

Attenuation of Pathological Tremors by Functional Electrical Stimulation I: Method

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In this study we explored the possibility of suppressing pathological tremors using closed-loop functional electrical stimulation (FES) to activate the tremorogenic muscles out-of-phase. A displacement signal monitored with a transducer was filtered so as to be “tuned” to the tremor frequency at the wrist or elbow. The filtered signal was used to amplitude-modulate the electrical stimulation. The design process was based on measurements of the open-loop frequency response characteristics of the forearm and hand to stimulation of the elbow and wrist flexors and extensors in a number of subjects. These data allowed us to identify closed-loop configurations, which attenuated 2–5 Hz tremors substantially, while only minimally attenuating functional movements in the 0–1 Hz range. There was a fairly delicate balance between efficacy and the risk of instability. However, designs were identified that offered enough tremor suppression and adequate immunity to muscle/load variations for the technique to be considered seriously for clinical application.

Keywords— Tremor, Electrical stimulation.

INTRODUCTION

About 50% of pathological tremors cannot be adequately controlled by medication (21). The only available alternative to control such tremors has been inertial loading of the affected limb (3). However, this generally tends to be viewed as a last resort, and often proves unsatisfactory, because the amount of loading required to attenuate a tremor by a useful amount usually weighs the limb down to the point where voluntary movement is impeded and the limb muscles rapidly fatigue. Viscous loading has been suggested as a further alternative, (8) the idea being to attach a device to the limb, which would offer an impedance to movement proportional to limb velocity.

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Pilot experiments along these lines have been promising, but so far the approach has not been implemented practically. Furthermore, it is likely that purely viscous loading would not be selective enough to impede pathological tremors whose power content is in the frequency range 2–5 Hz without also significantly impeding useful movements in the 0–1 Hz range. A combination of inertial, resistive, and viscous loading (8), providing a mechanical impedance with a sharply tuned band-pass characteristic, might be another option, but its practical implementation within acceptable size limits might prove very difficult.

Another approach reported recently (2,5) is to use closed-loop functional electrical stimulation (FES) to activate the tremorogenic muscles out-of-phase, thereby counteracting the tremor. The block diagram of Fig. 1 shows the basic idea: the neuronal activation of muscle generated by the patient's nervous system may be viewed as a disturbance, which the loop resists. However, only the fast tremorous components of movement are to be attenuated, leaving slower intentional movements unaffected. If $H(s)$ represents the transformation of neural activation (originating either from the subject's nervous system or from the electrical stimulator) into displacement of the inertial load by the muscle, the problem is to design the feedback filter $F(s)$ so that the overall loop gain $F(s)H(s)$ is maximal in the tremor frequency range, minimal at the lower frequencies of useful intended movement and consistent with stability in closed-loop operation. Closed-loop FES has been explored before to linearise the responses to externally generated movement command signals (1,15,16,19). Note that the present approach differs in principle from these systems, in that the sole purpose of the loop is to resist a particular component of movement *generated by the patient*.

With careful filter design, it is possible to attenuate 2–5 Hz tremors substantially, while only minimally attenuating functional movements in the 0–1 Hz range. A knowledge of the response characteristics $H(s)$ of the load-moving muscles is an essential prerequisite for the design process, the details of which are presented in this paper. Clinical trials are described in the companion paper (6).

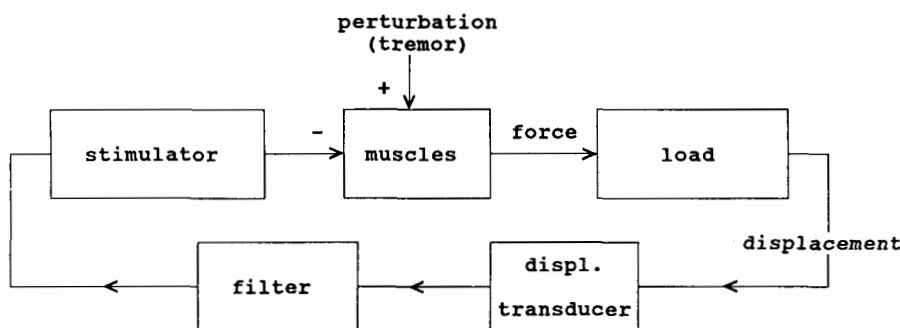


FIGURE 1. Block diagram of a closed-loop system, which attenuates tremor with electrical stimulation of an antagonist pair of muscles. The load comprises the viscoelastic and inertial impedance of the forearm and/or hand plus any external load being moved. With appropriate filter design, the loop resists tremor but not slow intended movements.

METHODS

Frequency Response Characterization of Load-Moving Muscle

Experimental Approach. The first step in the procedure was to establish the frequency response characteristics of the muscles moving the hand and the forearm. The responses to modulated electrical stimulation of antagonist groups of flexor and extensor muscles acting about the wrist and elbow were analysed in seven normal subjects, using methods described in detail previously (4). Subjects gave their written consent to the experiments, in accordance with the requirements of the University of Alberta Human Ethics Committee and the Declaration of Helsinki. For wrist movements, the right forearm was strapped to a comfortable horizontal support in a half-supinated position. The hand was strapped to an extension of the support, which could pivot freely in the horizontal plane about a fulcrum located under the wrist joint. For the elbow, the arm was stabilized and the forearm was free to pivot on a light horizontal support (Fig. 2). In both cases, displacement was monitored with a low-noise optical transducer. Surface electrodes (typically 2×3 cm) were used as cathodes to activate the flexors and extensors, selectively. These were either pregelled self-adhesive electrodes (Chattanooga Corp.) or moistened pads pressed onto the skin by thin stainless-steel plates. For forearm muscle stimulation, the indifferent electrode (anode)

