In the case of finite amount of data, smoothing the periodogram is superior to averaging periodograms of segments due to a better frequency resolution (see Table 1).

While this averaging or smoothing looks only technical it is based on deep mathematical insights. Instead of going into the mathematical details, we give an example for the result in the case of an unaverged squared modulus of the FT of the physiologic tremor of a healthy person (Fig. 2a). On the one hand, it is obvious that not every peak in this plot (Fig. 2b) can correspond to some oscillator; on the other hand, below this widely fluctuating curve one can imagine one broad peak.

Fig. 2c displays the smoothed periodogram of the data. The resulting curve confirms the impression from Fig. 2b that there is one broad peak in the spectrum of the data. Indeed, it has been shown that such a broad peak of hand tremor can be interpreted as a damped linear oscillator that is driven by the asynchronous firing motoneurons (Randall, 1973; Gantert et al., 1992). Fig. 3a–c shows the corresponding data for a Parkinsonian tremor.

The need for averaging or smoothing can be understood on mathematical grounds. It has been shown, for time series that do not yield periodic functions, an averaging or smoothing procedure has to be applied to obtain reasonable results (Brockwell and Davis, 1987; Priestley, 1989). A further result is that the degree of averaging or smoothing is a crucial quantity: Too few segments used for averaging or too few frequency bins included in the smoothing

Table 1

Peak frequency and peak amplitude for the Parkinsonian tremor time series of Fig. 3 determined by different numbers of averaged segments

No. of segments	Peak frequency (Hz)	Amplitude (mm)
1	4.39	3.211
5	4.39	4.010
10	4.39	4.773
16	4.21	4.519
20	4.68	3.189
32	4.68	4.083
40	4.68	4.341

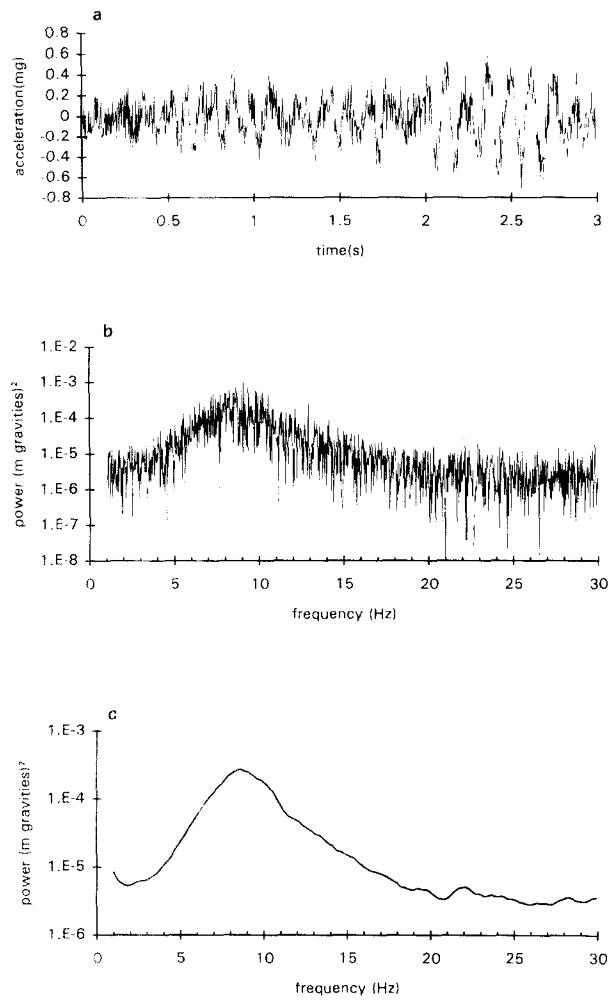

Fig. 2. Physiological tremor time series (a), periodogram (b) and estimated spectrum (c) based on the smoothed periodogram. The periodogram (b) displays a broad peak with several possible maxima.

