Health Wellness Monitoring using the Scaling Exponent: a Heartbeat Interval Time Series Analysis

Toru YAZAWA
Biology, Tokyo Metropolitan University
Hachioji, Tokyo, 192-0397, Japan

and

Hiroyuki KITAJIMA
Faculty of Engineering, Kagawa University,
Takamatsu, Kagawa, 761–0396, Japan

ABSTRACT

The cardio-vascular control system (CVCS) includes the heart, blood vessels, and neuronal/hormonal regulating systems. Ontogenetically and evolutionally, CVCS is designed, implemented and maintained by multi-cellular components. To endure proper operation as a mixture of different type of cells, CVCS functioning is automated with complex interaction with each other. When a certain state of CVCS becomes a malfunctioned state, physicians acknowledge that CVCS's sickness might get started even the malfunctioned state is acute and temporary. However, it is not easy to quantify the state of CVCS. Using the scaling exponent (SI, scaling index), we have recently introduced a novel health technology to check CVCS's state, which is "modified detrended fluctuation analysis (mDFA)". mDFA-method simply calculates SI based on the electrocardiogram data. If our health wellness conditions are practically healthy, SI is nearly 1.0. If we bear a stressful condition, the value of SI decreases toward to 0.5. Intriguingly, if we would be at risk, for example, we are approaching unpredictable cessation of heart-pumping, we found that SI increase toward 1.5. This mDFA-rule is beneficial and applicable to "hearted" animals, from crustaceans to humans. Here we propose that mDFA can distinguish between healthiness and sickness of CVCS.

Keywords: Cardio-vascular system, Heartbeat interval time series, mDFA and Scaling exponent.

1. INTRODUCTION

The cardio-vascular control system (CVCS) is a system that creates proper behavior of heartbeat. The timing of heartbeat is generated by cells in sinoatrial area (i.e., PM, the pacemaker). It may not be a question that you (audiences) have considered before. But contemplating it will introduce you to unseen world of the heart physiology. What happens when one PM drops dead? Nothing happen, because there are alternates. Someone said there are 200 PM cells in our heart but no crucial evidence. What happens when a PM cell acquires excess activity? The pacing heart might become chaotic in function. You might feel vomiting midnight like the Wolff-Parkinson-White syndrome, for example.

In a healthy heart, ventricle cells synchronously fire following an order from "commander in chief" that is PM cells. Therefore, heartbeat and cardiac rhythm carry important health information. We have intended to capture that information from electrocardiogram.

Our heart rhythm is apparently NOT regular. Cardiac rhythmicity is continuously changing, because CVCS is responding every second to stimulus from internal and outer world, such as blood oxygen and environmental stress. Marked irregularity and/or marked degree of regularity might be a wrong state in function. However, although the human heart system has long been studied far over a hundred year, there is no good answer to a question: what is a moderate health wellness condition? Progress in biomedical research is still demanded, because we suffer from sudden cessation of heartbeat in worst case scenario.

Lower animals such as crustaceans have the heart like human does. Crustacean CVCS has been well studied over one hundred years. For example, the English comparative biologist-anatomist Tomas Henry Huxley published about crayfish zoology in ca. 1901 [1]. And Swedish American physiologist Anton Julius Carlson has already documented detailed morphology and physiology of the heart of horseshoe crabs (*Limulus polyphemus*), in 1904 [2]. It is noteworthy that Carlson already considered invertebrate hearts as a model of our heart.

Until now, anatomy of cardiac-nerve of crustaceans is well documented. The crustacean animal has autonomic nervous system that controls the heart (see R. L. Cooper, for example [3], and legendary articles [4, 5]). Typically, crustacean heart is innervated by two acceleratory nerves and one inhibitory nerve (Figure 1, see [6]). Figure 2 shows diagrammatical view of cardiac nerves both in vertebrates and crustaceans. Crustacean diagram is based on our publication [6]. In summary, the cardiac inhibitory nerve mainly innervates PM cells (P in Figure 2) both in crustaceans and humans. In turn, the cardiac acceleratory nerve innervates not only PM cells but also myocardial cells (ventricle cells). As shown in the figure, it is important to acknowledge that nerve fibers of accelerator (CA) proceed into deep inside the heart. This fact presents an evidence for that CA nerve regulates not only rhythm of the heart but also strength of heart contraction. Figure 2 highlights an important issue in terms of evolution: the heart and its controller system resemble in both invertebrate and vertebrate. Further discussions about the resemblance are shown in [7]. Thus we strongly expect that a basic finding obtained from invertebrate animals is applicable to humans, according to evolutional view [7].

