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Pathological tremor management: Modelling, compensatory technology and evaluation

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Abstract. A great deal of effort has been devoted in the past decades in the generic area of tremor management. Specific topics of modelling for objective classification of pathological tremor out of kinematics and physiological data, compensatory technologies and evaluation rating tools are just a few examples of application field. This paper introduces a comprehensive review of research work in this generic field during the last decades. In particular special focus has been put on the systems approach and thus a specific section on modelling has been included. Aspects related to experimental protocol and tremor pattern identification are reviewed in detail with the aim of drawing a practical guideline when compensatory technology has to be developed.
The current status on ambulatory and non-ambulatory tremor reduction technologies is given in the section devoted to tremor management. Here compensatory technologies are classified according to the tremor isolation and the tremor reduction approaches. Eventually, we finish our discussion with those aspects related to tremor evaluation.

1. Introduction

Tremor is a rhythmic, involuntary muscular contraction characterised by oscillations (to-and-from movements) of a part of the body [1]. Although the most common types of tremor were subject to numerous studies, their mechanisms and origins are still unknown. The most common of all involuntary movements, tremor can affect various body parts such as the hands, head, facial structures, tongue, trunk, and legs; most tremors, however, occur in the hands. Tremor often accompanies neurological disorders associated with aging. Although the disorder is not life-threatening, it can be responsible for functional disability and social embarrassment [2].

There are many types of tremor and several ways in which tremor is classified. The most common classification is by behavioural context or position. There are five categories of tremor within this classification: resting, postural, kinetic, task-specific, and hysterical. It is accepted that the majority of the affected patients have either Parkinson disease or Essential tremor and that the most incapacitating are essential tremor, tremor due to Parkinson disease and cerebellar tremor.

Resting or static tremor occurs when the muscle is at rest, for example when the hands are lying on the lap. This type of tremor is often seen in patients with Parkinson's disease. Postural tremor occurs when a patient attempts to maintain posture, such as holding the hands outstretched. Postural tremors include physiological tremor, essential tremor, tremor with basal ganglia disease (also seen in patients with Parkinson's disease), cerebellar postural tremor, tremor with peripheral neuropathy, post-traumatic tremor, and alcoholic tremor. Kinetic tremor occurs during purposeful movement, for example during finger-to-nose testing. Task-specific tremor appears when performing goal-oriented tasks such as handwriting, speaking, or standing. This group consists of primary writing tremor, vocal tremor, and orthostatic tremor.

Tremor is a disorder that is not life-threatening, but it can be responsible for functional disability and social embarrassment. More than 65% of the population with upper limb tremor present serious difficulties performing daily living activities [37]. In many cases, tremor intensities are very large, causing total disability to the affected person.

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The effect of tremor on the patient depends on the clinical manifestation. In general it can be said that the more goal-directed movements are distorted by tremor, the more severe the difficulty in performing daily activities. On the other hand, rest tremor is seen by the patients as a cause for social exclusion.

There is no known cure for a lot of tremor diseases. The overall management is directed toward keeping the patient functioning independently as long as possible while minimising disability. In view of what is known at present, the treatment options available for tremor nowadays are medication, neurosurgical intervention, rehabilitation programs (psychotherapy) , brain stimulation, and to assist the limb with compensatory technology.

The standard and most effective treatment of tremor is medication. One of the main problems is that drugs are typically prescribed on a trial-and-error basis in order of decreasing expected effectiveness because the clinical phenomenological tremor classifications are not perfectly predictive of their success. If success in reducing tremor is found, it must be weighed against side effects and the potential for addiction [3].

Drug therapies have not been very successful in tremor treatment, giving rise to the need of alternative approaches to the problem of tremor suppression. For those cases of tremor in which there is no effective drug treatment, physical measures such as teaching the patient to brace the affected limb during the tremor are sometimes useful. The goals of rehabilitation programs include preservation of present function, improve range of motion, posture, strength, and endurance; prevention of disabling complications (e.g., respiratory, bowel, bladder, visual); family training; and maintenance of the patient's independence as long as possible.

More recently, there has been research interest in the use of deep brain stimulation of the globus pallidus or subthalamic nucleus as a treatment for people who suffer from tremor diseases, specially of some Parkinsonian symptoms, such as rigidity, bradykinesia, or akinesia. Caparros [4] in his work discovered that high-frequency electrical stimulation of ventralis intermedius suppresses Parkinson tremor, and Friston [5] stated that the suppression of tremor is associated to reduced blood flow in the cerebellum. A commercial example of this approach is the Medtronic® Active Tremor. The Activa® Tremor Control System (Medtronic Corp., Minnesota) has been approved by the FDA (Food and Drug Administration – US Department of Healthy and Human Services) for "unilateral thalamic stimulation for the suppression of tremor in the upper extremity in patients who are diagnosed with essential tremor or Parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability."

2. Modelling

As described above, tremor denotes an involuntary oscillation of limbs of the body. In this article we will mainly focus on upper limbs. Even healthy persons show tremor. Healthy tremor is clinically divided in "physiological tremor" and "enhanced physiological tremor" mainly by the criterion whether it can be observed by eye.

A number of works tried to model tremor but so far no tremor is understood completely. Most of the papers in the literature are concerned with physiological normal tremor. The objective of this paper is to review the work done in this area trying to show some light in the present literature on modelling tremor.

In this section we review the various hypotheses and existing knowledge related to the tremor modelling. First, a summary of the current experimental protocols to get the tremor data is shown. Secondly, a brief review of the patterns of the most common tremors is done. Eventually, we will briefly address the issue of tremor quantification.

2.1. Experimental protocol

The electrophysiological analysis of human tremor has a long tradition. The earliest works on this field usually investigated electromyography (EMG), recorded from different muscles and plotted with analog devices [6,7]. In the sixties, different techniques were used to measure the amplitude and frequency of tremor [8,9], spectral analysis was performed with analog computer devices. Later on, with the fast development of digital computers, researchers began to sample the tremor records to analyse the data off-line mainly by the new developed methods of spectral and cross-spectral analysis of stochastic processes. From this time, the tremor has been usually measured with piezoresistive accelerometers (ACC). In the following years research groups presented a lot of different approaches to measure and model tremor. In the meantime, the needed mathematical methods, e.g. the theory of linear stochastic processes or linear time series analysis, have been well investigated. 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 difficulty is rather the proper interpretation of results in terms of physiology and physics.

The experimental protocol is largely determined by the study goals, and it is concerned basically with three aspects:

- Type and number of sensors involved in the experimental procedure.
- Procedure for supporting the limbs and exciting the tremor.
- Data acquisition, treatment and interpretation.

Just a few papers focus on these issues related to pathological forms of tremor. Among them, there are some papers that draw some conclusions about kinds of tremor. In particular, Forssberg [49] characterises the nature of the oscillations regarding Parkinson disease, studying the action tremor during object manipulation in Parkinson's disease.

2.1.1. Type and number of sensors

Concerning the type and number of sensors, most authors use accelerometers for direct measure of tremor and EMG sensors for recording muscle activity at flexors and extensors. Usually piezo-resistive accelerometers are employed and a means of uncoupling gravity is provided by limiting the oscillation to a horizontal plane, otherwise the resolution is limited by the relative high amplitude of gravity.

In this context, and considering the low frequency characteristics of intention, kinetic and rest tremors, Adelstein [21] discused on the relative amplitudes of power spectral densities of position and acceleration measurements according to the following expression:

$$M_{\ddot{\theta}\ddot{\theta}}(f) = (2\pi f)^4 M_{\theta\theta}(f)$$

where $M_{\ddot{\theta}\ddot{\theta}}(f)$ is the amplitude of the power spectral density of the acceleration measurement, $M_{\theta\theta}(f)$ is that of the position measurements and $(2\pi f)^4$ is the amplification factor between acceleration and position as a function of frequency.

