The complete frequency spectrum of physiological tremor can be recreated by broadband mechanical or electrical drive

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Vernooij CA, Lakie M, Reynolds RF. The complete frequency spectrum of physiological tremor can be recreated by broadband mechanical or electrical drive. J Neurophysiol 113: 647–656, 2015. First published November 5, 2014; doi:10.1152/jn.00519.2014.—Two frequency peaks of variable preponderance have been reported for human physiological finger tremor. The high-frequency peak (20–25 Hz, seen only in postural tremor) is generally attributed to mechanical resonance, whereas the lower frequency peak (8–12 Hz, seen in both postural and kinetic tremor) is usually attributed to synchronous central or reflexive neural drive. In this study, we determine whether mechanical resonance could generate both peaks. In relaxed subjects, an artificial finger tremor was evoked by random mechanical perturbations of the middle finger or random electrical muscular stimulation of the finger extensor muscle. The high and the low frequencies observed in physiological tremor could both be created by either type of artificial input at appropriate input intensity. Resonance, inferred from cross-spectral gain and phase, occurred at both frequencies. To determine any neural contribution, we compared truly passive subjects with those who exhibited some electromyographic (EMG) activity in the finger extensor; artificially created tremor spectra were almost identical between groups. We also applied electrical stimuli to two clinically deafferented subjects lacking stretch reflexes. They exhibited the same artificial tremor spectrum as control subjects. These results suggest that both typical physiological finger tremor frequencies can be reproduced by random artificial input; neither requires synchronized neural input. We therefore suggest that mechanical resonance could generate both dominant frequency peaks characteristic of physiological finger tremor. The inverse relationship between the input intensity and the resulting tremor frequency can be explained by a movement-dependent reduction in muscle stiffness, a conjecture we support using a simple computational model.

Physiological hand tremor; mechanical resonance; thixotropy; finger tremor from posture to movement using a simple model, where the hand, muscles, and tendons act as a mechanical resonator driven by a broadband force input (Lakie et al. 2012). A key feature of the model is a substantial reduction in muscle stiffness with movement, which explains the related drop in tremor frequency.

Unlike hand tremor, physiological finger tremor has two spectral peaks “of variable preponderance” (Lakie 1992). The high-frequency peak (typically 20–25 Hz) is generally attributed to mechanical resonance (e.g., Elble 1996). Consequently, it is thought that a different explanation has to be invoked for the lower frequency peak (typically 8–12 Hz, or simply “10-Hz tremor”). Finger tremor at this frequency is particularly prominent during movement (Vallbo and Wessberg 1993) and is usually explained in terms of increased synchronized modulation of contributing motor units produced by reflex or central mechanisms (reviewed by McAuley and Marsden 2000).

Alternatively, our recent results suggest that both characteristic frequencies (including the 10-Hz component) of physiological finger tremor might be produced by a resonant mechanism (Vernooij et al. 2013). In this study, we compared isotonic finger tremor with its isometric counterpart, where movement, and thus resonance, was prevented. We found that only isotonic gain spectra always showed a peak. Moreover, this peak systematically decreased in frequency from ~20 to ~10 Hz with increased drive. Corresponding electromyography (EMG) spectra and the isotonic gain spectra did not show any peak at either of the tremor frequencies. We suggested that thixotropic changes in muscle stiffness produce a very large drop in the finger’s resonant frequency when it is moving, which causes kinetic tremor to be dominated by the 10-Hz component, whereas the high-frequency peak vanishes. Consistent with this suggestion, we were able to create a comparable range of artificial tremor frequencies by the use of appropriately sized, entirely random electrical stimulation of the relaxed finger extensor muscle. We therefore proposed that mechanical resonance could shape the complete frequency range of the physiological finger tremor spectra. However, a limitation of generating artificial tremor by random electrical stimulation was that a possible contribution of spinal neural input (motor unit synchronization due to stretch or other reflexes induced by our stimulation) could not be excluded, because we were unable to record EMG during muscle stimulation. In this study, we additionally employ a mechanical stimulation that permits EMG registration and enables us to control for any effect of central neural output and spinal reflexes. Additionally, we compare the phase relationship between EMG and tremor to determine whether mechanical limb
resonance can explain both the low- and high-frequency components of physiological finger tremor.

MATERIALS AND METHODS

Participants

Fifteen healthy, right-handed subjects (age 24.7 ± 10.1 yr, mean ± SD; 8 males) volunteered to participate in this study. All gave informed consent. Two subjects suffering from extensive large-fiber sensory neuropathy (dorsal root ganglia cell body problem) participated in one of the experiments. Ethical permission was received from the University of Birmingham, and the experiments were carried out in accordance with the Declaration of Helsinki.