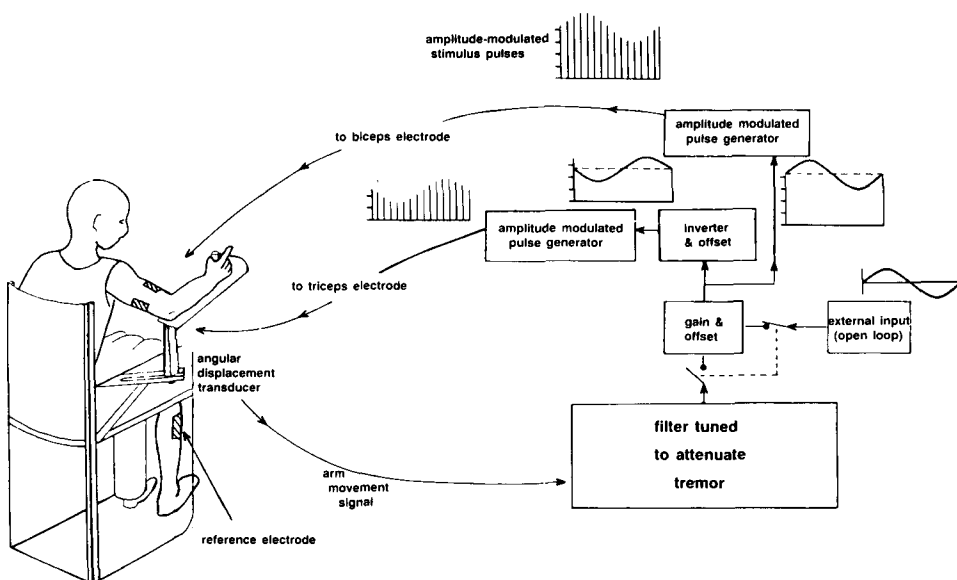


FIGURE 2. Experimental setup for forearm movements. Armrest pivots horizontally; displacement signalled by a transducer. Triceps and biceps brachii are selectively stimulated with surface electrodes. Stimulus pulse trains are interleaved, and amplitude-modulated so that as flexor stimulation increases, extensor stimulation decreases. Control is either open loop (external input: for characterization of frequency response of muscle/load) or closed loop (controlled by filtered movement signal). Filter is designed so that electrical stimulation is out-of-phase with tremor cycle, opposing and attenuating the tremor, while minimally affecting slower, useful movements.

consisted of a moistened sponge strip wrapped around the wrist. For arm muscles, the indifferent was a large moistened pad attached to the right leg anteriorly over the proximal end of the tibia. This location was found to be convenient, and avoided the cross talk between flexor and extensor activation, which was encountered if the indifferent was placed on an arm location (19).

Subjects were instructed to relax their arms and not react to the electrical stimulation. In initial trials, reflexive or voluntary reactions did sometimes occur. These were recognizable in that they were nonreproducibly related to the stimulus profiles. Within a few minutes of training, all subjects were able to suppress these reactions completely. In most trials, stimulation was not painful, though in some closed-loop trials with filters, which produced brief transients, pain was experienced, and so the use of these filters was discontinued (see later). Because painful levels of stimulation were avoided, we are confident that the responses documented in this and the subsequent paper were not contaminated by reflexive or voluntary reactions to pain.

Initial Isometric Adjustments. The following setting-up procedures were performed with either flexor stimulation alone or extensor stimulation alone. A low-compliance force transducer was attached to a wristlet to measure isometric elbow torque (4) or to a bar at the metacarpophalangeal joint to measure isometric wrist torque. The amplitude of the 30/s train of 100 μ s stimulus pulses was adjusted in the range 20–100 mA to produce a steady “offset” contraction corresponding to 2.5%, 5%, or 10% of maximal voluntary torque. The pulse train was now sinusoidally amplitude-modulated at 1 Hz to produce a sinusoidally varying torque, with a depth of modulation of about $\pm 2.5\%$ of maximal voluntary torque, centered about the offset torque.

When these adjustments had been made for the flexors and extensors separately, the force transducer was removed, allowing free movement of the extremity. Both channels of stimulation were switched on. Because the flexor and extensor pulse trains were interleaved, there was no interaction between the electric fields of individual pulses, ensuring independence of flexor and extensor activation. Modulation of the two channels was reciprocal (i.e., as flexor stimulation increased, extensor stimulation decreased). Because the stimulus parameters had been adjusted to produce equal flexor and extensor offset torques, the resulting movement was a sinusoid centered around the neutral position (90° for elbow, 180° for wrist). In practice, a slight deviation of the centre position occurred when the two channels were first switched on together. This was because of a slight mismatch between flexor and extensor offset torques, which were readily corrected with small adjustments of the stimulus offset parameters. Note that the aim of the offset procedure was to ensure a minimal level of co-contraction at the neutral position so that there would be no “dead zone” as one muscle became inactive and its antagonist became active.

Frequency Response Analysis. The subjects’ wrist or elbow movements and concomitant stimulator command signals were recorded on cassette tape (TEAC R61 instrumentation recorder) and some trials were videotaped. Movement responses to sinusoids of constant modulation depth and frequencies ranging from 0.5–10 Hz were logged. Subsequently, selected segments of the analogue data were digitised using a Cambridge Electronic Design (CED) 1401 laboratory interface linked to an Olivetti M28 microcomputer. The data were digitised, displayed, and printed (Hewlett Packard Laserprinter) with the use of CED “Massavg” software. This allowed us to align individual tremor cycles and collect them together into an average, typically of 10 cy-

cles. In some cases power spectral analysis was performed with CED "Waterfal" software. The amplitude and phase of the movement response was plotted against modulation frequency. Details of the software may be obtained from Cambridge Electronic Design, Science Park, Milton Road, Cambridge CB4 4FE, United Kingdom.

Filter Design. With the help of control systems software, (23) linear transfer functions were developed, which gave good fits to the frequency response curves for elbow and wrist. Next, treating these transfer functions as part of a feedback loop, we designed a compensating filter tuned to maximize the open loop gain in the range 2–5 Hz while minimizing net phase lag in the 0–10 Hz range. The aim was for the closed loop (which includes the muscle/load and the filter) stably to resist 2–5 Hz movements, while responding minimally to slow voluntary movements or high-frequency transducer noise. In the first instance, it was unclear as to whether suitable filter transfer functions would depend critically on parametric variations in the load-moving transfer functions of individual subjects. As will be seen, parametric sensitivity fortunately turned out to be quite low. The filter was realized with an array of linear operational amplifiers built into a purpose-designed prototyping device.

Closed-loop Experiments. The system was first evaluated in normal subjects performing voluntary tasks ranging from slow, goal-directed movements to rapid, tremor-like ones. In some experiments, a video recording of a moving-bar target was replayed to the subject, the surface of the video screen being just beyond the subject's fingertips. The attenuation of the amplitude of these various classes of movement during short periods of closed-loop stimulation of unexpected onset and duration was measured. After some experience with the system, a number of trials were conducted on patients with essential tremor, Parkinsonian tremor, and cerebellar tremor; these are described in the companion paper.

RESULTS

Open-Loop Trials

As just stated, the technique relies on accurately controlled electrical stimulation of the tremorogenic muscles, and as such, the first requirement was an accurate description of the way the load-moving muscles respond to smoothly modulated trains of electrical stimulus pulses. Figure 3 shows the frequency response characteristics of sinusoidal wrist flexion-extension movements in six normal subjects evoked by modulated electrical stimulation as described in the Methods. Separate symbols identify the amplitude and phase of the responses of each subject to command signal frequencies ranging from 1–12 Hz. The response amplitudes are expressed in decibels in relation to the response amplitude at 1 Hz. Phase is expressed in relation to the sinusoidal modulating signal. These trials were performed with 5% background (offset) co-contractions (i.e., the sinusoidal movements were elicited by modulating flexor and extensor stimulation about tonic levels, which separately produced torques 5% of maximal voluntary torque). The response characteristics were similar across subjects, showing low-pass properties, with 3 dB attenuation at about 2 Hz. f_{180} , the frequency at which the phase lag was 180° , lay between 3 and 4 Hz. As will be seen later, the f_{180} parameter has a special significance for closed-loop control, in that if the gain around the loop exceeds 1 at this frequency, positive feedback occurs, and the control system exhibits instability, manifested by oscillation.

