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**Fatigue reduces the complexity of knee extensor torque during fatiguing sustained isometric contractions**

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## **Abstract**

The temporal structure, or complexity, of muscle torque output reflects the adaptability of motor control to changes in task demands. This complexity is reduced by neuromuscular fatigue during intermittent isometric contractions. We tested the hypothesis that sustained fatiguing isometric contractions would result in a similar loss of complexity. To that end, nine healthy participants performed, on separate days, sustained isometric contractions of the knee extensors at 20% MVC to task failure and at 100% MVC for 60 seconds. Torque and surface EMG signals were sampled continuously. Complexity and fractal scaling were quantified by calculating approximate entropy (ApEn) and the detrended fluctuation analysis (DFA)  $\alpha$  scaling exponent. Global, central and peripheral fatigue were quantified using maximal voluntary contractions (MVCs) with femoral nerve stimulation. Fatigue reduced the complexity of both submaximal (ApEn from  $1.02 \pm 0.06$  to  $0.41 \pm 0.04$ ,  $P < 0.05$ ) and maximal contractions (ApEn from  $0.34 \pm 0.05$  to  $0.26 \pm 0.04$ ,  $P < 0.05$ ; DFA  $\alpha$  from  $1.41 \pm 0.04$  to  $1.52 \pm 0.03$ ,  $P < 0.05$ ). The losses of complexity were accompanied by significant global, central and peripheral fatigue (all  $P < 0.05$ ). These results demonstrate that a fatigue-induced loss of torque complexity is evident not only during fatiguing intermittent isometric contractions, but also during sustained fatiguing contractions.

**Keywords:** muscle; neuromuscular fatigue; non-linear dynamics; complexity; fractal scaling

## **Introduction**

The temporal structure, or complexity, of muscle torque output is believed to reflect the ability to adapt motor output accurately and rapidly in response to task demands (Vaillancourt and Newell, 2003) and acts as an indirect index of the functional capacity of the neuromuscular system (Pethick et al., 2016; Pethick et al., 2018). Measures of complexity refer to the predictability of a time-series independently from the amplitude of the fluctuations within it (Slifkin and Newell, 2000), and quantify the temporal irregularity and long-range (fractal) correlations present in a time-series (Pincus, 1994; Goldberger et al., 2002). The complexity of isometric torque output has been demonstrated to decrease with neuromuscular fatigue during maximal and submaximal intermittent isometric contractions (Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018), indicating a torque output that becomes smoother, more regular and more predictable as fatigue develops. This decrease in complexity is thought to be due to some effect on the output of the motor unit pool and is indicative of a decreased ability to adapt motor output in response to external perturbation (i.e. a loss of adaptability; Pethick et al., 2015).

Whilst fatigue-induced losses of muscle torque complexity have been repeatedly demonstrated during intermittent isometric contractions (Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018), the effect of sustained isometric contractions on muscle torque complexity has yet to be established. The ability to sustain submaximal force is of importance for activities of daily living (Enoka and Duchateau, 2009) and forms a key component of motor control. Furthermore, sustained isometric contractions have been extensively used in the study of neuromuscular output; providing excellent insight into the complex mechanisms of force production and fatigue (Garland et al., 1994; Hunter and Enoka, 2001; Castronovo et al., 2015).

Decreased torque complexity during intermittent contractions has been demonstrated to compromise motor control, motor adaptability and task performance (Pethick et al., 2016; Pethick et al., 2018), but to what extent torque complexity changes during sustained fatiguing contractions is not known.

It has been demonstrated that sustained isometric contractions result in a decrease in the complexity of surface EMG output in the quadriceps (Beretta-Piccoli et al., 2015; Boccia et al., 2015). Such decreases in the complexity of EMG output may also manifest in the complexity of muscle torque during sustained contractions. Indeed, the apparent coherence between muscle force fluctuations and motor unit spike trains (Farina et al., 2014; Farina and Negro, 2015) suggests an effect on the ensemble activity of the motor unit pool is likely involved in the loss of torque complexity (Pethick et al., 2018). Moreover, a decrease in the complexity of EMG output during sustained contractions has been associated with increased motor unit synchronisation (Mesin et al., 2009), which may be involved in the fatigue-induced loss of muscle torque complexity (Pethick et al., 2016; Pethick et al., 2018).

The aim of the present study was to determine the effect of sustained maximal and submaximal fatiguing contractions on the complexity of knee extensor torque output. The experimental hypotheses were that both maximal and submaximal sustained isometric contractions would result in a reduction in torque complexity (measured by decreased approximate entropy [ApEn]), which would be accompanied by a shift in temporal fractal scaling (measured by increased detrended fluctuation analysis [DFA]  $\alpha$  scaling exponent).

## Methods

### Participants

Nine healthy participants (7 male, 2 female; mean  $\pm$  SD: age  $24.6 \pm 5.5$  years; height  $1.74 \pm 0.07$  m; body mass  $68.9 \pm 10.3$  kg) provided written informed consent to participate in the study, which was approved by the ethics committee of the University of Kent, and which adhered to the Declaration of Helsinki. Participants visited the laboratory on three occasions, with a minimum of 48 hours between each visit. During their first visit, participants were familiarised with all testing equipment and procedures, and the settings for the dynamometer were recorded. The next two visits involved performance of fatiguing sustained maximal and submaximal isometric contractions.

### Dynamometry

Participants sat in the chair of a Cybex isokinetic dynamometer (HUMAC Norm; CSMi, Massachusetts, USA), with their right leg attached to the lever arm of the dynamometer and the seating position adjusted to ensure that the lateral epicondyle of the femur was in line with the axis of rotation of the lever arm. The relative hip and knee angles were  $85^\circ$  and  $90^\circ$ , respectively, with full extension being  $0^\circ$ . The lower leg was attached to the lever arm above the malleoli with a padded Velcro strap. Straps secured firmly across both shoulders and the waist prevented extraneous movement and the use of the hip extensors during the contractions. The seating position was recorded during the first visit and replicated for each subsequent visit.

