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Deterministic Recurrences of Sequential F-Wave Latencies

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ABSTRACT

PURPOSE: Historically, F-waves have been classified by various linear descriptors like persistence, latency, duration, amplitude, chrono-dispersion and number of repeater waves. But because physiological signals are notoriously nonlinear in nature, the objective of this study was to apply modern nonlinear methodology to F-waves sequences to assess the presence of underlying deterministic structures. Subtle changes in these sensitive markers could give early warnings for neurological problems. **METHODS:** F-waves were elicited in the left abductor pollicis breivs muscle by supra-maximally stimulating the median nerve percutaneously at the wrist. Approximately 200 stimuli were applied (0.5 Hz) to three subjects for at least four trials each. F-wave latencies were measured and assembled into sequences in proper order. Recurrence quantification analysis (RQA) was applied to these F-wave sequences from different dimensional perspectives. Controls were constructed by randomly shuffling the ordered sequences. RQA has a theoretical mathematical foundation and practical performance record on numerous other physiological systems. **RESULTS:** Recurrence analysis showed that sequential F-waves form recurrent patterns with parallel trajectories with deterministic and laminated structures. These features could be destroyed by randomizing the sequential orders of F-waves, upholding the hypothesis that sequences of F-waves are deterministically formed from underlying physiological rules. **CONCLUSIONS:** F-wave time series are fully amenable to recurrence analysis which provides a higher-dimensional perspective on the physiological dynamic. The recurrent patterns are complex, but not random, meaning that physiological rules dominate the sequence of F-waves. Disease processes within the central or peripheral nervous system may alter F-wave patterns. If so, RQA potentially may be a diagnostic tool to help discern subtleties between altered deterministic rules operating in disease.

Search Terms: F-waves, recurrence quantification analysis, F-wave latency recurrences, EMG, median nerve

INTRODUCTION

F-waves are intriguing, ubiquitous motor artifacts produced by antidromic activation of motoneurons commonly used in clinical neurophysiology (Fisher, 2003). Individual motoneurons in F-waves are activated infrequently (Schiller and Stälberg, 1978), and usually no more than several motor units constitute a single F-wave (Yates and Brown, 1979). As such, F-waves are inherently variable in latency, amplitude, and configuration and they may not be present after each stimulus. They are also low in amplitude, i.e. less than 5% of the amplitude of the associated direct motor response (M-wave). The latency of F-waves consists of three serial components: the antidromic conduction time from the distal stimulation site to the spinal cord, the time required for motoneuron activation, and then orthodromic conduction to the site of recording.

F-waves are analyzed following a series of stimuli delivered at some low, but constant stimulation rate (e.g. 0.5 Hz). The number of stimuli can range from 10 to 20, but up to 100 stimuli have been used in clinical reports (Macloed, 1987). Adequate evaluation of F-waves requires estimation of variables other than latency. These include response amplitudes, durations, chrono-dispersion (the difference between the minimal and maximal latencies in a series of F-waves), the persistence (the percentage of discernible F-waves following a series of stimuli), and the number of self-similar F-waves (repeater waves).

Since F-waves monitor conduction in motor axons to and from the spinal cord, they are used frequently in the evaluation of disorders of the peripheral nervous system. Arguably, F-waves are the most sensitive markers for motor conduction abnormalities following axonal injury (Fraser and Olney, 1991). F-waves are also the most reliable indicators for monitoring the time course of conduction depreciation in patients with neuropathies (Kohara et al., 1996). Because F-wave activation is dependent on the central excitability state of the associated segmental motoneuron pool, F-waves have been used to access the health status of the central nervous system (Lin and Floeter, 2004; Fisher, 2005).

In sum, F-waves arise from a complicated combination and multifaceted interaction of peripheral and central influences. For this reason, any meaningful analysis of F-waves can be rather complex. Given their clinical relevance, tools that would enhance meaningfully the assessment of F-waves are important. Since F-waves result from processes that are nonlinear, non–stationary and state-dependent, quantitative tools that evaluate such complex processes could be relevant for the assessment of F-waves. It is the purpose of this report to explore the feasibility of one such a tool, recurrence quantification analysis (RQA) (Webber and Zbilut, 2004), which has proven valuable in the assessment of numerous other physiological systems including fatiguing skeletal muscle electromyograms (Webber et al., 1995; Kankaanpää et al., 1997; Ikegawa et al., 2000), epileptic electroencephalograms (Thomasson et al., 2001, 2002) and normal electrocardiograms (Zbilut et al, 2002).