might result in a still fluctuating curve, while too many segments, or too heavy smoothing, might lead to loss in frequency resolution. In terms of mathematics, this is the conflict between the bias (the systematic misestimation) and the variance (the stochastic fluctuations): one can oversmooth sharp peaks and undersmooth broad peaks. The optimal smoothing depends on the unknown properties of the process under investigation. For example, it is obvious that the periodogram of the tremor recorded from a patient suffering from Parkinson's disease shown in Fig. 3 needs only minor averaging or smoothing compared to the periodogram of Fig. 2. In the extreme case of periodic processes any smoothing will lead to an underestimation of the true amplitude while averaging will lead to a misestimation of the peak frequency.

In order to deal with these problems it is necessary to determine the degree of averaging or smoothing depending on the given data. In general, different frequency ranges require different degrees of averaging, or smoothing. Since averaging the periodograms of segments corresponds to a fixed degree of smoothing, the algorithm we propose is based on a data-driven frequency-dependent smoothing algorithm of the periodogram of the entire set of data.

For estimating the spectrum by a smoothing procedure it is superior to use an unbalanced smoothing function instead of a balanced weighting. We chose a triangular smoothing window which includes $2h + 1$ frequency bin and, thus, our spectral estimate $S(f_k)$ is given by

$$S(f_k) = \sum_{i=-h}^{i=h} W_i P(f_{k+i}), \tag{3}$$

$$W_i = \frac{1}{h+1} - \frac{1}{(h+1)^2}|i|$$

The smoothing window is normalized, i.e. its components sum up to one, thus conserving the integral spectral power of the periodogram.

4. Confidence limits for the estimated spectrum

The periodogram is χ^2-distributed with two degrees of

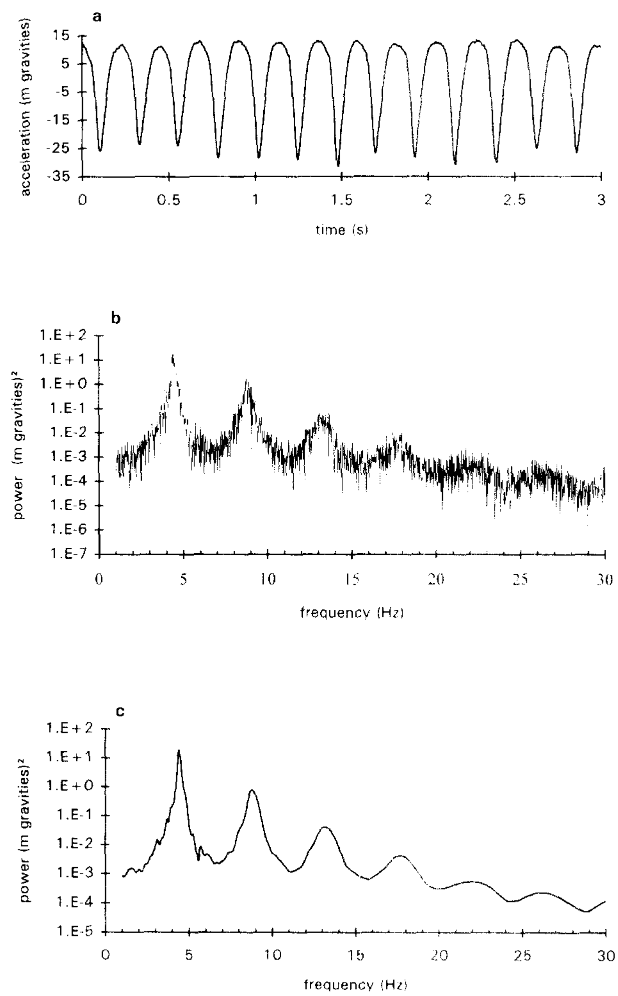

Fig. 3. Parkinsonian tremor time series (a), periodogram (b) and estimated spectrum (c) based on the smoothed periodogram. The periodogram (b) displays a sharp mean peak with unique frequency.