### Electromyography and femoral nerve stimulation

The EMG of the vastus lateralis was sampled using Ag/AgCl electrodes (32 x 32 mm; inter-electrode distance 35 mm; Nessler Medizintechnik, Innsbruck, Austria). As in our previous

work (Pethick et al., 2015; Pethick et al., 2016), the vastus lateralis alone was sampled as it should be representative of the knee extensors as a whole during isometric contractions. Furthermore, it has been demonstrated that the vasti are controlled primarily by a shared neural drive (Laine et al., 2015). The skin of the participants was shaved, abraded and cleaned with an alcohol swab over the belly of the muscle. The electrodes were placed in a direction parallel to the alignment of the muscle fibres over the belly of the muscle. A reference electrode was placed on prepared skin medial to the tibial tuberosity. The raw EMG signals were sampled at 1 kHz, amplified (gain 1000; Biopac MP150, Biopac Systems Inc., California, USA) and band-pass filtered (10-500 Hz; Biopac MP150).

The anode (100 x 50 mm; Phoenix Healthcare Products Ltd., Nottingham, UK) was placed on the lower portion of the gluteus maximus, lateral to the ischial tuberosity. The cathode, an Ag/AgCl electrode (32 x 32 mm; Nessler Medizintechnik, Innsbruck, Austria), was placed over the femoral nerve. The appropriate stimulator current was established as described in Pethick et al. (2015), using a constant-current, variable voltage stimulator (Digitimer DS7AH, Welwyn Garden City, UK). Briefly, current was incrementally increased (in steps of 20 mA) until knee extensor torque and the M-wave response to single twitches had plateaued, and was verified with stimulation delivered during a contraction at 50% MVC to ensure a maximal M-wave was also evident during an isometric contraction. The stimulator current was then increased to 130% of the current producing a maximal M-wave. In all subsequent trials, doublet stimulation (two 200  $\mu$ s pulses with 10 ms interpulse interval) was used.

## Protocol

Each visit began with the instrumentation of the participants and the (re-)establishment of the correct dynamometer seating position and supramaximal stimulation response. Maximal torque

was established as in Pethick et al. (2015). Participants performed a series of brief (3 second) MVCs, separated by a minimum of 60 seconds rest. The first MVC was used to establish the fresh maximal EMG signal, against which subsequent signals were normalised (Data analysis; see below). The second and third MVCs were performed with femoral nerve stimulation. During a plateau in torque, ~1.5 seconds into the contraction, a doublet was superimposed on the contraction to test its maximality and provide the fresh voluntary activation. A further doublet was delivered at rest 2 seconds after the contraction to establish the fresh potentiated doublet torque (Data analysis; see below). All subsequent contractions with femoral nerve stimulation were conducted in this manner. Participants then rested for 10 minutes before performing either the maximal or submaximal test.

#### Maximal test

Participants performed a sustained MVC for 60 seconds. This duration was chosen based on its use in previous research (Bigland-Ritchie et al., 1978). Participants were given feedback on their previous MVCs and were encouraged to equal or exceed these values during the first 2-3 seconds of the contraction. Participants were also informed to expect their torque to decline by more than 50% during the test, but to produce a maximal effort despite this occurrence. During the test participants were very strongly encouraged to maximise and maintain their torque. At the end of the 60 seconds, participants performed a 3 second MVC, accompanied by femoral nerve stimulation.

#### Submaximal test

Participants performed a sustained contraction at a target torque of 20% MVC, determined from the highest instantaneous MVC torque measured at the start of the visit. Participants were instructed to match their instantaneous torque with a target bar superimposed on a display in



front of them and were required to continue matching this torque for as long as possible. The fatiguing contraction was terminated either voluntarily or when the torque declined by 10% of the target value for greater than 5 seconds. Immediately at task failure, participants performed a 3 second MVC, accompanied by femoral nerve stimulation.

#### Data acquisition

Data acquisition was performed as described in Pethick et al. (2015). All devices were connected via BNC cables to a Biopac MP150 (Biopac Systems Inc., California, USA) and a CED Micro 1401-3 (Cambridge Electronic Design, Cambridge, UK) interfaced with a personal computer. All signals were sampled at 1 kHz. The data were collected in Spike2 (Version 7; Cambridge Electronic Design, Cambridge, UK). A chart containing the instantaneous torque was projected onto a screen placed ~1 m in front of the participant. A scale consisting of a thin line (1 mm thick) was superimposed on the torque chart and acted as a target, so that participants were able to match their instantaneous torque output to the target torque during the submaximal test.

#### Data analysis

All data were analysed using code written in MATLAB R2013a (The MathWorks, Massachusetts, USA).

The fluctuations in torque were quantified according to their variability and complexity. Each of the experimental trials was divided into 10 second bins, and the measures of variability and complexity calculated using the steadiest 5 seconds of each 10 second bin, identified by MATLAB code as the 5 seconds containing the lowest standard deviation (SD). The amount of variability was quantified using the SD, which provides a measure of the absolute amount

of variability in a time-series, and the coefficient of variation (CV), which provides a measure of variability normalised to the mean of the time-series. The complexity of torque was examined using multiple time domain analyses. The regularity of torque output was determined using approximate entropy (ApEn; Pincus, 1991), and the temporal fractal scaling was estimated using the detrended fluctuation analysis (DFA)  $\alpha$  scaling exponent (Peng et al., 1994). Sample entropy (Richman and Moorman, 2000) was also calculated, but as shown in Pethick et al. (2015) this did not differ from ApEn. Full details of the calculations of ApEn and DFA  $\alpha$  are detailed in Pethick et al. (2015). ApEn was calculated with the template length,  $m$ , set at 2 and the tolerance,  $r$ , set at 10% of the standard deviation of torque output, and DFA was calculated across time scales (57 boxes ranging from 1250 to 4 data points).

In order to analyse the torque data in the frequency domain, as well as the time domain, the fast Fourier transform was used to calculate the power spectra for frequencies within the torque output. This was accomplished, as with the measures of variability and complexity, using 10 second bins. The mean power frequency (MnPF) of the torque output was calculated as a spectral measure of central tendency in the frequency domain to provide information regarding the distribution of power.