This work argues that accelerometers are adequate for higher frequency and small displacement oscillations (physiological and Essential tremors) while lower frequency and large displacement tremors (intention, kinetic and rest) are better measured by goniometry or gyroscopes.

Some researchers, as Matsumoto [10], have the opinion that tremor research needs better validated methods of instrumental measurement and that a standard instrumental measurement of tremor has yet to be established. He developed a device to precisely measure the three-dimensional position of the fingertip during a postural task by combining three precision potentiometers placed orthogonally and sensing rotation of lightweight aluminium lever arms coupled with the tip of the patient index finger by a ring clamp. This device could quantify essential tremor severity during a postural task. The disadvantage is that this device does not measure tremor during a functionally relevant task. The measurements comprise mean three-dimensional velocity, mean three-dimensional dispersion, and power of the three-dimensional acceleration.

Bain [50], in 1993, in a rigorous validation study, reported that uniaxial accelerometry correlated poorly with tremor disability. One hypothesis is that this failure might be the result of the three-dimensional aspects of tremor which were not captured by this technique or to aspects of tremor which were best appreciated visually. Newer techniques address these possible problems, but as yet their correlation with tremor disabilities is unproved, so far.

Lately, some researches are using laser techniques in order to measure tremor amplitude, i.e., Roderick et al. [26,27] used laser displacement recording when trying to discriminate physiological and Parkinsonian tremors using time and frequency domain characteristics (Fig. 1). When measuring displacement of the affected limb, velocity and acceleration could be obtained by numerical differentiation of the raw displacement time series. Davis [11] measured the amplitude of physiological tremor using a novel method based on laser penlight that allow to determine the relative contributions of tremor generators at the wrist, elbow and shoulder, and to determine the degree of displacement in various planes.

2.1.2. Experimental procedure

In most of the reviewed papers the experimental tests are performed under upper limb support in such a way that only motion about a selected joint is allowed. Usually the selected joint is the wrist and the allowed motion is flexion-extension. The goal is to measure the influence of each joint in the overall tremor. To perform these experiments the patients were exposed to different levels of supporting systems.

Adelstein [21] argues that the muscle contracts to counterbalance the effect of gravity and this in turn could increase the effective stiffness of the biomechanical system under study. In order to prevent these ex-

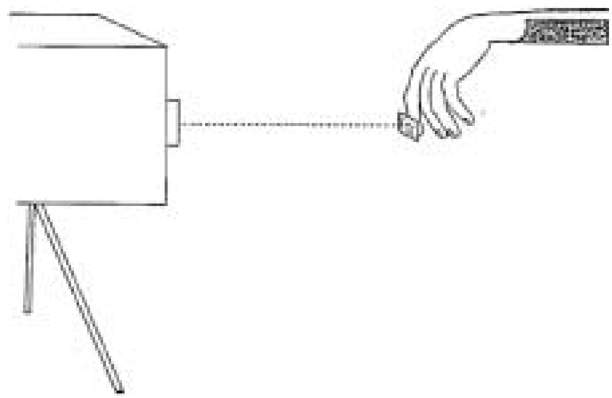

Fig. 1. Example of a laser experiment. The marker positioned in the finger tip is tracked by the laser pen light that estimates its position in three dimensions.

ternal effects, in general the motion is restricted to a horizontal plane. Usually a large enough number of subjects are involved to have a representative sample of different etiological groups. For instance, Elble [22] involves up to 44 subjects (25 men and 19 women). In the experiments related to the pathological forms of tremor, the groups of subjects contain healthy people and people with the disease; among the persons with the disease, there were people with and without medication, and they were classified by the degree of their disease.

Another interesting issue is the excitation of tremor. In those cases in which tremor appears under voluntary muscle contraction, i.e. postural, kinetic tremors, the subject is usually committed to perform a tracking task [3,9]. This involves the visual tracking of a reference signal of low frequency. Gonzalez [36,37] proposes as reference signals white noise filtered in the frequency band of 0.01 to 0.5 Hz. This procedure is of particular interest for the evaluation of active cancellation orthosis, in which one of the above-described tremor measures can be compared under control and active cancellation. Another way to evaluate patients who suffer from postural tremor is asking them to keep the arms outstretched in a horizontal position, against gravity. To evaluate the kinetic tremor, the patients are asked to execute a specific task, i.e. finger-to-finger test, finger-to-nose, and pronation/supinations. In the evaluation of rest tremor the patients should keep the limb in a rest position.

In some cases the subject is asked to maintain a posture while the degree of support is increased [16]. Morrison et al. [17] measure the finger tip physiological tremor under five experimental conditions, i.e. full limb support, upper arm support, forearm and upper arm support, the previous plus hand support and unsupported control condition. In this particular case, the aim was determining inter and intra limb tremor correlation as well as determining involuntary compensatory control of tremor.

2.1.3. Data acquisition, treatment and interpretation

In most of the reviewed papers both EMG activity and acceleration are simultaneously measured. When EMG data is involved in the experimental procedure, relatively low sampling frequencies are used. For instance, Stiles [16], samples at 1024 Hz while Elble [22] just at 200 Hz. When several EMG pickups are included in the tests, those measures including cross-talk are rejected by cross-correlation techniques.

In all cases, the EMG signal is rectified and averaged. In addition, Stiles high pass filters the EMG signal at 8 Hz to reject all possible motion artifacts. It is usually done at the pre-amplifier stage or later by a digital filtering approach.

In the studies involving tremor time series, acceleration or displacement, all the time series were low-pass filtered to remove the high-frequency components beyond the range of interest in the tremor analysis. In particular, Roderick used 20 Hz as cut frequency when evaluating physiological and Parkinson tremor.

When computing power spectral densities of the EMG signal, averaging of sequential time series is used to smooth the auto-spectra. Once the power spectral density is available, it is sometimes used to estimate the intensity of motor unit entrainment. Elble [22] estimated the EMG peak amplitude ratio as the ratio between the square root of the spectral power within the EMG peak and the total spectral power from 0 to 15 Hz.

Acceleration measures of tremor show lower frequency content. Depending on the paper, sampling frequencies are as low as 64 Hz and a similar data treatment is performed. In addition to all tremor measures presented in Section 4, sometimes, tremor amplitude is directly estimated from the power spectral density of the acceleration signal. This is done by the square root of the overall power at the tremor peak.

Power spectral analysis has been proposed as a statistical method of qualifying both the magnitude and the frequency parameters of body tremors in the unified schemes. Cross-spectral methods provide a powerful tool to investigate the relation between simultaneously recorded signals. These methods have been used in tremor research to study the relation between muscle activity (electromyogram (EMG)) and magnetoencephalogram (MEG), between EMG and electroencephalogram (EEG), between EMGs and mechanical measurements, between EMGs and between single units and EMGs.

2.2. Tremor patterns

Human physiological tremor is surrounded by a long history of controversy and general interest, dating back to the observations of Schafer et al. in 1886. Most of the interest is based on the beliefs that tremor offers some clue to the mechanisms of neuromuscular control in man and the clarification of physiological tremor will help to elucidate the origins of many pathological action tremors.

Pioneered in the work of Lippold [7,9], various experiments were performed to clarify the effect of reflex mechanisms on physiological tremor. According to Lippold the reflex mechanisms which stabilise a limb during maintained posture may also be responsible for physiological tremor. This possibility arises from the fact that there are substantial delays in the feedback from muscle so that at certain frequencies (8–12 Hz) the feedback is sufficiently delayed so that it adds to the next phase of the movement, rather than resisting the phase that produced it.

Based on the Lippold work, Stein and Oguzt öreli [12] introduced a deterministic model concerning the properties of muscles and the sensory feedback pathways from muscles in order to evaluate the tremor sources. Stein used a stochastic feedback system which applies a signoidal nonlinearity describing the activation function of the motoneurons. According to Stein, damped oscillations can arise in the absence of sensory feedback due to interaction of a muscle with inertial loads. Stein is one of the researchers that performed an experiment to clarify the effect of reflex mechanisms on physiological tremor.