freedom. The estimated spectrum $S(f_k)$ from Eq. (3) is χ^2-distributed itself as it is a sum of those χ^2-distributed random variables. The degrees of freedom of the resulting χ^2-distribution depend pointwise on the form of the smoothing window and on its size h. For an equal weighting window, they are two times the number of frequencies considered. In case of unequal weighting windows the resulting degrees of freedom ν can be calculated by

$$\nu = \frac{2}{\sum_{i=-h}^{h} W_i^2} \qquad (4)$$

Hence, for a given confidence level α the confidence interval around $S(f_k)$ is given by (Brockwell and Davis, 1987)

$$\left(\frac{\nu S(f_k)}{\chi^2_{1-\alpha/2}(\nu)}, \frac{\nu S(f_k)}{\chi^2_{\alpha/2}(\nu)} \right) \qquad (5)$$

The application of these procedures to detect different significant peaks in the estimated spectra of tremor time series will be given below.

5. Testing for white noise in spectra

For each time series it has to be decided whether there are any significant frequencies at all or whether it contains white noise only. In the latter case, the spectrum is flat and the periodogram fluctuates around a certain value which is given by the variance of the noise. To test whether a periodogram is consistent with such a flat spectrum for a given confidence level α the Kolmogorov-Smirnov test (KS-test) can be applied (Brockwell and Davis, 1987). For this test the normalized cumulative periodogram $CP(r)$

$$CP(r) = \frac{\sum_{k=1}^{r} P(f_k)}{\sum_{k=1}^{N/2} P(f_k)} \quad \text{with } r = 1, 2, \ldots, N/2 \qquad (6)$$

has to be calculated. For the flat spectrum of white noise $CP(r)$ is just the diagonal. The KS-test measures the maximal deviation of $CP(r)$ from this diagonal and decides if $CP(r)$ deviates significantly from this diagonal. Fig. 4 displays two examples. The cumulative periodogram of an EMG in Fig. 4a does not cross the chosen level of significance ($P = 0.05$) and is, therefore, consistent with white noise, i.e. unsynchronized, but the cumulative periodogram of a physiologic tremor in Fig. 4b does.

6. Estimating spectra and different peaks of a spectrum

Once it is established that a spectrum is different from white noise, significant peaks can be determined. As there is no mathematical way to decide which degree of smoothing is appropriate, any possible approach must be based on

