WHAT A PHYSICIST CAN LEARN FROM A SOMNOLOGIST?

INTRODUCTION

During the great Depression the American humorist Will Rogers with his characteristic sarcasm pointed out that: “The money was all appropriated for the top in hopes that it would trickle down to the needy.” Nowadays “Trickle-down economics” in United States politics refers to the idea that tax breaks or other economic benefits provided to businesses and upper income levels will benefit the less fortunate members of society by improving the economy as a whole. In a scientific rather than an economic context one observes that many or even most physicists are proponents of trickle-down physics. They believe that the development of medicine and life sciences can be and often is determined by the adoption of methods and techniques developed in the physical sciences. Such an opinion is not entirely without merit. It is difficult to envision modern medicine without sophisticated imaging such as computer tomography, nuclear magnetic resonance or positron emission tomography and radiotherapy that extends the life of thousands of cancer patients every year.

Physicists either intentionally or not often find themselves at the frontiers of medicine. In 1928 a neuro-psychiatrist Hans Berger started the series of publications on bioelectrical activity of human brain. His groundbreaking work was accepted by the medical community six years later. It took Alfred Lee Loomis, an investment banker turned physicist, only three years to extend Berger’s work and uncover the structure of human sleep in his private lab in Tuxedo Park, New York. This colorful individual was also instrumental in the development of radar thereby contributing to the Allied victory in World War II. However, such interdisciplinary research is a reciprocal interaction from which physicists also benefit. This paper is our testimony to that benefit.

FRACTAL GEOMETRY AND FRACTAL TIME SERIES

The term fractal was coined by the late Benoit Mandelbrot who championed its use in all manner of social and natural phenomena (Mandelbrot 1977). Since a picture is worth a thousand words in Fig. 1 we illustrate the generation of a geometric fractal - Koch’s snowflake. It is built by starting with an equilateral triangle, removing the inner third of each side, building another equilateral triangle of 1/3 the size at the location
where the side was removed. This process is repeated indefinitely each time with the same contraction of scale size.

What geometric fractals have in common is the repeating pattern at every scale. If the replication is exactly the same at every scale (as in Fig. 1), it is called a self-similar pattern.

Let us look at the self-similar pattern from the different perspective by examining a different geometric fractal. In the left column of Fig. 2 we present a branching tree in which the outermost “tip” of the branch is magnified to reveal the same branching structure at the next smaller scale. It is worth pointing out that such branching may be found in the architecture of the human lung and vascular system (West 2013). A mathematical fractal has no characteristic scale size and its defining pattern proceeds to ever smaller and ever larger scales. On the other hand, a natural fractal always terminates at some smallest and largest scale and whether or not this is a useful concept for the process considered depends on the extent of the interval over which the process appears to be scale-free. A rule of thumb is that if the scale-free character persists over two orders of magnitude then the fractal concept may be useful.

However it is not just spatially that the fractal concept has proven to have utility, but also for the time interval between events. Let us focus on data in Fig. 3, that being the time series \( W(t) \) of fractional Brownian motion (fractal time series for short) (Feder 2013). Here it is not the geometric structure that is repeated at successive scales, it is the statistics of the fluctuations that are self-similar. The statistics of the time series are determined by the probability density \( P(x,t) \) and the scaling is given by

\[
P(x,t) = \frac{1}{t^H} F\left(\frac{x}{t^H}\right),
\]

where \( F \) is a normal distribution in the scaled variable \( x/t^H \). In the time series data the scaling behavior of the fractal is seen through intermittent bursts of fluctuations interspersed between regions of relatively quiescent behavior. Upon magnification of a rectangular part of the top plot in Fig. 3, intermittent bursts between regions of relatively quiescent behavior can again be seen. More rigorously, the distribution function of the segment of the left trace with the horizontal axis magnified by a parameter \( b \) and the vertical axis by \( b^H \), according to the above equation is the same as that of the original trace. This scaling of the statistical distribution of the time series defines a fractal time series.

It turns out that the properties of the fractal time series defined above are determined by a single parameter — the Hurst exponent \( H \) (0<H<1). In particular, the standard deviation is proportional to \( t^H \), where \( t \) is the length of series. Said differently, the standard deviation increases as a power-law in time and the statistical distri-
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Hurst exponent are based on this scaling property.

A number of algorithms that are commonly used to calculate the Hurst exponent are based on this scaling property.

