Detrended Fluctuation Analysis on Cardiac Pulses in Both, Animal Models and Humans: A Computation for an Early Prognosis of Cardiovascular Disease

Toru YAZAWA
Department of Biological Sciences, Tokyo Metropolitan University,
Hachioji, Tokyo 1920397, Japan

and

Katsunori TANAKA
Tokyo Biophysical Cardiology Research Group, T. M. University,
Hachioji, Tokyo 1920397, Japan
and

Tomoyuki NAGAOKA
Tokyo Biophysical Cardiology Research Group, T. M. University,
Hachioji, Tokyo 1920397, Japan

and

Tomoo KATSUYAMA
Tokyo Biophysical Cardiology Research Group, T. M. University, and Department of Physics, Numazu
National College of Technology, Numazu, 4108501, Japan

ABSTRACT

We analyzed the heartbeat interval by the detrended fluctuation analysis (DFA) in models and humans. In models, the myocardium of the healthy heart contracted regularly. The deteriorated heart model, however, showed alternating beats so-called "alternans." The DFA revealed that if the heart is having "alternans" exhibited there is a declined scaling exponent (~0.5). In humans, the heart that had "alternans" also showed a low scaling exponent (~0.6). We consider that the coexistence of "alternans" and a low scaling exponent can be a risk marker in predictive and preventative diagnosis, supporting the idea that "alternans" can be a harbinger of sudden death.

Keywords: Heart, EKG, DFA, Scaling exponent, Model animal.

1. INTRODUCTION

The detrended fluctuation analysis (DFA) was developed by statistical physicists and has been reported as a useful method in the area of physiology and medicine. For example, it was applied to biology, one for DNA sequences, the other one for the heart rate in the '80s by researchers in Boston, USA. Consequently fluctuations contained useful "hidden" information about the underlying nonequilibrium control mechanisms [1,2].

It was a good development. However, in those days, it was difficult to obtain a fast speed, powerful, small enough and inexpensive computers, unlike the super-computer. Nowadays, two decades later, we practically have an improved high specification computer on the desk. We therefore have developed our own program, which is principally running like the same algorithm as the original DFA theorem. We utilized it to analyze EKG data recorded from animal models and humans. In those animal models study, it has already revealed that the DFA distinguishes the two types of hearts; i.e., (1) the isolated beating-hearts at a physiological condition in a dish exhibits the scaling exponents near ~0.5, and (2) the intact beating-hearts under conscious but immobilized conditions, which is apparently a very stressful and frightening condition for the animal, exhibits the exponent ~0.8 [3].

2. METHODS AND PROCEDURES

Our DFA-computation method has already been explained elsewhere [4]. Briefly, we describe it here.

Firstly, we recorded the heartbeat for about 10 min to one hour. We use EKG or finger pressure pulses. Using a brief-period recording of heartbeats for 5 minutes, we can roughly estimate the value of the scaling exponent. But, for safe, we usually recorded cardiac pulses for one hour from a single subject.

Secondly, pulse peaks were captured by our own program. By eye-observation on the PC screen, all real peaks were identified and noise peaks were removed.

Thirdly, using our own program, intervals of the heartbeat {Ii}, such as the R-R intervals of EKG, were calculated, which is defined as:

$$\{P_{i+1} - P_i\} = \{I_i\} \quad (1)$$

Forth, mean interval was calculated, which is defined as:

$$< I_i > \quad (2)$$

Fifth, fluctuation value was calculated by removing mean value from each interval data, which is defined as:

$$I_i - < I > \quad (3)$$

Then, a set of data for the DFA was obtained by adding each value in the equation (3), which is defined as:

$$\sum_i (I_i - < I >) \quad (4)$$

This is a method for investigating "random walk" time-series. Peng et al. [3] used different idea than ours. They are considering that behavior of the heartbeat fluctuation is a kind of phenomena belonging to the critical phenomena. Ours consideration is that behavior of heartbeat fluctuation is involved in "random walk" type. Peng et al. [3] used much restricted or strict idea than ours.

In the next step, we determine box size, τ , which represents the number of beats, and which ranges from beat-number-1 to maximum number of beats. So, the maximum number always depend on the length of each record to be analyzed. Then, we calculate valiance, which is defined as:

$$F^2(\tau) = < B_{i+\tau} - B_i > \quad (5)$$

Finally, we plotted variance against the box size. Then the scaling exponent is calculated from the slop of the plot.

We recorded heartbeatS from dissected hearts using conventional electrophysiological methodS, and from the heart of freely moving animals using permanently implanted metal electrodes. Signals were digitized at 1 KHz, stored, and processed by a Power Lab (ADI, Australia). Human heartbeats were recorded from the finger's blood pressure change, using a Power Lab.