METHODS

F waves were recorded in a standard fashion from the left abductor pollicis breivs muscles from three normal, volunteer subjects (JC, CW, and MF aged 36, 56, and 63 respectively). The median nerve was stimulated percutaneously at the wrist with the cathode proximal to avoid anodal block. As is usual, supramaximal stimulation was used. This has the advantage of providing a physiological consistent state for the recordings and enhances the prominence of F-waves both in terms of F-wave amplitudes and persistences. The F-waves were elicited at constant stimulus rate of 0.5 Hz. This low rate was used in order to provide for sufficient recovery time between stimuli. The recordings were monitored by a Nicolet Viking IV EMG machine (VIASYS^{TM} Healthcare, Madison, WI). Filter settings were 2Hz to 5 KHz, and F-wave recordings were made a sensitivity of 200 or 500 µvolts/division and a sweep of 5 or 10 milliseconds/division. M-waves were recorded at a sensitivity of 5 mV/division. All recorded F-waves had identifiable responses greater than 40µV measured peak-to–peak.

Experimental Protocol

The goal was for all subjects to receive at least 200 supramaximal stimuli for each of 5 trials given at the same recording session. About 5 minutes elapsed between trials. Evoked responses (stimulus artifact, M-waves and F-waves) of the abductor pollicis brevis muscle were amplified, recorded continuously (400 s), digitized (1000 Hz) (Labscribe Data Acquisition System, Iworx, Durham. NH), and saved in ASCII file format for off-line data analysis. F-wave latencies were computed manually by visually marking the times of occurrence of the delivery of the stimulus (S) and the initiation of the F-wave (F). F-wave latencies were computed as the F minus S times (1 ms resolution). By this means, time series of F-wave latencies were constructed with the number of F-waves proportioned to the F-wave persistence. Missing F-waves (undefined) were simply dropped from the latency series, a modified approach from the first pass on these data (Chawla et al. 2004).