The EMG output from the vastus lateralis was also analysed using 10 second bins, and the 5 seconds with the lowest SD. The EMG output was filtered (10-500 Hz) and full-wave rectified. The rectified EMG was then low-pass filtered, using a 4<sup>th</sup> order Butterworth filter with a 10 Hz cut-off, in order to obtain the EMG linear envelope. This linear envelope was then subjected to the same complexity analysis as the torque output (see above). A linear envelope was applied as analysis of the raw EMG indicated the output approximated uncorrelated white noise (DFA  $\alpha = \sim 0.5$ ). Given the coherence between motor unit spike trains and force fluctuations (Farina

and Negro, 2015), a 10 Hz filter was chosen based on the similarity of the resultant EMG noise colour with that of the torque output. The average rectified EMG (arEMG) was also calculated and normalised by expressing the arEMG as a fraction of the arEMG obtained during an MVC from fresh muscle performed at the beginning of the trial.

Measures of central and peripheral fatigue were calculated based on the stimuli delivered during and after the MVCs performed pre-test and at task end/failure. Peripheral fatigue was evidenced by a fall in the potentiated doublet torque. Central fatigue was evidenced by a fall in voluntary activation, assessed using the twitch interpolation technique (Behm et al., 1996):

$$\text{Voluntary activation (\%)} = (1 - \text{superimposed doublet/resting doublet}) \times 100$$

where the superimposed doublet was that measured during the contraction of interest and the potentiated doublet was measured at rest 2 seconds after the contraction.

### Statistics

All data are presented as means  $\pm$  SD, and results were deemed statistically significant when  $P < 0.05$ . The complexity, variability, frequency and EMG data were analysed using averages calculated over 30 seconds. Bonferroni-adjusted 95% paired-samples confidence intervals were used to identify specific differences between pre-test/task beginning and task failure values for MVC torque, potentiated doublet torque, voluntary activation, arEMG, torque variability, complexity and frequency, and EMG complexity.

## Results

### Global, peripheral and central fatigue

MVC torque significantly decreased over time in both conditions, indicating the presence of global fatigue. During the maximal test, MVC torque decreased from  $216.8 \pm 41.0$  to  $115.4 \pm 20.9$  N·m (95% paired samples confidence intervals (CIs)  $-122.5$ ,  $-80.4$  N·m). Task failure in the submaximal test occurred after  $256.4 \pm 54.5$  s, during which time MVC torque had decreased from  $220.2 \pm 35.7$  to  $109.7 \pm 21.4$  N·m (CIs  $-133.7$ ,  $-87.3$  N·m).

Potentiated doublet torque and voluntary activation significantly decreased over the course of both conditions, indicating the presence of peripheral and central fatigue, respectively. In the maximal test, potentiated doublet torque fell from  $93.1 \pm 16.1$  to  $45.5 \pm 16.3$  N·m (CIs  $-60.9$ ,  $-34.4$  N·m); while in the submaximal test it fell from  $94.2 \pm 16.3$  to  $63.0 \pm 17.0$  N·m (CIs  $-39.1$ ,  $-23.4$  N·m). During the maximal test, voluntary activation fell from  $92.4 \pm 3.1$  to  $74.9 \pm 11.1\%$  (CIs  $-26.7$ ,  $-8.4\%$ ); while in the submaximal test it fell from  $92.6 \pm 2.8$  to  $79.5 \pm 8.0\%$  (CIs  $-19.1$ ,  $-7.1\%$ ).

### EMG amplitude and complexity

Over the course of the maximal test, the vastus lateralis arEMG progressively decreased from  $97.2 \pm 13.6\%$  during the first 30 seconds to  $81.2 \pm 18.1\%$  during the last 30 seconds (CIs  $-23.9$ ,  $-8.5\%$ ). Over the course of the submaximal test, the vastus lateralis arEMG progressively increased from  $19.5 \pm 3.7\%$  during the first 30 seconds to  $52.8 \pm 14.9\%$  at task failure (CIs  $20.8$ ,  $45.9\%$ ). The complexity of the EMG linear envelope did not change over the course of either the maximal test (ApEn,  $0.31 \pm 0.01$  to  $0.29 \pm 0.01$ , CIs  $-0.003$ ,  $0.03$ ; DFA  $\alpha$ ,  $1.36 \pm$

0.01 to  $1.38 \pm 0.01$ , CIs  $-0.05, 0.01$ ) or the submaximal test (ApEn,  $0.36 \pm 0.01$  to  $0.33 \pm 0.01$ , CIs  $-0.02, 0.07$ ; DFA  $\alpha$ ,  $1.30 \pm 0.01$  to  $1.33 \pm 0.02$ , CIs  $-0.09, 0.02$ ).

#### Torque variability and complexity

During the maximal test, the SD increased from  $3.6 \pm 1.4$  N·m (first 30 seconds) to  $5.1 \pm 1.9$  N·m (last 30 seconds; CIs 0.03, 2.6 N·m), while the CV increased from  $2.4 \pm 0.9\%$  to  $5.2 \pm 2.5\%$  (CIs 1.3, 4.1%). During the submaximal test, the SD increased from  $0.8 \pm 0.2$  (first 30 seconds) to  $4.3 \pm 1.4$  N·m (task failure; CIs 2.4, 4.5 N·m), while the CV increased from  $1.8 \pm 0.4$  to  $9.7 \pm 3.1\%$  (CIs 5.7, 10.2%).

Complexity decreased over time in the maximal test, as evidenced by a fall in ApEn from  $0.34 \pm 0.15$  (first 30 seconds) to  $0.26 \pm 0.13$  (last 30 seconds; CIs  $-0.2, -0.01$ ; Figure 1a) and an increase in DFA  $\alpha$  from  $1.41 \pm 0.12$  to  $1.52 \pm 0.09$  (CIs 0.03, 0.2; Figure 1b). Complexity also significantly decreased over time in the submaximal test, as evidenced by a fall in ApEn from  $1.02 \pm 0.21$  (first 30 seconds) to  $0.41 \pm 0.13$  (task failure; CIs  $-0.8, -0.4$ ; Figure 1a). DFA  $\alpha$  did not change in the submaximal test ( $1.28 \pm 0.07$  to  $1.35 \pm 0.16$ ; CIs  $-0.3, 0.1$ ; Figure 1b). Raw torque outputs from the beginning, middle and end of representative contractions in the submaximal and maximal tests are shown in Figures 2 and 3, respectively, and individual data for each subject from the submaximal and maximal tests are shown in Figure 4.