Experimental Apparatus

Subjects sat in a comfortable chair with their pronated right forearm supported in a horizontal foam rest placed at waist height. The ring and index fingers, along with the knuckles and wrist, were very firmly strapped to a rigid U-shaped aluminum rest. This permitted unrestrained vertical movement of the middle finger exclusively, ensured that the second and fourth finger would not slip into the movement slot, and restricted any movements of the hand (see Fig. 2). Subjects were asked to sit as still as possible and to keep their forearm completely relaxed when the perturbations were applied.

A small accelerometer (12.7 × 20.32 mm, model SCA3000; Active Robots, Radstock, UK) encased in epoxy resin was attached on top of the distal phalanx of the middle finger to record vertical acceleration. A light duraluminium bar strapped to the finger acted as a splint to restrict movements to the third metacarpophalangeal (MCP-3) joint. A thin (diameter 2.5 mm) titanium crank extending from a miniature servomotor (type D; maxon motor, Sachseln, Switzerland) was attached to the distal end of the middle finger. The rotary axis of this low-inertia motor was aligned with the MCP-3 joint. The motor was connected as a torque servo (type 201583 amplifier; maxon motor), converting input voltage to torque. As well as imposing any desired torque perturbations, the motor supplied a minor offset torque to counteract the weight of the titanium linkage. For five subjects, a miniature strain gauge (model 632-124; RS Components, Northants, UK) was cemented to the titanium linkage to directly measure the torque applied to the finger. Analysis of this torque confirmed that it faithfully recreated the voltage signal supplied to the motor at the frequencies we employed.

Experimental Conditions

We studied three conditions. First, we measured physiological postural and kinetic tremor (tremor during a voluntary tracking task) in the absence of any other input. In the other conditions, we used a mechanical or electrical drive (“artificial input”), to the finger and muscle, respectively, to generate artificial tremor, as follows. In the second condition, artificial tremor was generated by random mechanical perturbation of the middle finger using the torque motor. In the third condition, tremor was generated by random electrical stimulation of the extensor digitorum communis muscle. It was impossible to reproduce the trajectory of the voluntary movement with the artificial stimuli. Therefore, to study the effect of increasing finger motion on the evoked tremor, we employed six different levels of random mechanical and electrical input. The smallest amplitude was tuned to evoke a barely visible finger movement. As artificial input size increased, finger movement also increased. We used six sizes of input so that we encompassed the amount of finger movement observed during both postural and kinetic physiological tremor. Each trial lasted 60 s with a freshly generated stimulus train. Rest periods were allotted between each of the 18 trials per subject.

Voluntary physiological finger tremor (voluntary condition). To record postural tremor, subjects were asked to hold their middle finger at a comfortable position midway between maximal flexion and extension of MCP-3. To record kinetic tremor, they were asked to sinusoidally flex and extend the finger at 0.1 Hz through a range of ~50° centered around their midpoint. Finger position was monitored by a laser range finder (model YP11MGV80; Wenglor Sensoric, Tettwang, Germany) and displayed as a white cross on the 17-in. computer screen placed ~1.5 m in front of the subject, along with the computer-generated target position, which was displayed as a red ball. Surface EMG of the extensor digitorum communis (EDC) muscle was recorded (Bagnoli system; Delsys, Boston, MA). The correct positioning of the EMG electrodes was confirmed by the appearance of a 0.1-Hz peak in the spectral analysis of the kinetic condition.

Tremor evoked by mechanically applied torque (mechanical condition). Continuous, randomly varying torque signals with a flat spectrum between 5 and 25 Hz were generated by applying a bandpass filter to white noise (4th-order Butterworth, cutoff frequencies 2 and 30 Hz). Torque was applied to the distal part of the relaxed, splinted middle finger by the crank connected to the miniature servomotor. The range of torque sizes was predetermined on an individual basis, according to the magnitude of the evoked finger acceleration. The lowest level of torque, level 1, generated tiny deviations in the noisy acceleration signal produced by the otherwise relaxed subjects (~0.15 ms⁻² peak to peak), and the upper level of torque, level 6, was set to produce an acceleration of ~7.5 ms⁻². Torque levels 2–5 were systematically set at intermediate values between torque levels 1 and 6. Note that the motor was not set in positional control mode and as such did not dictate the acceleration response. Surface EMG was recorded from the EDC muscle, as above.

Tremor evoked by electrical muscle stimulation (electrical condition). Random electrical stimuli were applied to the relaxed EDC muscle via two aluminum electrodes (~1 cm² each), placed over the belly of the muscle, using a computer-controlled constant current stimulator (50-μs pulse duration, model DSTA; Digitimer, Welwyn Garden City, UK). The 60-s stimulus trains had a flat frequency spectrum between 5 and 25 Hz and contained 10 stimuli per second on average. Each stimulus caused a brief contraction of the EDC muscle and therefore a small upward acceleration of the finger. For each subject, current intensity was individually tailored based on the response to a single stimulus, in exactly the same way as for the mechanical condition. The sensation of the stimuli varied from hardly noticeable to a clear tapping feeling. The stimuli were never painful or very uncomfortable.