Other studies address the problem of determining the excitation sources of normal tremor. In particular, Stiles [13] focuses on determining to what extent mechanical and neural factors are involved in the excitation of physiological tremor. In 1998, Timmer [14] used cross-spectral analysis to study the role of reflexes in physiological tremor. Cross-spectral analysis has the advantage of not perturbing the system, i.e. the stimulus for the reflexes is the tremor itself.

Timmer is one of the researchers that pay more attention to modelling tremor. Initially, the standard methods of stochastic and deterministic time series analysis were used to analyse data of various physiological and pathological forms of tremor. Timmer et al. had shown that the physiological tremor can be described as a linear stochastic process whereas pathological forms of tremor represent non-linear processes [15]. He used a stochastic feedback system which applies a sigmoidal nonlinearity describing the activation function of the motoneurons that was introduced by Stein. In this work Timmer gives evidence for the contribution of the reflexes to the tremor. However, there is no evidence in the data that reflex loops primarily cause the tremor. Reflex loops alter the frequency, relaxation time, and amplitude of existing oscillation to some degree. Therefore, Timmer supports that the primary cause of physiological tremor is the resonant behaviour of the hand and a synchronised EMG activity that is either generated centrally or due to the recruitment strategy of motoneurons.

Other researchers tried to model the behaviour of a limb affected by tremor. In 1973, Randall [16] suggested linear stochastic autoregressive processes to model the tremor data. Randall used digitised samples of hand acceleration in order to construct a stochastic time series model for hand tremor. This study showed that of the part of tremor variance which can be explained by the difference equation, the major portion was explained by a second-order difference equation having a natural frequency of about 10 Hz (ω_n) and a damping ratio of about 0,10 (ξ). The unexplained part was essentially white noise and would be the random noise driving the frequency-selective part, as illustrated by the following second-order difference equation:

$$y''(t) + 2\xi\omega_n y'(t) + \omega_n y(t) = 0$$

The different manifestations of normal or physiological tremor have been extensively analysed during the past decades. In particular, Morrison [17] studies the effect of progressively supporting upper limb segments in the physiological tremor at the finger tips. He also addressed the issue of inter and intra-limb correlation of the acceleration measures. Elble [18] carefully examined the relation between hand tremor and the 8–12 Hz component of finger tremor, that is the range of frequency that received the most attention, largely because of the work of Lippold [9] and Halliday and Redfearn [7].

Previous work [15] showed that physiological tremor can be regarded as a linear stochastic process consistent with the interpretation of a mechanical system of the hand as a damped linear oscillator driven by a uncorrelated firing of motoneurons. These results suggest that features, especially of nonlinear dynamics, may lead to a good classification of the different kinds of tremor. Gantert conduced a study to establish mathematical tests toward an objective classification of tremors on the basis of waveform characteristics of accelerometer recordings. The results indicated that features other than amplitude and peak frequency can provide better criteria to classify the various kinds of postural hand tremors.

Pathological tremor exhibits a nonlinear oscillation that is not strictly periodic. Timmer et al. [19] investigated whether the deviation from periodicity is due to nonlinear deterministic chaotic dynamics or due to nonlinear stochastic dynamics. To do so, Timmer applied various methods from linear and nonlinear time series analysis to tremor time series. The results of the different methods suggest that the considered types of pathological tremors represent nonlinear stochastic second order processes. Finally, Timmer investigated whether two earlier proposed features capturing nonlinear effects in the time series allow for discrimination between two pathological forms of tremor for a much larger sample of time series than previously investigated.

According to Timmer, tremor time series span a large range of different behaviours. The physiological tremor of healthy subjects represents a linear second order stochastic process driven by white noise originating from uncorrelated firing of motoneurons [14]. The enhanced physiological tremor can either be described by a stochastic linear second order process driven by colored noise or non-linear stochastic delay differential equation depending on the degree of the contribution of a central pacemaker or of reflexes [19]. Timmer also supports the view that pathological tremor, like essential, Parkinson, and Kinetic tremor, exhibits a nonlinear oscillation. The oscillation is not strictly periodic. Timmer is researching the possible reasons for the deviation from a strictly periodic, limit cycle type of dynamics. According to Timmer et al. [19] oscillation of the pathological tremors is best described by a nonlinear stochastic second order process. This affirmation contradicts the suggestion of Gresty et al. [20] that the variability observed in the considered pathological tremors should be interpreted as caused by frequency and/or amplitude modulated harmonic oscillators.

The different manifestations of normal or physiologic tremor have been extensively analysed during the past decades. As described below, there is sufficient evidence that supports the fact that oscillating limbs behave as second order biomechanical systems relating input muscle torque to output limb position. Adelstein [21] in his thesis gives evidence of this second order behaviour:

a) The frequency of the oscillating peaks in subjects with normal physiologic tremor is inversely related to the square root of the lumped sum of the inertia of the body part and the externally added mass, i.e. $\omega_n \propto \sqrt{1/I}$.
b) The effect of varying the limb stiffness (of the forearm) results in a frequency change directly related to the equivalent stiffness, i.e $\omega_n \propto \sqrt{K}$.

Modelling of the second order behaviour gives rise to estimations of the damping ratio that results in $\zeta \approx 0,1$. Likewise, the unloaded limb natural frequencies are reported to be:

– Finger ≈ 25 Hz
– Wrist $\approx$ 8–10 Hz
– Forearm $\approx$ 2–3 Hz

As stated above, most of the literature focusses on physiological tremor. Physiological tremor consists of two distinct oscillations that are present in normal subjects. The first component is a biomechanical resonant component and the second one is a frequency invariant component.

The frequency of the biomechanical component is largely determined by the limb inertia and stiffness. It is generally assumed that the background EMG fluctuation due to the random firing of motor units excites each limb in resonance. Following this model, the biomechanical characteristics of each limb define the filtering characteristics of the associated second order model.

On the other hand, the frequency invariant component is always associated to a modulation of the motor unit activity in the frequency band of 8 to 12 Hz. This frequency band shows a very low change when external loads (inertial or stiffness) are applied to the limb.

From the point of view of the applicability of tremor-suppression orthosis, we are mainly interested in Essential, Parkinsonian and kinetic tremor. The characteristic patterns of these forms of tremor are reviewed.

2.2.1. Essential tremor

Essential tremor is typically symmetric affecting both upper limbs, in particular the hands and forearms [1]. Koller [40] states that it appears most frequently in the hands, being abduction-adduction of fingers and flexion-extension of wrist typically affected. In some cases it also affects pronation-supination of the forearm.

It is postural and kinetic and a rest component is rarely found and always in the most advanced cases. It is always accompanied by a rhythmic entrainment of the motor units' discharge that forces the affected body into oscillation. This results in rhythmic bursts in the EMG of the involved muscles. Mechanical loading has little effect on the frequency characteristics of Essential tremor, typically <1 Hz [22].

The frequency band of Essential tremor differs according to the reporting author, while Jain [41] gives relatively narrow frequency band of 5 to 8 Hz, Cooper [42] and Elble [22] give 4 to 12 Hz and 3 to 11 Hz respectively.

For a given patient the Essential tremor frequency decreases at a rate of 0.06 to 0.08 Hz yearly, however, Elble [22] found that tremor frequency is a function of age but not of duration illness. The age, a, and frequency, f, of unit motor entrainment in the forearms of these patients show the following linear relationship:

$$f = -0.077a + 11.4.$$

Following with the characterisation of the essential tremor, Elble [22] found a logarithmic relationship between tremor amplitude, A, frequency, f, and the amplitude of the EMG, v:

$$\log(A) = \alpha \log(f) + \beta \log(v)$$

Few figures were found in the literature about Essential tremor amplitude. Just Elble [22] reports that the mean value of the tremor acceleration amplitude was 2 m/s^2. This figure was obtained with the forearm pronated and supported in such a way that only motion about the wrist was allowed.