Recurrence Quantification Analysis

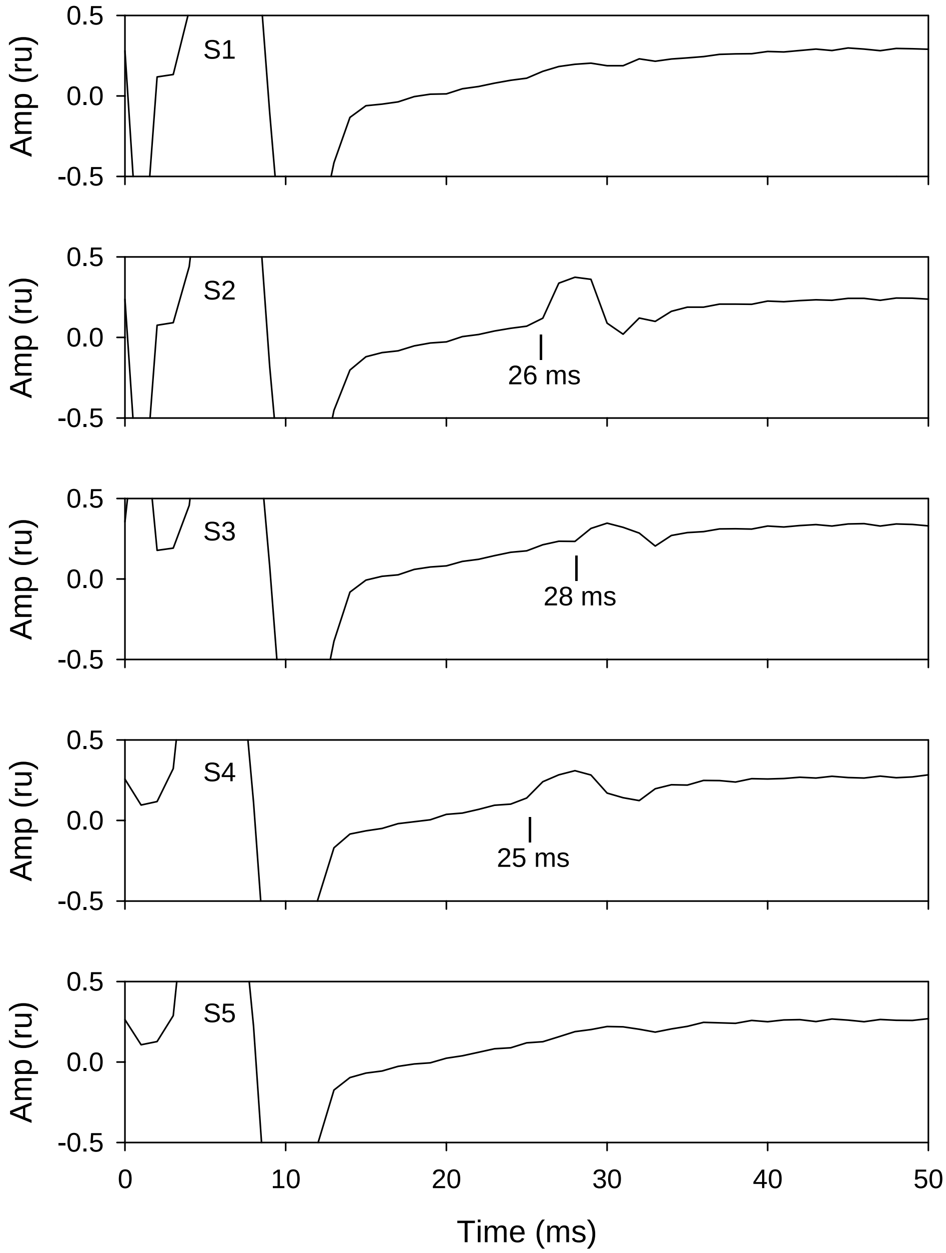
The F-wave latency time series were subjected to recurrence quantification analysis (RQA) (Webber and Zbilut, 1994). RQA is a nonlinear tool that has the ability to discriminate between the nonlinear ordering of signals, independent of their statistical distribution, non-stationarity, and presence of noise. In fact, RQA does not transform the data, but rather detects repeating patterns (recurrences) within the data. Eckmann et al (1987) originally described recurrence plots, but Zbilut and Webber (1992) and Webber and Zbilut (1994) showed how recurrence features could be extracted from the plots and quantified.

RQA has several parameters to set (Webber and Zbilut, 2004). For this study, the F-wave sequences were studied at: embedding dimensions = 5, 10, 15 and 20; delay = 1; Euclidean norm, maximum distance rescaling of the recurrence matrix. The radius parameter was automatically adjusted in order to accumulate a density of recurrent points at 5% recurrence (REC). By this means, recurrence plot features were compared at equal densities. Two recurrence quantifications were examined in this study, %determinism (DET) and %laminarity (LAM). DET measures the percentage of recurrent points in diagonal line structures; LAM measures the percentage of recurrent points in vertical line structures. The idea is that DET is a marker for parallel trajectories in the input time series whereas LAM is a marker for singularities in the input time series. The operating hypothesis posited was that sequences of F-wave latencies are deterministically ordered. This hypothesis was tested by shuffling each native F-wave sequence 10 times, and recomputing the DET and LAM values each time (see Zbilut et al., 2000). Averaged shuffled DET and LAM values were then compared against the native DET and LAM values. Embedding dimensions which gave the largest difference in native to shuffled RQA variables were selected. Details of the analyses are conveniently described in the results section. Recurrence software is available free of charge (Webber, 2006).

RESULTS

In all trials for each subject, percutaneous activation of the median nerve consistently elicited stimulation artifacts and M-waves in the abductor pollicis brevis muscle, followed inconsistently by late F-waves as shown in Figure 1. In this example, F-waves with latencies of 26 ms, 28, ms and 25 ms were evoked for stimuli S2, S3 and S4, respectively, but not for stimuli S1 and S5. Persistence is defined as the ratio of number of F-waves elicited to number of stimuli delivered as reported in the combined data in Figure 1. Upon stimulation of the median nerve, a stimulation artifact was elicited in the left abductor pollicis brevis muscle (time zero), followed first by a large M-wave and second by a delayed F-wave. In this example, three stimuli (S2, S3, S4) of five induced three F-waves with latencies of 26 ms, 28, ms and 25 ms respectively.