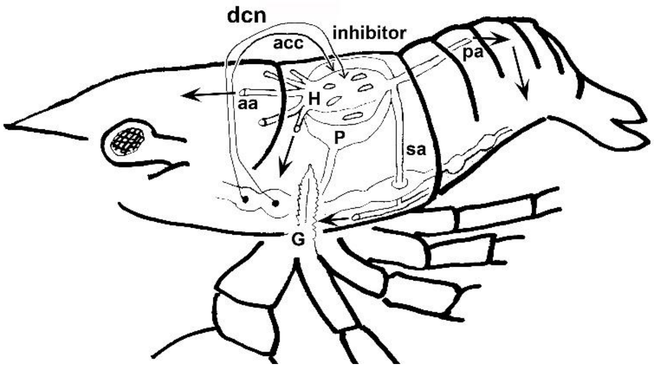

Figure 1. Crustacean CVCS. Autonomic-like regulation of the heart. Cardio-regulatory nerves: ***inhibitor***, cardio-inhibitory nerve; ***acc***, cardio-acceleratory nerve; ***dcn***, bilateral dorsal cardiac nerves. A dcn contains three nerve axons, one inhibitor and two acc nerves. Arrows, direction of blood flow. ***aa***, anterior artery; ***pa***, posterior artery; ***sa***, sternal artery. Blood is pumped out from the heart (H), returning to gill (G) where blood is oxygenated. After leaving from gill, blood return to pericardial sinus (P), and finally withdrawn into the heart through ostium.

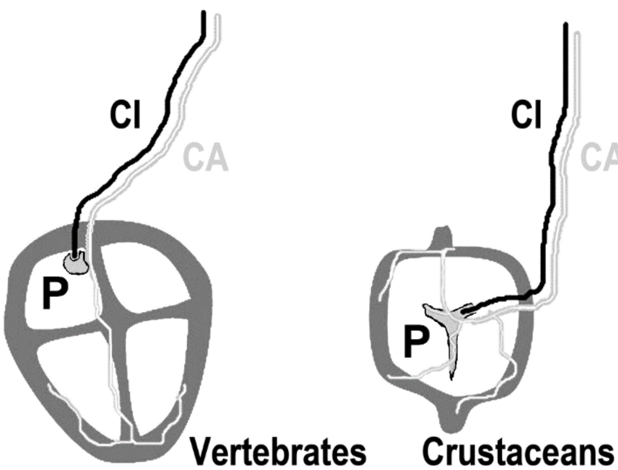

Figure 2. Resemblance in CVCSs. Evolutionary distant two different animals, vertebrates and crustaceans. The cardio-inhibitory (CI) and cardio-acceleratory (CA) nerves. P, pacemaker cells.