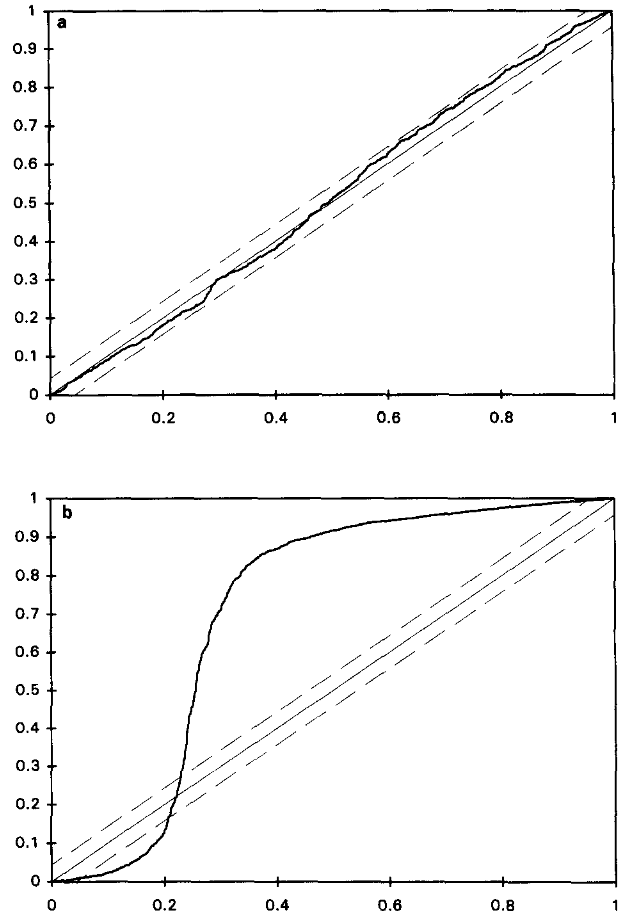

Fig. 4. Graphic display of the KS-test for white noise for two examples. Normalized cumulative periodograms (thick lines) of an EMG time series consistent with white noise (a) and a physiologic tremor with a significant preferred frequency (b). The diagonal line from (0,0) to (1,1) would correspond to a true spectrum of white noise. The parallel dashed lines represent the confidence limits ($P = 0.05$).

a heuristic idea not to oversmooth a periodogram similar to Fig. 3 but to smooth a periodogram similar to Fig. 2 sufficiently. Moreover, the width of the smoothing window has to change even in a given periodogram when there are large singular peaks in an otherwise fluctuating periodogram. We propose the following step-wise procedure which can be implemented in a computerized way to determine peaks of the spectrum automatically.

(1) A preliminary spectrum is estimated by smoothing the periodogram with the window of width h_0. According to our sampling rate and duration of measurement we found $h_0 = 0.5$ Hz as a practicable value.

(2) The standard deviation (SD) of this estimate is calculated by Eq. (5). This SD is included in the determination of local maxima: a local maximum is assumed if there are values left and right of the presumed local maximum which are at least 2 SD smaller. The peak frequency f_0 is defined as the largest of the detected local maxima.

(3) To further quantify the estimated spectrum, the 'half-width' of the peak frequency is defined in the follow-

ing way. The frequency values left and right of the peak are determined at which the amplitude is half the peak power, f_l and f_r, and the corresponding frequency interval $(f_r - f_l)$ is defined as the 'half-width' of the peak.

(4) In order not to oversmooth the periodogram, the smoothing width is determined first at the peak by

$$h(f_0) = \frac{(f_l - f_r)^2}{b} \tag{7}$$

where b is a parameter to be chosen. We found $b = 3.22$ Hz to be a reasonable value for b. Thus, the broader the peak, the larger is $h(f_0)$. Two straight lines are now constructed with the slopes s_l and s_r defined by

$$s_l = a\frac{f_l - f_0}{2h_0} \tag{8}$$

$$s_r = a\frac{f_r - f_0}{2h_0} \tag{9}$$

where a is a second parameter to be chosen. In our application we found $a = 0.2$ to be a reasonable value. The resulting frequency-dependent variable smoothing width $h(f_k)$ is defined as

$$h(f_k) = \begin{cases} \min(h(f_0) + s_l(f_k - f_0),\ h_{\max}), & f_k \le f_0 \\ \min(h(f_0) + s_r(f_k - f_0),\ h_{\max}), & f_k \ge f_0 \end{cases} \tag{10}$$

where $h_{\max}$ is an upper limit for the window-width, we choose $h_{\max} = 1$ Hz.

(5) Finally, the periodogram is smoothed again with the window of Eq. (3) but with the frequency-dependent width of Eq. (10). The final peaks are determined according to step 2.

This procedure will cause larger values for $h(f_k)$ for broad peaks in the calculation of the preliminary spectra in step 1 than for sharp peaks. Therefore, we get reasonable smoothing for periodograms similar to Fig. 2 but we do not oversmooth periodograms resembling that of Fig. 3. The variable width $h(f_k)$ of the smoothing window is designed to estimate the spectrum optimally around the maximal peak. Fig. 5 shows the result for two periodograms shown in Figs. 2 and 3. The resulting figures do not depend critically on the chosen parameters a and b.

7. The interpretation of tremor spectra

Following the appropriate mathematical treatment of tremor spectra, we still have to interpret them in physiological terms. According to our experience the following spectra have to be discussed.