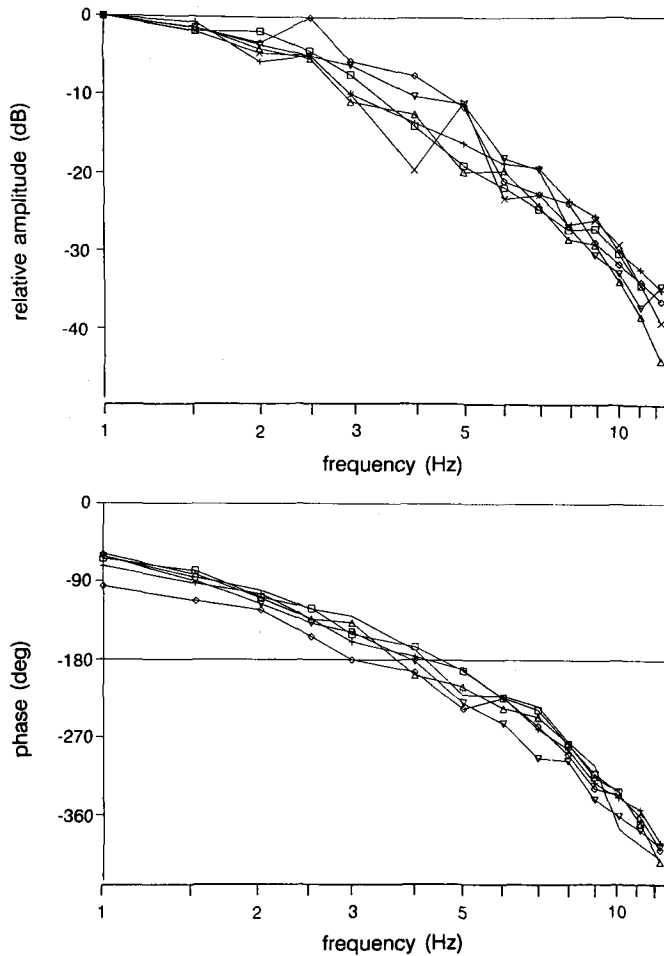


FIGURE 3. Frequency response characteristics of wrist flexion-extension movements in six normal subjects evoked by modulated electrical stimulation. Response amplitudes expressed in dB relative to the response amplitude at 1 Hz. Phase relative to that of the sinusoidal modulating signal. Note low-pass properties, with 3 dB roll-off at about 2 Hz and 180° phase lag at 4 Hz.

Next we fitted a linear transfer function to the averaged wrist data of Fig. 4. This was done with a control systems software package, Alcon, which computes and displays Bode plots of functions comprising up to 24 terms. In a large number of trial-and-error iterations, we developed the transfer function whose amplitude and phase characteristics are plotted in Fig. 4, and which is described in the frequency domain by the equation:

$$\frac{5 \times 10^9}{(s + 8.5)(s + 55)^5}, \quad (1)$$

where s is the Laplace operator.

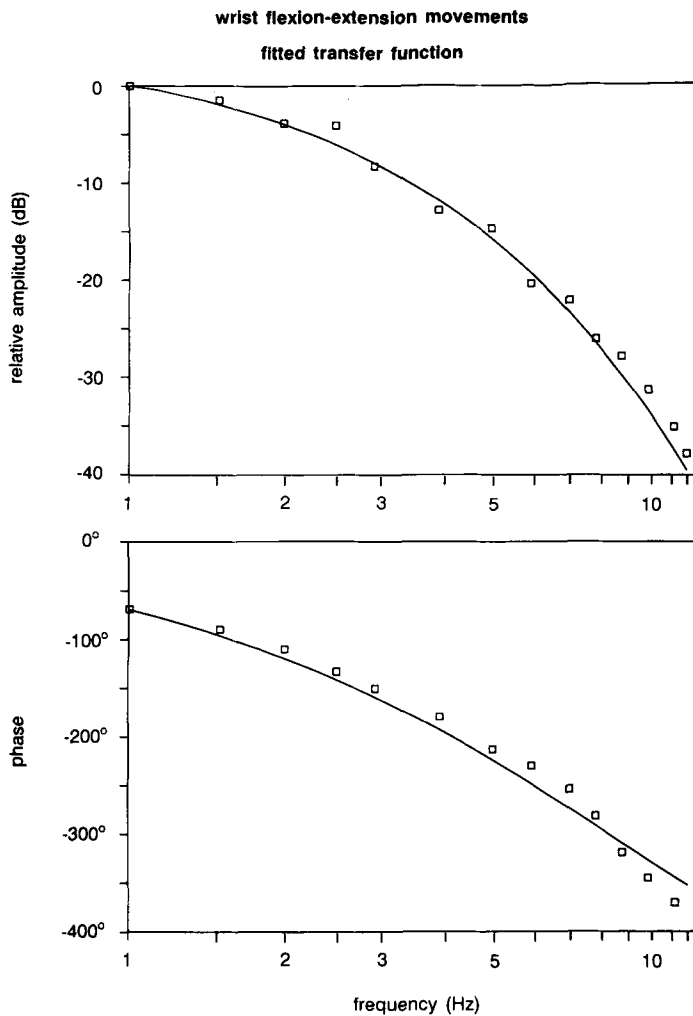


FIGURE 4. Averaged wrist data of Fig. 3 (squares) with fitted transfer characteristic described in text.

At the outset we did not know whether there would be a unique solution to this curve-fitting problem or not. In the event, we found a number of transfer functions with differing configurations of poles and zeroes, which gave good fits both to the amplitude and phase data. Furthermore, when these were used in combination with filters in the analysis of closed-loop stability to be described below, they led to similar conclusions regarding parameters such as f_{180} and gain margin. Thus, there is nothing absolute about the transfer functions we derived, nor did we attempt a mathematically rigorous optimization of them. Nonetheless, we feel that functions derived in this way are sufficiently representative and accurate for the present application. The general form of the response characteristics is, of course, a low-pass filter, as expected from previous measurements in both animal and human load-moving muscle (see (4) for review).