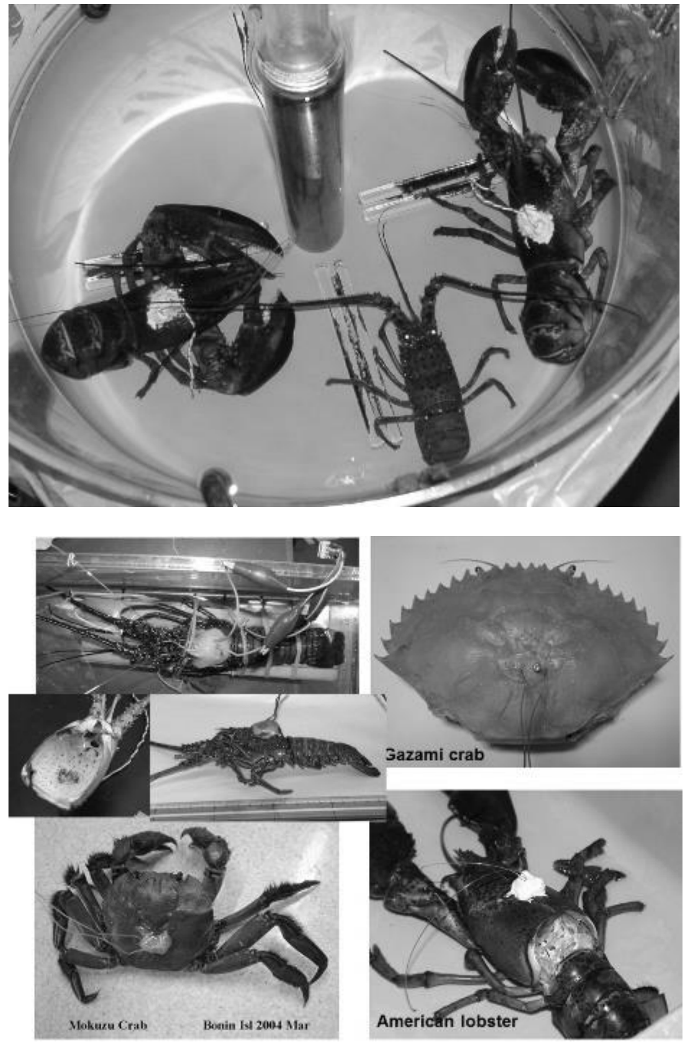

Figure 4. EKG test arena (sea water) and some specimens engaged in the tests. After mounting electrodes, EKGs were continuously recorded for the rest of their life. These specimens were terminally inconvenienced after a period of time, e.g., two weeks to two years.

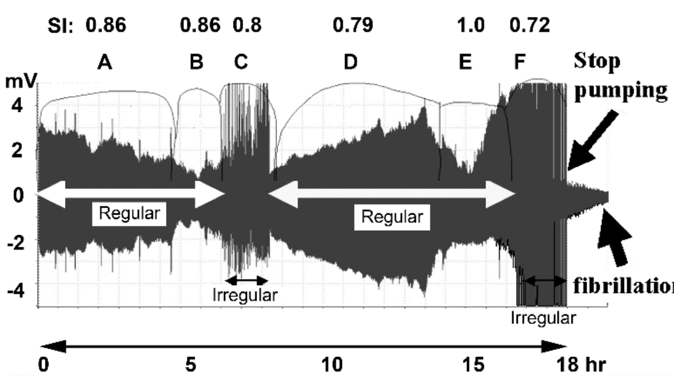

Figure 3. Natural death EKG, dying coconut crab (*Birgus latro*). From A to F, decrements in scaling exponents. Immediately after F, the heart stop pumping and fibrillation-like movements remained.

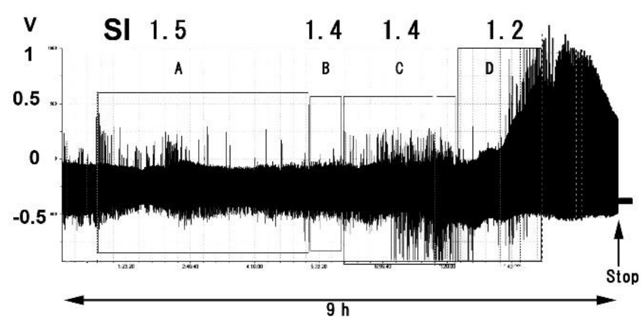

Figure 5. Unpredictable death EKG. An experiment similar to Figure 3, but this specimen's heart suddenly ceased at an arrow. Note, scaling exponents (SI) are very high, from A to D.

2. EXPERIMENTS - CRUSTACEANS

Therefore, we have been studied crustacean heart as a model of human heart (Figure 4) [6, 7]. Crab's EKGs were analyzed with mDFA that we innovated by our group [7], and discovered that dying crab hearts (Figure 3) show a low scaling exponent (SI, scaling index), and healthy crab hearts show a normal SI, near 1.0. Experiments on several animal species (crabs, lobsters, liga, crayfish, and insects) proved that natural death processes decrease SI, falling toward a low level, i.e., SI ≒ 0.5 [7, 10] (Figure 3). Then, we encountered strange specimens that exhibited a high SI, such as ~1.5. They died unpredictably (Figure 5): we noticed that high-SI-specimens are unique and they always had unpredictable death. Intriguingly, a key observation was that unpredictable-death-crab always had myocardial injury that were caused by mounting of artificial EKG electrodes (Figure 6).

Figure 5 shows an EKG data taken while unexpected dying process. We normally put two EKG electrodes into crustacean dorsal carapace. However, this crab (Figure 6) received three, an excess electrode. Why? Because its EKG signal was too weak. Why insufficient? Because EKG electrodes have not good contact with the surface of heart muscles, making EKG signal weak. We never want to damage the heart. However, this insufficient condition sometimes happened. Any electrode can cause this unwished outcome: damaging local myocardial cells. From this unexpected outcome, we got data that prove myocardial damage increase SI. Then, we got an idea from this crustacean phenomenon that human ischemic myocardium damage might be the same in terms of physiological nature, and heartbeat of damaged human heart might be able to be analyzed with mDFA (see below).