On two separate occasions, we measured electrically evoked tremor in two subjects living with long-standing large-fiber sensory neuropathy. Subject GL (55 yr old, female) has lost all muscular and cutaneous sense below the nose (Sarlegna et al. 2006), and subject JW (59 yr old, male) has lost all muscular and cutaneous sense below the neck (level C3) (Cole and Sedgwick 1992). Although touch and proprioception are lost in these subjects, they can feel some pain and temperature and could detect the stimulation. Importantly, neither subject exhibits stretch reflexes. If the stretch reflex does contribute to the physiological tremor, it would be expected to generate a finger tremor frequency of ~10 Hz (Durbaba et al. 2005; Lippold 1970). In nonimpaired persons, this tremor frequency becomes dominant at higher intensities of electrical stimulation (Vernooy et al. 2013). Therefore, to determine the effect of an absent stretch reflex on this particular frequency, we electrically stimulated the muscle of both impaired subjects at a level comparable to highest intensity applied to the nonimpaired (“control”) volunteers. Three repeats at this level were applied per subject.

Data analysis. EMG signals were amplified 1,000 times. Artificial input signals (torque and electrical stimuli), acceleration, and EMG were sampled at 1,000 Hz and digitized using a MC6026 PCI card. EMG signals were then bandpass filtered between 40 and 300 Hz and rectified. Because the muscle torque generated by electrical stimula-
tion could not be directly measured, we estimated this torque so that it could be compared with the torque applied to the finger in the mechanical condition. We used a low-pass filter (Bawa and Stein 1976) with a time constant of 34 ms to filter the artificial input signal for the electrical condition only. This time constant turned out to best represent the muscular force twitch constant produced by a single stimulus and by a train of electrical stimuli that we measured in our previous study (Vernooij et al. 2013). The spectra were converted to torque spectra by multiplying the force by a finger moment arm (estimated at 10 cm).

All signals were processed using Matlab (release 2011a; The MathWorks, Natick, MA). Fast Fourier transforms (FFTs) were calculated for torque, acceleration, and rectified EMG (voluntary and mechanical conditions only) at a resolution of 0.12 Hz using Neuro-Spec-software for Matlab (version 2.0, 2008; for a theoretical framework, see Halliday et al. 1995). Cross-spectral analysis was used to determine gain and phase between input (EMG or torque) and output (acceleration). This provided two accepted indicators of mechanical resonance (e.g., Bach et al. 1983); a peak in the gain spectrum between torque and finger acceleration, and a 0° phase angle between torque and finger velocity (see Knudsen and Hjorth 2002). For both the electrical and mechanical conditions, resonant frequencies derived from gain and phase were analyzed using repeated-measures ANOVA. Since the use of post hoc tests following repeated-measures ANOVA is controversial (Howell 2010) and the trend was clear, we decided not to check any post hoc differences between frequency bins.

For the mechanical condition, we found that some subjects displayed a level of EMG activity larger than expected for passive musculature. This may have been caused by incomplete relaxation or by reflex components. This provided a serendipitous opportunity to evaluate the effect of adding neural coloration of central or spinal origin to resonance. We grouped trials on the basis of the amplitude of the EMG spectrum. EMG spectra with an average amplitude clearly larger than that during the rest trial (>10⁻² mV), which also often contained a small peak, were considered “active” and were split from the spectra showing an amplitude <10⁻³ mV (“passive”) (see Fig. 4). We found that 4 of 15 subjects were consistently active, whereas 11 were consistently passive. We therefore analyzed tremor spectra separately for these two subject groups. EMG-acceleration coherence was also calculated separately for both groups, at a resolution of 0.98 Hz to obtain a reliable statistical estimate of linear relationship.

Tremor model. In a previous study, we used a single spring-mass-damper model to support our suggestion that physiological hand tremor is mainly caused by resonance (Lakie et al. 2012). This simplified model represented the hand as a mass connected to an underdamped torsional spring, which represented the muscle-tendon complex. Driven by white noise, the model successfully recreated the main characteristics of hand tremor. A substantial but plausible reduction in muscle stiffness and a slight reduction in damping were sufficient to reproduce changes in tremor between postural and movement conditions. In the present study, we use the same model adjusted for finger properties to test our supposition that both the high and low finger tremor frequencies could be generated by a single resonator, e.g., the finger-tendon-muscle complex. We examine whether the observed finger tremor spectra generated in the mechanical and electrical condition can be recreated by the model. The difference between these two conditions is that during electrical stimulation the muscle is active, and thus the force input driving the model is a low-pass filtered version of the input (Bawa and Stein 1976). Details of the model are described in the Appendix.