A similar procedure was followed for movements about the elbow. Figure 5 shows the averaged data from six subjects. In this case we measured the frequency response characteristics for background (offset) torques of 2.5% and 5% of maximal voluntary torque, respectively. The fitted transfer function represented in the figure is the following:

$$\frac{30,000}{(s + 12)^4} \quad (2)$$

Filter Design for Closed-Loop Stimulation

The next task was to develop filters that, when combined with the above model transfer functions, would result in frequency response curves with sharp peaks at

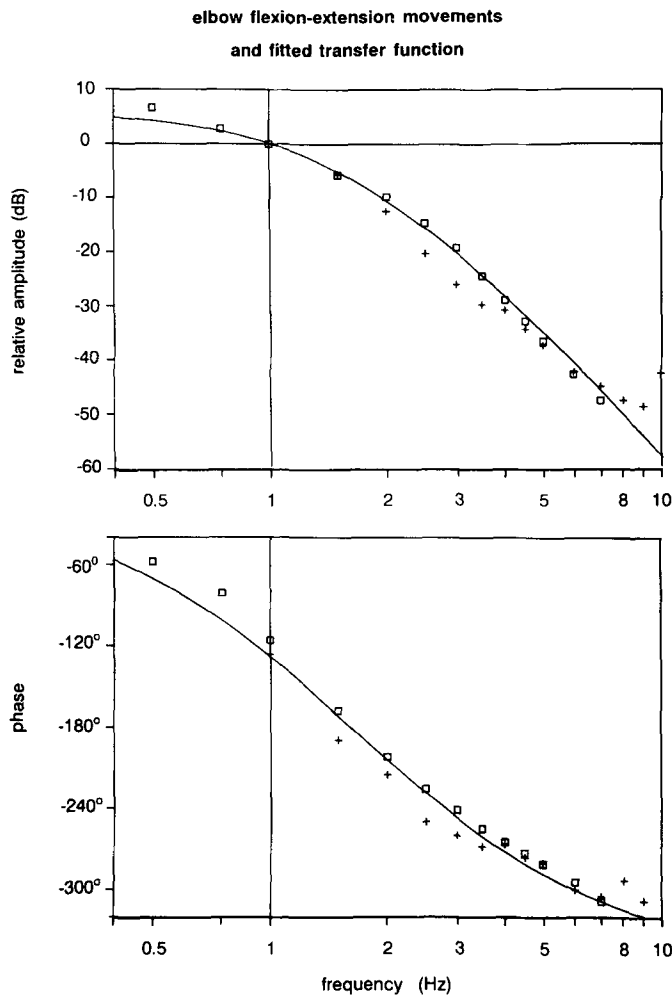


FIGURE 5. Averaged elbow characteristics with fitted transfer function. Squares: modulation about a 5% background co-contraction; crosses: modulation about a 2.5% background co-contraction.

tremor frequencies of 2–4 Hz, together with phase shifts consistent with stable closed-loop operation. In the closed loop, the tremor may be viewed as an external perturbation, which the loop resists and attenuates (by out-of-phase activation of the selfsame muscles *producing* the tremor). Intuitively, a notch filter tuned to the tremor frequency seemed the most logical design to try. Figure 6a shows the individual and combined characteristics of the wrist model (Eq. 1 above) and a 3 Hz notch filter, the transfer function of which was:

$$\frac{1,100}{(s + 0.5 + j20)^2(s + 0.5 - j20)^2} \quad (3)$$

The amplitude characteristic of the combined (wrist + notch filter) function showed the desired peak at 3 Hz. The gain margin (the difference between peak amplitude and amplitude at f_{180}) was 23 dB. The significance of this is as follows. Instability occurs in a closed feedback loop when the gain around the loop exceeds 1 at f_{180} . In the example of the notch filter characteristic of Fig. 6a, if the amplitude (gain) at f_{180} were raised to 1 (0 dB), the *peak* amplitude at 3 Hz would rise to 23 dB (13 in absolute terms); that is, instability would just occur when the gain at 3 Hz was 13 (the gain margin). Thus, a loop gain of say 12 should in theory be attainable at 3 Hz without making the system oscillate at f_{180} . Now a negative feedback loop attenuates an external perturbing input by a factor of:

$$(1 + \text{open loop gain}) \quad (4)$$

(i.e., the response to the perturbation is reduced by this factor compared to the response in the absence of feedback). So with a gain of 12 permissible from a stability point of view, the use of this particular notch filter in the closed loop should in theory have resulted in a 13-fold attenuation of tremor. We implemented the filter with analogue circuitry, and set up a closed-loop experiment of the type illustrated in Fig. 2 with a normal subject. However, we were disappointed to find that although the subject found it more difficult to produce 3 Hz tremor-like movements, there were long-lasting after-oscillations, which grossly interfered with voluntary movements of 0.5 to 1 Hz frequency content. Indeed, any voluntary movements at all gave rise to such after-oscillations. With hindsight, the reason for this is fairly obvious: although the loop incorporating the notch filter does not become completely unstable until the gain at 3 Hz exceeds 13, it is grossly under-damped even at gains as low as 1 or 2. This was confirmed in computed step responses and in root locus plots, which revealed trajectories starting from close to the imaginary axis and slowly approaching it as gain increased. We tried mitigating this by shifting the starting positions of the notch filter poles away from the j -axis to $(s + 2 \pm j20)$, but this merely reduced the gain margin to about 10 dB, without sufficiently damping the system.

A more satisfactory filter is shown in Fig. 6b. Although the combined wrist + filter transfer function had a less selective bandpass characteristic than the notch filter, and the gain margin for closed-loop operation was only 9 dB; this filter operated well, allowing gains of 2 to 2.5 to be used in patients (3 to 3.5-fold tremor attenuation), without noticeable after-oscillations or attenuation of slow voluntary movements. The transfer function of this filter was:

