Form and Its Nonlinear Analysis for the Use of Electrogastrogram as a Gastrointestinal Motility Test

Yasuyuki Matsuura[1] and Hiroki Takada[2*]

[1]*Graduate School of Information Science, Nagoya University, Furo-cho, Nagoya 464-8603, Japan*
[2]*Graduate School of Engineering, University of Fukui, 3-9-1 Bunkyo, Fukui 910-8507, Japan*
[*]*E-mail address: takada@u-fukui.ac.jp*

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Conventional gastrointestinal motility tests cause pain; therefore, newer noninvasive methods are desired. Non-invasive methods facilitate the measurement of motility close to the normal physiological state, provide new valid findings, and may contribute to the development of associated fields. Electrogastrography (EGG) measures the electrical activity of the stomach through electrodes placed over the abdomen, which is primarily rhythmical. Compared with other gastrointestinal motility measurement methods such as the gastric emptying and internal pressure measurement, EGG is noninvasive and allows measurement under minimum restriction and therefore, allows prolonged measurement. In addition, since EGG measures gastrointestinal electric activity, which cannot be quantified using other methods, it can be used for the evaluation of the state of the body and pathological condition, and may provide new findings such as those useful for the prevention of gastrointestinal dysfunction associated with various disorders. EGG is also useful for preventing disorders associated with abnormal gastrointestinal activity such as functional dyspepsia, which has become frequent in recent years, and constipation, which is an extremely frequent complaint in the elderly. Thus, EGG is of marked importance in public health. However, the range of EGG application is still limited. Therefore, we outlined the measurement/analysis methods, listed advantages and disadvantages of EGG and electrogastroenterography (EGEG), described their clinical importance, and commented on studies at the forefront on form and its nonlinear analysis by EGG. We also evaluated the prospects of EGG.

Key words: Electrogastrogram (EGG), Electrogastroenterogram (EGEG), Non-invasive Measurement, Gastrointestinal Motility, Biological Signal

1. Introduction

With progress in science and technology, techniques of biomedical measurements have also improved. Biological signals that have been difficult to measure became measurable due to improvements in biomedical measurement technologies. Also, biological signals are widely used by visualization as waveforms of electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (EMG), stabilometry, etc., for evaluation of the autonomic and central nervous systems, muscle fatigue, and equilibrium function. Various biological signals are used in not only clinical practice but also biomedical engineering, human engineering, and psychology, but papers on the evaluation of digestive activities using biological signals have been scarce.

Studies of biological signals began at the end of the 19th to the beginning of the 20th century as biological signals such as ECG, blood pressure, and EEG were first measured in humans. Waveforms obtained by employing these modalities are used for evaluation of the autonomic and central nervous systems, muscle fatigue, and equilibrium function. Various biological signals are used in not only clinical situations, but also biomedical engineering, human engineering, psychology, etc.

Since examinations of the gastrointestinal motor function are generally stressful to humans, the establishment of noninvasive methods is anticipated. Also, as noninvasive methods can measure the psychological and physiological phenomena in a close-to-normal condition, they are expected to provide novel findings and contribute to the development of related fields. Electrogastrogram (EGG) evaluates the gastrointestinal motor function by measuring electrical activities of the gastrointestinal system as biological signals.

EGG is a method to measure electrical activities that control the movements of the digestive (gastrointestinal) tract without restraining the subject. In 1921, Alvarez first attempted to record electrical activities of the human stomach from the body surface (Alvarez, 1922). He named the record an electrogastrogram. However, EGG required special equipment and was likely to be affected by EMG due to respiratory movements of the diaphragm and ECG, because the evoked potentials of the gastrointestinal system detected on the abdominal wall are weak, the development of research was long hampered. Recently, however, their recording has been facilitated by the development of measurement devices and digital circuit technology, leading to a marked increase in clinical research. In addition, the electrogastrography designed exclusively for EGG, and electrogastroenterogram (EGEG), i.e., measurement of motor functions of the small intestine and colon as well as the stomach, as an extension of EGG (intestinal movements have also been discussed as EGG), have appeared.

Recently, also, diseases associated with abnormal gastrointestinal activities such as constipation and functional dyspepsia (FD) have emerged as issues, and these abnormalities may lead to lifestyle-related diseases. Particularly, constipation is considered to be complained of frequently by patients with latent FD and elderly individuals, and this topic is also of marked interest regarding hygiene.

Since EGG can be performed noninvasively and without restriction compared with other tests of gastrointestinal motor function such as the gastric emptying method and internal pressure measurement, measurements in a state close to the physiological condition or over a long period are possible. Therefore, it is expected to also be applied to the evaluation of biological conditions, diagnosis of diseases, and pathological evaluation, provide novel findings, and contribute to the further development of research on gastrointestinal activities.

In this paper, therefore, methods for the measurement and analysis of EGG and EGEG are outlined, and their clinical significance is discussed. Also, the latest research trends related to mathematical models to describe EGG are reviewed, and future prospects are discussed.

2. Background

2.1 Historical background of EGG and research trends

In this paper, therefore, methods for the measurement and analysis of EGG and EGEG are outlined, and their clinical significance is discussed. Also, the latest research trends related to describe EGG are reviewed.

The activation of gastrointestinal movements by a warm poultice to relieve constipation is widely performed not only in clinical nursing but also by the general public. However, this treatment is based on experience and lacks physiologic evidence. Also, diseases due to abnormal gastrointestinal activities such as constipation and FD have recently emerged as problems. Constipation is defined as the absence of bowel movements for 3 days or longer or a feeling of residual stools despite daily bowel movements (Matsushita and Okazaki, 2009). About 5 million Japanese adults are estimated to have constipation, and it is particularly prevalent in people aged 75 years and above (Health and Welfare Statistics Association, 2009). In the United States, there are more than 5.7 million adults with constipation, and the annual number of consultations due to constipation is 2.5 million, with 100,000 admissions (Sonnenberg and Koch, 1989; Martin and Barghout, 2004). The authors developed diagnostic criteria for constipation based on EGG findings and evaluated the effects of epigastric warm fomentation inducing a skin temperature about 4°C higher than usual on gastrointestinal movements in young females complaining of chronic constipation (Matsuura *et al.*, 2003). Chronic constipation is generally classified into spastic and atonic types. Spastic constipation is caused as the intestine becomes hyperactive due to autonomic dysfunction, movements of intestinal contents are blocked by contraction of the lower colon, particularly the sigmoid colon, due to frequent spasms, and water absorption from stools increases to make them resemble rabbit feces. Patients with this type of constipation have a strong desire to defecate and have a sense of residual stools even after bowel movements. Atonic constipation is considered to be the most frequent type of constipation and is caused by reduced intestinal peristaltic activities (Fusamoto, 1995). Our experiments suggested that gastrointestinal activities are enhanced by warm abdominal fomentation in young females with symptoms of spastic constipation, and the further development of hygienic research on this treatment is awaited.