#### Frequency

The MnPF increased from  $3.94 \pm 0.01$  to  $4.00 \pm 0.05$  Hz (CIs 0.03, 0.08 Hz) over the course of the maximal test and from  $4.16 \pm 0.18$  to  $4.57 \pm 0.35$  Hz (CIs 0.1, 0.7 Hz) over the course of the submaximal test.

## Discussion

The major novel finding of the present investigation was that sustained fatiguing isometric contractions of the knee extensors resulted in a decrease in torque complexity, regardless of whether the knee extensors were driven maximally or submaximally. This reduced complexity was quantified by decreased entropy and increasingly Brownian fluctuations (DFA  $\alpha = 1.50$ ) during the maximal contractions. Interestingly, in contrast to our hypothesis, the decrease in entropy during the submaximal contractions was not accompanied by a shift towards a Brownian torque output. In contrast to the loss of complexity and smoothing of torque time-series previously observed during intermittent submaximal fatiguing contractions (Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018), the loss of complexity during the sustained submaximal contractions appeared to be characterised by increasingly sinusoidal behaviour (Figure 2). These results extend previous findings regarding the loss of torque complexity during intermittent fatiguing contractions, providing the first indication that the complexity of muscle torque output also decreases during sustained fatiguing contractions.

### Fatigue-induced reduction in torque complexity

Maximal and submaximal sustained fatiguing contractions both resulted in significant decreases in torque complexity, as measured by decreased ApEn and increased DFA  $\alpha$  during the maximal test, and by decreased ApEn alone during the submaximal test. (Figure 1). This extends our previous findings indicating a loss of torque complexity during intermittent fatiguing contractions (Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018) to sustained fatiguing contractions and provides further evidence that neuromuscular fatigue compromises the control of muscle torque production and reduces the adaptability of motor

output (Pethick et al., 2015). Though such a fatigue-induced loss of torque complexity has not been previously observed during sustained contractions, decreased complexity of surface EMG output has been frequently observed during sustained fatiguing contractions of various muscle groups (Mesin et al., 2009), including the knee extensors (Beretta-Piccoli et al., 2015; Boccia et al., 2015).

In contrast to previous studies, we did not observe a decrease in the complexity of surface EMG output. This could be attributed to methodological differences: previous research has utilised high-density surface EMG arrays and calculated the fractal dimension (Beretta-Piccoli et al., 2015; Boccia et al., 2015), whereas we used a bipolar EMG setup and calculated ApEn and DFA  $\alpha$ . Such differences may arise from our use of bipolar EMG, which simply provides the interference pattern of a single channel, compared to the multiple channels of high-density arrays. Alternatively, differences may arise due to the use of different complexity metrics, which quantify different aspects of physiological outputs and which may not be correlated. We have hypothesised that changes in muscle torque complexity are a result of changes in motor unit behaviour (Pethick et al., 2015). It has been demonstrated that, due to factors such as amplitude cancellation and summation, bipolar surface EMG is not a faithful representation of neural drive and ensemble motor unit activity (Farina et al., 2004; Keenan et al., 2006). Thus, it may not be possible to detect the changes in motor unit behaviour we hypothesise are responsible for the loss of muscle torque complexity using bipolar EMG. We therefore suggest that high-density EMG arrays (or intramuscular EMG), from which individual motor unit spike trains can be decomposed, represent the best way to analyse the complexity of EMG output.

That ApEn significantly changed during the submaximal test but DFA  $\alpha$  did not is of interest, since our previous studies using intermittent contractions have shown changes in both metrics

(Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018). ApEn and DFA quantify very different aspects of physiological outputs; ApEn measures the regularity or randomness of a time-series only across one time-scale, while DFA estimates the temporal fractal scaling and noise colour across multiple time-scales (Seely and Macklem, 2004). Thus, while we have previously observed congruence between changes in ApEn and DFA  $\alpha$ , such agreement is not guaranteed and insensitivity of one complexity metric to experimental intervention does not imply that other metrics will also lack meaningful relationships to the functionality of the system (Manor and Lipsitz, 2013). The lack of a significant increase in DFA  $\alpha$  during the submaximal test is likely due to individual differences in the response: several participants exhibited decreased rather than increased values (Figure 4).

Although a fatigue-induced loss of complexity was observed during the sustained submaximal contractions in the present study, the nature of this change did not appear, visually at least, the same as that previously observed for intermittent contractions (Pethick et al., 2015; Pethick et al., 2016; Pethick et al., 2018). During intermittent fatiguing contractions, the loss of torque complexity is manifest as a progressively smoother output with fewer high frequency fluctuations, whereas in the submaximal contractions in the present study there were progressively greater low frequency fluctuations that appeared to manifest as a more periodic and sinusoidal output (Figure 2). Nevertheless, both the smoothing of a time-series and more sinusoidal activity are indicative of increased regularity and predictability, and therefore decreased complexity (Pincus, 1991; Pincus and Goldberger, 1994). It is possible that the increasing periodicity in torque complexity during the submaximal contractions relates to physiological tremor, an approximately rhythmic and roughly sinusoidal movement with a dominant frequency of 8-12 Hz (Elble and Koller, 1990; McAuley and Marsden, 2000). As fatigue developed during the submaximal contractions there was a shift in the spectral



components of the torque output towards higher frequencies, as evidenced by an increase in MnPF, and, indeed, it has previously been demonstrated that tremor increases during sustained fatiguing contractions (Löscher et al., 1996; Hunter and Enoka, 2001), and that there is a shift in the spectral components of torque towards higher frequencies (from 0-3 to 8-12 Hz) with fatigue (Kouzaki et al., 2004; Singh et al., 2010). Fluctuations at a greater magnitude and higher frequency imply greater periodicity (i.e. decreased complexity) in an output (Singh et al., 2010).