$$\frac{100(s + 3.3)^6(s + 100)^2}{(s + 15)^6(s + 300)^2} \quad (5)$$

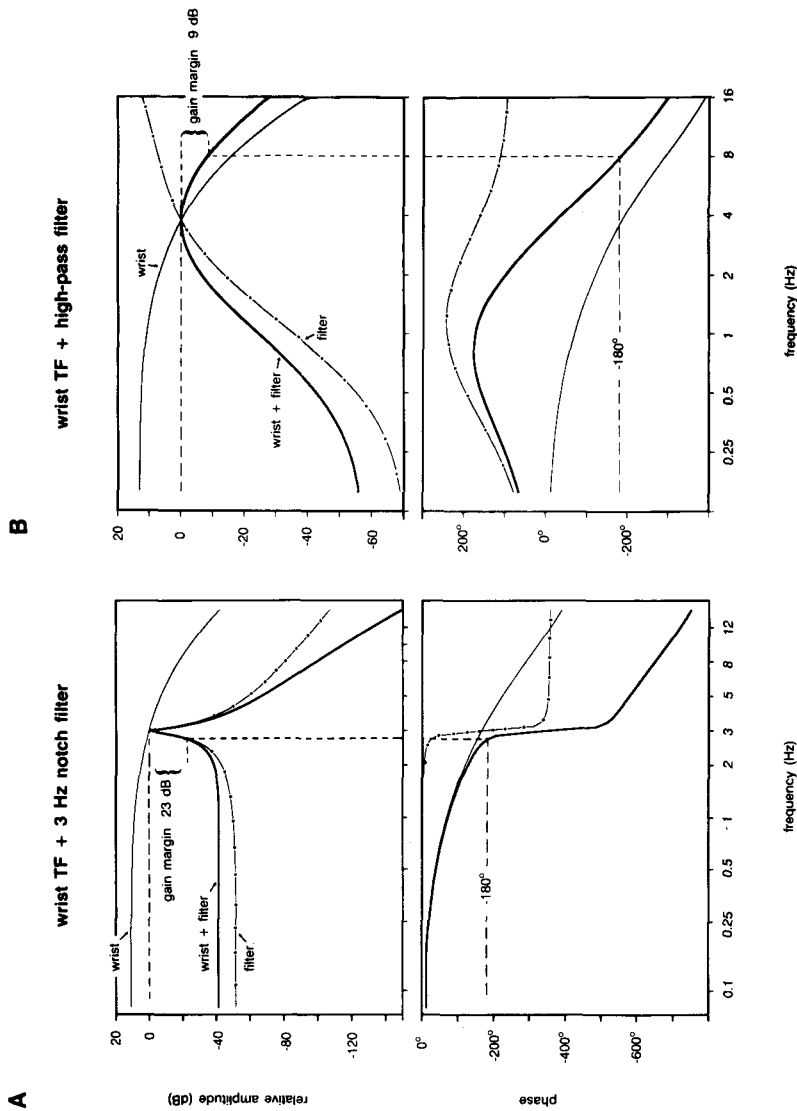


FIGURE 6. Two filters (a: notch, b: high-pass) designed to cause maximal attenuation of 3–4 Hz tremor, with minimal attenuation of 0.1–1.0 Hz “useful” movements. Thin lines: wrist model (Fig. 4); dash-dot: filter; thick lines: combined characteristics. Amplitudes normalised to 0 dB at peaks of combined characteristics. Relative amplitude at f_{180} (frequency at which net phase lag is 180°) is “gain margin,” a measure of potential efficacy of loop in attenuating tremor. Paradoxically, though gain margin was greater in a, overall performance of system b was superior.

In fact, this was a truncated version of the following design, which gave a slightly better gain margin of 11 dB (4-fold tremor attenuation):

$$\frac{800(s + 3.3)^6(s + 100)^4}{(s + 15)^6(s + 300)^4} \quad (6)$$

However, in closed-loop trials on two normal subjects and two patients, this full version, though very effective at attenuating tremor, tended to produce large high-frequency transients of stimulation, which were uncomfortable and at times even painful with the surface electrodes used. Furthermore, stability was less robust than with the truncated version, in that there was a tendency for high-frequency (10–12 Hz) oscillations to develop at certain wrist orientations. Pain is generally less of a problem with intramuscular stimulation, so this design might be suitable for systems based upon implanted electrodes (7,17).

Filters were also designed for attenuation of tremor about the elbow. We first developed the filters shown in Fig. 7b for a 3-Hz tremor. The gain margin of 15 dB (corresponding to an absolute value of 5.6) would in theory allow a maximal tremor attenuation of 6.6:1, though in practice we found that instability tended to occur above gains of about 3. Again, this was a truncated version of an even more effective filter, which offered a closed-loop gain margin of 25 dB; however, in trials this had the same drawback of high-frequency transients as the optimal wrist filter. The transfer function describing the 3 Hz truncated design is:

$$\frac{800(s + 4)^6(s + 100)^2}{(s + 21)^6(s + 310)^2} \quad (7)$$

Closed-Loop Trials

Prior to evaluating these systems in patients, we tested and optimised them in normal subjects performing tremor-like and slow tracking movements. Figure 8 shows three such tests of the 3-Hz elbow system with the loop gain adjusted to be about half (–6 dB) that which caused instability (from Fig. 7b the loop gain was, therefore, 15 dB – 6 dB = 9 dB; that is, an absolute value of 3). The 5-Hz tremor-like movements were attenuated by about 3.5:1, which is close to the expected attenuation of 4:1 for a loop gain of 3. Figure 8 bottom panel shows that slow (0.4 Hz) self-paced movements were only slightly attenuated, which is of course an important requisite of a functionally useful tremor-suppression system.

As will be seen in the following paper, the 3-Hz truncated elbow filter worked well in normal subjects mimicking a 3-Hz tremor, but unsatisfactorily in patients with cerebellar tremor. In reviewing our results, we found that the cerebellar tremors had been of a somewhat lower frequency (1.5–2.5 Hz), so for future work we have developed the 2-Hz truncated design shown in Fig. 7a.

$$\frac{50(s + 2.5)^6(s + 50)}{(s + 12)^6(s + 150)} \quad (8)$$

Figure 9 shows similar tests of the wrist system. Tremor-like movements were attenuated by about 2:1 for a gain adjusted to 6 dB below instability, and about 3:1 at

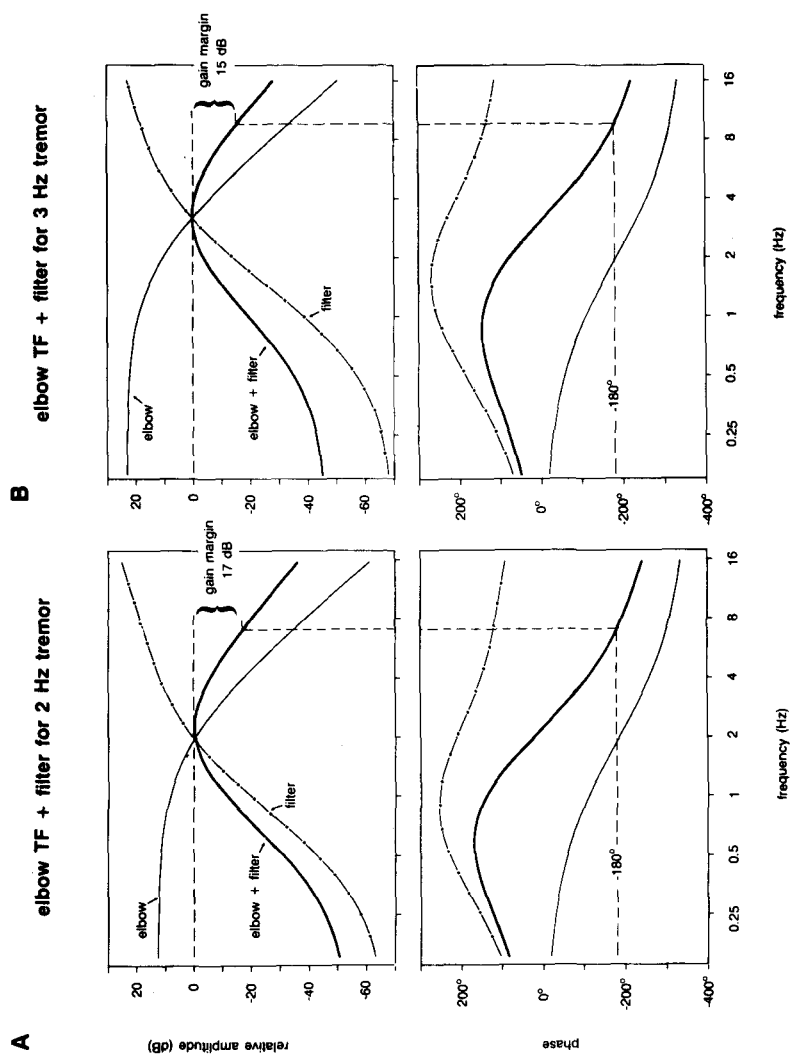


FIGURE 7. Filters designed to attenuate (a) a 2-Hz; and (b) 3-Hz tremor about the elbow. Thin lines: elbow model of Fig. 5; dash-dot: filter; thick lines: combined characteristics.