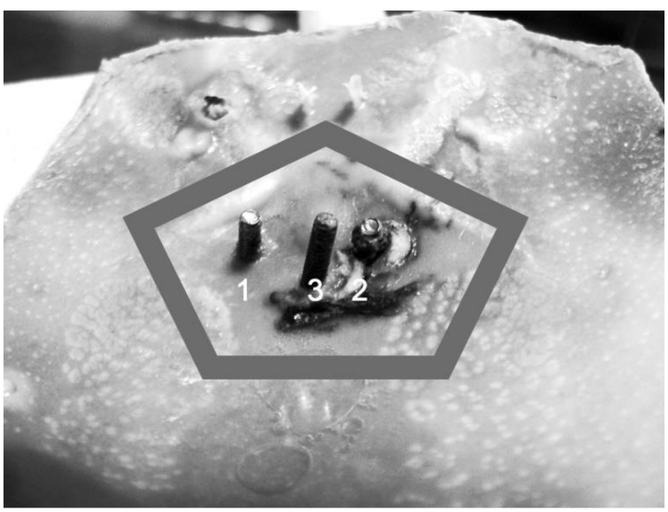

Figure 6. Inside view of a crab carapace. Gazami Crab, *Portunus trituberculatus*. Approximate size of the heart is shown by thick lines. This picture was taken after the crab's death. Electrode-1, -2, and -3, for EKG. One can see the electrode-3 is too long in size to damage the heart immediately beneath the carapace. Myocardial damage caused unpredictable cessation of heartbeat. It took two weeks before this crab's death, happened in an unpredictable manner (see Figure 5).

We have believed that crustacean heartbeat is continuously persisting, that is, their heart beats like the human heart does. But it was not the case (Figure 7). With EKGs from freely moving lobsters/crabs, we found that the heartbeat pattern is not continuous but intermittent if animals are not disturbed (Figure 7). This intermittency, (see repetitive slowdown in Figure 7) is induced by the activity of cardio-inhibitory nerve (Figure 8) [6]. Then, EKG analysis revealed that relaxed lobster exhibits an SI near 1.0 and nervous lobster exhibits an SI near 0.5 (Figure 9). These results proved that SI can quantify psychology of lobster. In short, stressful stimuli decrease lobster's SI significantly, and electro-physiologically, the nervous/stressful state is a state of acceleration dominant and lost-inhibition-controls of the heart (Figure 7).

According to our guideline, normal SI ranges approximately: 0.8~0.9 < SI < 1.1~1.2 [7, 10]. We have long been doing neurobiology of crustaceans [6]. However, due to the crustacean experiments, our viewpoint was extended to human hearts.

3. EXPERIMENTS - HUMANS

All experimental subjects were treated as per the ethical control regulations of universities (Tokyo Metropolitan University; Tokyo Women's Medical University; Universitas Advent Indonesia, Bandung; Universitas Airlangga, Surabaya, Indonesia). Volunteers never get paid for.

We have tested so far over 500 human individuals [7]. We have learned that SI is a useful indicator about job related stress and/or contentment of everyday life, as well as for heart disease. Typical results from them are shown in Table 1. When a person replies to an interview, "Stress level is fairly low," the person's SI is near 1.0. In turn, stressful person has a low SI such as 0.7-0.8 (Table 1). Those who have ischemic heart disease, i.e., those who have damaged myocardium, have a high SI such as 1.2-1.4 (Table 1). Actually, we conceived correlation between a high SI and myocardial damage, when we conducted crustacean experiments (Figures 5 and 6).

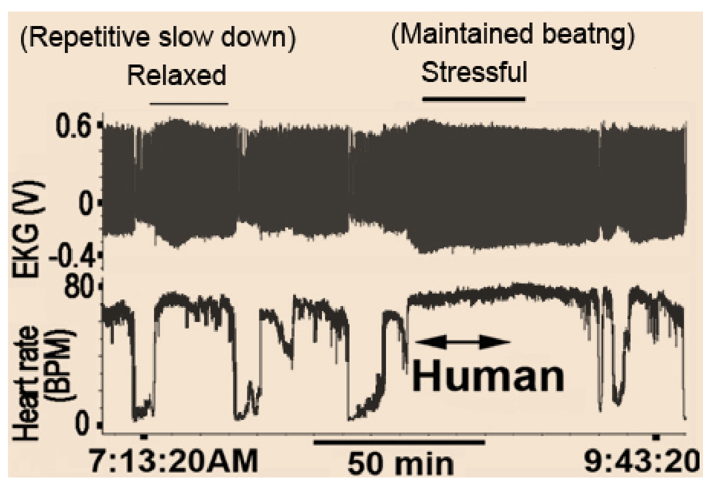

Figure 7. Intermittent pattern of heartbeat of lobster (Panulirus japonicas). The intermittency ceased when a human approaches the lobster tank. Note; an increasing tendency of heart rate, during human's presence (between arrows).