Figure 1: F-waves



Representative F-wave recordings with markers at onset latencies and two stimuli (S1, S5) without recordable F-waves.

Table 1 summarizes the persistence and latency data for the F-waves analyzed in this study. Persistences characteristically have a wide range in normal subjects. Latency values will vary directly with the limb length or height of the subject and, to a lesser degree, with age.

TABLE 1: Linear F-wave Characteristics

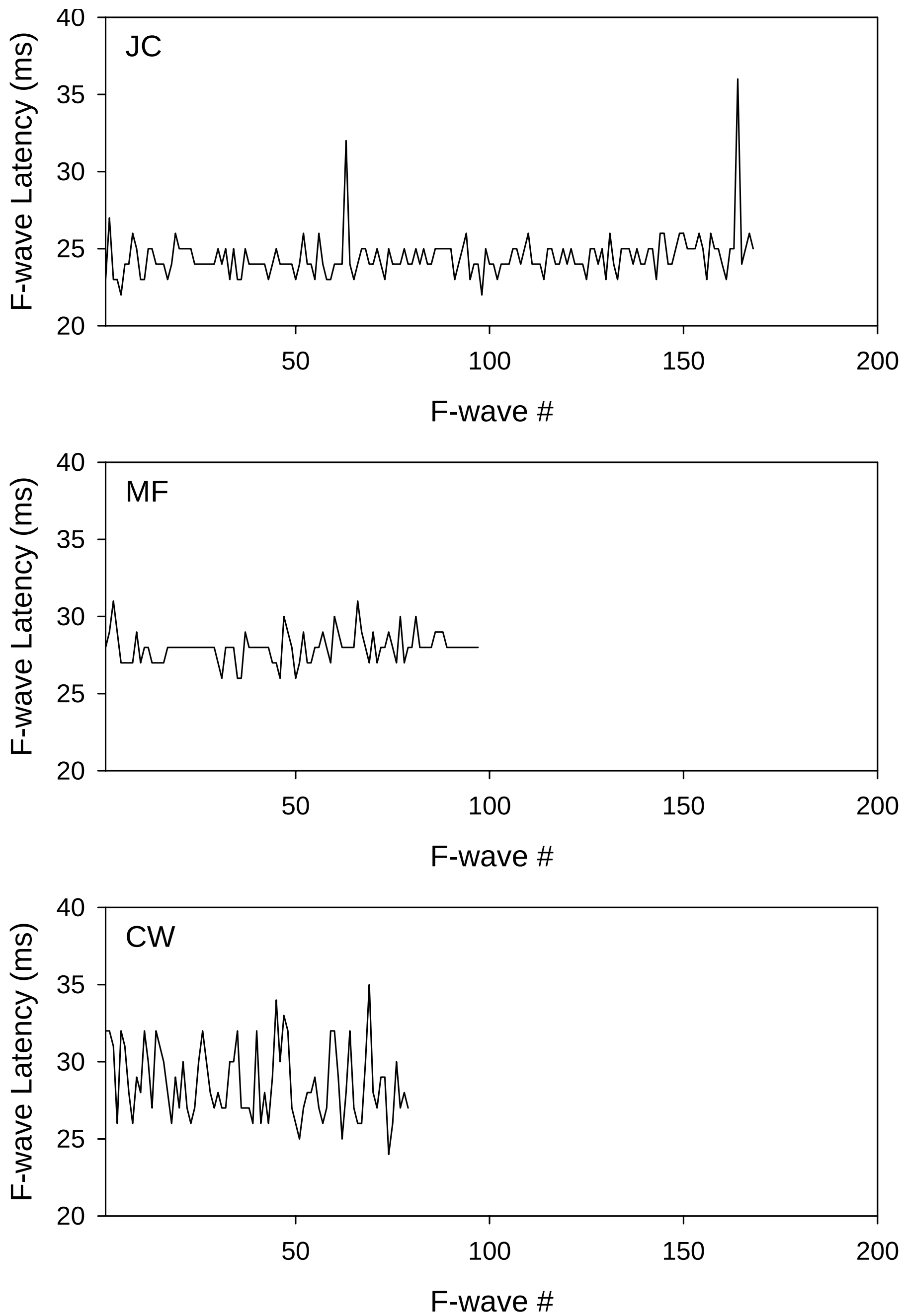
Subject	#Stimuli	#F-waves	Persistence	Mean (ms)	Stdev (ms)	Covar	Max (ms)	Min (ms)
JC1	205	186	90.7%	23	1	0.035	26	21
JC3	199	164	82.4%	25	2	0.087	38	22
JC4	200	168	84.0%	24	1	0.057	36	22
JC5	198	167	84.3%	25	2	0.068	36	23
mean=	201	171	85.4%	24.3	1.5	0.062	34.0	22.0
stdev=	3	10	3.7%	1.0	0.6	0.022	5.4	0.8
Subject	**#Stimuli**	**#F-waves**	**Persistence**	**Mean (ms)**	**Stdev (ms)**	**Covar**	**Max (ms)**	**Min (ms)**
MF1	202	87	43.1%	30	3	0.084	35	24
MF2	205	85	41.5%	32	2	0.068	35	27
MF3	200	98	49.0%	28	1	0.032	33	27
MF5	200	97	48.5%	28	1	0.034	31	26
mean=	202	92	45.5%	29.5	1.8	0.055	33.5	26.0
stdev=	2	7	3.8%	1.9	1.0	0.026	1.9	1.4
Subject	**#Stimuli**	**#F-waves**	**Persistence**	**Mean (ms)**	**Stdev (ms)**	**Covar**	**Max (ms)**	**Min (ms)**
CW2	191	57	29.8%	30	2	0.066	35	27
CW3	200	80	40.0%	29	2	0.071	33	25
CW4	200	79	39.5%	29	2	0.083	35	24
CW5	198	53	26.8%	29	3	0.102	38	25
mean=	197	67	34.0%	29.3	2.3	0.081	35.3	25.3
stdev=	4	14	6.7%	0.5	0.5	0.016	2.1	1.3