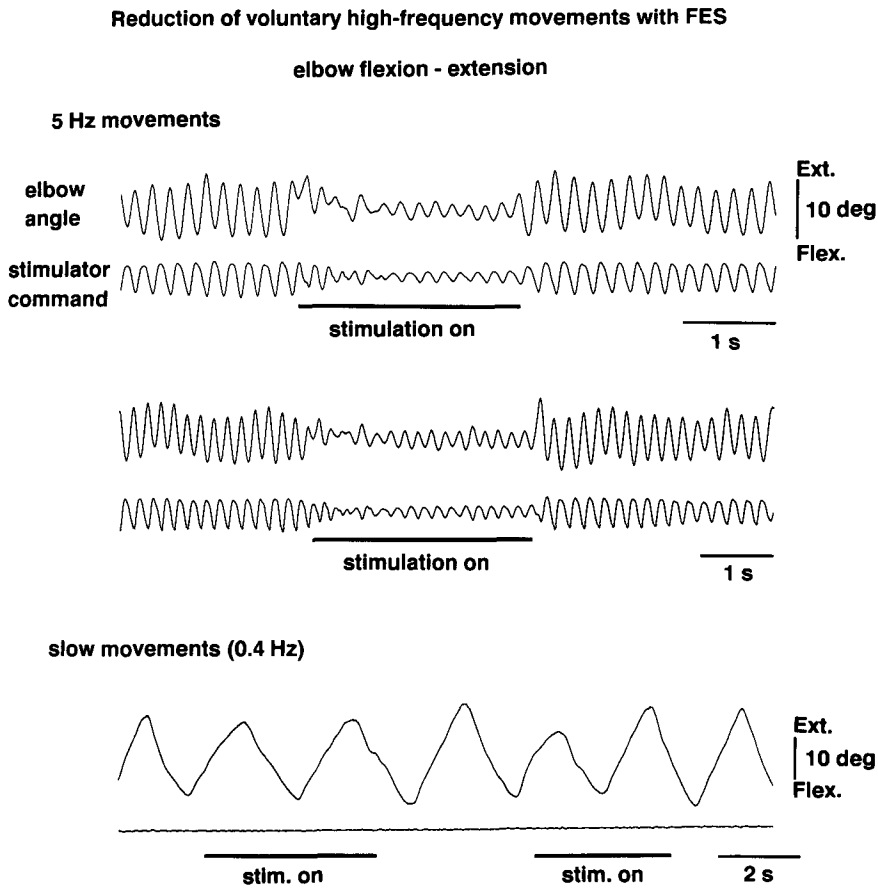


FIGURE 8. Normal subject performing tremor-like (top) and slow self-paced triangular movements (bottom) with and without closed-loop stimulation using the system in Figure 7b (horizontal bars indicate periods when stimulator was on). Tremor was strongly attenuated, while the slow movements (ca. 0.4 Hz) were little affected.

3 dB below instability. These attenuations were in line with the corresponding predictions based on the 9 dB gain margin shown in Fig. 6.

Effect of Inertial Loads

A system of the type just described would be of little practical use if tremor suppression were reduced, or if instability occurred whenever the patient's hand became inertially loaded. *A priori*, this seemed quite possible in that the dynamic response characteristics of muscle are known to be load-dependent (11): large loads could cause changes in the combined frequency characteristic, substantially reducing overall gain at the tremor frequency and destabilizing the closed loop. We addressed this issue by first measuring the open-loop frequency responses at wrist and elbow in normal subjects with loads consisting of 50-mm-wide strips of lead wrapped around the wrist or proximal phalanges. The weights were selected to cover the range of common house-

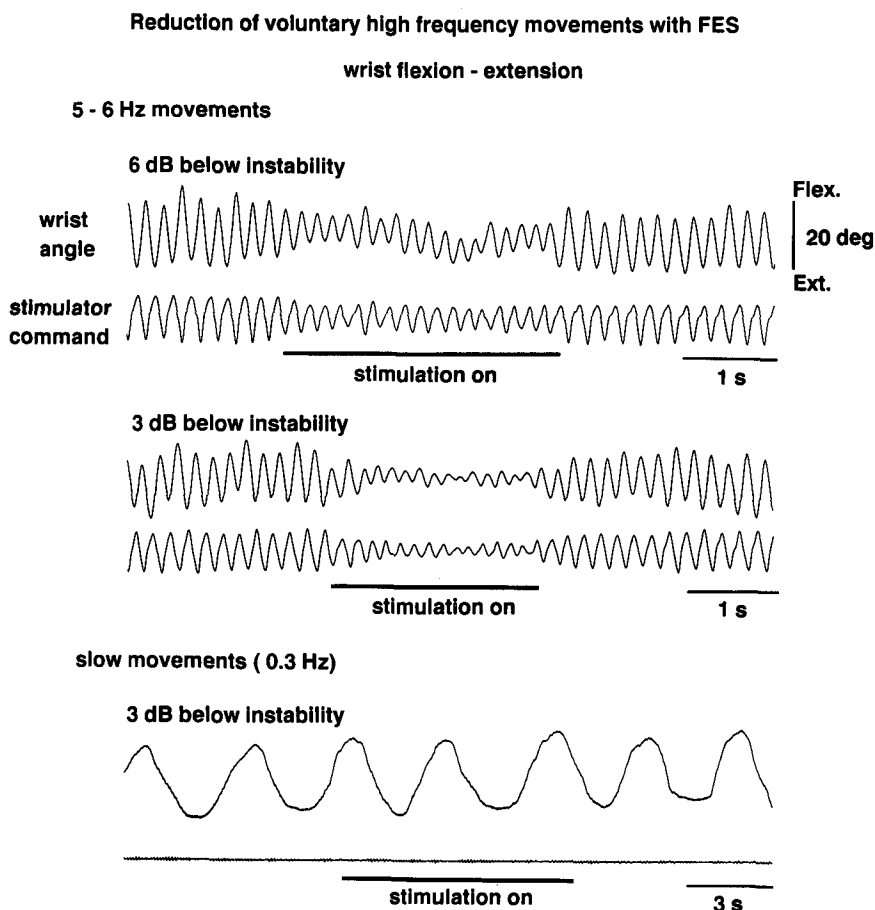


FIGURE 9. Similar tests to Fig. 8 of the wrist system of Fig. 6B. Tremor was attenuated by about 2:1 for a gain adjusted to 6 dB below instability, and about 3:1 at 3 dB below instability (accurate spectral analysis of attenuation is presented in the following paper). Slow movements were little affected.

hold objects. For elbow trials, up to six 0.35-kg weights were attached concentrically about the wrist (i.e., the net load was increased in 0.35-kg increments to a maximum of 2.1 kg). Assuming mean forearm moments of inertia about the elbow of 0.07 kg/m^2 (12), we calculated that each 0.35-kg wristlet increased the moment of inertia on average by 20%, the maximal increase therefore being 120%. The frequency response characteristics in Fig. 10a illustrate the main result, that loading in this limited but utilitarian range caused changes in amplitude of maximally 10 dB and in phase of maximally 60° . Larger changes were seen at the wrist, where from one to four of the same 0.35-kg weights were wrapped around the fingers. From Winter's data (22) we estimated the mean moment of inertia of our subjects' hands to be 0.005 kg m^2 , and each weight to add 0.004 kg m^2 . (i.e., 80% increments to a maximum of 320%). At this maximal load, changes of up to 20 dB in amplitude and 120° in phase were recorded (Fig. 10b).