In our literature review we have only found estimations on the power for Essential tremor due to Kotovsky [43]. They assume the tremor to follow a sinusoidal pattern with a frequency of 3 Hz and tremor amplitude of $\pm 30^\circ$ (severe tremor). They adopt a worst case assumption to establish an upper bound on the power that should be dissipated by an active orthosis. They assume that:

1. The muscle torque exciting the tremor is not reduced with the addition of the orthosis.
2. All the muscle torque in the presence of the orthosis must be dissipated by the orthosis itself (none is applied to the elastic and innertial elements).

Under these conditions the power to be dissipated results in 1.7 W.

2.2.2. Parkinsonian tremor

Parkinsonian tremor is a rest tremor affecting flexion-extension of the thumb against the index finger, flexion-extension of the wrist and pronation-supination of the forearm. The voluntary muscle contraction typically suppresses Parkinsonian rest tremor, but it is generally followed by a mild to moderate action tremor.

As reported by Elble [22], in many patients the rest tremor persists during posture and movement, typically with lower amplitude, but with no change in frequency or EMG characteristics. In other patients the action tremor has slightly higher frequency.

The frequency band of this tremor ranges from 3 to 6 Hz, as reported by Jain [41]. Cooper [42] supports that Parkinson tremor is commonly associated with a 4–6 Hz rest tremor that is often asymmetric. It is originally distal and extends to more proximal body parts as Parkinson progresses.

2.2.3. Cerebellar tremor

The most common form of cerebellar tremor is an intention tremor of frequency lower than 5 Hz. The tremor is typically bilateral and symmetric when caused by a degenerative or toxic disorder [42].

The most thorough study on the pattern of intention tremor is due to Adelstein [21]. It was conducted on a group of patients exhibiting intention tremor of diverse etiological origins. It was conducted under two conditions, namely free wrist rotation and complete isometric restrain. The tremor characteristics as reported by Adelstein are as follows:

– The frequency band ranges from 2 to 4 Hz.
– The frequency band is independent of external loading both under additional viscous damping and isometric constrain.
– The EMG shows synchronous bursts in flexors, extensors or both simultaneously.
– Under isometric constrain tremor activity is found in the measured torque.

- All the measured signals (EMG, acceleration and torque) are stationary.
- The comparison of torque densities associated to the isometric tremor spectral peaks and estimated from free oscillation trials indicated that the torque driving the oscillating tremor is independent of the magnitude of externally applied loads.

Other works, see Manyam [23], show that the kinetic cerebellar tremor is characterised by oscillation of variable amplitude and perpendicular to the direction of movement. Proximal muscles are most commonly affected, and the tremor amplitude can reach up to ± 30 degrees. According to Manyam the frequency of cerebellar kinetic is commonly described as being 3–5 Hz, but studies have shown that the frequency of cerebellar is inversely proportional to limb inertia, resulting in frequency being dependent on the part of the affect limb. In the upper extremities, kinetic tremor has a frequency of 3–8 Hz, and in the lower extremities is usually 3 Hz. The truncal tremor usually has a frequency of 2–4 Hz.

2.3. Tremor quantification

A number of papers discuss the quantification of tremor. Quantification of tremor is of clinical interest as an aid to diagnosis and to evaluate objectively the effect of treatment. Hand writing and drawing patterns are often used to examine tremor. Recording such patterns using a digitising tablet has been introduced as one way to provide precise quantification.

Clinical classification of tremor is based on the body parts involved, position of maximum activation, morphology, and frequency. From the point of view of tremor quantification, the two most important factors are the frequency and the amplitude. Frequency of tremor has been often given much importance and is used in classification [44]. Amplitude of tremor is easily quantifiable and is classified as middle, moderate, and severe on various rating scales. It is important to show up that the amplitude of tremor in patients with the same disease may vary and can be increased by physical and emotional stress.

Gao [24] used dynamical systems theory in order to discriminate between essential and Parkinsonian tremors and has shown that pathological tremors can be characterised as diffusional processes. He concluded that the quantities that might be able to discriminate among different pathological tremors should be purely of dynamical origin, since quantities that are purely of dynamical origin characterise more the similarities than the differences among different pathological tremors, as summarized in his studies. Gao used a non-dynamical quantity L/T, which is the ratio between the embedding delay time and the mean oscillation period, and concluded that it is a much more promising figure of merit in discriminating between essential and Parkinsonian tremors. On the other hand, Timmer showed that these kinds of tremor can be characterised as different non-linear processes.

According to Elble [44], tremor is well suited to spectral analysis, the most popular method of tremor quantification, because of its oscillatory characteristic. The idea is to calculate a power spectral density function indicating the signal power at different frequencies across the spectrum. The dominant frequency of tremor is evident in the form of a peak in the power spectral density, while the average tremor amplitude can be determined from the area under the peak. Riviere [25] used a computational method, the weighted frequency Fourier linear combiner (WFLC), for quantification of tremor. This technique rapidly determines the frequency and amplitude of tremor by adjusting its filter weights according to a gradient search method. It provides continual tracking of frequency and amplitude modulations over the course of a test.

Others researchers, i.e. Beuter and Edwards [26,27], focused their studies on the use of time and frequency domain characteristics to discriminate among the various types of tremor. Their studies showed that time domain and frequency domain characteristics can enhance the diagnostic power of tremor and could eventually be used by clinicians and epidemiologists to detect subclinical changes in tremor.

3. Tremor suppression via biomechanical loading

As already pointed out in the introduction, biomechanical loading has appeared as a potential tremor suppression alternative. Biomechanical loading relies on an external device that either passively or actively acts mechanically in parallel to the upper limb. Significant results have been obtained in reducing hand tremor by applying mass, friction, and viscous resistive forces. This can be approached in two ways [45]:

- Isolate the task from the tremorous limb in a frequency selective manner.
- Decrease the amplitude of tremor.

The big challenge in this approach is to distinguish error from intended motion before error cancelling can

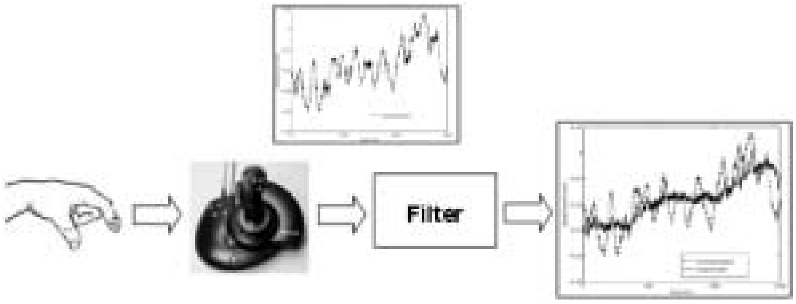

Fig. 2. Scheme of task isolation. Signals retrieved from the joystick are filtered removing the tremorous component from the signal sent to the controller subsystem.

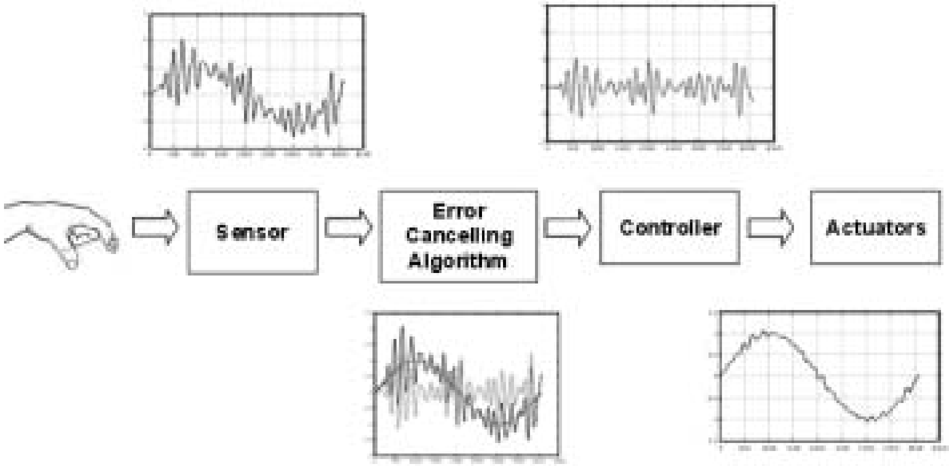

Fig. 3. General overview of an error compensating system. The hand movement is measured by sensors, an error cancelling algorithm discriminate the voluntary movement from the tremorous motion, this information is sent to a controller that generates the actuator commands that interact with the upper limb removing the tremor from the overall movement.

occur. This requires real-time error estimation. There have been studies in recent years on the use of signal filtering for tremor attenuation, primarily dealing with pathological tremor.