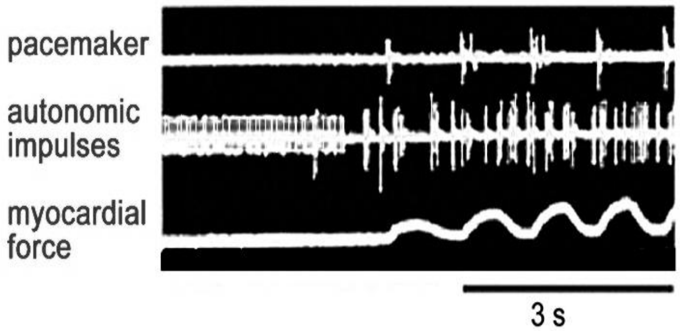

Figure 8. Simultaneous electro-physiological recording: Heart (pacemaker), cardio-regulatory nerve (autonomic impulses), and mechanical transducer (myocardial force, peak=approximately 1mg). An increase of a nerve activity completely stops heartbeat. The smallest spikes in amplitude are the cardio-inhibitory impulses. The other two, the cardio-acceleratory impulses. Specimen, hermit crab (*Aniculus aniculus*, modified from Yazawa and Kuwasawa, 1992 [6]).

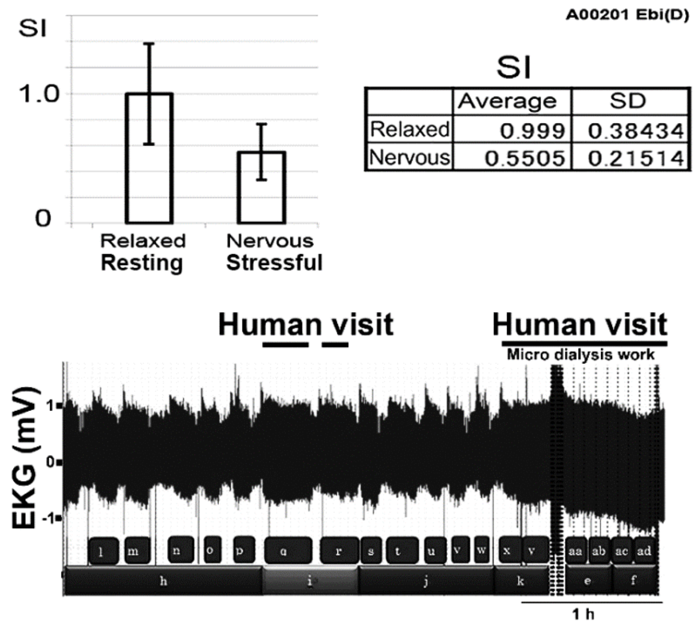

Figure 9. A long EKG recording (below). Human visit changes heartbeat pattern. In relaxed and nervous conditions: SI ≒ 1, and SI ≒ 0.6, respectively (upper inset). SI distinguishes lobster's psychology.

Table 1. Typical mDFA results.

Subject	Categories/Cardiac disease	Age	Stress level (Interview)	SI
1	A company owner	50s, M	Fairly low	1.03
2	A company owner	50s, M	High	0.72
3	University President	60s. M	High	0.84
4	University Vice President	40s, F	High	0.84
5	University Dean	40s, M	High	0.72
6	Secretary of President	40s, F	High	0.76
7	Ordinary teaching professor	50s, M	Fairly low	1.0
8	Ordinary teaching professor	50s, F	Fairly low	0.98
9	Patient, stent placement	60, M	Daily life OK	1.26
10	Patient, bypass surgery	45, M	Daily life OK	1.38
11	Patient, implantable cardioverter	53, M	Daily life OK	1.22
12	Patient, ventricular septal defect (surgery 20 y ago)	48, F	Daily life OK	1.41
13	Healthy representative, housewife	46, F	Daily life OK	1.03

4. EKG-mDFA GADGET

Health wellness monitoring has been advancing in healthcare and medical applications [9]. We especially focus our attention to heartbeat-interval checking. Figure 10 shows lab-made data logging and mDFA computing devices for a real-time detection and measurement. Figure 10A shows electrodes for EKG, commercially available, in-hospital use, using for a prematurely-born baby in an incubator, Vitrode V, Nihon Koden, Tokyo, Japan. Figure 10B shows an EKG-amplifier, heartbeat interval calculator, Bluetooth radio transmitter. This EKG-amplifier (Figure 10B) receives live body EKG signal from the two end terminals (Figures 10C, two electrodes, the third one is spare electrode). Figure 10A shows an iPod (Apple, USA), which has a computation program: We incorporated mDFA [7] in it (not for sale). This system (Figure 10) is commercially available except for (1) mDFA program and (2) modified the electrode attachment (Figure 10B). Ready-made goods (Figure 10B) have the inconvenience in precision recording of the heartbeat signal.