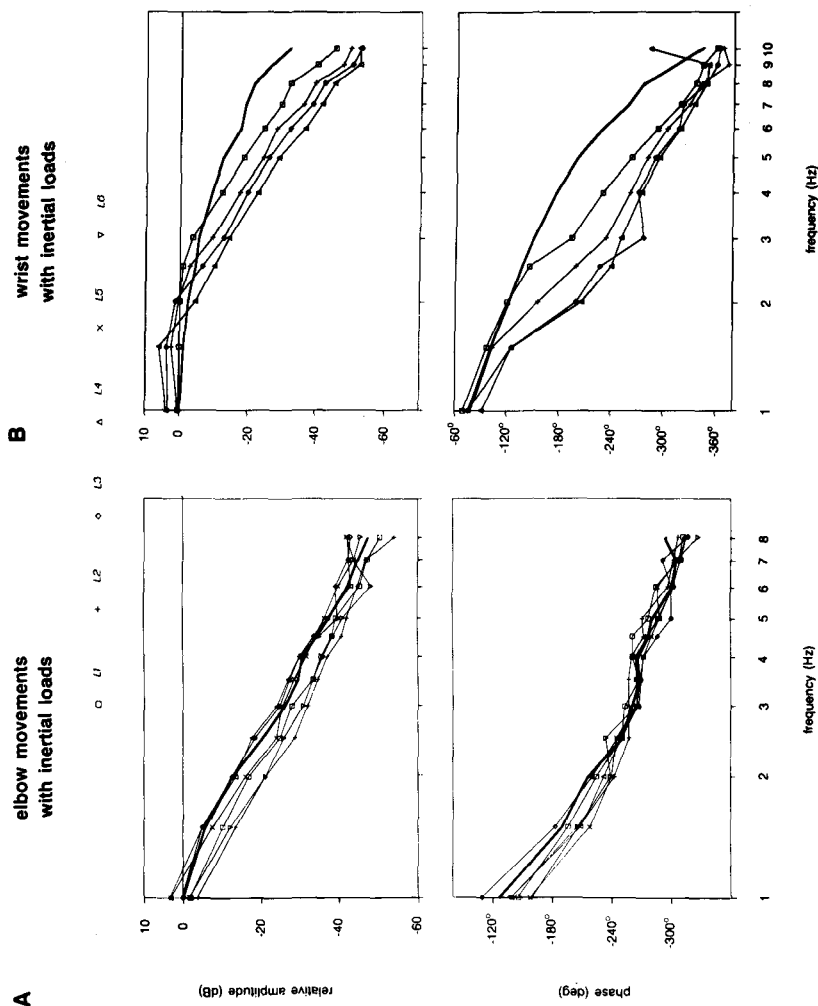


FIGURE 10. Effect of inertial loading on frequency response of electrically elicited movements at (a) elbow; and (b) wrist. Load was incremented by fixed amounts (elbow: six increments (L1–L6) each representing 20% of moment of inertia of forearm; wrist: four increments (L1–L4) each representing 80% of moment of inertia of hand). Solid lines show no-load responses. Wrist characteristics were significantly altered as load increased.

To see how this heavy loading of the hand might affect closed-loop operation, we combined the worst-case open-loop characteristics of Fig. 10b (4 weights = 1.3 kg; cubic curve-fit:Supercalc 5 software) with the transfer function of the antitremor filter (Fig. 6b). The result, shown in Fig. 11b, is contrasted with the no-load characteristics in Fig. 11a, obtained by combining the no-load plots of Fig. 10b with the same filter transfer function. Two points emerge from the comparison: (a) The amplitude characteristic remains bell-shaped with the heavy load, though the peak is shifted from 4 Hz to 2 Hz; (b) the gain margin with the heavy load is larger than that with no load. This would imply that for a 3-Hz tremor, closed-loop operation would remain stable and effective with heavy loading. We confirmed this in closed-loop trials with gain adjusted to 3 dB below that causing instability of the *unloaded* hand: addition of the largest load did not cause instability, and tremorous movements, already attenuated by the load itself, were further attenuated by the closed-loop stimulation.

DISCUSSION

In this paper we have presented the technical details of a new method to attenuate pathological tremor with functional electrical stimulation. The basic idea is to stimulate the tremorogenic muscles out-of-phase so as to suppress the tremor, while minimally interfering with useful volitional movements. Our approach was first to measure the frequency-response properties of two pairs of load-moving muscles often involved in pathological tremors: the elbow and wrist flexors and extensors. This was done in normal subjects, and allowed us to fit model transfer functions to the averaged results. Filters were then designed which, when combined with these models in the closed loop, gave bandpass characteristics causing attenuation of 2–4 Hz tremor with barely noticeable effects on slower voluntary movement.

Validity of Linear Analysis

It is often pointed out that the neuromuscular system exhibits nonlinear properties, and that linear modelling such as we have used is therefore invalid. Yet we found in our study that predictions regarding gain margins, resonant frequencies and tremor attenuation derived from the linear models were accurate and dependable when evaluated in closed-loop experiments. The most likely explanation for this is that for the relatively small movements seen at the onset of instability and in tremor, muscle/load properties are in fact adequately described by linear transfer functions, at least to the level of precision required for our application. This is not to deny that a nonlinear systems approach might provide more accurate or more general models, which might enable one to design filters with better closed-loop performance and greater stability margins. Indeed, even within the constraints of linear modelling, we are by no means sure that we managed to identify the best possible filters. Our purpose at this stage is to present the general approach and some workable solutions, which provide enough tremor suppression to be considered seriously for practical clinical use.