(1) In the case of a sinusoidal oscillation, the spectrum exhibits one sharp peak at the corresponding frequency. In our experience, such a case does not occur in human tremors.

(2) In the case of deterministic but non-linear oscillations the spectrum shows a sharp peak with higher harmonics. Usually, in tremor time series the higher harmonics appear at two-fold multiples of the fundamental frequency. This pattern is commonly seen in pathologic tremors and can be interpreted as a sign of asymmetric flexion and extension movements.

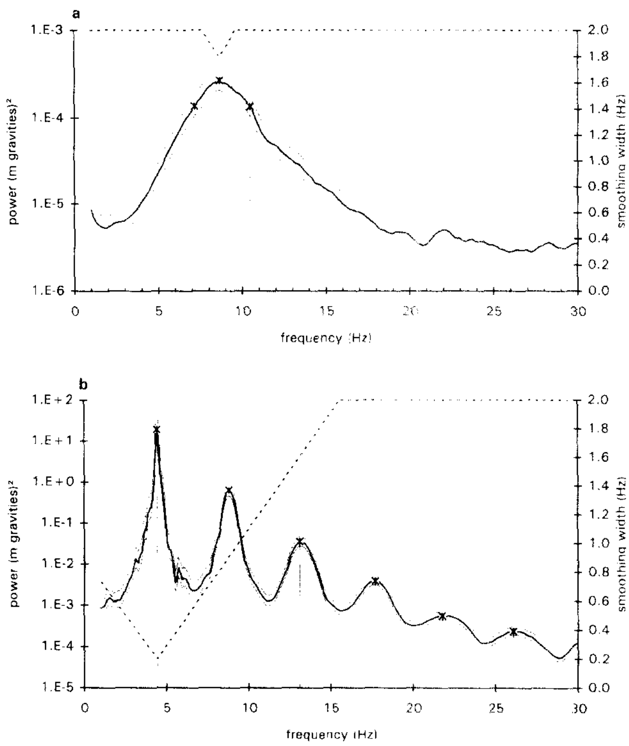

Fig. 5. Spectra of the accelerometer data of a normal subject (Fig. 2a) ((a), thick line) and of a patient with Parkinson's disease (Fig. 3a) ((b), thick line) estimated with a frequency-dependent window width $h(f_k)$, displayed as dotted line with regard to the right vertical axis. The thin lines display the 95% confidence levels. The local maxima found by the algorithm are displayed as plain vertical lines. The dashed vertical lines in (a) show the 'half-values'; in (b) these lines are not displayed due to the small 'half-value-width' (approximately 0.12 Hz).

(3) In the case of a stochastic oscillation the spectrum shows a broad peak. This does not indicate that there are several oscillators but this is a feature of a single damped oscillator showing decreasing frequency contributions to both sides of the oscillators peak frequency. This is most often seen in physiologic tremor (Randall, 1973; Gantert et al., 1992).

(4) In the case of a loaded hand, records of (enhanced) physiologic tremor often display two different frequencies being harmonically unrelated (Elble and Randall, 1978). In this case significant peaks can be accepted with the procedure proposed in this paper with a defined probability.

(5) Finally, EMGs of some normals do not exhibit significant synchronization at all. This results in a spectrum consistent with the flat spectrum of a white noise process at a given level of significance. In this case, no further conclusions can be drawn from the spectrum.

8. Determination of tremor amplitude and frequency

The natural definition of the amplitude is the standard deviation as a statistical measure of the amplitude (Randall and Metzger, 1963).For this purpose we first consider the original time series $x(t)$.If there is any DC-offset we first have to subtract the mean from the time series. The variance of the tremor curve is now determined according to

$$\mathrm{var}(x) = \frac{1}{N-1}\sum_{i=1}^{N} x_i^2 \qquad (11)$$

The standard deviation is given by the square root of the variance.