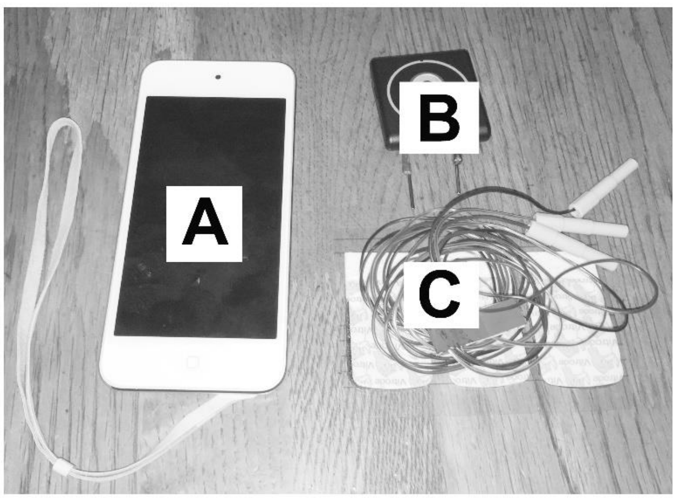

Figure 10. A lab-made device system. Electrocardiogram recording, then peak-to-peak interval timeseries construction, and mDFA calculation.

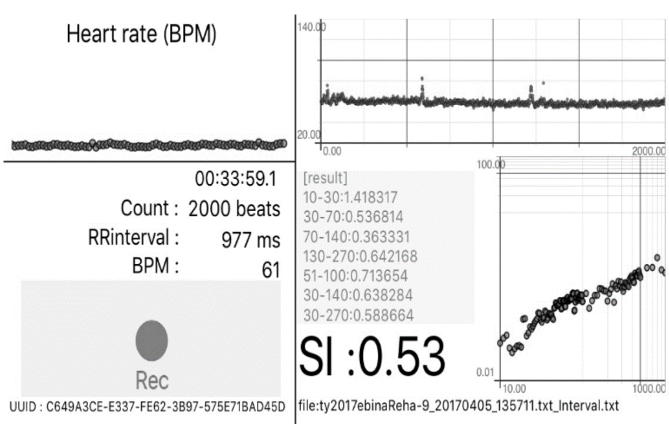

Figure 11. An example screen view of iPod (lab-made, not for sale).

Figure 11 shows a practical view of iPod touch screen. To start recording, an operator can touch the "Rec" button, and then after completing capture of 2000 beats, it automatically computes SI. As can be seen in the figure, SI is 0.53 (Figure 11). Generally, the system computes various SIs. These SIs are computed from various box size ranges (see the reference [7] in detail), which are as follows: [10; 30], [30; 70], [70; 140], [130; 270], [51; 100], [30; 140], and [30; 270]. For the final SI-result, we use the last one, here it is 0.531390 [30; 270], as explained in [7]. Computational and mathematical explanation about mDFA are presented in [7].

5. A CASE STUDY: DRIVING SAFELY

Figures 12, 13, and 14 show fourteen results of consecutive and automated mDFA computation. A volunteer (a man age 66) drove a car from his home to a town 150 km away to see his mother-in-low who is hospitalized. He has been driving the road a number of time, thus he is familiar with the road conditions every corner. Furthermore, he drove safely as possible as he can by obeying the speed limit. We recorded his EKGs while driving, and computed the scaling exponents using the device shown in Figure 10.

Driver's heart rate was monitored by a device commercially available as aforementioned (Figure 10B). Figure 11 shows an example result of mDFA computation. Figure 12B represents a 2000 beat recording, a time series. Figure 12A shows an expanded time series of heart rate recording (arrows). Interval signals were transferred to an iPod and stored in it. The iPod has our mDFA program [7]. The program instantaneously computed the scaling exponent (SI) from the heart rate time series immediately after 2000 heartbeats were captured (Figure 12C). Figure 12D shows a summary of the characteristics of the data {i.e., the file-name (interval.txt), 37 min and 0.2 sec recording total-time for the 2000 beats, R-R interval value and heart rate (beat per min, BPM) for the last heartbeat.} Figure 12C indicates that driving safely gives a perfect healthy scaling exponent near 1.0. Here, the SI is 0.99.