EGG has been used for research on the mechanism of gastric dyskinesia in digestive disorders, diabetes, and neurological disorders, effects of a meal, hormones, and drugs on EGG, early detection of gastric dyskinesia, and prediction of autonomic neuropathy such as Parkinson's disease. It has also been used in studies of FD (Thor *et al.*, 1996) and kinesia (Tokumaru *et al.*, 2003). Recently, also, studies of the effects of listening to music (Celebi and Bor, 2007) and alcohol intake on gastrointestinal activities (Lin *et al.*, 2007) and the effects of warm fomentation on gastrointestinal activities as a possible treatment for constipation have been conducted (Matsuura *et al.*, 2003).

2.2 Physiologic mechanism of EGG

EGG is a method to percutaneously record electrical activities of the stomach with electrodes attached to the abdominal body surface. Therefore, EGG can be performed noninvasively without restricting the subject, and the motor function and autonomic activities of the upper digestive tract can be evaluated objectively by analyzing the graphics.

Rhythmic electrical activities consisting of alternating depolarization and repolarization are observed in the stomach and small intestine, as in the heart. The pacemaker of electrical activities of the stomach is located on the greater curvature side of the upper third of the body of the stomach and discharges impulses 3 times per minute (3 cycle per minute, cpm) toward the pylorus (Berne and Levy, 1998). This pacemaker is controlled by parasympathetic activities but spontaneously discharges periodically due to a cell network called interstitial cells of Cajal (ICCs) (Cajal, 1911; Homma, 1997). ICCs were identified only recently as pacemaker cells causing movements of the digestive tract.

In 1998, ICCs were directly found to show rhythmic changes in electric currents and induce spontaneous contractions, and were confirmed to be pacemaker cells of the digestive tract (Hirota *et al.*, 1998; Thomsen *et al.*, 1998). Although ICCs were shown to be involved in spontaneous activities of the digestive tract and neural regulation of its movements, problems such as the mechanism by which they generate rhythms and which cell structures constitute the pacemaker mechanism remain unanswered, and research on these problems is in progress (Nakamura *et al.*, 2002). Electrophysiolgically, ICCs are present in the muscle layer of the digestive tract, which discharges rhythmic action potentials and contracts spontaneously, and they determine the intensity and frequency of electrical activities of the stomach under the influence of neural and humoral factors (Takayama *et al.*, 2002; Torihashi *et al.*, 2005).

In electrical activities of the stomach, periodic vibration is generated in the excitation conducting network of smooth muscle cells with modification by ICCs and nerve activ-

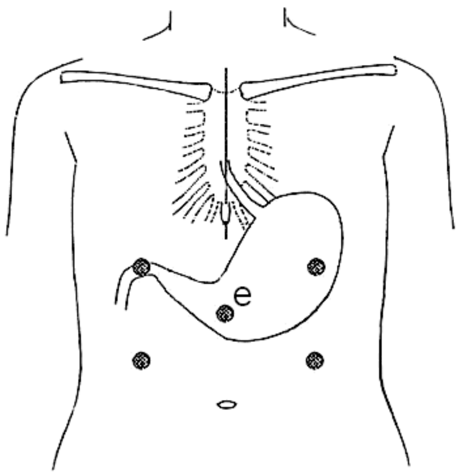

Fig. 1. An arrangement of EGG electrodes in Nipro Electrogastrograph EG (Unipolar) (e is a reference electrode) (Yoneda *et al.*, 2002).

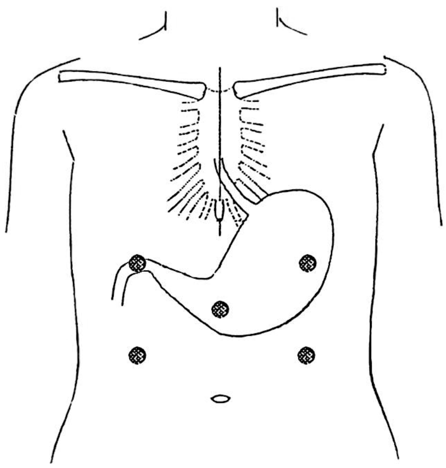

Fig. 2. An arrangement of EGG electrodes in accordance with the method of Okuno *et al.* (Unipolar) (a reference electrode sets the back of right hand) (Okuno *et al.*, 1988).

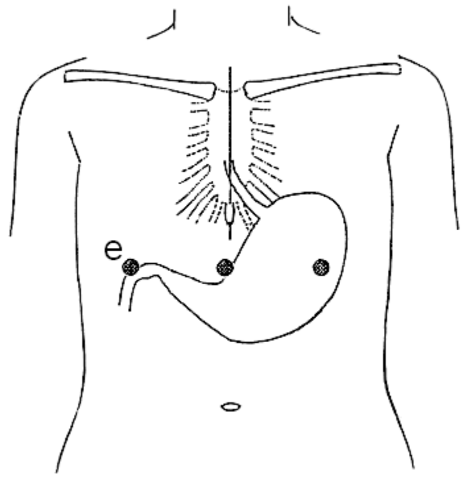

Fig. 3. An arrangement of EGG electrodes as described in the Handbook of Electrogastrography (Bipolar) (e is a reference electrode) (Kenneth and Robert, 2004).

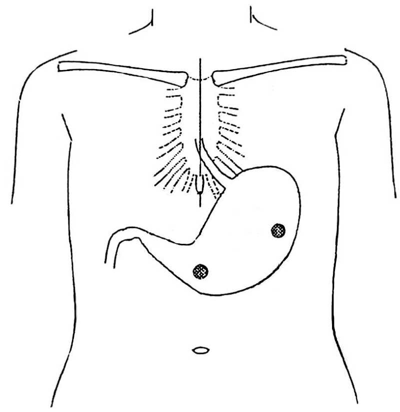

Fig. 4. An arrangement of EGG electrodes in accordance with the method of Kaneoke *et al.* (Bipolar) (a reference electrode is placed arbitrarily) (Sagami and Hongo, 2007).

ities. However, peristaltic activities are not generated by electric impulses discharged by ICCs alone. Action potentials are generated when the electrical activities surpass the contraction threshold during depolarization and produce peristaltic activities. There are 2 types of these electrical activities: They are Electrical Control Activity (ECA) and Electrical Response Activity (ERA) unaccompanied and accompanied by peristaltic activities, respectively (Smout *et al.*, 1980). EGG measures both ECA and ERA but cannot distinguish them, so it does not directly record peristaltic activities (Smout *et al.*, 1980; Chen and Mccallum, 1994).