#### Physiological bases for changes in neuromuscular system behaviour

The loss of torque complexity observed during the sustained maximal contractions was likely directly related to a loss of agonist torque generating capacity (Pethick et al., 2015). However, if the loss of torque complexity during the submaximal contractions reflects a loss of motor control it must, by definition, be due to some effect of central or peripheral processes modulating the excitatory and inhibitory properties of the motor unit pool (Kilner et al., 1999; Pethick et al., 2015). Both central and peripheral fatigue developed during the progression of the submaximal contractions and, indeed, both central and peripheral mechanisms have been linked to the fatigue-induced loss of torque complexity (Pethick et al., 2016).

It has previously been demonstrated that during intermittent contractions, complexity only declines as a function of time above the critical torque (Pethick et al., 2016). The submaximal intensity used in the present study was likely above the critical torque, which typically occurs at ~15% MVC for sustained contractions (Monod and Scherrer, 1965; Hendrix et al., 2009). As metabolite-mediated peripheral fatigue is the dominant fatigue mechanism above the critical torque, this further suggests that the fatigue-induced loss of complexity is, in some way, related to peripheral fatigue (Pethick et al., 2016). However, it remains unclear whether the peripheral

adjustments that occur above the critical torque (i.e. phosphocreatine depletion, inorganic phosphate and proton accumulation; Jones et al., 2008; Vanhatalo et al., 2010), directly contribute to the loss of complexity or are merely prerequisites for central adjustments, which then cause a loss of complexity (Pethick et al., 2016).

One of the central adjustments hypothesised to be involved in the fatigue-induced loss of muscle torque complexity is common synaptic input (Pethick et al., 2016). A necessary consequence of common synaptic input is the correlated discharge of action potentials, known as motor unit synchronisation (Farina and Negro, 2015). Common synaptic input and motor unit synchronisation have been suggested to be the main determinants of torque variability (Farina et al., 2014). It has been demonstrated that common synaptic input and motor unit synchronisation increase with both increasing contractile intensity and the development of fatigue (Castronovo et al., 2015), just as muscle torque complexity decreases under such conditions (Pethick et al., 2015; Pethick et al., 2016). The use of bipolar EMG electrodes in the present study did not allow us to address the potential link between motor unit synchronisation and muscle torque complexity, as the bipolar EMG comprises the sum of contributions made by active motor units rather than detecting activity of single motor units (Farina et al., 2004). Direct measurement of individual motor units via high-density surface EMG arrays is necessary to confirm such a link, and, indeed, studies using this methodology have linked the decrease in surface EMG complexity with increased motor unit synchronisation (Mesin et al., 2009; Beretta-Piccoli et al., 2015).

## Conclusions

Fatiguing sustained isometric contractions of the knee extensors led to a significant reduction in the complexity of torque output. This reduction in complexity was manifest as a decrease in

ApEn and increase in DFA  $\alpha$  during maximal contractions and a decrease in ApEn alone during submaximal contractions. The reduced complexity during the submaximal contractions appeared to manifest as increasingly sinusoidal behaviour, unlike the loss of complexity previously observed during intermittent contractions, which was manifest as a smoothing of the time series. This suggests that the nature of the fatigue-induced loss of muscle torque complexity is task dependent.

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**Competing interests:**

The authors report no competing interests for this work.

## References

- Behm, D.G., St-Pierre, D.M.M. and Perez, D. (1996). Muscle inactivation: assessment of interpolated twitch technique. *Journal of Applied Physiology*, **81**, 2267-2273.
- Beretta-Piccoli, M., D'Antona, G., Barbero, M., Fisher, B., Dieli-Conwright, C.M., Clijsen, R. and Cescon, C. (2015). Evaluation of central and peripheral fatigue in the quadriceps using fractal dimension and conduction velocity in young females. *PLoS One*, **10**, e0123921.
- Bigland-Ritchie, B., Jones, D.A., Hosking, G.P and Edwards, R.H.T. (1978). Central and peripheral fatigue in sustained maximum voluntary contractions of human quadriceps muscle. *Clinical Science and Molecular Medicine*, **54**, 609-614.
- Boccia, G., Dardanello, D., Beretta-Piccoli, M., Cescon, C., Coratella, G., Rinaldo, N., Barbero, M., Lanza, M., Schena, F. and Rainoldi, A. (2015). Muscle fiber conduction velocity and fractal dimension of EMG during fatiguing contraction of young and elderly active men. *Physiological Measurement*, **37**, 162,
- Castronovo, A.M., Negro, F., Conforto, S. and Farina, D. (2015). The proportion of synaptic input to motor neurons increases with an increase in net excitatory input. *Journal of Applied Physiology*, **119**, 1337-1346.
- Elble, R.J. and Koller W.C. (1990). Tremor. The John Hopkins University Press, Baltimore, Maryland.

Enoka, R.M. and Duchateau, J. (2008). Muscle fatigue: what, why and how it influences muscle function. *Journal of Physiology*, **586**, 11-12.

Farina, D., Merletti, R. and Enoka, R.M. (2004). The extraction of neural strategies from the surface EMG. *Journal of Applied Physiology*, **96**, 1486-1495.

Farina, D., Negro, F. and Dideriksen, J.L. (2014). The effective neural drive to muscles is the common synaptic input to motor neurons. *Journal of Physiology*, **592**, 3427-3441.

Farina, D. and Negro, F. (2015). Common synaptic input to motor neurons, motor unit synchronization and force control. *Exercise and Sport Sciences Reviews*, **43**, 23-33.

Garland, S.J., Enoka, R.M., Serrano, L.P. and Robinson, G.A. (1994). Behaviour of motor units in human biceps brachii during a submaximal fatiguing contraction. *Journal of Applied Physiology*, **76**, 2411-2419.

Goldberger, A.L., Amaral, L.A., Hausdorff, J.M., Ivanov, P.C., Peng, C.K. and Stanley, H.E. (2002). Fractal dynamics in physiology: alterations with disease and aging. *Proceedings of the National Academy of Sciences*, **99**, 2466-2472.