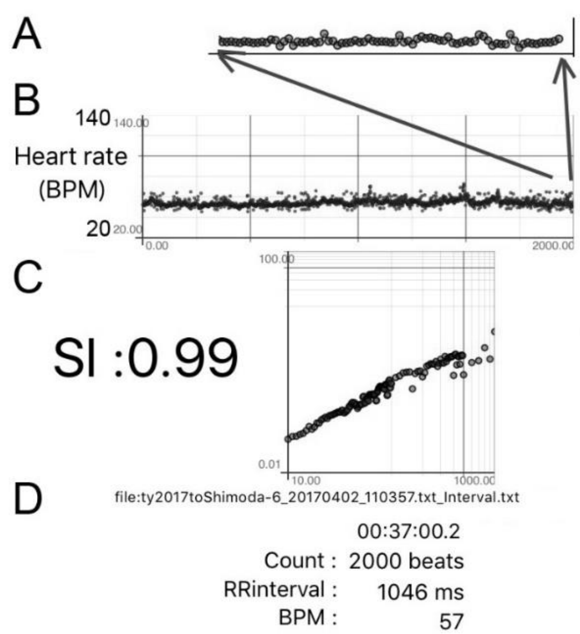

Figure 12. EKG monitoring and mDFA results.

2017Apr2, Driving a car to see relatives		SI
1 Talk about Gas, driving route, etc., before the express way		0.84
2 Express way, driving at about 70km by legal speed		1.03
3 Ordinary road, driving at about 40km by legal speed		1.09
4 Ordinary road, driving at about 40km by legal speed		1
5 Ordinary road, driving at about 40km by legal speed		1.03
6 Ordinary road, driving at about 40km by legal speed	*	0.99
7 Ordinary road, driving at about 40km by legal speed		1.04
8 Ordinary road, driving at about 40km by legal speed		1
9 Lunch, Chinease restaulant, sweet-sour pork, special black vineger		0.61
10 Visit hospital, meeting elderly mom-in-low, nervous		0.64
11 In the hospital, nervous		0.53
12 Ordinary road, driving safely, super market		0.84
13 Super market, driving safely ordinary road		0.99
14 Meeting/greeting brother-in-law, nervous conversation		0.77

Figure 13. Fourteen EKG monitoring and mDFA results (SI).

Figure 13 summarize results of driving-mDFA test. SI showed a low value (SI=0.84, Figure 13, number 1). This can be explained that the driver handled many worries about fuel Gas, driving route and so force. After taking express way, the driver kept a speed limit (70 km/h) and enjoyed blue sky of a spring morning day (SI=1.03, Figure 13, number 2). Many vehicles over-took his car one right after the other although some law-abiding cars followed his car. He continued driving safely (Figure 13). One can see that his safe-driving gave good values of SI, i.e., near 1.0 as can be seen in the SI values from 2 to 8 (Figure 13).

It is a unique result that a specific behavior (eating lunch) decreased the SI value (SI=0.61, Figure 13, number 9). We can explain this result as followings: the mind (his brain function, i.e., autonomic nerve function) concentrated to enjoy foods, digesting them in the stomach and even pay less attention to environment. It seems that a dynamic CVCS response to environment is not dominant when eating lunch.

One can see that SI decreased when the subject walked into the hospital and visited/stayed the room of his mother-in-law (see Figure 13, number 10 and 11, SI=0.64 and 0.53, respectively). After going out from the hospital, SI recovered: during driving and shopping at the super market (see Figure 13, number 12 and 13). We would like to conclude that mDFA can capture anxiety/worry of a subject.

The last result (Figure 13, number 14, SI=0.77) is of interesting. When meeting a new person (the driver's brother-in-low) to greet him, SI decreased again to a very low value (Figure 13, number 14, SI=0.77), which indicates that he is very nervous. He said that he tried NOT to display an ungentlemanly attitude, because he is son of mother-in-law.

Figure 14 shows two example iPod-mDFA screen view. This might give convincing evidence for the idea that "stressfulness decreases SI." It seems that iPod-mDFA is beneficial more than we have expected.

In conclusion, stress deceases SI down to a lower value. We would like to emphasize that three examples, SI=0.64, and SI=0.53, SI=0.77, are great results of iPod-mDFA gadget, and read-out time after 2000 heartbeat detection is only one to two second. All of SI-monitorings were instantaneously computed by iPod-mDFA system as shown in Figure 13.