3. RESULTS

"Alternans" is recognized that it is a harbinger of sudden cardiac death [5](D. S. Rosenbaum et al. 1994). Alternans may reflect on an unhealthy condition of the heart.

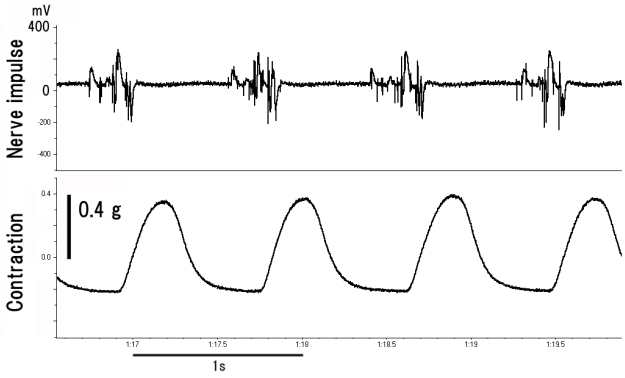

Figure 1. Pacemaker discharge and force of contraction recorded from dissected heart of hermit crab.

Alternans in animal modelS

We have noticed that crustacean hearts can exhibit alternans. As shown in Figure 1, a normal but dissected heart (cut-opened for experimental purpose) exhibited a regular rhythm, if it was fresh. However, preparation was necessary but deteriorated time after time, and then the heart exhibited irregular beats. Specifically, alternating beats are frequently observable (Fig. 2). For our DFA, 3000 beats are necessary. Alternans in Figure 2 did not last for such length; we cannot perform DFA on this data.

An isolated, but not cut-opened, intact whole heart preparations also exhibited alternans and it lasted for a rather long time (Fig. 3). We performed DFA on this data (Figs, 3 and 4). The scaling exponent was about 0.5. It is very low in value comparing it with a healthy heart**,** which is known to exhibit 1/f fluctuation, the scaling exponent of 1.

An unhealthy heart that received isolation and dissection sooner or later stops its beat. So, finally, we concluded that isolation and dissection of the heart easily induces alternans. However, it is uncertain that a reduced scaling index has a 1:1 correlation with alternans or to any deterioration or both. But, at least, deterioration strongly correlated with alternans.

Clinically, it is said that subtle electrical alternans may serve as a maker of vulnerability to ventricular arrhythmia [5]. So, lowering the scaling index may be associated with a cardiac electrical instability.

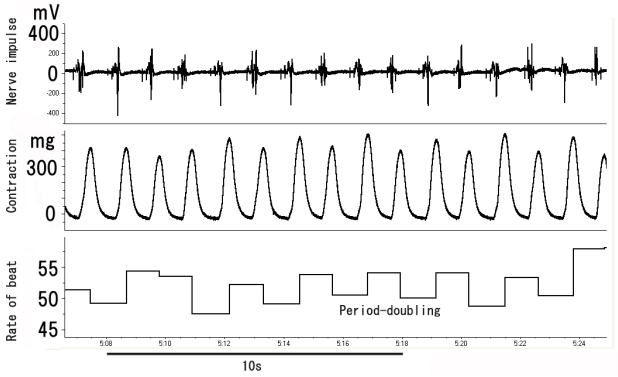

Figure 2. Alternative beats. The same heart in Figure 1.

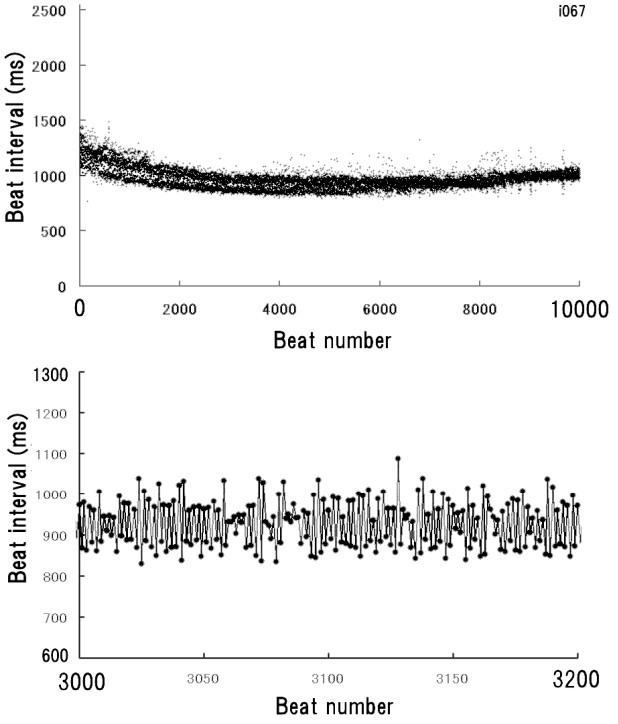

Figure 3. Example Alternals, a spiny lobster isolated heart. Saline perfusion experiments. Upper, beat number, successive 10,000 beat are shown. Lower, 3000 – 3200 is enlarged.