As to whether EGG truly reflects electrical activities of the stomach, Pezzolla and Homma performed EGG before and after total gastrectomy in stomach cancer patients and observed the complete disappearance of periodic activities at 3 cpm, which are characteristic of the stomach, after surgery (Pezzolla *et al.*, 1989; Homma *et al.*, 1995). This established that EGG is truly a record of electrical activities of the stomach.

In the small intestine, also, ECA is known to be transmitted from the duodenal pacemaker toward the anus by gradually reducing the frequency, which is 10–12 cpm in the duodenum but 8–10 cpm in the ileum (Kaneoke *et al.*, 1992; Ozawa and Fukuda, 2009). There have been papers that these intestinal electrical activities can be detected as signals with a frequency of 8–12 cpm from the body surface, and EGEG, or recording of electrical activities of the stomach and small intestine by spectral analysis, has been proposed, but it has not gained as wide support as EGG (Kaneoke *et al.*, 1992). In addition, the frequency of potential changes due to respiration-induced abdominal wall movements is close to that of electrical activities of the small intestine, and the frequency components due to respiration may be difficult to isolate. Furthermore, intestinal activities have been studied by a small number of groups, and papers regarding them have been insufficient to establish their clinical usefulness.

Table 1. Examples of high-pass and low-pass filters used in EGG and EGEG.

EGG	High-pass filter	Low-pass filter
Handbook of Electrogastrography	0.016 Hz	0.25 Hz
(Kenneth and Robert, 2004)	(1 cpm)	(15 cpm)
Nipro Electrogastrograph EG	0.03 Hz	0.08 Hz
(Naruse *et al.*, 2000)	(1.8 cpm)	(4.8 cpm)
Kaneoke *et al.*	0.016 Hz	0.1 Hz
(Sagami and Hongo, 2007)	(1 cpm)	(6 cpm)
Matsuura *et al.*	DC	0.15 Hz
(Matsuura *et al.*, 2009)		(9 cpm)
EGEG	High-pass filter	Low-pass filter
Kaneoke *et al.*	0.016 Hz	0.3 Hz
(Kaneoke *et al.*,1992)	(1 cpm)	(18 cpm)
Homma *et al.*	0.032 Hz	0.5 Hz
(Homma *et al.*,1998)	(1.9 cpm)	(30 cpm)

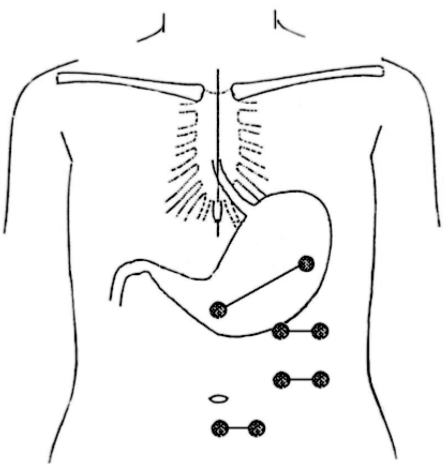

Fig. 5. An arrangement of EGEG electrodes in accordance with the method of Kaneoke *et al.* (1992).

2.3 Methods of EGG and EGEG

EGG measures electrical activities associated with gastrointestinal movements as evoked potentials on the abdominal surface (Cheung and Vaitkus, 1998). Therefore, it is carried out by attaching electrodes on the abdominal surface near the stomach and intestine. The electrodes may be unipolar or bipolar, but measurements using unipolar electrodes are more common. Three to 5 electrodes are attached to the abdomen, and an indifferent electrode is placed on the abdomen or the back. Concerning bipolar electrodes, a pair of electrodes (2 electrodes) is attached to the abdomen, and an indifferent electrode is placed on the abdomen, back, or dorsum of the hand. Bipolar electrodes are usually placed near the gastric pacemaker. Okuno *et al.* and Imai *et al.* attached 5 electrodes to the abdomen, performed EGG using unipolar electrodes first, and employed bipolar electrodes in the analytical stage (Okuno *et al.*, 1988; Imai *et al.*, 1996).

The positions of unipolar and bipolar electrodes are variable (Chen and Maccallum, 1993), but typical examples are presented here. In EGG using unipolar electrodes, 4 electrodes are attached to the abdomen for Nipro Electrogastrograph EG (Fig. 1) (Yoneda *et al.*, 2002), but Okuno *et al.* placed 5 electrodes in the abdominal region (Fig. 2) (Okuno *et al.*, 1988). Concerning EGG using bipolar electrodes, the Handbook of Electrogastrography describes a method using 3 electrodes in the abdomen (Fig. 3) (Kenneth and Robert, 2004), and Kaneoke *et al.* placed 2 electrodes near the gastric pacemaker (Fig. 4) (Kaneoke *et al.*, 1992; Sagami and Hongo, 2007).

EGEG measures electrical activities associated with gastrointestinal movements as evoked potentials on the abdominal surface. Therefore, it is performed by placing electrodes on the surface of the abdominal wall near the stomach and intestine (Kaneoke *et al.*, 1992). According to the proposal by Kaneoke *et al.*, bipolar electrodes are placed as shown in Fig. 5 (Kaneoke *et al.*, 1992).

EGG and EGEG are more sensitive to changes in DC due to electrode resistance and depolarization because of a markedly lower frequency of signals than in EEG or ECG. To avoid their effects, using electrodes with less potential changes and reducing the inter-electrode resistance by carefully wiping the skin using an alcohol disinfectant or skin pretreatment agent is necessary (Naruse *et al.*, 2000; Shen *et al.*, 2003).

EGG or EGEG is usually performed in the supine position to avoid artifacts due to body movements, but the seated position is also tolerated for measurements with meal loading, for example.

Since the amplitude of the signals recorded by EGG is small at 100–500 μV, they are likely to be affected by abdominal muscle EMG and ECG, the amplitude of which is several mV, or show baseline instability due to body movements. The stability of signals must be secured by eliminating the effects of sudden noise due to the simultaneous occurrence of these artifacts. A smoothing filter using a moving average and the elimination of abnormal values are necessary to cope with sudden noise due to interference by EMG.