3.1. *Isolation of the task from tremorous limb*

Task isolation of the tremorous limb could be done by filtering both mechanically or electronically. The issue of physically isolating the task from the tremorous limb has been attempted in the context of tremor in patients with ataxia. It involves the manipulation through a series linkage (conceptually similar to suspensions) or using systems that execute the task [43].

The concept of electronically isolating of a task has been largely used in the microsurgery research area. The two approaches available for this application are either filtering the command signal during teleoperation or active oscillation control. In the teleoperative scenario, the human operates a master interface. Input signals from this master are processed to drive a slave manipulator, which performs the surgery. If tremor motion can somehow be distinguished from intended motion, it can be removed from the drive signal sent to the slave. In this approach the following drawbacks can be mentioned, which make attenuating tremor motion be more interesting:

- Tactile sensation is virtually eliminated.
- Control of tool dynamics is more difficult.
- Tool force is limited by the series mechanism compliance.
- The series linkage is potentially intrusive.

Activities such as driving a wheelchair, manipulating a rehabilitation robot or accessing a computer require a standard input device (mice, joystick. . .). In this case, the goal is filtering out tremor related frequencies in the tracking signal obtained from input devices when used by patients affected by pathological tremor, generating an intermediate signal which is sent to the controlled subsystem (wheelchair, robot arm or cursor), as illustrated in Fig. 2. This approach is similar to the teleoperative scenario.

3.2. Decreasing the amplitude of tremor

The approach of actively suppressing tremor is based on tremor reduction devices that act mechanically in parallel to the oscillating limb. They are energy dissipaters that apply a shunt load between the limb and a fixed reference frame. These are fixed-based restraints and they can be divided in ambulatory and non-ambulatory devices.

The effects of load and force on tremor have received considerable attention by the research community. Among others, David [28], has studied the effects of mechanical loading on the amplitude of the movement in different frequency ranges. He concludes that both load-dependent and load-independent oscillations of the affected limb occur.

Viscous damping appears as one of the most promising approaches for tremor suppression. Rosen et al have shown experimentally that people who suffer from tremor are disable because the magnitudes of their purposeful actions [29], what suggest that a loading orthosis could be designed to selective suppress tremor while allowing voluntary movement.

Adelstein, in his thesis [21], has conducted a thorough analysis of the applicability of viscous loading as a means for active reduction of intention tremor. He modelled the upper limb as a second order biomechanical systems relating input muscle torque to output limb position:

$$Ms^2 + Cs + D = T(s)$$

This model helps us understand how the application of biomechanical loading could reduce upper limb tremor. Figure 4 illustrates the effect of adding mass and damping to the upper limb movement.

As a result, Adelstein reports that significant and steady reductions of tremor amplitude are observed as the viscous loading is increased. The following results are worth mentioning:

- The tremor amplitude shows steady and significant decreases as the damping constant is varied from the unload condition up to a maximum of 1,13 (N-m)/(rad/s).
- All the patients presented a resonance peak in the range of 2–4 Hz. The magnitude of these peaks in the accelerometer spectral density showed the same trend to decrease as the damping was increased.
- The magnitude of the transfer function between reference and tracking response was used as a measure of the amplitude fidelity during the tracking task. This fidelity factor was constant and independent of the damping setting.
- Mean tracking phase lags of the transfer function showed a slight growth of 2 degrees on average from the unloaded to maximally loaded cases.

Biomechanical loading for tremor reductions can be approached either by ambulatory orthotic devices or by non-ambulatory table or wheelchair mounted devices. The former approach is characterized by selective tremor suppression through internal forces at particular joints, while the later relies on global application of external forces that leads to the overall tremor reduction.

While wearable tremor suppression devices are already a matter of research, non-ambulatory systems have lead to commercial products, see, for instance, the so-called Neater Eater [46]. In addition, the MIT damped joystick [47], the controlled Energy-Dissipation Orthosis, CEDO [48], or the Modulated Energy Dissipation Arm, MED, (cited in [43]), are realizations of non-ambulatory wheelchair mounted tremor suppression prototypes.

As far as wearable tremor suppression concepts are concerned, just the well-know wearable tremor-suppression orthosis [43], has been reported in the literature. This is a passive damping loading device, which acts mechanically in parallel to the wrist in flex-extension. It completely constrains both wrist abduction-adduction and prono-supination. In general, as noted by Kotovsky [43], the design goals of any tremor suppression orthosis should consider:

- *Selective tremor reduction:* the orthosis should minimise involuntary limb movements while preserving the voluntary limb motion.
- *Compliance:* the elastic stiffness of the orthosis should be minimised so that the user does not have to impart significant force levels to hold non-neutral positions.
- *Safety:* should not harm the user limb during use.
- *Range of motion:* the orthosis should not limit the amplitude of voluntary wrist motion.

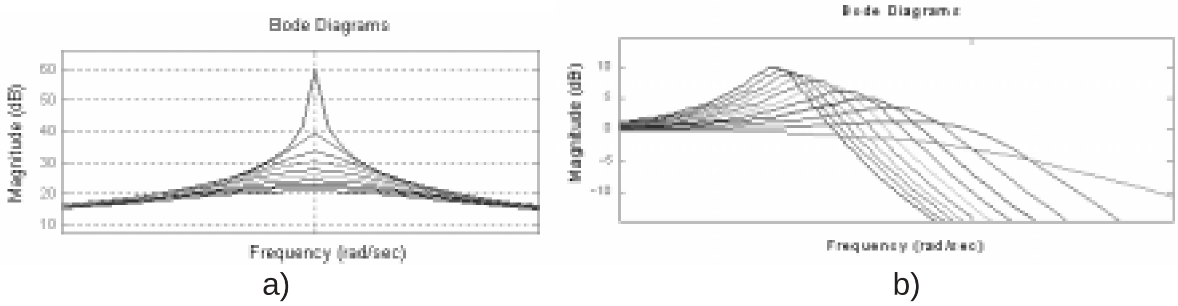

Fig. 4. Modification of biomechanical characteristics of the upper limb. a) Applying viscous to the motion; b) adding mass to the upper limb.

– *Comfort:* the orthosis should impose minimal loads (weight, moment of inertia...) and should not produce unreasonable pressures on the skin. Another important point is the damper dissipation tremor power in order to assure that the orthosis remains comfortable to wear.
– *Ease of use:* Final solutions should be easy to don, adjust, use and remove.

A number of issues remain to be investigated regarding the effect of sustained, permanent application of viscous loads. Arnold et al. [30] note that muscle fatigue, carryover of attenuation effects after damping is removed and long term strengthening of muscles due to orthosis imposed exercise all require study.

3.2.1. Estimation techniques

As already pointed out, both ambulatory and non-ambulatory concepts can be implemented though passive and active systems. In active systems [46] and [48], active actuators generate an equal but opposite motion, based on a real time estimation of the involuntary component of motion, actively compensating and effectively subtracting the tremor for the overall motion.