RESULTS

Characteristics of physiological and artificial finger tremor. Figure 1A shows the average acceleration spectrum of voluntary postural tremor (linear scale). As described in the literature (e.g., Lakie 1992; Stiles and Randall 1967), a broad spectrum is shown with increased activity at two frequencies, in this case at 26 and 9 Hz. This was not true of every subject, and the considerable variation is evident from the standard error. The kinetic tremor spectrum (Fig. 1B) has a different shape and is an order of magnitude larger than postural tremor with a single large peak at ~9 Hz. An additional peak can be seen at the very low frequency of the tracking movement (0.1 Hz), due to inevitable accelerometer tilt. To facilitate comparison between trials, all results are henceforth plotted with a logarithmic vertical axis. Figure 1C shows the EMG spectrum with a sharp peak at the frequency of movement (0.1 Hz) for the kinetic trial, but not for the postural trial. This confirms that we were measuring EMG from a relevant part of the muscle controlling finger extension. The kinetic EMG spectrum is two to three times larger than for the postural trial. They both show a broad range of activity with a maximum of ~14 Hz for the postural trial and ~9 Hz for the kinetic trial. Figure 1D displays the acceleration spectra from Fig. 1, A and B, replotted on a

Fig. 1. Physiological finger tremor: frequency spectra averaged per trial over all subjects. A: postural tremor acceleration plotted on a conventional linear scale. The anticipated twin peaks in postural tremor acceleration at ~9 and ~26 Hz are evident. B: kinetic tremor acceleration plotted on a conventional linear scale (an order of magnitude larger than in A). The kinetic tremor acceleration spectrum displays a single sharp peak at ~9 Hz. C: surface electromyography (EMG) of extensor digitorum communis (EDC). The EMG in the kinetic trials has a frequency peak at the frequency of movement (0.1 Hz). The kinetic EMG spectrum is larger than the postural spectrum: both show most activity frequencies from ~8 to 20 Hz. D: tremor acceleration from A and B replotted on a logarithmic scale. E: cross-spectral gain from EMG (C) to acceleration (D). The gain spectra (between C and D) strongly resemble the acceleration spectra, because the EMG spectra (C) are fairly flat. Shaded areas represent standard error (SE).
semilogarithmic scale. The peak frequencies of tremor appear less sharp. The shapes of the cross-spectral gain spectra (EMG to tremor) (Fig. 1E) are very similar to the acceleration spectra. For the postural trial, there are small peaks at ~9 and ~26 Hz. The gain for the kinetic tremor is peaked at ~9 Hz.

Figure 2 displays the results of artificially evoked tremor in a representative subject. This includes spectra of the input stimuli, the evoked tremor, and the cross-spectral gain (between artificial input and tremor). The correspondence to Fig. 1 is clear. For the mechanical condition (Fig. 2, top), all applied torque spectra were flat between ~5 and 25 Hz, tailing off above and below these limits. Finger acceleration at the lowest amplitude of driving torque (Fig. 2, top center) shows a defined peak at ~26 Hz. Increasing the torque level produces a drop in peak frequency, down to ~10 Hz at the highest level, and a systematic increase in acceleration magnitude. Consequently, the gain (Fig. 2, top right) between torque and acceleration also displays a peak at 26 Hz for the lowest input, similarly dropping to ~10 Hz at the highest. For the electrical condition (Fig. 2, bottom), the electrical stimuli were converted into estimated applied torque to the finger, to enable comparison with the mechanical condition. This was done by filtering the stimulation signal using an empirically derived time constant to mimic the low-pass properties of the muscle (see MATERIALS AND METHODS). This process resulted in an applied torque that decreases with frequency (Fig. 2, bottom left). Increasing the current level generated a systematic increase in estimated torque across all frequencies. The resulting finger acceleration spectrum (Fig. 2, bottom center) peaks at ~26 Hz at the lowest level of stimulation. As the input stimulus increases in magnitude, so does the acceleration spectrum, whereas its peak frequency drops to ~9 Hz and becomes more sharply tuned. Similarly, gain (Fig. 2, bottom right) is peaked at ~26 Hz for low intensities, and the frequency peak decreases to ~9 Hz with increased current. There is a slight increase in gain at higher stimulation levels. Figure 2 thus shows that the high (20–25 Hz) and the low (~10 Hz) frequencies of physiological finger tremor can be reproduced with both artificial techniques.

There are two proofs that spinal or central synchronized input is not responsible for either of the dominating tremor peaks: by confirming a resonant origin and by examining tremor in the absence of a synchronized neural drive. The following two sections study these two issues.