Hendrix, C.R., Housh, T.J., Johnson, G.O. Mielke, M., Camic, C.L. Zuniga, J.M. and Schmidt, R.J. (2009). Comparison of critical force to EMG fatigue thresholds during isometric leg extension. *Medicine & Science in Sports & Exercise*, **41**, 956-964.

Hunter, S.K. and Enoka, R.M. (2001). Sex differences in the fatigability of arm muscles depends on absolute force during isometric contractions. *Journal of Applied Physiology*, **91**, 2686-2694.

Jones, A.M., Wilkerson, D.P., DiMenna, F., Fulford, J. and Poole, D.C. (2008). Muscle metabolic responses to exercise above and below the “critical power” assessed using <sup>31</sup>P-MRS. *American Journal of Physiology*, **294**, R585-R593.

Keenan, K.G., Farina, D., Merletti, R. and Enoka, R.M. (2006). Amplitude cancellation reduces the size of motor unit potentials averaged from the surface EMG. *Journal of Applied Physiology*, **100**, 1928-1937.

Kilner, J.M., Baker, S.N., Salenius, S., Jousmäki, V., Hari, R. and Lemon, R.N. (1999). Task-dependent modulation of 15-30 Hz coherence between rectified EMGs from human hand and forearm muscles. *Journal of Physiology*, **516**, 558-570.

Kouzaki, M., Shinohara, M., Masani, K. and Fukunaga, T. (2004). Force fluctuations are modulated by alternate muscle activity of knee extensor synergists during low-level sustained contraction. *Journal of Applied Physiology*, **97**, 2121-2131.

Laine, C.M., Martinez-Valdes, E., Dalla, F., Mayer, F. and Farina, D. (2015). Motor neuron pools of synergistic thigh muscles share most of their synaptic input. *Journal of Neuroscience*, **35**, 12207-12216.

Löscher, W.N., Cresswell, A.G. and Thorstensson, A. (1996). Central fatigue during a long-lasting submaximal contraction of the triceps surae. *Experimental Brain Research*, **108**, 305-314.

Manor, B. and Lipsitz, L.A. (2013). Physiologic complexity and aging: Implications for physical function and rehabilitation. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, **45**, 287-293.

McAuley, J.H. and Marsden, C.D. (2000). Physiological and pathological tremors and rhythmic central motor control. *Brain*, **123**, 1545-1567.

Mesin, L., Cescon, C., Gazzoni, M., Merletti, R. and Rainoldi, A. (2009). A bi-directional index for the selective assessment of myoelectric manifestations of peripheral and central muscle fatigue. *Journal of Electromyography and Kinesiology*, **19**, 851-863.

Monod, H. and Scherrer, J. (1965). The work capacity of a synergic muscular group. *Ergonomics*, **8**, 329-338.

Peng, C.K., Buldyrev, S.V, Havlin, S., Simon, M., Stanley, H.E. and Goldberger, A.L. (1994). Mosaic organization of DNA nucleotides. *Physical Review E*, **49**, 1685-1689.

Pethick, J., Winter, S.L. and Burnley, M. (2015). Fatigue reduces the complexity of knee extensor torque fluctuations during maximal and submaximal intermittent isometric contractions in man. *Journal of Physiology*, **593**, 2085-2096.

Pethick, J., Winter, S.L. and Burnley, M. (2016). Loss of knee extensor torque complexity during fatiguing isometric muscle contractions occurs exclusively above the critical torque. *American Journal of Physiology*, **310**, 1144-153.

Pethick, J., Winter, S.L. and Burnley, M. (2018). Caffeine ingestion attenuates fatigue-induced loss of muscle torque complexity. *Medicine & Science in Sports & Exercise*, **50**, 236-245.

Pincus, S.M. (1991). Approximate entropy as a measure of system complexity. *Proceedings of the National Academy of Sciences*, **88**, 2297-2301.

Pincus S.M. (1994). Greater signal regularity may indicate increased system isolation. *Mathematical Biosciences*, **122**, 161-181.

Pincus, S.M. and Goldberger, A.L. (1994). Physiological time-series analysis: what does regularity quantify? *American Journal of Physiology*, **35**, H1643-H1656.

Richman, J.S. and Moorman, J.R. (2000). Physiological time-series analysis using approximate entropy and sample entropy. *American Journal of Physiology – Heart and Circulatory Physiology*, **278**, H2039-2049.

Singh, N.B., Arampatzis, A., Duda, G., Heller, M.O. and Taylor, W.R. (2010). Effect of fatigue on force fluctuations in knee extensors in young adults. *Philosophical Transactions of the Royal Society A*, **368**, 2783-2798.



Slifkin, A.B. and Newell, K.M. (2000). Variability and noise in continuous force production. *Journal of Motor Behavior*, **32**, 141-150.

Søgaard, K., Gandevia, S.C., Todd, G., Petersen, N.T. and Taylor, J.L. (2006). The effect of sustained low-intensity contractions on supraspinal fatigue in human elbow flexor muscles. *Journal of Physiology*, **573**, 511-523.

Vaillancourt, D.E. and Newell, K.M. (2002). Changing complexity in human behavior and physiology through aging and disease. *Neurobiology of Aging*, **23**, 1-11.

Vaillancourt, D.E. and Newell, K.M. (2003). Ageing and the time and frequency structure of force output variability. *Journal of Applied Physiology*, **94**, 903-912.

Vanhatalo, A., Fulford, J., DiMenna, F.J., and Jones, A.M. (2010). Influence of hyperoxia on muscle metabolic responses and the power-duration relationship during severe-intensity exercise in humans: a <sup>31</sup>P magnetic resonance spectroscopy study. *Experimental Physiology*, **95**, 528-540.

## Figure legends

### Figure 1

Complexity and fractal scaling analysis of knee extensor torque. Panel A, approximate entropy (ApEn); Panel B, detrended fluctuation analysis (DFA)  $\alpha$  scaling exponent. Open circles represent the maximal test; closed circles represent the submaximal test. \* indicates a significant difference from test beginning

### Figure 2

Raw torque output from a representative participant from the submaximal test. The top panel shows the whole of the trial. The bottom panels represent, respectively, 0.5 second snapshots from the beginning, middle and end of the test.