The pulse variation is 1 Hz, respiratory variation is 0.25 Hz, blood pressure variation is 0.1 Hz, and body fluid volume variation is 0.17 Hz. Here, as the frequencies of pulse variation and body fluid volume variation differ from those of EGG or EGEG signals, and as the effect of the blood pressure variation is very weak, despite the presence of blood vessels at the sites of electrode placement, they pose no problem. Respiratory variation must be eliminated using a low-pass filter, because its frequency is close to that of intestinal electrical activities. Particularly, during measurement in the supine position, the respiratory rate is likely to slow to 0.15–0.2 Hz. Therefore, respiratory components must be eliminated by respiration control or the use of a low-pass filter. Generally, the interference by ECG and respiration is prevented using a high-pass filter of DC-0.032 Hz and a low-pass filter of 0.05–0.2 Hz for EGG and a high-pass filter of DC-0.032 Hz and a low-pass filter of 0.3–0.5 Hz for EGEG.

3. Methodology to Evaluate EGG

3.1 Advantages and problems of EGG

Since EGG is noninvasive and requires no restraint, it has no contraindication and can be applied widely. It can be performed safely even in children, disabled adults, and elderly people. It also causes little additional stress before or after its execution, such as prolonged fasting before endoscopy and the use of a laxative after barium radiography.

Presently, by EGG, few organic diseases can be diagnosed, but electrical activities of the stomach, which cannot be detected by other examinations such as endoscopy and radiography, can be evaluated. EGEG is as reliable as EGG, and as it allows the simultaneous evaluation of electrical activities of the stomach, small intestine, and colon, it is expected be useful for a more detailed assessment and diagnosis of gastrointestinal disorders, including the coordination of the stomach and small intestine.

On the other hand, since the measurement of weak electrical signals was difficult until recently, and since EGG was developed after the 1980s, the accumulation of basic research has been insufficient, hampering its clinical application. Also, the clinical application of EGG has not widened compared with ECG and EEG, because spectral analysis of the frequency and amplitude, by which EGG data are usually analyzed, does not yield much information. This restricts the fields of its application compared with ECG and EEG.

Spectral analysis methods including Fast Fourier Transform (FFT) are usually employed to analyze EGG and EGEG records (Kenneth and Robert, 2004), and instances using complex analytical methods have been few. By spectral analysis, evaluation can be made by measurements of about 5 minutes because of its high temporal resolution (Kenneth and Robert, 2004). However, while spectral analysis is useful for the evaluation of electrical activities characteristic of the stomach, spectral analysis alone is presently considered insufficient, unlike spectral analysis of heart rate variation. Also, in consideration of the complexity of biological activities, evaluation using techniques of complex systems analysis including chaos analysis and nonlinear analysis is considered indispensable. Further, our test of linearity using the surrogate method indicated that EGG may be nonlinear (Matsuura, 2009).

3.2 Analytical methods for EGG and EGEG

3.2.1 Linear analysis for EGG EGG is known to reflect the transmission of electrical activities of the stomach and their rhythmic changes corresponding to the pacemaker frequency of the stomach, which is about 3 cpm. Therefore, time series analysis of EGG is generally performed using numerical data sampled in a frequency range of 0.5–2.0 Hz. Also, the duration of the time window for time series analysis of EGG is usually 1–15 minutes.

Time series analysis of EGG is made primarily by spectral analysis, which is commonly performed by Fourier transform or Wavelet analysis. Spectral analysis of EGG is performed to analyze temporal changes in the frequency and amplitude of EGG waves. Analysis using FFT is performed every 256 or 512 seconds. Temporal resolution at this level is usually sufficient for clinical objectives, but Wavelet analysis is more suited for the closer analysis of temporal changes (Tokmakçi, 2007). Also, in spectral analysis of EGG, spectra are segmented at a fixed duration, and segmented spectra are superimposed to visually evaluate changes in electrical activities of the stomach. This method, called Running Spectrum Analysis (RSA), is often employed (Van Der Schee and Grashuis, 1987; Kenneth and Robert, 2004).

Other examples of spectral analysis are the method using an Autoregressive (AR) model (Matsuura *et al.*, 2007) and the EGG analysis system using the minimum root-raised cosine spectral method (Kim *et al.*, 2000). Attempts at research level include the extraction of EGG alone using independent component analysis (ICA) (Zhishun *et al.*, 1997).

An important point concerning EGG is that it noninvasively provides data on the periodic control process and is a method to evaluate the autonomic function of the digestive system. In the stomach of healthy individuals, changes occur at a rate of about 3 times a minute during rest or a period after a meal. Normal cycles of EGG changes are reportedly 2.4–3.7 cpm (Kenneth and Robert, 2004), with some variation among papers (Chen and Macclum, 1993; Kenneth and Robert, 2004).

In normagastria, the EGG cycle on recording during rest in the supine position is 2.4–3.7 cpm, but its frequency decreases by 0.2–0.5 cpm 5–10 minutes after a meal. This temporary slowing of the EGG cycle after a meal is called the postprandial dip, which reflects the vagus nerve activities. The amplitude usually increases 1–3 fold after a meal. Rhythms slower than 2.4 cpm are called bradygastria, those faster than 3.7 cpm tachygastria, and the absence of a regular rhythm is called arrhythmia; all are considered abnormal (Kenneth and Robert, 2004). The absence of a postprandial dip is also judged to be abnormal, and suggests vagus nerve dysfunction.

3.2.2 Linear analysis for EGEG EGEG is usually analyzed by frequency analysis. Using RSA, temporal changes in the cycle length and amplitude are analyzed every 256 or 512 seconds.

In the duodenum, the basic rhythm of electrical activities is about 11 times per minute. Electrical activities of the stomach affect the activities of the duodenal smooth muscle via the longitudinal muscle and intestinal nerve system extending from the stomach to the duodenum. Under the influence of slow waves transmitted from the stomach, the slow wave of the duodenum is intensified approximately every 5 waves (Berne and Levy, 1998).

Segmental movements are often observed in the small intestine. Their frequency is close to that of slow waves of the small intestine, being 10–12 cpm in the duodenum and 8–10 cpm in the ileum. However, the contraction frequency of segmental movements is not necessarily as stable as that of slow waves.

In the jejunum, there are periods in which contraction weakens or disappears, and contraction occurs intermittently usually at intervals of about 1 minute. This pattern is called the micro-rhythm of the jejunum.

In the colon, contraction waves called mass peristalsis occur about 1–3 times a day. These movements resemble peristaltic waves, and constricted parts remain constricted for a period, driving the colon contents toward the anus over a considerable distance.

There are 2 types of smooth muscle cell that generate rhythms in the colon. One is located near the submucosal border of the circular muscle and produces classic slow waves about 6 times a minute. The waveform of these slow waves resembles that of slow waves recorded in the stomach and consists of rapid rising, plateau, and repolarization phases (Berne and Levy, 1998; Ozawa and Fukuda., 2009). The other type of pacemaker cell is located between the longitudinal and circular muscles and generates small and irregular potential oscillations between the muscle layers, the frequency of which is about 20 cpm.