Resonance inferred from gain and force-velocity phase. At resonance, the velocity of a moving body will be in phase with the applied force (or torque), and there will be a peak in the gain between input and output (measured here as acceleration) (Knudsen and Hjorth 2002; Timmer et al. 1998). Figure 3 shows the phase and gain results for all subjects. Figure 3A is an illustration of the phase and gain graphs of a representative subject (for levels 2 and 6 in both conditions). The frequencies at which torque and velocity are in phase (0° phase crossing)
are marked with a vertical dashed line. The crossing frequencies are similar for electrical and mechanical conditions. The 0° phase crossing points as well as the gain peaks show a lower frequency at level 6. Figure 3B shows the average frequencies of these peak gain and phase crossing points of all subjects for both conditions. There was no significant difference between these two methods for estimating the point of resonance [Fig. 3B; \( F_{(1,140)} = 3.95, P = 0.06 \)]. However, there was an interaction between frequency and method (gain vs. phase) for the mechanical condition \([F_{(5,140)} = 6.23, P < 0.001]\). ANOVA confirms a significant decrease in the peak frequency of both gain and phase shift \([F_{(5,70)} = 27.16, P < 0.001]\) as input size increases. Although both mechanical and electrical conditions produced a progressive decline in frequency, the extent and form of the reduction were not identical (Fig. 3B). This was expected because of the differences in their method of generating finger velocity; electrical stimulations activate the muscle, which consequently generates finger movement, but finger movement generated by the mechanical torques moves the muscle to a lesser extent because of the compliant coupling of the tendon. This is further considered in the Discussion.

**Tremor in absence of a neural drive.** In the mechanical condition, 4 of 15 subjects displayed a level of EMG activity that was larger than their passive rest level (average spectral amplitude >10^{-3} mV), caused either by subjects not being completely relaxed or by some form of reflex activity. This provided an opportunity to compare acceleration spectra between subjects without any neural input versus those with central or reflexively induced EMG. Figure 4 shows a comparison of EMG and acceleration spectra between these groups. EMG spectra of the passive group confirmed a flat and low level of EMG for all torque levels, comparable to the rest trial (Fig. 4, left). In the active subjects, a variable peak can be seen between 12 and 18 Hz. Despite this pronounced group difference in EMG, the acceleration spectra between both groups of subjects are strikingly similar (Fig. 4, center). Whereas the peak frequency occurs at a slightly lower frequency and is somewhat more sharply tuned in the
passive subjects, the overall shape and amplitude of the spectra are almost identical. In physiological tremor, coherence between EMG and acceleration has been cited as supporting evidence for a neural contribution to tremor causation (e.g., Halliday et al. 1999; Kakuda et al. 1999; Williams et al. 2009, 2010). We therefore compared EMG-acceleration coherence between the passive and active subjects (Fig. 4, right). As expected for passive subjects, coherence is minimal (~0.03) and flat for all. In contrast, active subjects show a peak in coherence where acceleration is largest. An unpaired t-test on the mean coherence level per input intensity showed that this difference between the groups was significant [P = .0033, t(10) = 3.8336]. However, the degree of coherence made no obvious difference to the artificial tremor (Fig. 4, center) that was produced.

In addition, we recorded tremor in two deafferented subjects, who do not have a spinal reflex. Acceleration spectra evoked by high-intensity electrical stimulation of the two subjects are depicted in Fig. 5, along with the associated average spectrum from the control (healthy) subjects. The tremor spectra are almost identical in shape, peak frequency, and size.

Resonance model. Using a simple computational model (see Appendix), we generated the tremor spectra that would result from a simple resonant system driven by white noise. To account for muscle thixotropy, we decreased the model joint stiffness when the artificial input size was larger. In addition, we made the simplest possible change to the model to account for the difference between the mechanical and electrical conditions, which was to filter the input in electrical conditions to account for the known low-pass property of muscle tissue (see also our method for generating torque from electrical stimulations) (Bawa and Stein 1976). Figure 6 compares measured tremor of a representative subject versus modeled tremor and confirms a good approximation of the recorded acceleration spectra. At low input levels, the measured tremor spectra show a high-frequency peak (~26 Hz) whether electrically or mechanically energized. The modeled equivalents show a peak at a slightly lower frequency, namely, ~24 Hz. The shape of the spectra between measured and modeled acceleration is very similar otherwise. For the empirical data, some difference between electrical and mechanical conditions becomes apparent at high levels of input, with the electrical condition showing a larger decay toward higher frequencies. The modeled tremor reproduces the drop in frequency and increase in tremor amplitude, and also strikingly replicates the difference between the mechanical and electrical condition. The model is able to produce this difference simply by including the low-pass filtering properties of the muscle.
PHYSIOLOGICAL TREMOR CAN BE RECREATED BY BROADBAND DRIVE

DISCUSSION

We discuss five main findings. First and foremost, we have demonstrated that the low- and high-frequency peaks found in the spectra of postural and kinetic physiological finger tremor can both be reproduced when tremor is artificially generated by applying appropriately sized random inputs to relaxed subjects. Second, we have confirmed that this artificial tremor is due to mechanical resonance that occurs at a frequency that decreases as input size increases. Third, we have confirmed that modulated EMG is not usually associated with artificial tremor. Fourth, we have reproduced the resonant behavior with a very simple computational model that requires only one change reflecting muscle engagement to simulate the difference between mechanical and electrical conditions. Finally, on the basis of the resonant properties of the finger that we describe, we suggest a novel explanation for the long-known presence of two peaks in physiological postural finger tremor and for the large, (kinetic) ~9-Hz tremor that accompanies voluntary movement.