Parametric Variation Between Subjects

At the outset we wondered whether it would be necessary to optimise a filter design for each individual based on his or her particular muscle/load properties. This turned out not to be the case: the interindividual variation in frequency responses

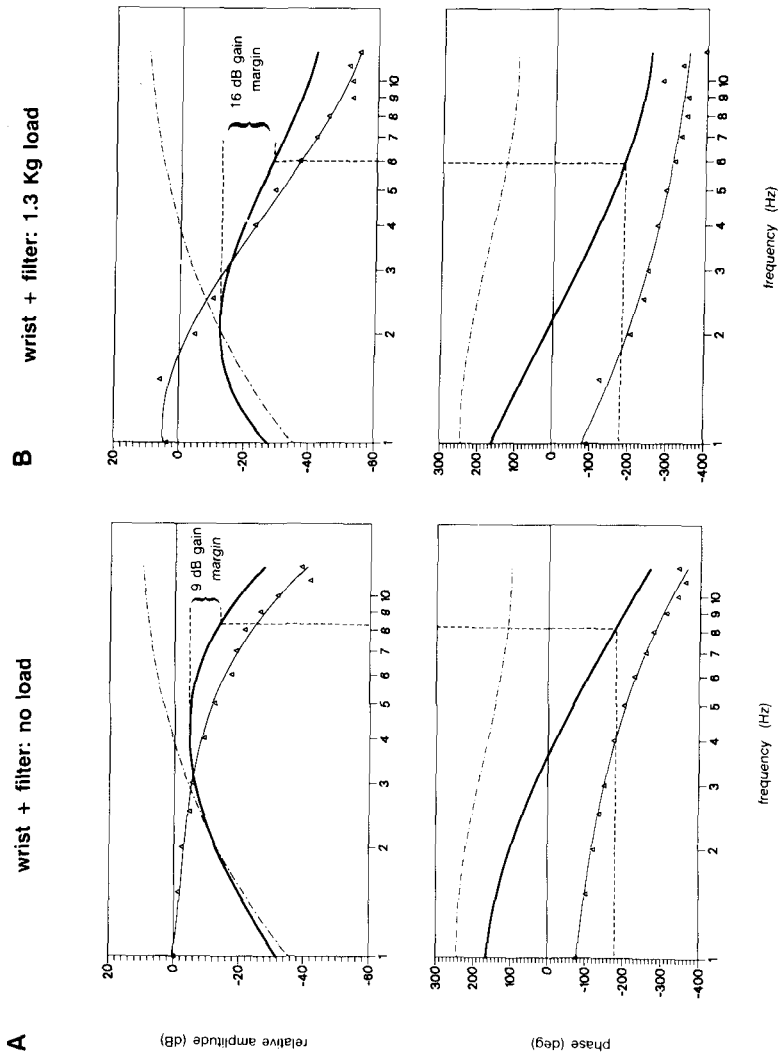


FIGURE 11. Impact on closed-loop operation of largest load of Fig. 10b. (a) Triangles, fitted curves: no-load characteristics (from Fig. 10b); dash-dot curves: antitremor filter (from Fig. 6b); thick curves: combined response showing peak at 4 Hz. (b) Triangles, fitted curves: 1.3-Kg load (from Fig. 10b, curve L4); dash-dot curves: antitremor filter (from Fig. 6b); thick curves: combined response showing shift of peak to 2 Hz. Curves in b indicate that closed-loop operation remains stable and effective (see text).

(e.g., Fig. 3) was small enough to allow the same filters to be used successfully on all subjects. Furthermore, the relative insensitivity of the system to the variations in muscle/load characteristics illustrated in Fig. 11 was considerably more favourable than expected. On the other hand, it became evident that a filter appropriate for a 4-Hz tremor might not attenuate a 2-Hz tremor sufficiently (see following paper [6] which follows in this issue). This means that for the best outcome, a filter should be chosen from a standard set to suit a particular patient's tremor frequency. We would expect that some form of self-tuning might eventually be used to optimize filters for particular patients. This would best be implemented with digital controllers.

The loading studies revealed an interesting difference between hand and forearm, which has implications for normal central nervous system (CNS) control of movement. A 1.3-kg weight attached to the hand attenuated higher frequency movements more at the wrist than at the elbow. Let us assume that forearm and hand movements are controlled with closed-loop proprioceptive feedback and that in many individuals stability margins are quite low (14). *A priori*, one might suspect that inertial loading would destabilize the hand first because of its larger effect on the overall transfer function. To compensate, the CNS could adaptively adjust the dynamics of central transmission, or it could simply operate the wrist loop at a lower gain to start with (consistent with the greater briskness of tendon jerks in arm vs. forearm muscles). On the other hand, depending on the overall transfer characteristics, loading may in fact make wrist (and elbow) control *more* stable, as exemplified in Fig. 11.

The scope of this study was to explore the basic feasibility of attenuating tremor with electrical stimulation. A more rigorous analysis of the sensitivity of various closed-loop configurations to parametric variation is now called for, partly because it might lead to better filter designs, and partly for the insight it would no doubt give on the organization required within the CNS to control movement in the face of parametric variation in muscles and their loads.

Limitations

There were three main areas of difficulty and unreliability in suppressing tremor with the systems described above.

Stimulation. Accurate placement of surface electrodes was required for reproducibility of open-loop responses and for correct operation of the closed loop. In some subjects it was quite difficult to locate appropriate sites. Surface electrodes, even of the new self-adhesive type tend to be somewhat cumbersome, cosmetically unappealing and time-consuming to don and doff. Percutaneous intramuscular electrodes (7,9,10,13,17) bypass these difficulties, but introduce some problems of their own. They are invasive and so tend to be reserved for use in severely disabled individuals only. Implanted stimulators controlled by percutaneous telemetry (e.g., (20)) may provide viable alternatives in the future but at this stage are only commercially available for stimulation of the common peroneal nerve. Any implanted device would have to include a displacement sensor, either externally mounted or implanted (18).

Displacement Transduction. It is relatively easy to fit a suitable low-noise, high-resolution transducer to a pivoting armrest or handrest. However, if unrestricted movement of the arm is to be allowed, the task of reliably sensing joint displacement becomes much harder. In some trials, we spanned the elbow or wrist with a minia-

ture displacement transducer consisting of an elastic band attached to a small cantilever strain gauge. The ends of the gauge were attached to the skin with double-sided adhesive tape. This arrangement worked reasonably well, except that instability tended to occur at lower gains than in the stabilized forearm. The reason seemed to be that mobility of the muscle belly over which the transducer was attached caused a modulation of the displacement signal additional to the displacement of the joint. This was not taken into account in the open-loop transfer functions. The result was a high-frequency instability consisting of rapid muscle "bouncing" with little joint displacement, but with discomfort caused by the large rhythmical bursts of electrical stimuli. Goniometric transducers of the type manufactured by Penny and Giles (Blackwood, Gwent, United Kingdom) might circumvent this problem, in that their attachment is distributed along the extremity, and so their responses are less likely to be distorted by local muscle bulging. For very long-term applications, a fully implanted displacement transducer would be desirable (18).

Multiple-Joint Tremor. The clearest difficulty we see in applying the technique to patient populations relates to the practical difficulties of simultaneously suppressing tremor about more than one joint. This problem, and some possible solutions to it, will be discussed in detail in the subsequent paper.

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