Persistency and latency data for the 3 subjects studied in this report. As can be seen, subject JC had the highest average persistence (85.4%), subject MF had a moderate persistence (45.5%), and CW had the lowest persistence (34.0%). Covar – covariance; Max – longest latency response; Min – shortest latency response.

Time series were constructed by sequencing F-wave latencies into vectors, skipping all stimulations trials not evoking F-waves. Example time series are plotted in Figure 2, with F-wave latencies that were not constant, but varied in time as quantified by the standard deviation and coefficient of variation (Table 1). In this limited data set, there was no apparent correlation between F-wave variability (coefficient of variation) and persistence.

RQA was performed on each of the F-wave latency time series, four per subject. An example recurrence plot from subject JC1 is shown in Figure 3. The same time series is plotted horizontally and vertically along the axes of the recurrence plot (F-lat) in milliseconds. The RADIUS was automatically adjusted to achieve a 5% density of recurrent points (excluding the central diagonal). As can be observed, many of these points form diagonal line structures of varying length (indicating the position of parallel trajectories) as well as vertical line structures of varying height (indicating laminated parallel trajectories). In this case, %DET computed to 89.4% and %LAM computed to 40.4% (Table 2). Shuffling the F-wave latency time series 10 times yielded 10 new %DET and %LAM values which averaged 87.2% and 28.2%, respectively. That is, shuffling caused the %DET to fall by 2.2% and the %LAM to fall by 12.2%, leading to the conclusion that the deterministic and laminar structuring of the F-wave latencies is sequence dependent (i.e. non-random).