SCALING IN PHYSIOLOGICAL TIME SERIES

Fractal fluctuations have been found in heartbeat dynamics (Peng et al. 1995), respiration (Altemeier et al. 2000, Mutch et al. 2005), human locomotion (Hausdorff et al. 1996), posture control (Collins and Luca 1994) and cerebral hemodynamics (Latka et al. 2004). See (West 2013) for a thorough review of scaling in physiologic time series. They have been the focus of interdisciplinary research for more than two decades. One outcome of this research has been a profound change in our understanding of the significance of homeostasis. Homeostasis — an organism’s tendency to maintain, through negative feedback, approximately constant values of vital biological parameters, such as heart rate or blood pressure, has been the cornerstone of modern physiology since the turn of the twentieth century. However, the intrinsic variability of many physiological phenomena seems to reflect the adaptability of the underlying control systems and argues against the traditional view of homeostasis.

The view of many scientists is that the neurons of the human brain form the most complex dynamical network in existence. It is therefore hardly surprising that this complexity is reflected in electroencephalograms (EEG) — recordings of electrical activity of the brain from electrodes mounted on the scalp. Like most other biological time series, the EEG exhibits stochastic properties. Even when a person is quietly resting with eyes closed her EEG is irregular. However, an EEG time series is not simply uncorrelated noise but contains structure, such as alpha, beta, gamma and delta wave packets. Consequently, EEG waveforms are non-stationary and require special methods for their analysis. A number of research groups have argued that EEG time series have scaling properties, with a standard deviation that increases as a power law in time. The prevalent method used to determine the power-law index \( H \) and to take into account the issue of non-stationarity is detrended fluctuation analysis (DFA) (Peng et al. 1994). DFA is intended to remove the non-stationary components of the time series, called trends, and to provide a measure of the standard deviation of the detrended fluctuations as a function of the data window length. Let us elucidate this algorithm.

All physiological time series such as EEG are bounded. The largest amplitudes of EEG are observed during sleep. The amplitude of delta waves with frequencies between 0.5 and 2 Hz seldom exceeds 300 \( \mu \)V (Schomer and Lopes da Silva 2010) and the amplitudes of the other rhythms are significantly smaller. To transform the EEG signal into a potentially fractal time series we convert bounded measured values \( x_i \) into the unbounded process \( X_t \)

\[
X_t = \sum_{i=0}^{t} (x_i - \bar{x})
\]
DFA is applicable in short-time limit (Ignaccolo et al. 2010b). To emphasize the importance of this problem in Fig. 5 we present the DFA analysis of EEG segment extracted from channel O2 of a polysomnographic recording (Ignaccolo et al. 2010a). Some researchers suggested that there were not merely two but even three scaling regions in EEG signals as indicated in Fig. 5 by straight-line segments.

It is worth emphasizing that DFA is one of the most frequently used algorithms for fractal analysis of experimental time series. The paper that introduced the DFA technique (Peng et al. 1994) has been cited over 2000 times as of 2013. The “DFA” query in PUBMED database returned about 500 papers focused exclusively on biomedical applications. The initial study of heart rate variability using DFA, that being to the intermittency of inter-beat interval time series, revealed the existence of two distinct regimes of scaling with the crossover taking place at approximately 10 heart beats (Peng et al. 1995). Interestingly enough, the short-time scaling exponent turned out to be clinically significant. For example, this measure was the most accurate predictor of all-cause mortality in a cohort of 446 survivors of acute myocardial infarction (Hukuri et al. 2000). The “two exponent” approach was used to quantify heart rate variability in various physiological conditions (Mäkikallio et al. 1999, Tulppo et al. 2001, Beckers et al. 2006, Mourot et al. 2007), dynamics of arterial blood pressure (Beckers et al. 2009, Castiglioni et al. 2009) and cerebral blood flow (Latka et al. 2004). Interestingly enough, until recently, no one proved in a mathematically rigorous way that DFA is applicable in short-time limit (Ignaccolo et al. 2010b). To emphasize the importance of this problem in Fig. 5 we present the DFA analysis of EEG segment extracted from channel O2 of a polysomnographic recording (Ignaccolo et al. 2010a). Some researchers suggested that there were not merely two but even three scaling regions in EEG signals as indicated in Fig. 5 by straight-line segments.