Physiological and artificial tremor. Our 15 subjects demonstrated very typical physiological tremor spectra. The average result for postural tremor (Fig. 1) showed two peaks, one at ~9 Hz and one at ~26 Hz. The standard error of the data in Fig. 1 reinforces the well-known considerable variability in absolute and relative size of these peaks (e.g., Lakie 1992; Stiles and Randall 1967). One aspect that has been noted only more recently is that during movement there is a shift to a much larger and slower form of tremor. This is also clearly shown in Fig. 1. This kinetic tremor was attributed by Vallbo and Wessberg (1993) to a shift to an intermittent or discrete form of neural control during movement and has formed the basis for a hypothetical model of intermittent control (Bye and Neilson 2010). However, we have recently suggested an alternative explanation (Vernooij et al. 2013) that is in line with the current results. We believe that the low-frequency peak is produced by a thixotropic reduction in muscle stiffness and damping, excited by broadband noise from the active muscles. Consequently, the postural resonance shifts systematically to a lower frequency and becomes much larger during movement (Lakie et al. 2012; Vernooij et al. 2013). Thus our suggestion is that the alteration in size and shape of the spectrum going from posture to movement is a consequence of altered mechanical behavior rather than different neural behavior.

It is a simple matter to record real postural tremor (while holding the finger still) and real kinetic tremor (while carrying out a movement using an appropriate tracking task). It is less trivial to artificially mimic these conditions in relaxed subjects. Our solution was to use random electrical muscle stimulation and mechanically applied torque at a range of input intensities. The smallest intensities produced a barely visible dither of the digit. This approximated to postural tremor. As the intensity increased, the size of the movement also increased until, with the highest level, the finger’s movement became a random dance of considerable amplitude. Despite the inevitable lack of precise correspondence between the artificial and voluntary conditions, the artificial frequency peaks occurred at frequencies very similar to the subjects’ physiological tremor in both postural and kinetic conditions (i.e., ~9 and ~26 Hz) as shown in Figs. 2, 3B, and 4. This signifies that an entirely random input to the muscle-tendon-finger complex could generate both the high and the low frequencies seen in physiological tremor. The similarity between artificial and voluntary tremor, and between the active and passive groups in Fig. 4, suggests that any frequency-specific signal generated by central or spinal means is not required to cause tremor.

Although our main finding is that both artificial random inputs could reproduce physiological tremor frequencies, we noticed some differences in other spectral characteristics. Whereas tremor in the electrical condition has a spectral shape that closely resembles physiological tremor, the mechanically generated spectrum is slightly different. In particular, there is a disproportionately large amount of high-frequency tremor in trials with a high-intensity input. This can be explained by muscle properties (see A simple model reproduces the main findings). The torque produced by the muscle (in physiological and electrically generated tremor) is a low-pass filtered version of the white noise input (Fig. 2; see e.g., Bawa and Stein 1976). In contrast, the mechanical perturbations were applied directly to the finger and thus were not low-pass filtered. This results in a relatively larger amount of high-frequency acceleration in the mechanical condition.

Gain and phase suggest a resonance at a frequency that decreases as input size increases. In the literature, generally only the high-frequency (20–25 Hz) component of finger tremor is attributed to mechanical resonance. The evidence usually cited is that only this peak decreases in frequency when finger inertia is artificially increased (e.g., Halliday et al. 1999; Stiles and Randall 1967). However, recent work suggested a main role for mechanical resonance in shaping the complete finger tremor spectrum (Raethjen et al. 2000; Vernooij et al. 2013). In the current study, in addition to the previously employed cross-spectral gain, we strengthened this suggestion by employing a secondary corroborative technique to indicate resonance, the phase relationship between torque and velocity. For any mechanical system, the applied force (or torque) and resulting velocity will be in phase precisely at the point of resonance (Knudsen and Hjorth 2002; Timmer et al. 1998). We observed that the frequency at which this occurred corre-
sponded well to the peaks in gain. For both methods, the estimated resonant frequencies ranged from ~10 to >20 Hz, depending on the level of the driving input (Fig. 3). The gain and phase data showed a systematic decrease in peak frequency with increasing stimulus amplitude for both artificial inputs.