In passive concepts, a mechanical damper is used [43,47], thus the dissipative force usually results from shear forces at the damper's fluid. One of the main drawbacks of passive systems is that the dissipative force is also loading the patient's voluntary motion. As a consequence, the user feels a mechanical resistance to the motion. Even though in active systems this could be avoided, to the authors' knowledge, the prototypes reported in the literature do not filter out voluntary motion, and thus, the dissipative force also affects voluntary motion.

Estimation techniques have been developed for tremor suppression. The most used algorithm to estimate tremor is the weighted-frequency Fourier linear combiner (WFLC) developed by Riviere in the context of actively counteracting physiological tremor in microsurgery. The WFLC is an adaptive algorithm that estimates tremor using a sinusoidal model, estimating its time-varying frequency, amplitude, and phase [31]. Riviere also investigated the application of neural networks to augment manual precision by cancelling involuntary motion [32]. The system proposed by Riviere is conceptually different to tremor suppression through biomechanical loading. Riviere's approach is based on an active system that acts in series with the surgeon. It computes the tremorous component and modifies the tool position accordingly.

Other techniques have been used in order to separate the voluntary and involuntary motion. Riley and Rosen [33], among others, have investigated low pass filtering. Most of this work involves either finite impulse response linear equalizers trained on tremor recordings [36], or linear low-pass or bandstop filtering approaches, which aim to attenuate the full frequency band of tremor, while passing frequencies below 1 or 2 Hz, which are assumed to be voluntary. Linear filters are successful in attenuating tremor in many applications, but their inherent time delay [34] is a drawback in active noise control, with its demand for zero-phase compensation. Furthermore, low-pass filtering is not sufficiently selective to form an explicit tremor model for use as an actuator command. Effective active tremor compensation requires a zero-phase system which generates a specific tremor estimate to be used as an opposing vibration.

A different approach is proposed by Gonzalez [35] who addresses the problem of smoothing the tracking signal through the optimal design of a signal equaliser. Designing an optimal equaliser is a mathematical optimisation problem in which a filter of a given class is optimised according to the maximisation of a measure of closeness between reference and tracking signal. The author defines and uses the F-MSEd index as the closeness indicator, see next section. They developed a digi-

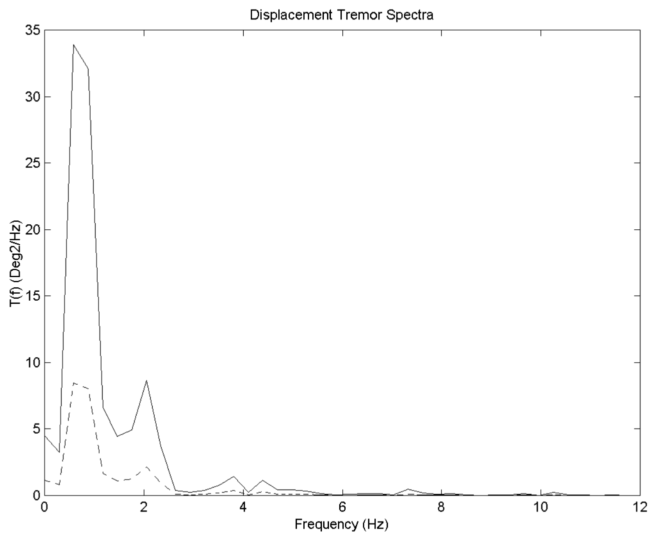

Fig. 5. Tremor power spectral density $T(f)$. The continuous line represents the conditioned tremor power spectral density of the undamped motion, while the dashed line shows the same indicator of the damped motion.

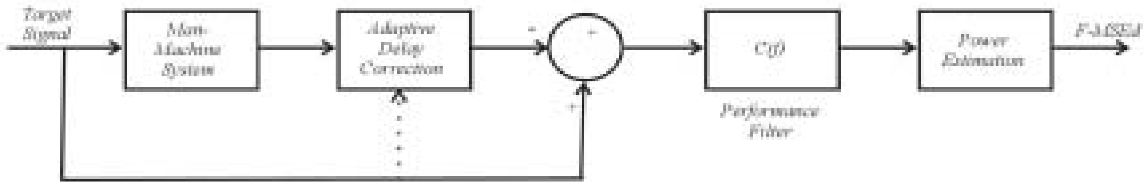

Fig. 6. Sequence of operations required for computing F-MSEd.

tal filtering algorithm that utilised an optimal equaliser to equilibrate a tremor contaminated input signal and a target signal that the subject attempted to follow on a computer screen [36]. Most attempts to develop such systems have involved teleoperative approaches, such as those of Hunter et al. [37] and Schenker et al. [38].

Pledgie [39] developed a methodology that incorporates quantitative performance criteria as well as position, rate, and acceleration feedback into the design of a non-adaptive tremor suppression through impedance control system. In spite of the above mentioned, Pledgie concluded that non-adaptive tremor suppression systems that utilise impedance control to achieve a specified reduction in tremor power can be successfully designed when accurate open-loop human-machine models are available.

To the authors' knowledge, no active compensating orthosis has been published so far, but some work is being conducted with this technology due the advantage of offering a small resistant force to the voluntary motion. However the drawback of consuming more energy than the passive one is to be taken into account. This challenge is being faced by the European project DRIFTS. The DRIFTS project (EU QoL QLK6-CT-2002-00536) was launched on April 2002 with the main objective of validating the concept of active suppression of pathological tremor through ambulatory orthotic devices [51].

4. Evaluation of tremor suppression technologies

When developing a tremor suppression system, some tools for evaluating the performance of the orthosis are required. The patient does the final evaluation of the system but this evaluation is very subjective, therefore, some tools for objectively evaluating the performance of the orthosis are required. These indicators quantify the tremor suppression orthosis effectiveness. According to the above-presented goals in the design of a tremor suppression orthosis, the tremor reduction evaluation process should consider:

– Selective reduction of tremor frequencies.
– Zero phase lag suppression.

Table 1
Tremor characteristics

Tremor type	Affected limbs	Frequency pattern	Mechanical characteristics	Remarks
Essential (postural and kinetic)	Abduction-adduction of fingers; Flexion-extension of wrist; Pronation-supination of forearm	5 to 8 Hz (Jain et al.), 4 to 12 Hz (Cooper et al.), 3 to 11 Hz (Elble) Invariant upon mechanical loading ($<$ 1 Hz)	Mean tremor amplitude of 13 rad/s^2 (Elble); Amplitude increases with aging or progression; Power estimation: 1.7 W (wrist $\pm 30°$ @ 3 Hz).	Frequency decrease with time (0.06–0.08 Hz yearly); Rhythmic bursts in EMG Symmetric.
Parkinsonian (rest)	Flexion-extension of fingers, i.e. "pill-rolling movement"; Flexion-extension of wrist; Pronation-supination of forearm	3 to 6 Hz		Suppression under voluntary muscle contraction; Originally distal, extending to proximal body parts
Cerebellar (intention and kinetic)	Proximal muscles are more commonly affected; Flexion-extension of wrist	2 to 4 Hz; Invariant upon external loading	Muscle torque driving the oscillation independent of external loads; Tremor amplitude up to $\pm 30°$.	Bilateral and symmetric Synchronous EMG in flexors, extensors or both;EMG, acceleration and torque are stationary.

– Preservation of the reference motion amplitude of tracking tasks (posture is a particularisation of tracking task in which the reference is set to zero).

The most general parameter to evaluate tremor reduction is by direct comparison of the RMS amplitude of the uncompensated limb motion with that of the compensated motion. Other approaches rely on comparing the undamped and damped tremor power. Rosen [48] et al. examined the magnitude and phase of the transfer function relating the target and response trajectories averaged over the target frequencies, to monitor the selectivity of the tremor reduction. Riviere [31] computed the uncompensated and compensated error by subtracting the estimated voluntary motion from the uncompensated and compensated, relatively. Then, the uncompensated and compensated error RMS values were compared. In the opinion of Riviere, this provides a more stringent evaluation that accounted for motion at all frequencies, rather than only within the tremor band. Pledgie [39] used the tremor movement power as a measure of the tremor attenuation during a task specific execution in his closed-loop system.