### Paradox of the Ornstein-Uhlenbeck Langevin Equation

To address the question concerning the applicability of DFA to physiological data, we (Ignaccolo et al. 2010b) adopted a simple stochastic model which exhibited short-time power-law scaling and incorporated a fundamental property of physiological control systems-negative feedback. This model, is known in physics literature as the Ornstein-Uhlenbeck (OU) Langevin equation (Lindenberg and West 1990):
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\[
\frac{dX(t)}{dt} = -\lambda X(t) + \eta(t),
\]

where \( \lambda \) is the dissipation rate and \( \eta \) is a random force with ordinary Gaussian distribution. We already know that in order to determine the scaling exponent it is necessary to calculate the standard deviation of a signal (with or without detrending) for data segments of different lengths. However, there are two ways of carrying out the average. In some experiments and in all computer simulations it is possible to generate number of data segments of a chosen length and average \( X(t) \) and \( X^2(t) \) over this collection of realizations of the time series to obtain a standard deviation. This way of doing the average is known as ensemble averaging. In medicine it is seldom possible. Imagine asking a patient to undergo repetitive EEG measurements to fulfill your need to average standard deviation over, let say 20 trials. It is obviously out of the question.

The second way to do an average is to partition the observational data into segments of increasing lengths, such as in the DFA algorithm described earlier, and to average the time series separately over each of the segments. This procedure is known as time averaging. But are these two approaches equivalent?

In general whether ensemble and time averages are equivalent is a subtle and difficult question to answer. When the two methods yield the same result the system is said to be ergodic, otherwise the system is non-ergodic. However, every student of physics knows that the OU Langevin model is stationary and ergodic and consequently "... One can then cut the record in pieces of length \( T \) (where \( T \) is long compared to all periods occurring in the process), and one may consider the different pieces as the different records of an ensemble of observations. In computing average values one has in general to distinguish between an ensemble average and a time average. However, for a stationary process these two ways of averaging will always give the same result...". This quote comes from the classic paper by (Wang and Uhlenbeck 1945).

The reader should not be surprised that we were convinced that ensemble or time averaging should yield the same value for the standard deviation for the OU Langevin equation. We were wrong. In Fig. 6 we compare the dependence of standard deviation on the length of data segments for both type of averaging. It turns out that the long-time (asymptotic) value for time averaging is twice as large as that for ensemble averaging. When we realized the discrepancy it was not difficult to understand the reason and analytically calculate the values of the standard deviation for both ensemble and time averaging.

The question arises as to whether our unexpected discovery may be of interest to someone other than a statistical physicist. The standard deviation is certainly the most often used measure of time series variability. In light of the difference between ensemble and time averaging one can easily envision the situation when their simultaneous application appears rational but ultimately leads to a systematic error. For example, one may perform the measurements on a cohort of subjects to determine variability of a physiological quantity. However, when the variability for a given patient is compared with that of a cohort one may be inclined to improve the statistics by cutting the time series into pieces and performing averaging over them. We now know that this may lead to gross overestimation of the standard deviation, see the curves in Fig. 6.

We must admit as physicists that we felt that we benefited the most from this interdisciplinary research. We were able to identify the fundamental property of time series analysis using the model which has been the integral part of statistical physics since its inception. Unfortunately, we understood the pitfalls and limitations of application of fractal analysis to EEG signals (Ignaccolo et al. 2010a). Nevertheless, when a somnologist...
invites you to a research project do not reject the offer out of hand. You may not only help him/her to solve some research problems but you may learn, as we did, something totally unexpected.

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Summary

There is controversy concerning the proper fractal scaling of human EEG. In order to resolve it we applied the most commonly used algorithm — detrended fluctuation analysis (DFA) to the time series generated using a fundamental model of statistical physics: the Ornstein-Uhlenbeck Langevin equation whose scaling properties can be determined analytically. In the process we uncovered the totally unexpected difference between time and ensemble averaging for this stationary and ergodic model.

CZEGO FIZYCY MOGA NAUCZYĆ SIĘ OD BADACZY SNU?

Streszczenie

Długotrwałe, fractalne fluktuacje zaobserwowano w wielu fizjologicznych szeregach czasowych. Wyznaczenie fractalnych współczynników skalowania sygnałów elektroencefalograficznych (EEG) na podstawie trudności związane ze słabym zrozumieniem własności jednego z najczęściej stosowanych algorytmów statystyki fractalnej — DFA (ang. detrended fluctuation analysis). W celu rozwiązania tego problemu przeprowadziliśmy analizę DFA szeregów czasowych wygenerowanych za pomocą równania Ornstein-Uhlenbeck Langevin — fundamentalnego modelu fizyki statystycznej, którego własności mogą być opisane analitycznie. W trakcie badań odkryliśmy zaskoczającą własność tego modelu dotyczącą różnic w sposobie obliczania wartości średnich za pomocą uśrednienia po czasie i po zespole statystycznym. Zaobserwowane różnice są w sprzeczności z powszechnie przyjętą interpretacją własności modelu Ornstein-Uhlenbeck Langevin sformułowana 70 lat temu.

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