ACTA PHYSIOLOGICA

Did you know? Using entropy and fractal geometry to quantify fluctuations in physiological outputs

Journal:	*Acta Physiologica*
Manuscript ID	Draft
Manuscript Type:	Editorial
Date Submitted by the Author:	n/a
Complete List of Authors:	Pethick, Jamie; University of Essex, School of Sport, Rehabilitation and Exercise Sciences Winter, Samantha; Loughborough University, School of Sport, Exercise and Health Sciences Burnley, Mark; University of Kent, School of Sport and Exercise Sciences

Did you know?

Using entropy and fractal geometry to quantify fluctuations in physiological outputs

Jamie Pethick[1], Samantha L. Winter[2], Mark Burnley[3]

[1]School of Sport, Rehabilitation and Exercise Sciences, University of Essex, UK

[2]School of Sport, Exercise and Health Sciences, Loughborough University, Leicestershire, UK.

[3]Endurance Research Group, School of Sport and Exercise Sciences, University of Kent, Kent, UK.

Corresponding author

Dr Jamie Pethick

School of Sport, Rehabilitation and Exercise Sciences

University of Essex

Wivenhoe Park

Colchester

CO4 3WA

United Kingdom

jp20193@essex.ac.uk

Physiological outputs are characterised by constant fluctuations, even under resting conditions.[1] Quantifying and characterising this variability represents an important methodological challenge. Variability in physiological outputs has traditionally been quantified according to its magnitude, using measures such as the standard deviation (SD).[2] Such magnitude-based measures have provided substantial insight into the analysis of physiological outputs; with changes in the magnitude of variability associated with adverse events in a number of systems.[2] However, physiological outputs are characterised by irregular self-similar fluctuations ("complexity") over multiple orders of temporal magnitude (i.e. seconds, minutes, hours); a property magnitude-based measures cannot quantify.[3] Complexity measures derive from non-linear dynamics, and include metrics related to information theory (e.g. entropy statistics), which provide a measure of the apparent regularity or randomness of a system's output, and metrics drawn from fractal geometry, which identify long-range correlations present in an output.[4] It has been suggested that neither magnitude- nor complexity-based metrics should be used as the sole indicator of system characteristics; rather, they should be used in conjunction, in order to provide a more complete understanding of variability.[2,5]

Entropy statistics

Entropy, as embodied in the Second Law of Thermodynamics, is a measure of disorder or randomness that tends towards a maximum in an isolated system.[6] As it relates to dynamical (i.e. physiological) systems, entropy is thought of as the rate of information generation and can be used to quantify the apparent randomness or regularity (i.e. complexity) of an output. To understand entropy statistics and contrast them with magnitude-based measures of variability, consider the following example.[7] There are two time-series: 1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2…. and 1, 2, 2, 1, 1, 1, 2, 2, 1, 1, 2, 1, 2, 2…. The first time-series continually alternates between 1 and 2. In the second time-series, each value is either 1 or 2, but randomly chosen

with probability ½ of either value. Statistics such as the mean and SD cannot distinguish between these time-series. However, the first time-series is perfectly regular; knowing that one value is 1 allows us to predict that the next value will be 2. In contrast, the second time-series is random; knowing that one value is 1 gives no indication whether the next term will be 1 or 2. Entropy statistics, therefore, can distinguish between such clearly different time-series and allow the determination of differences in regularity.[7] This is illustrated in a physiological output in Figure 1.

Approximate entropy (ApEn) derives from Kolmogorov-Sinai entropy in an information theory sense, and was developed as a model-independent quantification of the regularity of a time-series.[8] It provides an index of the predictability of future values in a time-series based on past events. ApEn is equal to the negative natural logarithm of the conditional probability that a template of length m is repeated, within a specific tolerance r, during a time-series.[8] ApEn measures the difference between the logarithmic frequencies of similar runs of length m and runs with length m+1. Values close to 0 indicate that the prevalence of repetitive runs of length m and m+1 do not differ significantly and reflect greater regularity and low complexity.[6] Values close to 2 correspond to greater irregularity and high complexity. High entropy values, though, such as that of white noise, are not necessarily physiologically complex. Therefore, other metrics that can differentiate random (i.e. white noise), statistically self-similar (i.e. pink or 1/f noise) and Brownian outputs are necessary to fully characterise physiologic complexity.[9]

ApEn is, however, not without shortcomings. It has been criticised due to the algorithm counting each sequence as matching itself, meaning it can be sensitive to the size of the time-series, giving uniformly lower than expected values when the time-series is short, and resulting in a lack of relative consistency.[6,10] This led to the development of sample entropy (SampEn),

which discounts self-matches on the basis that entropy is the rate of information generation and, in this context, comparing data with themselves is meaningless.[10] SampEn is precisely the negative natural logarithm of the conditional probability that two sequences similar for *m* points remain within the tolerance *r* at the next point, without allowing self-matches.[10] As with ApEn, low values of SampEn (approaching 0) indicate greater regularity and low complexity.