Gonzalez [36] reports that standard measures of the tracking error such as the Mean Square Error (MSE) or the Mean Absolute Error (MAE) are severely affected by tracking delays. For instance, delays in the range of 0.2 s can result in reductions of the MSE on the order of 30% depending on the target used. On the other hand, delays are always present in any tracking task and they are not always indicators of poor performance.

Other performance indicators try to overcome this problem by considering the tracking components that are linearly coherent with the reference as a normal result of the tracking task and attribute the task error just to non-coherent tracking components. This is the case of Adelstein [21] that proposed the ratio between the RMS of the conditioned tremor power spectral density under external viscous damping (max. D) and free oscillations ($D = 0$):

$$\sqrt{\int T(f,D)df \Big/ \int T(f,D)df_{D=0}}$$

The conditioned tremor power spectral density, T(f), is obtained from the weighted spectrum of the subject response in such a way that incoherent activity, i.e. activity not linearly related to the reference signal, is weighted heavily. In addition, this conditioned spectrum considers only those frequencies above the range of voluntary motion:

$$T(f) = \begin{cases} 0 & f < f_c \\ M_{rr}(f)[1-\gamma_{tr}^2(f)] & f \geqslant f_c \end{cases}$$

Where, $M_{\mathrm{rr}}(f)$ is the power spectral of response records, $\gamma_{\mathrm{tr}}^2(f)$ is the coherence factor and f_c is the cut off frequency.

The definition is limited to tremor frequencies by defining f_c as the frequency up to which 99% of the reference power is present. Figure 5 illustrates the use of the conditioned tremor power spectral density as an indicator; it shows the trend to decreasing tremor with addition of compensating system.

Adelstein also defines a signal-to-noise ratio, R, between voluntary motion and tremor:

$$R = \sqrt{\int_0^{f_c} |M_{\mathrm{tr}}(f)|df} \Big/ \sqrt{\int_{f_c}^{\infty} T(f)df}$$

This signal-to-noise ratio, R, relates the power of the voluntary activity (cross-correlated with the target) to the tremor variance. Less tremor or greater purposeful tracking power lead to higher R, this can be viewed as quantifying better tracking performance.

A different approach is proposed by Gonzalez [3], based on a three-step approach, as illustrated in Fig. 6. First, the tracking delay is corrected according to a delay estimator; secondly, a delay corrected tracking error is computed subtracting the aligned tracking signal form the target; and thirdly, a linear time invariant filter, called the performance filter, is applied to enhance the frequencies of interest. The mean square value of the filtered output constitutes the measure of performance and it is called the F-MSE$_d$ (filtered mean-square error with delay correction).

5. Conclusions

The present paper introduced a thorough literature review in the topic of technological management of pathologic tremor, specifically focused on upper extremity tremor. A summary of the main characteristics of upper-limb tremor can be seen in Table 1.

Tremor is very disabling and some kinds of tremor can be efficiently removed by means of pharmacological tremor, therefore the design of non-invasive wearable orthotic devices can represent a useful solution. Tremor is still an unknown issue. Physiological tremor has been deeply studied, and is quite well described in the literature, but there are still some mismatches between different authors about its sources. The pathological kinds of tremor are even less known than physiological tremor. Some kinds of pathological tremors are better described (i.e. Parkinson tremor), but again aetiology is unknown in most cases.

There is no consensus in the optimal way to objectively measure tremor in the upper limb. Accelerometers have been widely used but they are efficient only for measuring postural and rest tremor, due to the coupling of gravity component. The authors believe that gyroscopes and goniometers among other kinds of instrumentation can be very useful for the objective measurement of tremor.

Although pathological tremor signal seems to be quite non-linear, approximations of tremor as a linear second-order system have proven to be sufficient to implement some strategies of tremor suppression. One big issue regarding the future implementations for tremor suppression is the behaviour of the user when the tremor suppressing device is active. This issue has not received sufficient attention in the literature. The displacement of tremor to other segments (proximal in the limb or contra-lateral) or some other side effects should be taken into account. Therefore some a-priori successful techniques can produce unexpected results.

Until now, approaches to overcome tremor problems can be classified between:

– Digital suppression of tremor in input interfaces with computers.
– Fixed apparatus intended for specific tasks (drawing, eating, etc).

Very little effort has been made in ambulatory devices. Just the realization of a passive ambulatory system [43] is reported in the literature. In the authors' opinion this lack of ambulatory devices could be explained by the immature state of some actuator technologies necessary to produce an ambulatory device. There are some projects trying to solve these difficulties with the use of novel technologies such as magnetorheological fluids and/or electro active polymers [51].

Most of the approaches reported in the literature are based on increasing the damping of the biomechanical oscillating system (tunning brakes, viscous friction, etc). The authors believe that active approaches could be more comfortable to the users, reducing the perceived sensation of braking produced by the passive approaches. The challenge relies on the power consumption. Aesthetics and weight are the other big issues that an ambulatory device needs to solve in order to overcome the status of laboratory orthoses.

References

[1] A. Anouti and W. Koller, Tremor disorders: diagnosis and management, *The Western Journal of Medicine* **162**(6) (1995), 510–514.
[2] National Institute of Neurological Disorders and Stroke, 2001, Accessed May 09, 2002. Available at: http://www.ninds.nih.gov/health_and_medical/disorders/tremor_doc.htm.
[3] M. Aisen, et al., Glutethimide treatment of disabling action tremor in patients with multiple sclerosis and traumatic brain injury, *Arch Neurol* **49** (1991), 513-515.
[4] D. Caparros-Lefebvre, S. Blond and P. Vermesch, et al., Chronic thalamic stimulation improves tremor and l-dopa induced dyskinesias in Parkinson's disease, *J Neurol Neurosurg Psychiatry* **56** (1993), 268–273.
[5] K. Friston, R. Frackowiak, F. Mauguière and A.L. Benabid, Thalamic stimulation and suppression of Parkinson tremor. Evidence of a cerebellar deactivation using positron emission tomography, *Brain* **116** (1993), 267–279.
[6] J. Marshall and E.G. Walsh, Physiological tremor, *J Neurol. Neurosurg. Psychiatry* **19** (1956), 260.

[7] O.J.C. Lippold, J.W.T. Redfearn and J. Vuco, The rhythmical activity of groups of motor units in the voluntary contraction of muscle, *J. Physiol.* **137** (1957), 473.

[8] J.E. Randall and R.N. Stiles, Power spectral analysis of finger acceleration tremor, *J. Appl. Physiol.* **19** (1964), 357.

[9] O.C.J. Lippold, Oscillation in the stretch reflex arc and the origin of the rhythmical, 8–12 Hz component of physiological tremor, *J. Physiol.* **206** (1970), 359.

[10] Y. Matsumoto Joseph, W. Dodick David, N. Stevens Lorna, C. Newman Randall and E. Caskey Patrick, Fjerstad Wayne. Three-dimensional measurement of essential tremor, *Movement Disorders* **14**(02) (1999), 288–294.

[11] J. Davis Bradley, O'Connel John. Shoulder, elbow and wrist components of physiologic tremor amplitude as measured using a laser penlight, *European Neurology* **43** (2000), 152–154.

[12] R.B. Stein, M.N. Oguztöreli, Tremor and other oscillations in Neuromuscular systems, *Biol. Cybernetics* **22** (1976), 147–157.

[13] R.N. Stiles, Mechanical and neural feedback factors in postural hand tremor of normal subjects, *J. Neurophysiol* **44**(1) (1980), 40–59.

[14] J. Timmer, M. Lauk, Pfleger and G. Deuschl, Cross-spectral analysis of physiological tremor and muscle activity: I Theory and application to unsynchronized electromyogram, *Biol. Cybern.* **78** (1998), 349–357.