4. Solutions and Recommendations

4.1 Nonlinear analysis

Attractors can be reconstructed using dynamical equation systems such as the Duffing equation, Henon map, and Lorenz differential equation. It is very interesting to note that the structure of an attractor derived from time series data obtained by EGG can also be represented in a phase space (an embedding space). The form of the attractor is regarded as a subject of mathematical interest and can be measured by using Wayland (Wayland *et al*., 1993) and Rosenstein's algorithm (Sato *et al*., 1987; Rosenstein *et al*., 1993).

The Wayland algorithm is a method to calculate the divergence of close trajectories along the tangential direction in an attractor reconstituted in an embedded space as E_{trans} and is a method to evaluate the degree of determinism of the dynamics that generate a time series.

The Lyapunov exponent is a quantity indicating the mean divergence of 2 points on an attractor with the lapse of time and represents widening behavioral deviation derived from a minute divergence in the initial state (Lyapunov, 1892; Eckmann *et al*., 1986). The maximum Lyapunov exponent(MLE) is called λ, and, if it is positive, the time series may be chaotic, the oscillation waveform is more irregular, and the trajectory is more complex, as its value is larger (Sato, 1970).

However, non-linear analysis shows poor temporal resolution compared with spectral analysis, and developments such as further evaluation of the analytical technique and proposal of indices using mathematical models are awaited (Matsuura *et al*., 2008).

4.2 Examples

4.2.1 Mathematical model of EGG Most previous studies focused on clinical applications, and the subjects were patients. There have been few studies on the EGG dynamics of healthy subjects (normal EGGs). However, some studies have discussed solutions for the forward and inverse problems associated with the dynamics responsible for generating the gastric electrical potential (Kothapalli, 1993). These studies suggest that it is convenient to use current dipoles in an ellipsoid, as well as computer simulations to generate a mathematical model of the EGG for the stomach. However, the results available from the non-linear analyses of EGGs have been insufficient.

Sarna *et al*. proposed a mathematical model of the electrically controlled activity of a dog's stomach (Sarna *et al*., 1972) as follows:

$$\dot{x} = \alpha(y - grad\ f(x)) \tag{1a}$$

$$\text{and} \quad y = -\frac{x}{\alpha} \tag{1b}$$

$$s.t. \quad f(x) = \frac{1}{12}x^4 - \frac{1}{2}x^2 \tag{1c}$$

where x represents the gastric electrical activity and α represents the damping coefficient of the dependent valuable in this Van der Pol equation, which is a non-linear differential equation of the second order and is well known as a mathematical expression for a transition of two states (Fig. 2). In terms of physiology, these states may be referred to as the depolarized and repolarized states in ICCs (Homma, 1997). By improving the precision of the mathematical model for normal EGG data, we can qualitatively evaluate abnormal EGG data, for instance, in the case of tachygastria (increased rate of electrical pacemaker activity in the stomach, defined as being above 4 cpm) (Hongo and Okuno, 1992) or bradygastria (defined as being below 2 cpm).

The waveform of the electric potential in ICCs is similar to the graphs of the numerical solutions to the Van der Pol equation (Fig. 6). We thus added the Van der Pol equation to a periodic function and random white noise was used to represent intestinal motility and other biosignals.

$$\dot{x} = y - \alpha\ grad\ f(x) + s(t) + \mu w_1(t) \tag{2a}$$

$$\dot{y} = -x + \mu w_2(t). \tag{2b}$$

The function $s(t) = \sin \omega t$ and white noise $w_i(t)$ respectively represent the weak and random intestinal movements and other biosignals ($i = 1, 2$). The double-well potential, $f(x)$, generates depolarization and repolarization in ICCs.

4.2.2 Experimental procedure The subjects were 14 healthy people (7 males and 7 females) aged between 21 and 25 years. A sufficient explanation of the experiment was provided to all the subjects, and a written consent was obtained from them.

EGGs were obtained at 1 KHz for 150 min for a subject in the supine position by using an A/D converter (AD16-16U (PCI) EH; CONTEC, Japan). The EGGs were amplified using a bio-amplifier (MT11; NEC Medical, Japan) and recorded using a tape recorder (PC216Ax; Sony Precision Technology, Japan).

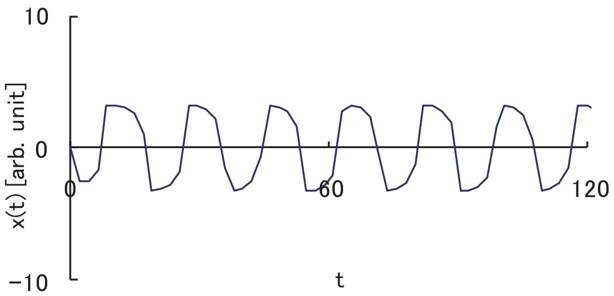

Fig. 6. A graph of the numerical solution obtained with van der Pol equation (1).

In this experiment, nine disposable electrodes (Vitrode Bs; Nihon Kohden Inc., Tokyo, Japan) were affixed to ch1–ch8 and e, as shown in Fig. 7. The electrode affixed on e was a reference electrode. Prior to the application of the electrodes, the skin resistance was sufficiently reduced by using SkinPure (Nihon Kohden Inc., Tokyo, Japan). The EGG data obtained on ch5, which is the position closest to the pacemaker of gastrointestinal motility, were analyzed.

To remove the noise from the time series of the EGG data $\{y_j | j = 0, 1, 2, \ldots, N-1\}$ obtained at 1 kHz, resampling was performed at 1 Hz. For the analysis, we obtained a resampled time series $\{x_i | i = 0, 1, 2, \ldots, (N/1000) - 1\}$ as follows:

$$x_0 = \frac{1}{1000}\sum_{j=0}^{999} y_j, \quad x_1 = \frac{1}{1000}\sum_{j=1\times1000}^{1999} y_j, \ldots,$$
$$x_i = \frac{1}{1000}\sum_{j=i\times1000}^{i\times1000+999} y_j.$$

To remove the noise from the time series of the EGG data $\{y_j | j = 0, 1, 2, \ldots, N-1\}$ obtained at 1 kHz, resampling was performed at 1 Hz. For the analysis, we obtained a resampled time series $\{x_i | i = 0, 1, 2, \ldots, (N/1000) - 1\}$ as follows:

The following delay coordinates were used:

$$\{\vec{x}_t = (x_t \quad x_{t+1} \ldots x_{t+(m-1)})\}.$$

Here, m represents the embedding dimension. These delay coordinates could be used to reconstruct a continuous trajectory without intersections in an embedding space having a large m. The embedding delay, τ, is defined as the minimum delay ($\tau \geq 0$) when the auto-correlation coefficient is zero. The linear correlations must be left between the vicinal components of the delay coordinates unless the time series data is resampled for every embedding delay, τ. The auto-correlation function, $\hat{\rho}(t)$, was estimated from the time series data (Matsumoto and Nishimura, 1998). In this study, we assumed that there was no correlation when $\hat{\rho}(t)$ initially decreased to a value below $1/e$ ($t \geq 0$).