Fractal geometry

Fractals are traditionally viewed as complex geometric structures, which display self-similarity regardless of the scale used to examine them (e.g. the Sierpinski triangle).[3] However, in the 1960s, the mathematician Benoit Mandelbrot realised they represent a suitable geometry to describe the complex shapes of nature. The example he proposed was a coastline,[11] which appears to maintain the same degree of self-similarity across multiple length-scales. From a physiological perspective, many anatomic structures (e.g. the bronchial tree, dendrites in the nervous system) exhibit fractal-like geometry and self-similarity.[3] Physiological outputs can also be fractal, generating irregular fluctuations over multiple time-scales, analogous to objects with branching structures across multiple length-scales.[3]

The fractal dimension (FD) was the original measure Mandelbrot developed and characterises the self-similarity of a time-series.[12] It is calculated using a box-counting method. The time-series is superimposed onto a grid and the number of boxes it passes through is counted, with this procedure repeated as box-size is varied. The slope of a plot of the logarithm of the number of boxes entered versus the logarithm of the inverse of the box-size gives the FD. Unlike traditional Euclidian geometry where lines, planes and volumes have dimensions of 1, 2 and 3, respectively, a fractal time-series will have a dimension between 1 and 2, with higher values occurring for more irregular time-series.[6]

Detrended fluctuation analysis (DFA) detects long-range correlations in a time-series, thus providing an indication of temporal fractal scaling.[13] To calculate DFA, a moving window of size n is used to study how the fluctuation $F(n)$ grows with n for the time-series.[6] The relationship between $F(n)$ and n can be graphed, with a fractal correlation present if the data is linear on a graph of log $F(n)$ versus log (n). The slope of this line determines the scaling exponent α,[6] which theoretically ranges from ~0.5 to ~1.5 for physiological outputs.[3] When α = 0.5, each value in a time-series is completely random (i.e. white noise) and independent from previous values. When α > 0.5, each value is correlated, to some extent, with previous values. An α of 1.0 (i.e. 1/f or pink noise) is typical of physiological outputs and consistent with statistically self-similar fluctuations and long-range correlations. An α of 1.5 is indicative of Brownian noise, and a smooth output with long-term memory.[3]

Conclusion

There has, in recent years, been increasing interest in the analysis of variability in physiological outputs. This has led to the development of numerous new techniques, in addition to those described above, to characterise physiologic complexity. Numerous studies on a diverse range of physiological outputs (including, *inter alia*, heart rate, the electroencephalogram, gait and muscle force) have demonstrated that entropy and fractal scaling measures are sensitive to both acute (e.g. neuromuscular fatigue)[4] and chronic (e.g. ageing)[9] perturbations. Thus, entropy and fractal scaling measures represent important techniques for characterising and differentiating physiologic outputs.

References

1. Goldberger AL, Rigney DR, West BJ: Chaos and fractals in human physiology. Scientific American, 262: 42-49, 1990.

2. Pincus SM, Goldberger AL: Physiological time-series analysis: what does regularity quantify? American Journal of Physiology, 35: H1643-1656, 1994.

3. Goldberger AL, Amaral LA, Hausdorff JM, Ivanov PC, Peng CK, Stanley HE: Fractal dynamics in physiology: alterations with disease and aging. Proceedings of the National Academy of Sciences, 99: 2466-2472, 2002.

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

5. Slifkin AB, Newell KM: Noise, information transmission, and force variability. Journal of Experimental Psychology, 25: 837-851, 1999.

6. Seely AJ, Macklem LT: Complex systems and the technology of variability analysis. Critical Care, 8: 1-18, 2004.

7. Pincus SM, Keefe DL: Quantification of hormone pulsatility via an approximate entropy algorithm. American Journal of Physiology, 262: E741-754, 1992.

8. Pincus SM: Approximate entropy as a measure of system complexity. Proceedings of the National Academy of Sciences, 88: 2297-2301, 1991.

9. Goldberger AL, Peng CK, Lipsitz LA: What is physiologic complexity and how does it change with aging and disease? Neurobiology of Aging, 23: 23-26, 2002.