A finger tremor frequency of 10 Hz is actually quite similar to the resonant frequency of the hand. However, the 10-Hz tremor that we report here is not due to hand oscillations, because the wrist and all other digits were strapped to a rigid device and were completely unable to move. Additionally, Lakie and Robson (1988) have previously reported a similar range of relaxed finger resonance frequencies using different apparatus and technique where the hand was also completely immobilized.

Why does resonant frequency of the finger decrease as it moves more? We propose that muscle thixotropy explains this phenomenon. Only minimal muscle movement is required to greatly reduce muscle stiffness (Lakie et al. 2012; Loram et al. 2007; Prosk et al. 1993). The precise mechanism is not fully established, but it is likely to be due to a decrease in the number of attached actin-myosin cross-bridges following movement or activity (Campbell 2010; Campbell and Lakie 1998). When the muscle subsequently remains still, bonds reform, the muscle becomes stiff again, and the resonant frequency rises (time constant of both thixotropy and tremor, 2–4 s; see e.g., Campbell and Moss 2000; Reynolds and Lakie 2010). This would explain why, with increasing intensity of artificial input, and thus more muscle movement, we observed a systematic drop in resonant frequency (Fig. 3). There is a difference in the pattern and extent of this frequency change between mechanical and electrical conditions. Figure 3B shows that as mechanical input size is reduced, frequency rises, and the rise becomes more dramatic for the smallest inputs. This behavior closely approximates the nonlinear behavior that has been observed at other limbs (Lakie et al. 1984) and is a consequence of the short-range stiffness of muscle so that with the smallest inputs to the finger, the amount of muscle movement becomes tiny. With electrical stimulation, the rise in frequency proceeds more linearly as input size is reduced, and frequency does not increase to quite the same extent. Presumably, with electrical stimulation at even the lowest intensity, there is more appreciable movement of the musculature.

We suggest that under physiological conditions, muscles have a stiffness that is almost binary. That is, they are either nearly stationary and very stiff, or moving and much less stiff. Because the sensitivity of muscle to movement is very high (e.g., Campbell 2010), only small movements are required to cause a low stiffness configuration of the muscle, immediately resulting in a resonance frequency close to ~10 Hz. This is why intermediate values of resonant frequency are not normally observed.

**Modulated EMG is not necessary to generate tremor-like behavior.** In the present study we examined reflex involvement in tremor in two ways. First, we used mechanical perturbations that permitted us to record EMG activity associated with the movement. Second, we used electrical stimulation in two subjects with a very rare neurological disorder that renders them areflexive. In mechanically driven artificial tremor, extensor EMG was insignificant and displayed a flat spectrum in the majority of our relaxed subjects; neural input was not implicated in their artificial tremor spectrum. Some subjects did exhibit some EMG, either because they were not well relaxed or because the movement caused some driving of the EMG. However, in this group there was no systematic relationship between peak frequency of EMG and the tremor that was generated (Fig. 4). This suggests that spinal and/or central neural input did not directly specify the physiological characteristics of finger tremor.

Several studies have cited coherence between neural activity (motor cortex activity, motor unit firing, or EMG) and tremor as evidence in favor of a specific neural drive causing the observed tremulous movement (e.g., Halliday et al. 1999; Kakuda et al. 1999; Williams et al. 2009, 2010). Such logic would imply that the EMG-to-acceleration coherence peaks that we observed at 10–15 Hz in active subjects only (Fig. 5) would also indicate neural driving of tremor at these frequencies. However, any effect of this coloration is so subtle as to be invisible, because as shown in Fig. 4, the acceleration spectra were indistinguishable in the subjects who showed, and did not show, EMG. Thus, although the coherence peaks could mean that an element of tremor is dependent on EMG, this cannot explain the acceleration spectra observed in passive subjects who show a negligible coherence. It seems more likely that in some, but not all, subjects, the resonant tremor may drive the EMG to some extent, inevitably producing a degree of coherence that is greatest where the signal-to-noise ratio is largest, that is, at resonance.

The application of random stimulation to two subjects with widespread sensory neuronopathy supported the above mentioned observations. Electrical stimulation at the extensor muscle of these areflexive subjects produced identical tremor spectra to the “control” subjects, suggesting a minimal role for stretch reflexes in generating tremor. The gain of stretch reflexes is known to be directly related to the background level of muscle activity (e.g., Marsden et al. 1972, 1976; Mirbagheri et al. 2000). Our measurements were made while subjects were relaxed and EMG levels were intended to be zero, so gain would have been at its lowest level. Some of our subjects were evidently unable to suppress all EMG activity. Their tremor was indistinguishable from that of subjects with silent EMG, which suggests that for their particular level of EMG, any reflex contribution was insignificant. Experience has shown that when involuntary EMG is recorded, it is invariably in the antigravity, i.e., extensor, muscles. However, we did not record flexor EMG activity, so it is possible, but unlikely, that reflex activity could occur in that group of muscles.