4.2.3 Calculation procedure In this study, we numerically solved Eqs. (2a) and (2b) and verified the stochastic resonance in the SDEs. We converted Eqs. (2a) and (2b) into difference equations and obtained numerical solutions using the Runge–Kutta–Gill formula for the numerical calculations. The initial values were set to $(0, 0.5)$.

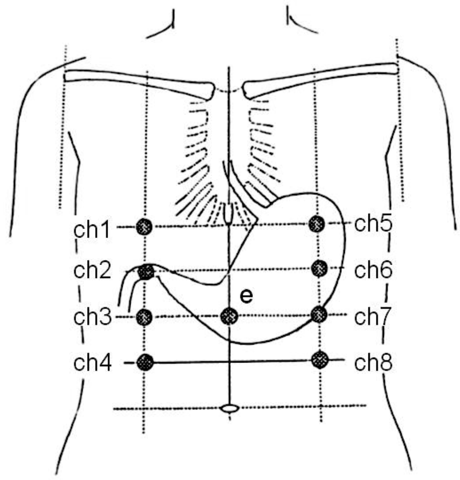

Fig. 7. An arrangement of EGG electrodes used in our study. EGG data recorded at ch5 were analyzed.

Pseudorandom numbers were substituted for $w_i(t)(i = 1.2)$. These pseudorandom numbers were generated by using the Mersenne Twister (Matsumoto and Nishimura, 1998). These numerical calculations were performed for $N = 24000$ time steps. Each time step was 0.05 units.

The values of the numerical solutions were recorded after every 20 time steps, which is equivalent to a signal sampling rate of 1 Hz. For each value of μ, we obtained 20 numerical solutions to Eqs. (2a) and (2b).

1) Using Wayland and Rosenstein's algorithms, estimate the translation errors (E_{trans}) and MLEs (λ) in the attractors generating EGG data, except for 30 min after the postural change (Fig. 8). Then, project the stationary EGG onto the $E_{\text{trans}} - \lambda$ plane.

2) Calculate the mean values ($m(i)$) of E_{trans} and λ for all of the projections obtained in (1). According to statistical theory, 95.5% of the EGGs would project onto the region $\{\Re_s^2 | m(E_{\text{trans}}) \pm 2\sigma(E_{\text{trans}}) \times m(\lambda) \pm 2\sigma(\lambda)\}$, as shown in Fig. 9.

3) Calculate the standard deviations ($\sigma(i)$) of E_{trans} and λ for all of the projections obtained in (1).

4) Project the numerical solutions of Eq. (2) onto the $E_{\text{trans}} - \lambda$ plane obtained in (1).

5) Count the number of numerical solutions projected onto region $\Re_s^2$ of the $E_{\text{trans}} - \lambda$ plane.

6) Calculate the conformity ratio of the number counted in step (5) to 20, i.e., the number of numerical solutions for each value of μ.

4.2.4 Results

4.2.4.1 Subjective evaluation

We analyzed the EGG data shown in Fig. 10. Regular 3-cpm slow waves could be observed, but the amplitude of the waves fluctuated irregularly (Figs. 10 and 11). Wayland and Rosenstein's algorithms were applied to the attractors in the case of all 252 (14 subjects × 18 × 10 min − EGGs = 252 EGGs) EGG data items.

The attractors of the EGGs were reconstructed in accordance with Takens' embedding method (Fig. 11) (Takens, 1981). The form of the attractors could be evaluated by the translation error (E_{trans}) and MLEs (λ).

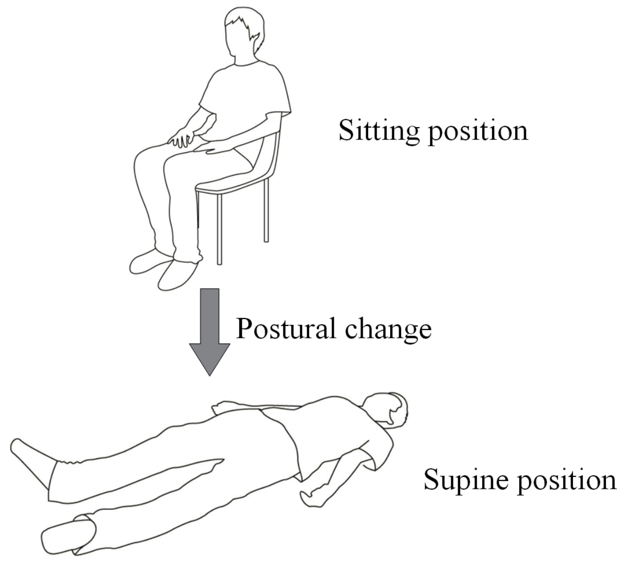

Fig. 8. Postural change.

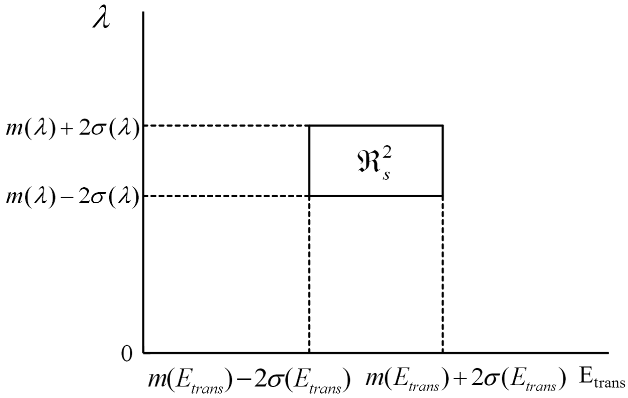

Fig. 9. Region $\Re_s^2$.

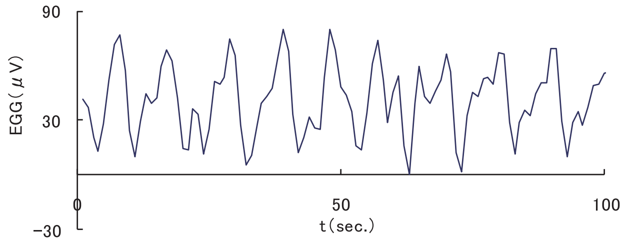

Fig. 10. A typical EGG. The EGG at ch5 was recorded for 1 min after the start of the measurement.