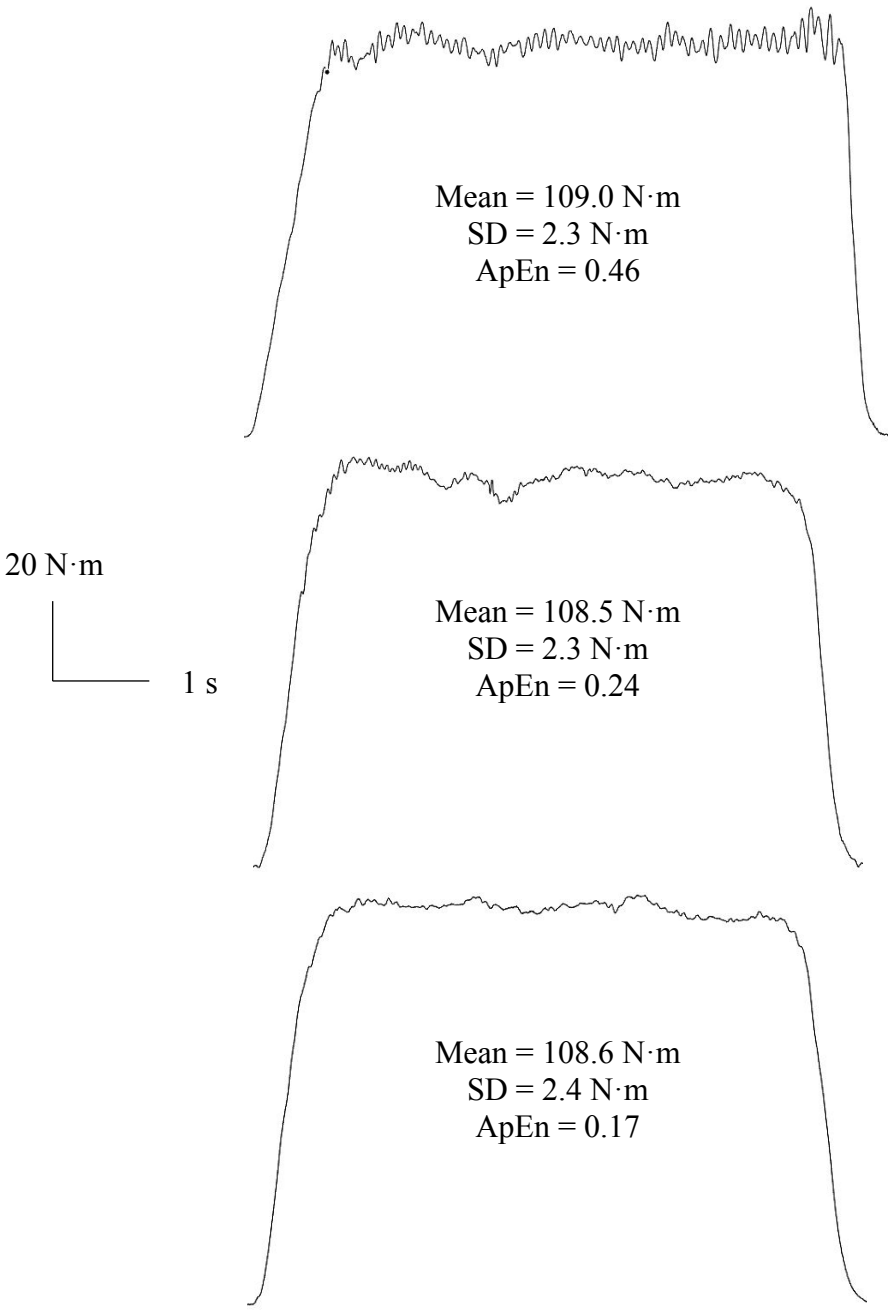
10. Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. American Journal of Physiology, 278: H2039-2049, 2000.

11. Mandelbrot B: How long is the coast of Britain? Statistical self-similarity and fractional dimension. Science, 156: 636-638, 1967.

12. Mandelbrot B: The fractal geometry of nature. New York, WH Freeman, 1983.

13. Peng CK, Buldyrev SV, Havlin S, Simons M, Stanley HE, Goldberger AL: Mosaic organization of DNA nucleotides. Physical Review E, 49: 1685-1689, 1994.

Figure 1 caption: Illustration of how entropy statistics are able to differentiate physiological outputs, in this case muscle torque during contractions performed at 40% of a participant's maximal voluntary contraction, with the same mean and magnitude of variability.


Mean = 109.0 N·m
SD = 2.3 N·m
ApEn = 0.46
20 N·m
1 s
Mean = 108.5 N·m
SD = 2.3 N·m
ApEn = 0.24
Mean = 108.6 N·m
SD = 2.4 N·m
ApEn = 0.17