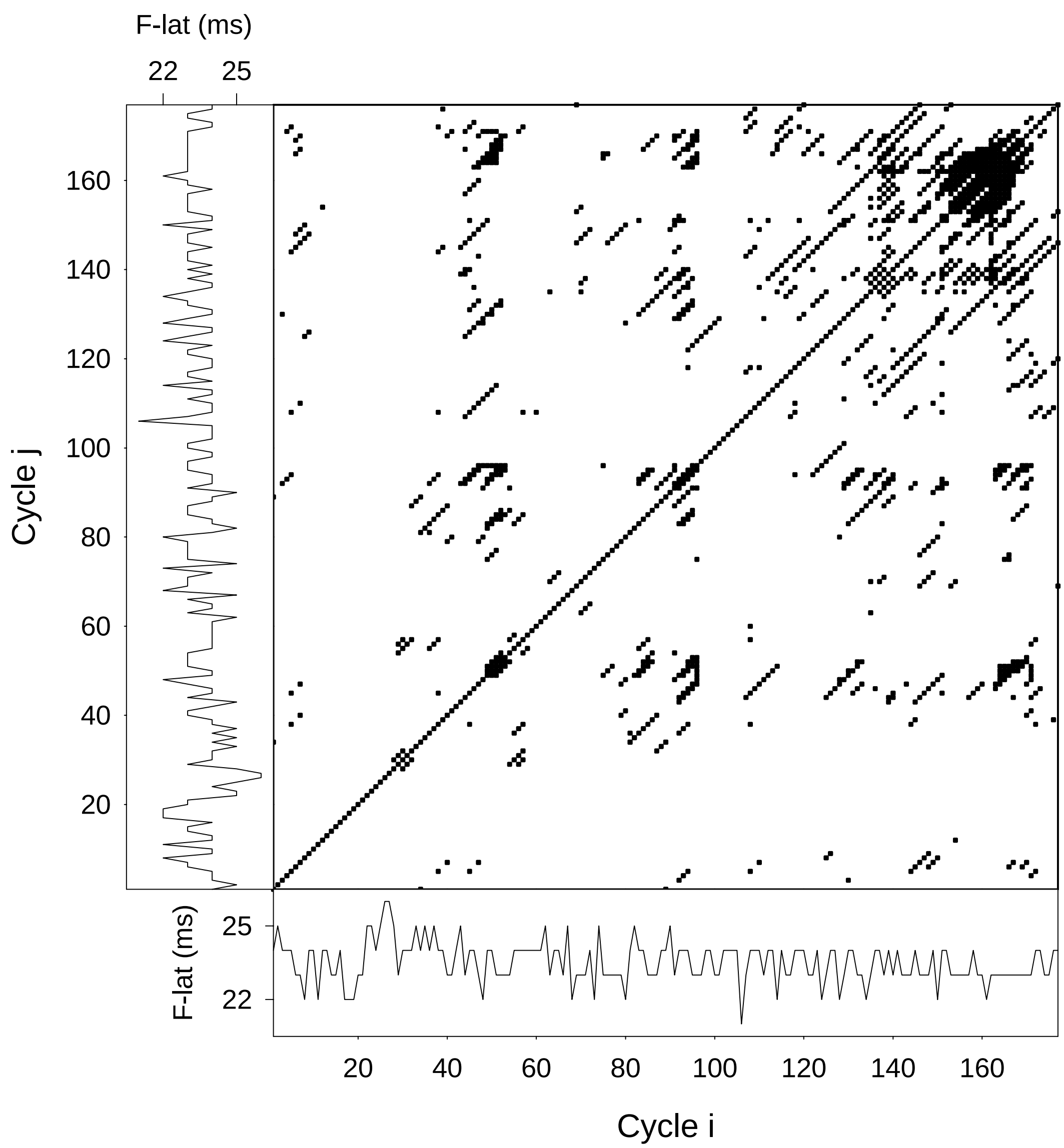
Figure 2: Time Series of Sequential F-wave Latencies.



As F-wave latencies were measured they were placed in the native orders. The time series show complex behaviors with F-wave seldom repeating themselves. The length of each series is proportional to F-wave persistence Data from subject JC4, subject MF5, and subject CW4.

Each F-wave time series was examined at four embedding dimensions: 5, 10, 15 and 20. The results from the third time series of subject JC (JC3) are displayed in Figure 4. In the upper panel, the native %DET values (black bars) are consistently higher than the corresponding shuffled %DET values (light grey bars) at all embedding dimensions. In the lower panel, the differences in native minus averaged-shuffled %DET values are shown (black bars), along with the standard deviation of 10 shuffled trials (light gray) for all embedding dimensions. Taking the ratio of %DET to standard deviation (dark gray bars) defines the factor which in this case is highest for embedding dimension of 5 (starred). The summary results are listed in Table 2. For each of four trials in each of three of three subjects, data are reported at embedding dimensions that yielded the highest factors. If factor values exceeding 1 are assumed to be significant, 8 or the total of 12 trials reached significance.