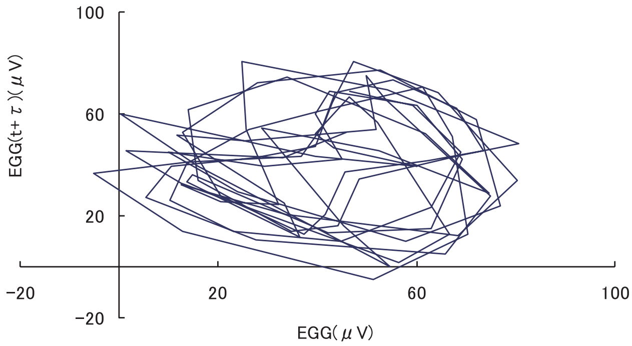

Fig. 11. An attractor reconstructed from the EGG time-series data, as shown in Fig. 10.

The translation errors were distributed from 0.23 to 0.61 (Fig. 12). The average ± standard deviation in the E_{trans} was found to be 0.45 ± 0.10. Of the 252 E_{trans} values for the supine position, 178 were less than 0.5.

The embedding delays and embedding dimensions were distributed from 2 (s) to 4 (s) and from 2 to 7, respectively. Large MLEs were obtained from some EGG data obtained for a subject in the supine position. The average ± standard deviation in the MLEs was 0.75 ± 0.024.

The MLEs were distributed from 0.67 to 0.81 (Fig. 12). All of the MLEs were greater than 0. The average ± standard deviation in the MLEs derived from the EGG data was found to be 0.75 ± 0.024.

4.2.4.2 Simulation evaluation

In the 24000 time steps, there was no exception wherein the numerical solutions did not diverge for $\mu = 1, 2, \ldots, 20$; the value of τ derived from the first component of the numerical solution was not different from that derived from the second component. We compared this numerical solution with the EGG data (Fig. 13). The temporal variations in the numerical solutions were similar to those in the EGG data. Based on Takens' embedding method, the attractors of the mathematical models were also reconstructed, as shown in Fig. 14.

The cross-correlation coefficient between the observed signal, $x(t)$, and the periodic function, $s(t)$, was calculated as a substitute for the SNR used in previous studies in which the occurrence of the stochastic resonance was investigated. Figure 15 shows the cross-correlation coefficient between the numerical solutions, $\dot{x}$, and the periodic function, $s(t)$, in Eq. (2a). The cross-correlation coefficient was maximized for a moderate value of noise intensity, $11 < \mu \leq 12$ (Fig. 15). Thus, the stochastic resonance could be generated using Eqs. (2a) and (2b) with $11 < \mu \leq 12$. Numerical solutions were projected onto the $E_{\text{trans}} - \lambda$ plane (Fig. 16).

With respect to the EGG data taken 30 min after the postural change, the amount of EGG data projected onto region $\Re_s^2$ was less than the statistical standard, as shown in Table 2. In contrast, 100% of the stationary EGG data was projected on the following region.

$$\{m(E_{\text{trans}}) \pm b\sigma(E_{\text{trans}})\} \times \{m(\lambda) \pm b\sigma(\lambda)\}.$$

We quantitatively examined the conformity of the numerical solutions in region $\Re_s^2$ of the $E_{\text{trans}} - \lambda$ plane. The conformity ratio for $\mu = 11.6$ was the highest (Fig. 17). Equations (2a) and (2b) for $\mu = 11.6$ could be regarded as a mathematical model of the stationary EGG. Therefore, the stochastic resonance appropriately describes the stationary EGG data.

4.3 Mathematical models of EGG

While the precision of EGG has been improved, as mentioned above, it has been applied to various diseases in experiments mostly for future clinical use, and few models of mechanisms of EGG traces in healthy individuals have

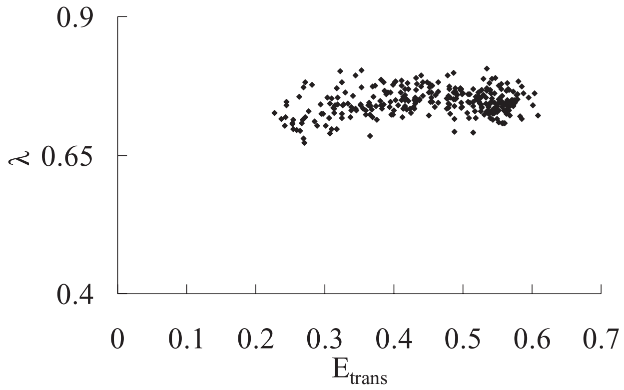

Fig. 12. Subjective results from the $E_{\text{trans}} - \lambda$ plane.

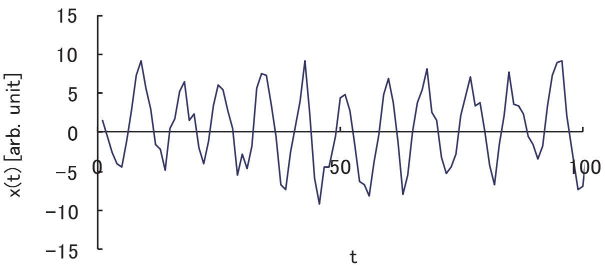

Fig. 13. A graph of the numerical solution obtained using stochastic differential equation (2) for $\mu = 11$.

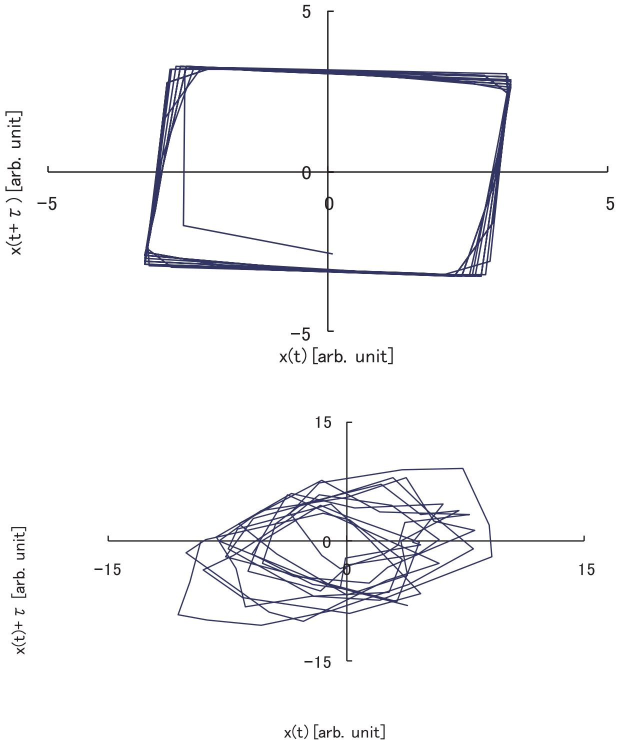

Fig. 14. (a) An attractor reconstructed from the numerical solution obtained using van der Pol equations, as shown in Fig. 6. (b) An attractor reconstructed from the numerical solution obtained using the stochastic differential equations, as shown in Fig. 13.