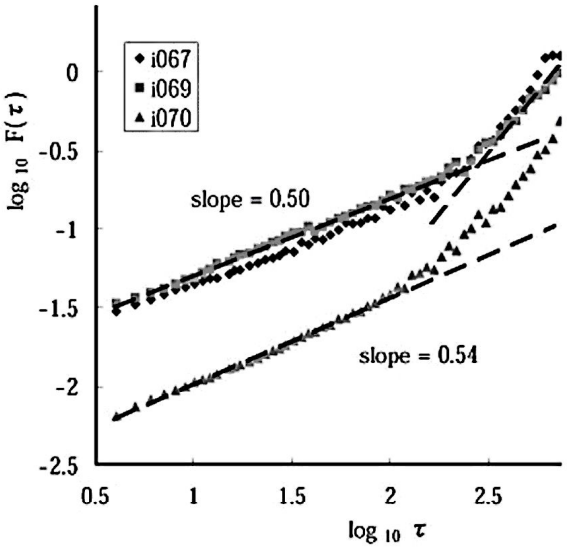

Figure 4. DFA of Alternans. Three examples of isolated hearts of Japanese spiny lobsters. All slop exhibited ~0.5.

Alternans in freely moving animals

Figure 5 demonstrates EKG of freely moving animals. This crayfish has no heart injury and was kept in a dark and silent place. Abrupt excitement was induced by unknown stimulation, probably internal emotional stress. It always occurred spontaneously. Figure 6 shows other typical alternans of the same animal. From two examples, one can see alternans occurres at a maximal-rate-period of beating. Alternans lasted for 6 second in median value (Fig. 7). Excess excitation seems to induce alternans.

In freely moving specimen, alternans did not last for a long period, enough to perform the DFA. So, we cannot do DFA on a live crayfish alternans. Lobster data in Figure 3 enabled us to do DFA on alternans.

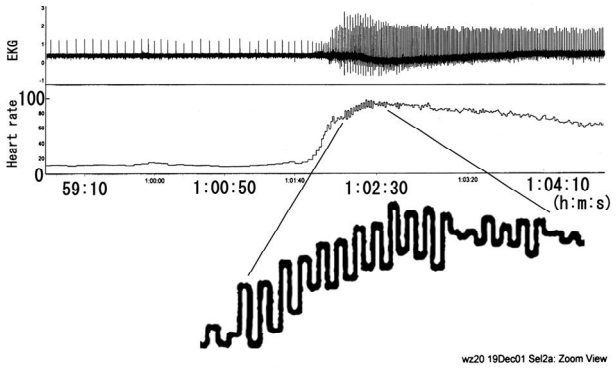

Figure 5. Spontaneously occurred alternans in freely moving mutant (white) crayfish. Upper trace, EKG. Lower trace, heart rate.

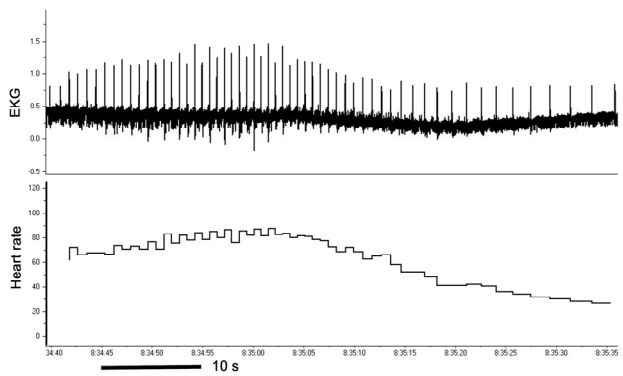

Figure 6. Alternans occurrs at the top speed. Freely moving mutant (white) crayfish. The same crayfish in Figure 5.