Figure 3: Recurrence Plot of F-wave Time Series



With an RQA embedding dimension of 10, the radius was automatically adjusted to give a recurrence density of 5%. At this low density, recurrent points form patterns including parallel trajectories (diagonal line structures; %DET) and laminated trajectories (vertical line structures; %LAM).

TABLE 2: Non-linear F-wave Characteristics

Subject	Embed	Factor	%Det-n	%Det-s	%Det-diff	%Det -sd	%Lam-n	%Lam-s	%Lam-diff
JC1	10	1.445	89.410	87.226	2.184	1.511	40.393	28.179	12.214
JC3	5	1.779	79.947	72.845	7.102	3.992	54.679	31.853	22.826
JC4	10	0.524	88.869	88.181	0.688	1.312	26.750	23.871	2.879
JC5	10	2.333	93.115	88.555	4.561	1.955	46.230	32.035	14.195
MF1	5	1.300	77.193	73.800	3.393	2.611	26.901	29.183	-2.282
MF2	5	0.243	73.457	72.300	1.157	4.759	8.025	7.444	0.581
MF3	20	0.905	96.178	93.534	2.644	2.921	33.758	32.026	1.732
MF5	10	1.443	91.444	85.787	5.657	3.920	85.561	39.520	46.041
CW2	10	1.494	92.857	82.500	6.931	10.357	10.714	18.214	-7.500
CW3	15	0.766	93.519	90.311	4.187	3.208	36.111	26.931	9.180
CW4	15	1.627	92.308	87.254	3.106	5.055	25.962	18.038	5.720
CW5	15	1.308	94.595	89.682	3.756	4.913	43.243	21.078	22.165

%DET and %LAM data reported with embedding dimensions adjusted to produce the highest factors (see text). Note differences in these values between native (n) and shuffled (s) data indicating that structuring of F-wave latencies is non-random.