[15] G. Gantert, Honerkamp and J. Timmer, Analysing the dynamics of tremor time series, *Biol. Cybern.* **66** (1992), 479–484.

[16] J.E. Randall, A stochastic time series model for hand tremor, *J. appl. Phys.* **34** (1973), 390–395.

[17] S. Morrison and K.M. Newell, Postural and resting tremor in the upper limb, *Clin Neurophysiol* **111**(14) (2000), 651–663.

[18] R.J. Elble and E. Randall James, Mechanistic components of normal hand tremor, Physiology Section, *Medical Sciences Program, Indiana University* (1997).

[19] J. Timmer, S. Häußler, M. Lauk and C.H. Lücking, Pathological tremors: Deterministic Chaos or non-linear stochastic oscillators? *CHAOS* **10** (2000), 278–288.

[20] M. Gresty and D. Buckwell, Spectral analysis of tremor: understanding the results, *J Neurol Neurosurg Psychiatry* **53** (2000), 976–981.

[21] B.D. Adelstein, *Peripheral mechanical loading and the mechanism of abnormal intention tremor*, MIT thesis, 1981.

[22] R.J. Elble, Essential tremor frequency decreases with time, *Neurology* **55**(10) (2000), 1547–1551.

[23] B.V. Manyam, Uncommon forms of tremor, in: *Movement Disorders: Neurologic Principles and Practice*, R.L. Watts and W.C. Koller, eds, New York: McGraw-Hill, Inc., 1997, pp. 387–403.

[24] J.B. Gao, Tung Wen-wen, Pathological tremors as diffusional processes, *Biological Cybernetics* **86** (2002), 263–270.

[25] N. Riviere Cameron, G. Reich Stephen and V. Thakor Nitish, Adaptive Fourier modelling for quantification of tremor, *Journal of neuroscience methods* (1997), 77–87.

[26] R. Edwards, Beuter Anne. Using time frequency characteristics to discriminate physiologic and Parkinsonian tremors, *Journal of Clinical Neurophysiology* **16** (1999), 484–494.

[27] R. Edwards, Beuter Anne. Using time domain characteristics to discriminate physiologic and Parkinsonian tremors, *Journal of Clinical Neurophysiology* **17**(1) (1999), 87–100.

[28] D.E. Vaillancourt and K.M. Newell, Amplitude changes in the 8–12 Hz, 20–25 Hz and 40 Hz oscillations of finger tremor, *Clinical Neurophysiology* **111**(10) (2000), 1792–1801.

[29] M. Rosen and B. Aldenstain, The effect of mechanical impedance on abnormal intention tremor, in: *Proceedings of the 9th Annual Northeast Bioengineering Conference*, N.Y. Elmsford, New York: Pegamon Press, Inc., 1981.

[30] A. Arnold and M. Rosen, Evaluation of a controlled energy dissipation orthosis for tremor suppression, *J Electromyogr Kinesiol* **3**(3) (1993), 131–148.

[31] C.N. Riviere, R.S. Rader and N.V. Thakor, Adaptive Cancelling of Physiological Tremor for Improved Precision in Microsurgery, *IEEE Transactions on Biomedical Engineering* **45**(7), (1998).

[32] C.N. Riviere and K. Khosla Pradeep, Augmenting the human-machine interface: improving manual accuracy, *Proc IEEE Int, Conf, on Robotics and Automation, New Mexico* (1997), 20–25.

[33] P.O. Riley and M. Rosen, Evaluating manual control devices for those with tremor disability, *J. Rehabil. Res. Dev.* **24** (1987), 99–110.

[34] A.V. Oppenheim and R.W. Schaefer, Discrete-time Signal Processing. Englewood Cliffs, *NJ: Prentice-Hall* **5** (1989), 204.

[35] J.G. Gonzalez, E.A. Heredia, T. Rahman, K.E. Barner and G.R. Arce, Optimal digital filtering for tremor suppression, *IEEE Transactions on Biomedical Engineering* **47**(5) (2000), 664–673.

[36] J. Gonzalez, E. Heredia, T. Arman, K. Barner and G. Arce, Filtering involuntary motion of people with tremor disability using optimal equalisation, ıtProc. IEEE Int. Conf. On Systems, Man, and Cybernetics **3**(3) (1995).

[37] I.W. Hunter, T.D. Tilemachos, S.R. Lafontaine, P.G. Charrete, L.A. Jones, M.A. Sagar, G.D. Malllinson and P.J. Hunter, A teleoperated microsurgical robot and associated virtual environment for eye surgery, *Presence* **2** (Fall 1993), 265–280.

[38] P.S. Schenker, E.C. Barlow, C.D. Boswell, H. Dias, S. Lee, T.R. Ohm, E.D. Paljug, G. Rodriguez and S.T. Charles, Development of a telemanipulator for dexterity enhanced microsurgery, *Proc. 2nd Intl. Symp. Med. Robot Comput. Assist. Surg.* (1995), 81–88.

[39] S. Pledgie, K. Barner and S. Agrawal, Tremor suppression through impedance control, *IEEE Transactions on rehabilitation engineering* **8**(1) (2000).

[40] W.C. Koller and K.L. Busenbark, Essential tremor, in: *Movement Disorders: Neurologic Principles and Practice*, R.L. Watts and Koller, eds, New York: McGraw-Hill, Inc., 1997, pp. 365–375.

[41] S.S. Jain and S.C. Kirshblum, Movement disorders, including tremors, in: *Rehabilitation Medicine: Principles and practice*, 2nd ed., eds, Joel A and DeLisa JB, Lippincott Company, Philadelphis, 1993.

[42] G. Cooper and R. Rodnitzky, The many forms of tremor, *Precise classification guides selection of therapy Postgrad Med* **108**(1) (July, 2000), 57–58, 61–64, 70.

[43] J. Kotovsky and M.J. Rosen, A wearable tremor-suppression orthosis, *J. Of Rehabilitation Research and Development* **35**(4), (1998).

[44] R.J. Elble, The pathophysiology of tremor, in: *Movement Disorders: Neurologic Principles and Practice*, R.L. Watts and W.C. Koller, eds, New York: McGraw-Hill, Inc., 1997, pp. 405–417.

[45] W. Koller, *Handbook of Parkinson's disease*, New York: Marcel Dekker, 1987.

[46] J. Michaelis, Introducing the neater eater, *Action Res* **6**(1) (1988), 2–3.

[47] J. Hendriks, M. Rosen and S. Huang, A second-generation joystick for people disable by tremor. Proceedings of the 14th Annual RESNA Conference; 1991 Jun 21–26; Kansas City, MO Washington, DC: RESNA Press, 1991, 248–251.

[48] M.J. Rosen, A.S. Arnold, I.J. Baiges, M.L. Aisen and S.R. Eglowstein, Design of a controlled-energy-dissipation orthosis (CEDO) for functional suppression of intention tremors, *J. Of Rehabilitation Research and Development* **32**(1) (1995), 1–16.
[49] H. Forssberg, P.E. Ingvarsson, N. Iwasaki, R.S. Johansson and A.M. Gordon, Action tremor during object manipulation in Parkinson's disease, *Movement Disorders* **15**(2) (2000), 244–254.
[50] P.G. Bain, L.J. Findley, P. Atchison, M. Behari, M. Vidailhet, M. Gresty, J.C. Rothwell, P.D. Thompson and C.D. Marsden, Assessing tremor severity, *J Neurol Neurosurg Psychiatry* **56**(8) (1993), 868–873.
[51] M. Manto, M. Topping, M. Soede, J. Sanchez-Lacuesta, W. Harwin, J. Pons, J. Williams, S. Skararup and L. Normie, Dynamically Responsive Intervention for Tremor Suppression, *IEEE Engineering in Medicine and Biology* **22**(3) (June, 2003), 120–132.