However, there are at least three reasons that hinder the direct use of Eq. (11) to determine the tremor amplitude. First, especially for low amplitude physiological tremors, observational noise (due to the piezo-crystal or amplifiers) will contribute significantly to the variance. Second, slow trends caused by voluntary movements sometimes occur. Both effects would lead to an overestimation of the tremor amplitude using Eq. (11). Third, in the case of two peaks harmonically unrelated amplitudes have to be assigned to each oscillation individually.

Since both phenomena exhibit specific spectral properties it is plausible to estimate the tremor amplitude based on the spectrum. This is usually done by choosing the square root of the spectral peak value (Calzetti et al., 1987; Cleeves and Findley, 1987; Pozos and Iaizzo, 1991; Bain et al., 1993b).This procedure will lead to an underestimation in the case of broad peaks because the variance of the original time series is equal to the sum of the estimated spectral power:

$$\mathrm{var}(x) = \sum_{k=0}^{N/2} S(f_k) \qquad (12)$$

To enable a reliable estimation of the tremor amplitude for the whole variety of possible spectra, we propose the following adaptive procedure. By Eq. (12) the variance of the original time series is displayed as a function of frequency. The power of an oscillation can be calculated as the sum over the spectrum of its frequency range. Since the true oscillation has a preferred frequency range, whereas the observational noise is equally distributed and trends show up in low frequency components, we suggest isolating the frequency band representing the real tremor activity around the peak-frequency. Therefore, we determine those frequencies around the peak which have just half the power of the peak (half-power frequencies f_l and f_r from above) and choose the sum over the spectrum between these half-power frequencies as estimate $\widehat{\mathrm{var}}(x)$ for the variance of the tremor:

$$\widehat{\mathrm{var}}(x) = \sum_{f_k=f_l}^{f_r} S(f_k) \qquad (13)$$

It should be noted that, apart from this technical use of the half-power width f_r–f_l, this quantity carries physiologic information since it is a measure for the coherence of the oscillation.

In order to obtain the position $s(t)$ from acceleration $x(t)$ the latter has to be integrated twice. This is easily performed in the frequency domain. The spectrum $S_{pos}(f_k)$ of position is obtained from the acceleration spectrum $S_{acc}(f_k)$ by

$$S_{\mathrm{pos}}(f_k) = \frac{S_{\mathrm{acc}}(f_k)}{(2\pi f_k)^4} g^2 \qquad (14)$$

where g = gravitational constant.

Now, we give three examples for the application of the proposed procedure.

(1) We compare the results of our algorithm with the usually applied averaging of segmentwise periodograms to the Parkinsonian tremor shown in Fig. 3. Table 1 shows the results for a different number of segments used. Our procedure gives a peak frequency of 4.39 Hz. (see Fig. 5b), and an amplitude of 4.43 mm. From the table, it is obvious that the estimated peak frequency depends on the number of segments chosen and may vary by approximately 0.3 Hz. The estimates of the amplitude depends also on the number of segments used and can differ by up to 50%.

(2) Table 2 shows the results for the physiologic tremor shown in Fig. 2 for a different number of segments used. The estimated peak frequencies differ by up to 0.9 Hz. Our procedure gives a peak frequency of 8.64 Hz (see Fig. 5a), and an amplitude of 0.0201 mm. There is a remarkable difference between the estimated amplitudes for the two different procedures. Since, for real data, the true amplitude is not know, we will use simulated data to decide which method yields the more reliable result.

(3) According to Randall (1973) and Gantert et al. (1992) physiologic tremor can be modelled by an autoregressive (AR) process with observational noise. We chose an AR process, whose spectrum resembles Fig. 2 with a frequency of 10 Hz. The amplitude of this process is fixed to 1 in arbitrary units and the observational noise exhibits a variance of 0.3. Table 3 shows the result corresponding to Table 2. Our procedure results in an estimate for the frequency of 9.91 Hz. and an amplitude of 0.732 units. Again, the results of the two methods differ substantially up to a

Table 2

Peak frequency and peak amplitude for the physiologic tremor time series of Fig. 2 determined by different numbers of averaged segments

No. of segments	Peak frequency (Hz)	Amplitude (mm)
1	9.11	0.0051
5	8.64	0.0067
10	9.08	0.0069
16	8.43	0.0082
20	8.78	0.0101
32	8.43	0.0110
40	8.20	0.0131

Both peak frequency and peak amplitude depend on the number of segment chosen.