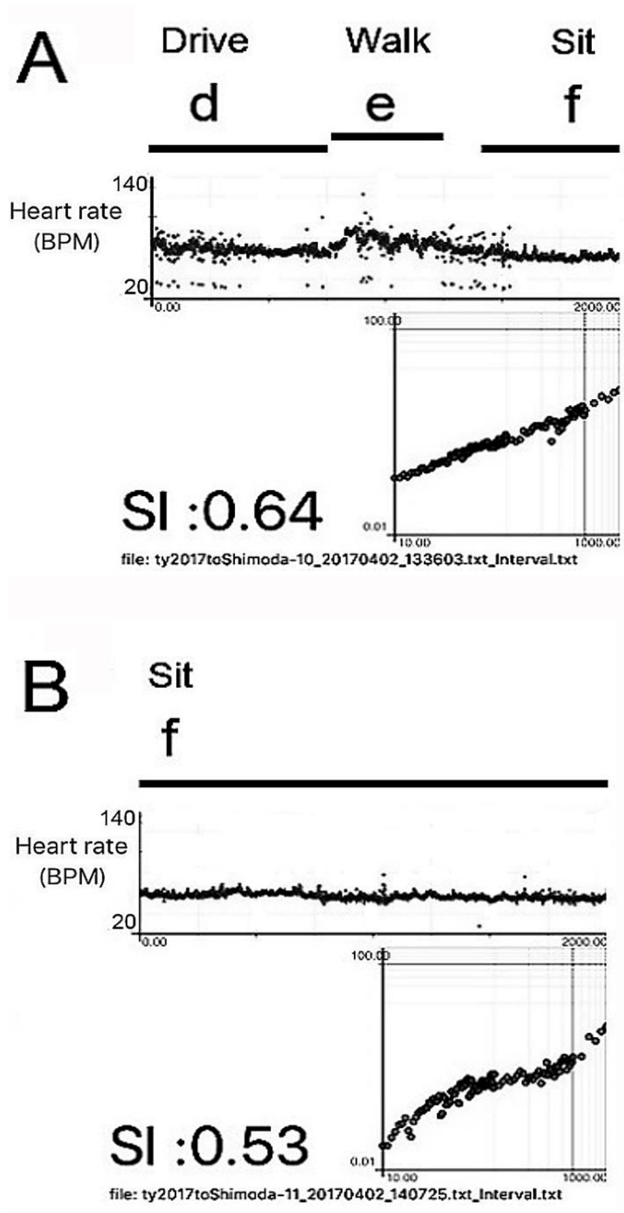

Figure 14. Two typical low-SI examples of iPod-mDFA results which is shown in Figure 13. A, corresponding to Figure 13, number 10. B, corresponding to Figure 13, number 11. Five min break of recording between A and B. Driving the car (d), walking into the hospital (e), sitting in the room of patient (f).

6. DISCUSSION AND CONCLUSION

This study suggests that the scaling exponents computed by mDFA can quantify stress. Furthermore, mDFA results were intriguing: Cardiac muscle injury can be detected using mDFA. An ischemic heart has a high SI. Before this finding, we already have proven in animal models that injured crustacean hearts exhibited a high exponent [7].

Although we need much more comprehensive examples, we propose that mDFA is helpful and beneficial computation tool in the research on emotion, particularly fear and anxiety disorders, understanding how emotion is encoded in the heartbeat time series, in animal models and humans.

If the body is tortured by stimuli from environment, and/or if some stimuli would harm us internally, which is invisible from outside, we would be upsetting for the nervous system. If we use mDFA, we can realize that stimuli is distorting the autonomic nerve function, little of which has been understood by human being until today [8], although we spend everyday life under advanced science and technology. We would like to emphasize that, using mDFA computation, we can numerically evaluate/quantify the state of our body, even it is invisible to us.

Although we (basic scientists, biologists) cannot make by ourselves, making a gadget is very rewarding. It is the right time to start making it. The gadget can work: (1) recording 2000 consecutive heartbeats without missing even a single pulse, (2) computing automatically the scaling exponent that can check the scaling exponent = 1.0, which is perfectly healthy state [7, 10], and finally (3) the gadget would capture what is going on in front of, around, and inside our mind. It gives us health information, each time we use it, for example, on an everyday basis.

In the present paper, we would suggest that we have entered the world experiencing seeing inside without sight. Sometimes a new technology does not have to be supercomplicated. mDFA computation is a kind of high school level mathematics instead of sophisticated nonlinear measures and/or linear complex computation like the HRV, the heart rate variability. mDFA looks at how the brain communicate with the heart and also with the world. mDFA is a tool that enable us to explore previously uncharted territories. For both preventive and post-diagnostic health wellness monitoring [9], we hope that market might find this beneficial nature of mDFA.

Acknowledgements
This work was supported in part by the JSPS Grant 17K01364.

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