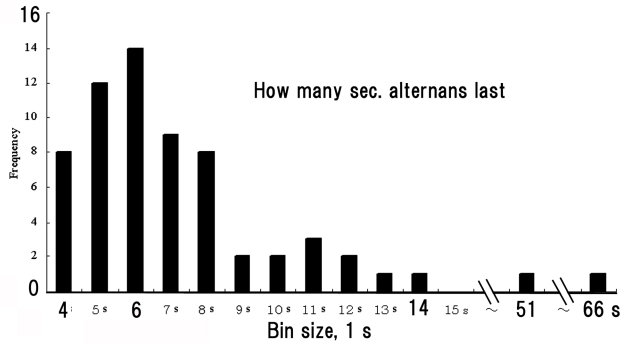

Figure 7. Alternans occurred during 37 hours. Alternans last for 6 second in average.

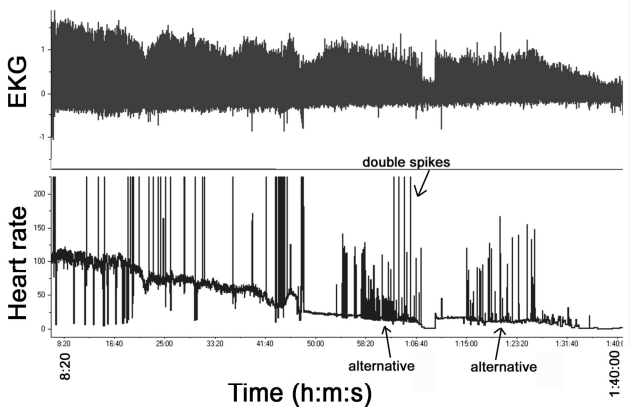

Figure 8. One and a half hour long EKG was taken at the last moment of the crayfish's life. Alternans occurred when this wild crayfish died.

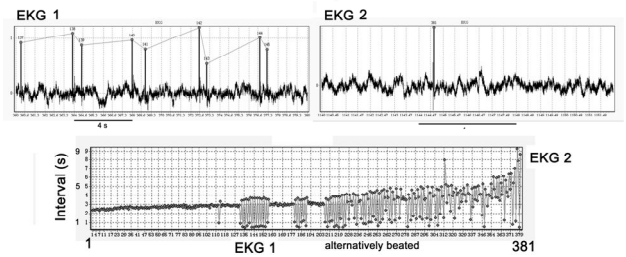

Figure 9. Serious alternans appeared within the successive 281 beats. In 2/3 of data period, double-spike beat (or alternans) are typical irregularity. Figure. 8.was partially enlarged.

Alternans in dying crayfish

Although it is not completely recognized, "alternans" is related to a cardiac death in humans. It is interesting that we observed a similar irregularity in the dying crayfish (Figs. 8 and 9). We already reported that a dying crustacean exhibits a lowering of scaling exponent [6]. An electro-physiological mechanism for alternans in a crustacean heart is uncertain. However, our observations underscore that if a candidate has emotional stress and a heart injury such as ischemia, a diagnosis shown in this paper may help to prevent future cardiac events. We confirmed that intact-hearts of animal models or isolated-hearts of animal models, both of which exhibited a long lasting alternans. This was a sign of feeling that this experiment must be over soon.

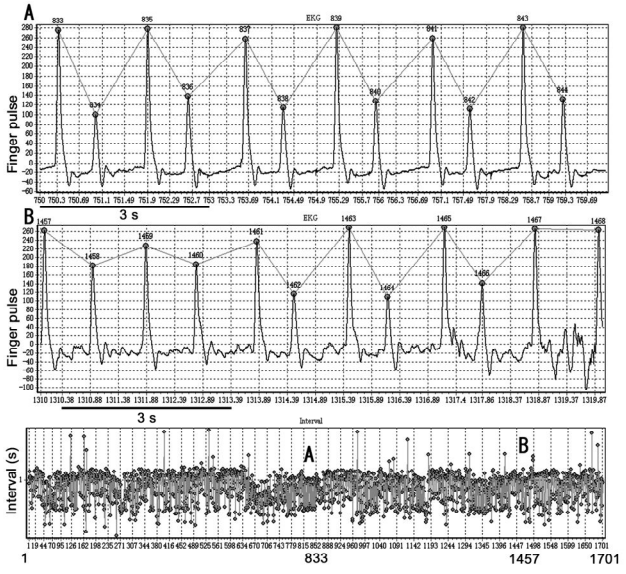

Figure 10. Human alternans. Finger pulses were obtained from a friend of us, ~1700 beats.