Table 3

Peak frequency and peak amplitude for a simulated tremor time series showing a spectrum similar to the physiologic tremor time series of Fig. 2 determined by different numbers of averaged segments

No. of segments	Peak frequency (Hz)	Amplitude (mm)
1	9.58	0.144
5	9.52	0.219
10	9.66	0.295
16	9.84	0.343
20	9.93	0.346
32	9.37	0.410
40	9.37	0.456

The amplitude of the time series is 1 in arbitrary units. This table shows the underestimation of the amplitude of an oscillation with a broad peak by the peak amplitude.

factor of 5. Since the true amplitude is known, this simulation confirms the peak amplitude heavily underestimates the true amplitude in the case of a broad peak.

These examples show that the proposed method is able to reliably estimate the peak frequency as well as the amplitude for the various different dynamics observed in tremor time series.

9. Discussion

Several problems need to be considered when applying mathematical methods to tremor time series. The aim of our study was to develop a sound mathematical approach to quantify accelerometric or position data of tremor.

The major problem emerges from the fact that tremor can be due to at least two mechanisms: a peripheral mechanic oscillation of the limb and central mechanisms driving the EMG and, hence, the limb. This includes several possibilities for central oscillators or feedback loops which are beyond the scope of the present paper and the reader is referred to appropriate reviews (Elble and Koller, 1990; Deuschl, 1994). The amplitude of tremor may vary up to 3 orders of magnitude between normals and patients depending on whether such rhythmic EMG oscillations are present or not. This is accompanied by significant changes of the waveforms which demand different or adaptive algorithms for power spectral analysis. Leaving the periodograms unsmoothed does not bear large errors in case of highly synchronized and large amplitude tremors as long as only the peak frequency is considered. However, for small amplitude tremors the determination of the amplitude, the peak frequency and, especially, the detection of various peaks might be significantly erroneous.

Moreover, any periodogram will have a highest peak, which does not mean that a significant peak exists. Hence, a formal test to exclude white noise is required, especially for tremor records with EMG. The present approach solves this problem by applying the KS-test.

The question has to be addressed whether the proposed procedure for the detection of multiple frequencies of the periodogram is able to detect different biologic oscillations. We decided to accept a local maximum if there are values right and left being at least 2 SD smaller. With such a procedure we cannot exclude that further biologically relevant peaks do exist. But, the level of confidence for such errors can be chosen depending on the specific physiologic application.

To calculate the amplitude of a tremor record is not a trivial problem. In order to illustrate this, we have calculated the maximal tremor amplitudes for patients with tremor according to the procedures proposed in some recent publications. We found amplitudes of 0.94 mm for severe essential tremor and 70 cm for 'shivering tremor'.Such values are obviously nonsense and the major reason for these errors is problems with the mathematical analysis of these data including calibration.

Using the variance of the time series to estimate the amplitude will lead to an overestimation due to observational noise and trends or multiple oscillators. Using the square root of the maximal power (at the peak frequency) will result in an underestimation of the real amplitude in the case of broad peaks. Another approach (Elble, 1986; Hömberg et al., 1987) has been to calculate the power for a fixed frequency range between −1 Hz and +1 Hz of the peak frequency. We generalized this approach by a data-driven adaptive method that is able to deal with the whole variety of real tremor dynamics and developed a procedure balancing the underestimation in case of measuring at the peak only and the overestimation when considering the full frequency range.

The proposed procedures may help to prevent erroneous frequency and amplitude detection.

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