Figure 4: Native versus Shuffled %DET

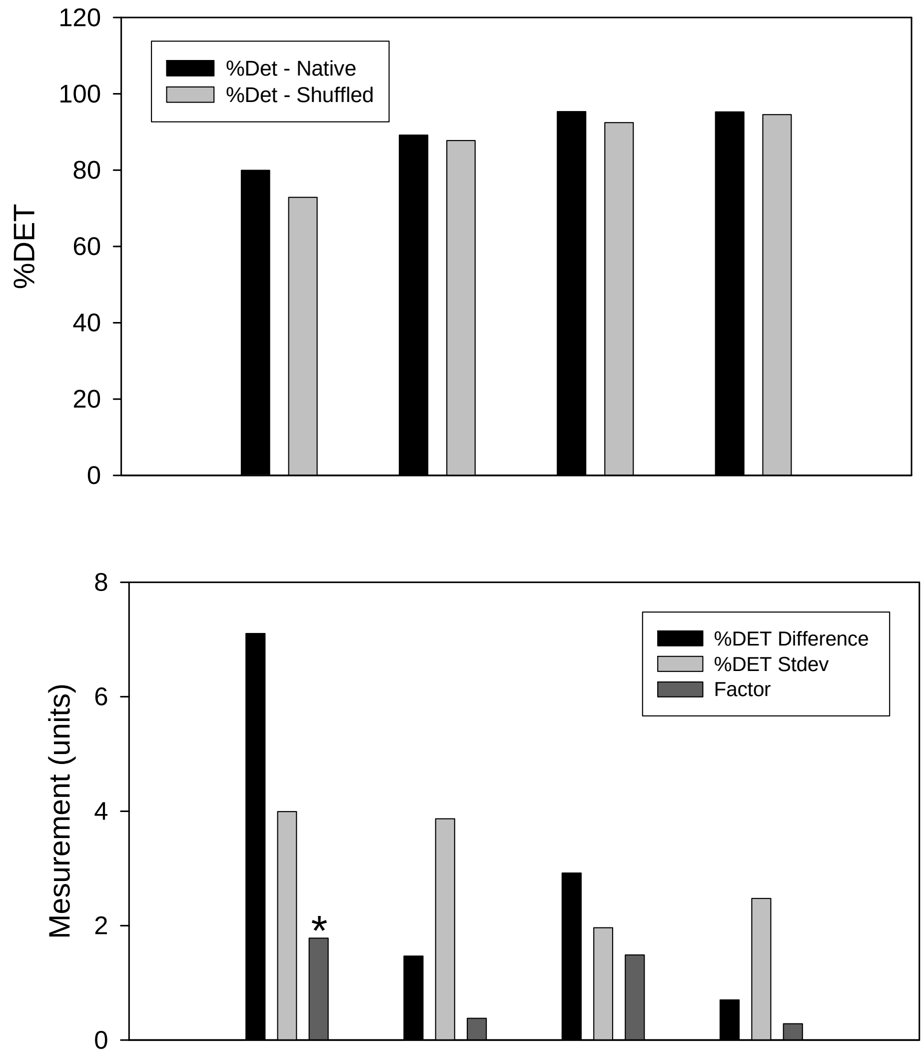


Figure 4 illustrates the effect of shuffling F-wave latency sequences on recurrence quantifications at four embedding dimensions (M = 5, 10, 15 and 20). Upper panel: shuffling decreases %determinism at all embedding dimensions. Lower panel: shuffling gives the highest change in %determinism (%DET difference) and largest factor (%DET difference/%DET stdev) at embedding dimension of 5 (star). Data from subject JC 3.

DISCUSSION

Linear or near-linear systems possess a regularity and simplicity that are readily open to scientific investigations. Yet most animate physiological systems possess numerous complexities that are at best non-linear. A common feature of both living and non-living systems resides in their shared property of recurrence. As signals grow in complexity, recurrences become rarer, until total random sequences lose any structural repeats. The presence of patterned recurrences, however, points to underlying rules derived from fundamental physiological principles (Eckmann et al., 1987).

This study demonstrates that sequences (trajectories) of F-waves can be subjected to nonlinear recurrence quantification analysis (RQA). Of seven recurrence variables defined to date (Webber and Zbilut, 2004), utility in this study was found for %DET and %LAM. Setting the density of recurrent points to 5% insured that compared trajectories were close in distance, but above the noise floor. As controls, F-wave latencies were randomly shuffled to destroy the phasic information carried in the native sequences. Since shuffling resulted in significant decreases in %DET and %LAM, this constitutes sufficient evidence that F-waves possess deterministic structuring. Indeed, the ordering of F-waves was found to be deterministic in each of the three normal subjects in the majority of trials. Thus F-wave recurrences in normal subjects are complex, structured and organized, but definitely non-random. This nonlinear characteristic adds to the other historical descriptors of F-waves, including persistence, mean latency, mean duration and mean amplitude.

This RQA approach to F-wave sequences should be clinically useful. For example, the recurrence of individual F-waves in disorders of the PNS varies. At times, repeater waves can be prominent (Petajan, 1985; Macloed, 1987). Analyses of these differing patterns of recurrent F-waves should therefore help characterize differing patterns of peripheral nerve dysfunction. Patterns of F-waves are altered differentially by different types of CNS injury (Fisher, 1983a,b). Consistent with different patterns of motor unit activation, cross correlations of different linear F-wave parameters varies in patients with upper motor neuron, cerebellar, or extra-pyramidal syndromes. These types of evaluations should be performed with greater accuracy and sensitivity using non-linear variables.

Although 100 stimuli have been used for F-wave analysis in patients (Macloed, 1987), this number of supramaximal stimuli is not really feasible for routine clinical work. This is equally true for the 200 stimuli used in this study. This problem could be obviated by eliciting F-waves with submaximal stimuli even if this required more stimuli to obtain the number of F-waves comparable to that obtained with supramaximal stimulation. RQA analysis of F-wave sequences, in addition to latency, may also allow for meaningful results based on data from a number of stimuli commonly used for the evaluation of F-waves in the clinical situation.

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