What do these results imply for physiological tremor under normal conditions where reflexes may operate at a higher gain and voluntary drive will be present (Catthers et al. 2004)? We propose that a parsimonious possibility is that the frequency of physiological tremor is primarily dictated by the stiffness of the musculature operating around the joints. Most of this muscle will be inactive under postural conditions, and its stiffness will decrease with movement in the same way as in our artificial tremor experiments. Thus physiological tremor will also be at a high frequency when it is small and at a low frequency when it is larger. Entirely random input of appropriate amplitude was sufficient to produce high and low tremor frequencies under passive conditions and therefore could do so under active conditions, as well. The implication is that specific central or reflex mechanisms that are usually suggested to produce tremor...
The spectrum of physiological postural movement can also be explained in terms of muscle filtering properties. We suggest that the time domain record of finger tremor combinations (e.g., Lakie 1992). These are seen in frequency domain transforms of time domain data typically lasting 30–60 s. There has always been an assumption that the high- and low-frequency tremor peaks are simultaneously present. We propose an alternative explanation. The nearly static postural condition. Conventional frequency analysis combined this postural tremor time record into a composite spectrum with two peaks. We suggest this mechanism is similar for hand tremor, but, because the relative difference between postural and kinetic tremor frequencies is much less for the hand, the two peaks will merge and only one tremor peak is seen. Inevitably, during movement the record is dominated by low-frequency kinetic tremor (for either limb). An analysis of the time-varying behavior of the physiological tremor spectrum will be able to test this view.

**APPENDIX**

* Tremor model. We have previously modeled the hand as a second-order torsional oscillator (Lakie et al. 2012). The limb was viewed as a moment of inertia \( J \), which is connected to a muscle-tendon complex with damping \( c \) and angular stiffness \( k \) (Fig. A1). Stiffness \( k \) represents the series-coupled muscle stiffness \( km \) and tendon stiffness \( kT \). We use the Laplace transfer: \( G(s) = 1/(Js^2 + cs + k) \), where \( s \) is the Laplace operator.

We use the model to simulate both the mechanical and electrical methods of tremor generation. The difference between these two conditions is that, unlike for the mechanical condition, the white noise torque driving the finger for the electrical condition is previously filtered by the muscle. We employ the same muscle filter as described to estimate the generated muscle torque in the experiment, i.e., a low-pass filter with a time constant of 34 ms. Our main intention here was to show that our results for both electrical and mechanical conditions could be reproduced by a single simple resonance model by making this single change. All other parameters are identical between conditions and physiologically justifiable values are used. We drive the model with a white noise signal with intensity similar to those used in the real experiment.

Chosen parameter values for the finger model (i.e., moment of inertia, angular stiffness, and damping) are mainly taken from the literature. We use a moment of inertia of 0.0001 kg·m² (based on a cylindrical finger with an estimated length of 10 cm and an average mass of 35 g; Stiles and Randall 1967). Angular stiffness drops considerably with movement (~15 times; e.g., Loram et al. 2007). On the basis of a simple strength comparison between the finger and hand extensors, we estimate the cross-sectional area of the musculature

![Fig. A1. Model of the limb viewed as a moment of inertia \( J \), which is connected to a muscle-tendon complex with damping \( c \) and angular stiffness \( k \), and where \( s \) is the Laplace operator.](http://jn.physiology.org/)

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(e.g., Schantz et al. 1983) acting on the middle finger to be eight times less than that acting on the hand. Assuming joint stiffness correlates with muscle area (e.g., Given et al. 1995), we modify our previous stiffness values used for the hand to fit the finger. This gives a muscle stiffness estimate of 15 N·m/rad when postural and 1 N·m/rad when moving. Finger tendons are approximately twice as stiff as hand tendons (Ward et al. 2006). Taking these estimates together with the 8-fold decrease in cross-sectional area, we estimate a tendon stiffness of 2 N·m/rad. With movement, damping slightly decreases (Halaki et al. 2006) from 0.004 N·m·s·rad⁻¹ to posture to 0.003 N·m·s·rad⁻¹ for movement.

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Sarlegna FR, Gauthier GM, Bourdin C, Vercher JL, Blouin J. Internal stiffness values used for the hand to fit the finger. This gives a muscle stiffness estimate of 15 N·m/rad when postural and 1 N·m/rad when moving. Finger tendons are approximately twice as stiff as hand tendons (Ward et al. 2006). Taking these estimates together with the 8-fold decrease in cross-sectional area, we estimate a tendon stiffness of 2 N·m/rad. With movement, damping slightly decreases (Halaki et al. 2006) from 0.004 N·m·s·rad⁻¹ to posture to 0.003 N·m·s·rad⁻¹ for movement.

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