### Figure 3

Raw torque output from a representative participant from the maximal test. The top panel shows the whole 60 seconds of the trial. The bottom panels represent, respectively, 0.5 second snapshots from the beginning, middle and end of the test.

### Figure 4

Individual changes in complexity and fractal scaling during the submaximal and maximal tests. Panel A, approximate entropy from the submaximal test; Panel B, approximate entropy from the maximal test; Panel C, detrended fluctuation analysis  $\alpha$  from the submaximal test; Panel D, detrended fluctuation analysis  $\alpha$  from the maximal test.

**Figure 1**

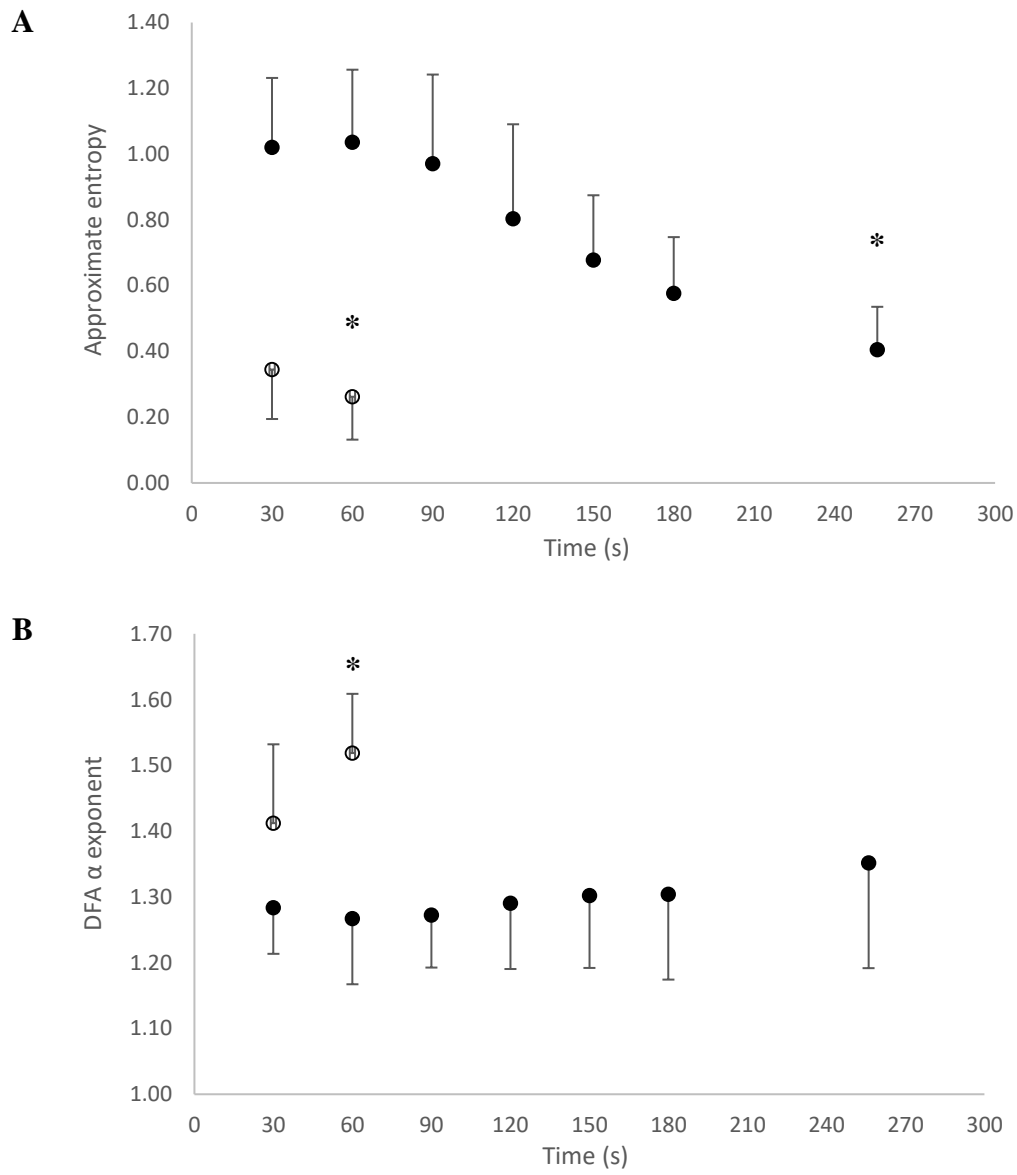
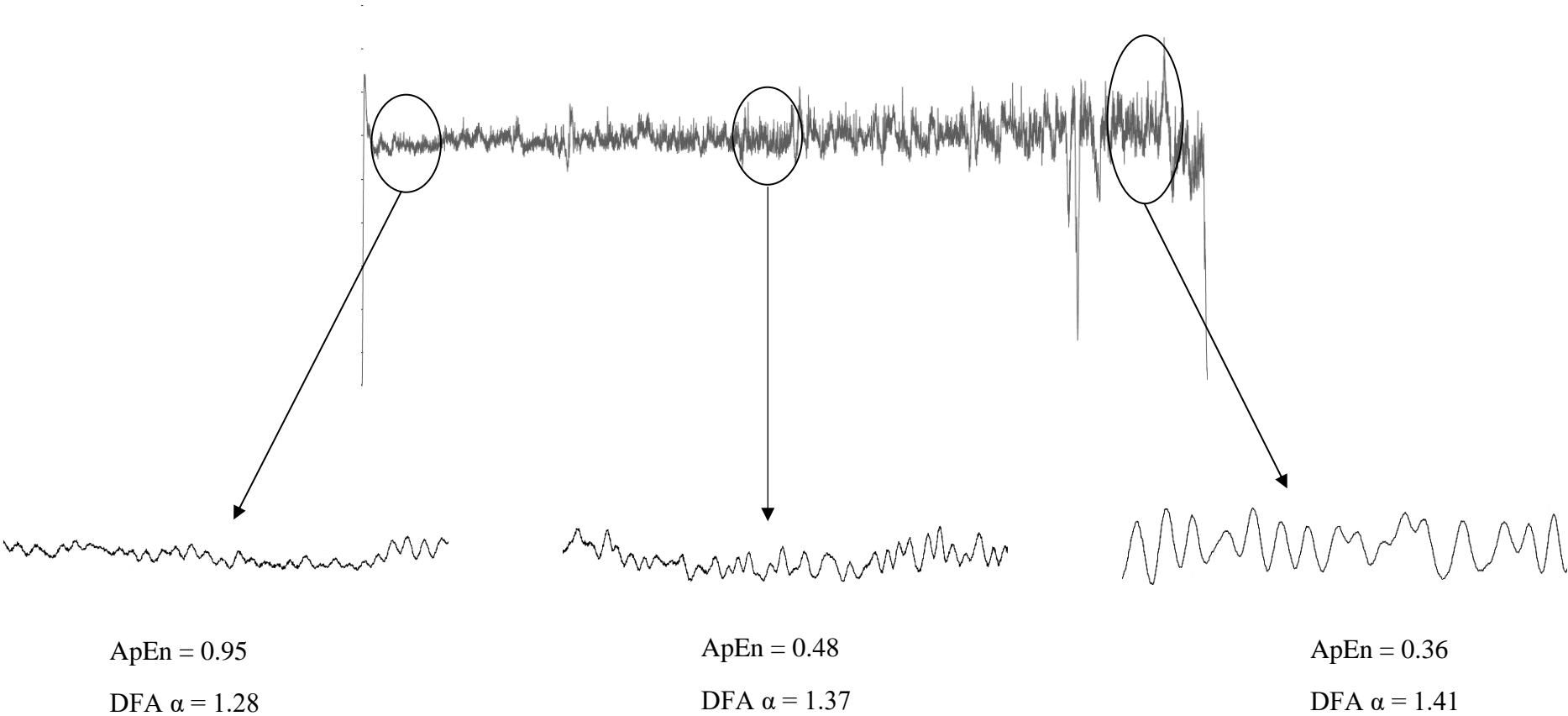
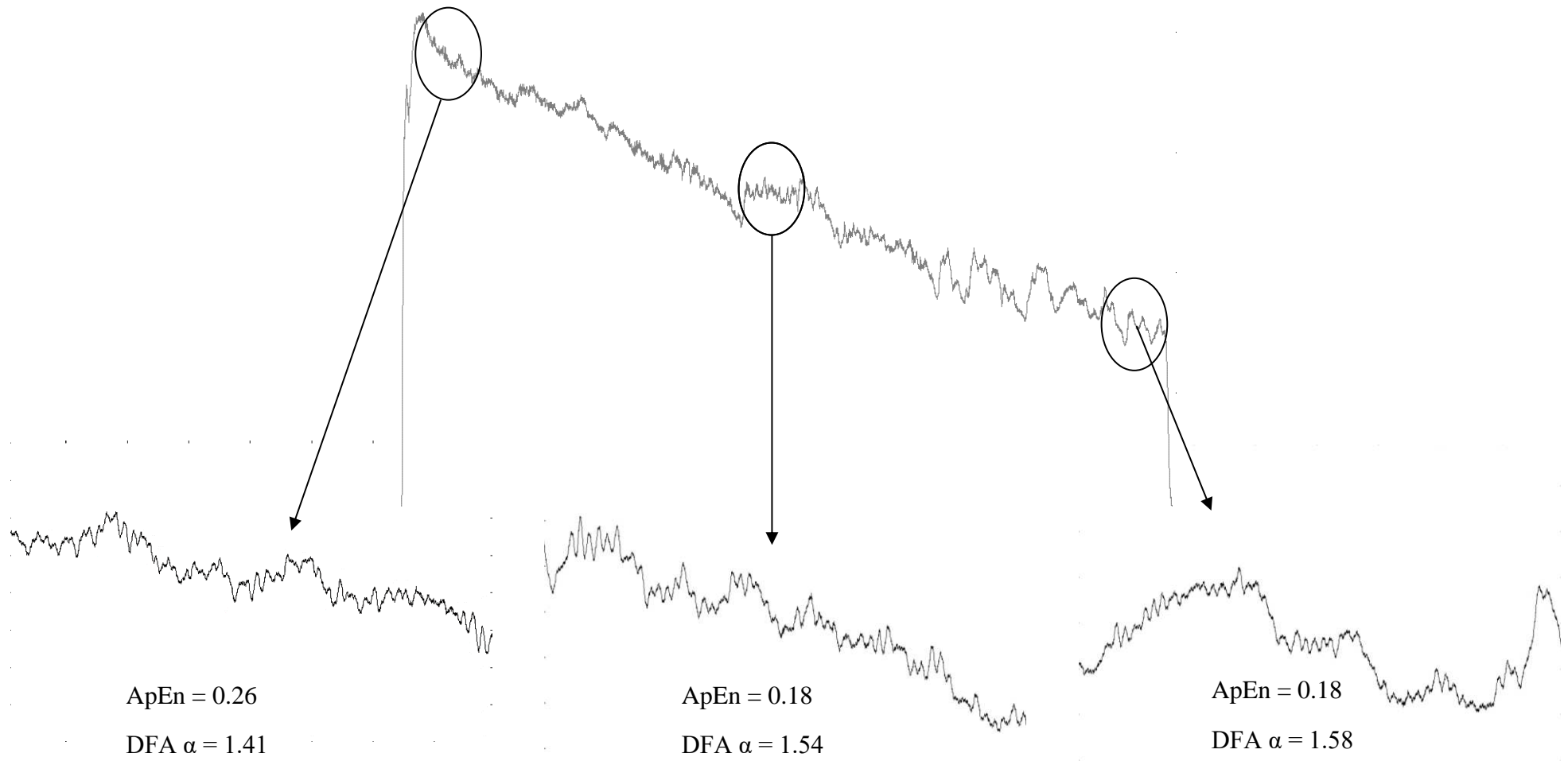


Figure 2



**Figure 3**



**Figure 4**