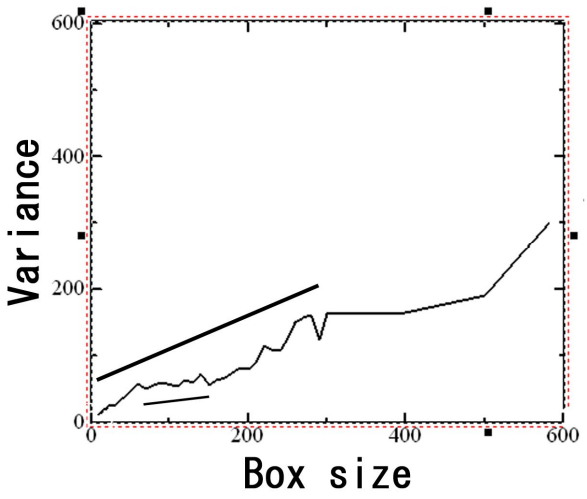

Figure 11. DFA of human alternans (data, Fig. 10). Slope demonstrating a scaling exponent in short-range. The long regression line corresponds to the box-sizes about 1-300, and the short one for 30-60.

Alternans in human case study

A volunteer, a friend of us, has arrhythmic heart beats (Female, 65 age, she also had colon cancer surgery, edema in pericardial space) who kindly offered us her finger for pulse testing (Fig. 10). Two samples - records shows alternans (Fig. 10 A and B). Interval time series shows arrhythmic beat. In this analysis, the total number of beats was 1,701. These are not enough numbers of beats for our DFA, but we can estimate the scaling exponent (Fig. 11). We consider that the scaling exponent, calculated from a small box-size beat-number, was relatively reliable because a relatively large number of data was retained (see DFA theorem), as can be seen from 1 to 300, the number of data points looks larger than the area over 300 (Fig. 11). One can see the slope is far smaller than 1.0 (see the strait long line in the graph.). We estimated it about 0.6. In this subject, the scaling exponent that characterizes the short-range control is apparently much decreased. From a 30-60 beat-number box-size, the slop is more declined in this subject (see short line in the graph.).

4. DISCUSSION

The present analysis on crustaceans revealed that the results on the models are applicable to the human heart. For establishing a tight connection between scaling exponent and body condition (both heart condition and controller condition), further experiments are necessary. Radical and daring experiments such as an artificial heart damage may be helpful to interpret the meaning of DFA results [6,7].

Biomedical technology is advancing very fast, such as telemedicine and Health Watch. Probably a new system of the next generation may use a nonlinear method like the DFA in the watch that involves a predictive and preventative computation for the diagnosis of the heartbeat

The odds that a particular individual will have a heart attack are so far unknowable. But, further detailed experiments on model animals, such as DFA on the heart of lobsters, provide us a supplement information, though we sacrifice them. Bio-physico-medical researche may improve the way to predict with far accuracy the percentage in groups of living-animals who will have a heart cessation.

5. ACKNOWLEDGEMENTS

We thank G. J. P. Channell for her English revise.

6. REFERENCES

[1] Havlin S et al. (1997) Scaling properties of DNA sequences and heartbeat rate. The physics of complex Systems (Proceedings of the International School of Physics Enrico Fermi, Course CXXXXIV) pp. 445-472

[2] Stanley HE, et al. (1999) Statistical physics and physiology: Monofractal and multifractal approaches. Physica A, 270:309-324.

[3] Yazawa T et al. (2004) Neurodynamical control systems of the heart of Japanese spiny lobster, Panulirus japonicus. Izvestiya VUZ. Applied Nonlinear Dynamics Vol.12. No. 1-2. pp114-121

[4] T. Katsuyama, T. Yazawa, K. Kiyono, K. Tanaka, and M. Otokawa 2003 Scaling analysis of heat-interval fluctuation in the in-situ and in-vivo heart of spiny lobster, *Panulirus japonicus*. Bull. Univ. Housei Tama Vol. 18, 2003, 97-108 (Japanese).

[5] D. S. Rosenbaum, L. E. Jackson, J. M. Smith, H. Garan, J. N. Ruskin, and R. J. Cohen, Electrical alternans and vulunerability to ventricular arrythmias. The New England J. of Medicine, Vol. 330, 1994, pp235-241.

[6]Yazawa T et al. (2005) Neurodynamical Control of the Heart of Healthy and Dying Crustacean Animals. CCCT 2005 July 24-27, 2005 – Austin, Texas, USA. Proceedings, Vol. 1. pp367-372.

[7]Yazawa T et al. (2006) DFA on Cardiac Rhythm: Fluctuation of the Heartbeat Interval contains useful Information for the Risk of Mortality in Both, Animal Models and Humans. WMSCI 2006 July 16-19,Orlando, Florida, USA. Proceedings Vol. IV. pp212-217.