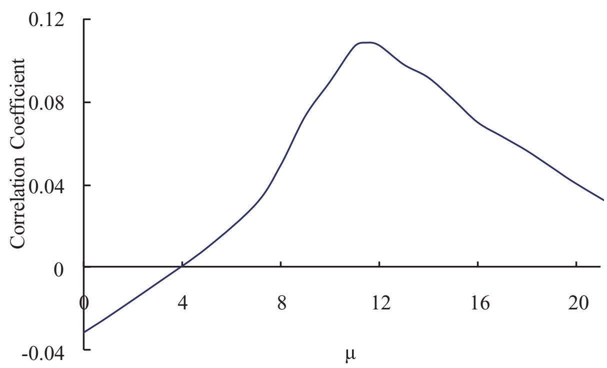

Fig. 15. A graph of the cross correlation function for the periodic function $s(t)$ and numerical solutions.

been reported. Creating precise models of normal EGG in healthy individuals may lead to the quantitative differentiation of EGG abnormalities associated with gastrointestinal disorders. This increases the possibility of diagnosing asymptomatic gastrointestinal disorders such as non-ulcerative dyspepsia by EGG and the application of automatic EGG to screening. EGG is thus expected to contribute to the early detection and prevention of gastrointestinal disorders associated with various diseases.

Nelsen and Sarna *et al.* described electrical activities of the canine stomach using the Van der Pol equation, which explains self-oscillatory systems (Nelsen and Becker, 1968; Sarna *et al.*, 1971). However, the Van der Pol equation is a deterministic differential equation. In addition, our analysis using the Wayland algorithm showed that actual EGG records are not necessarily composed of deterministic mathematical models (Matsuura and Takada, 2009). We are, therefore, attempting a description using stochastic differential equations (Matsuura and Takada, 2009).

5. Future Research Directions

Recently, disorders associated with abnormal gastrointestinal activities such as FD have emerged as problems. However, in FD, gastrointestinal symptoms are complained of despite the absence of organic abnormalities, and it is presently diagnosed basically by inquiry. In the future, FD may be detected and diagnosed by EGG, and EGG is expected to be useful for the prevention and early treatment of gastrointestinal disorders associated with various diseases. In addition, as shown in previous studies, it may also be applied to the evaluation of burdens due to overtime work or stressful situations, management of work burdens, and screening for gastrointestinal diseases.

The health management of astronauts during prolonged stays on the international space station is an important problem. However, as the station cannot be equipped with large examination instruments such as endoscopic and radiographic systems, ECG and blood pressure are monitored, and inquiries and counseling are made by physicians. Research on EGG in the space shuttle is being conducted in view of its application to the health management of astronauts (Deborah *et al.*, 2002). EGG may also contribute to clarification of the mechanism of space motion sickness.

Endoscopy and barium radiography are invasive exami-

Table 2. Comparison of the conformity ratios.

b	Statistical standard	30 min after postural change	Stationary EGG
1	68.3%	54.8%	57.1%
2	95.5%	95.2%	100%

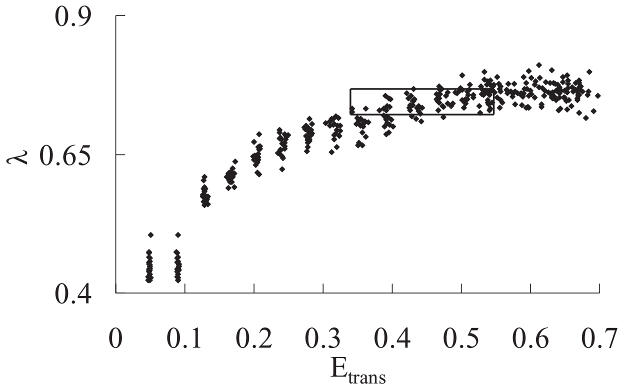

Fig. 16. Simulation results for the $E_{\text{trans}} - \lambda$ plane. The rectangular region shows $\Re_s^2$ for $b = 2$.

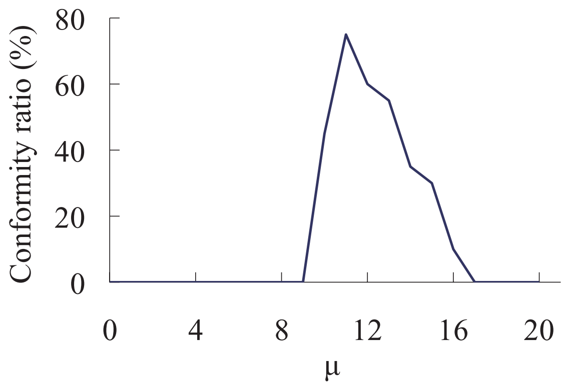

Fig. 17. Conformity ratio for $\mu = 1, 2, \ldots, 20$.

nations. If EGG is carried out before these modalities to select patients requiring these examinations or as a disease-specific examination, it is considered to not only reduce the patients' burden, but may also be incorporated in health-checking instruments and applied to medical services for remote areas. To achieve this, the accumulation of basic research, development of more precise analytical methods, and establishment of the evaluation method are needed.

EGG is a measurement technology that has not been applied to the diagnosis of gastrointestinal disorders or medical engineering, but shows considerable potential for future application and development. Constipation and FD have been treated primarily with drugs, but the clinical application of EGG to the treatment of these conditions and the development of products using EGG are considered to contribute to the early diagnosis and treatment of diseases based on abnormalities of gastrointestinal activities. Because of the simplicity of the EGG procedure, the burden of examination will also be reduced. Also, the development of measurement and health-check instruments incorporating EGG will promote new attempts at its application.

To advance research using EGG, it is important to accumulate data by performing studies on the gastric motor function in patients with various gastrointestinal disorders before and after surgery and in patients with FD before and after drug treatment, as well as studies on qualitative diagnosis by the multi-channel mapping of lesions of gastrointestinal dyskinesia and their changes over time. Developing the procedure and evaluation criteria of EGG as a noninvasive objective examination to make it clinically applicable and using it for the treatment of constipation and diarrhea are also of benefit to epidemiology. Also, the availability of a simple examination such as EGG reduces the physical burden to patients. Further, EGG can be made self-administrable, and the data can be made self-assessable using simple criteria, to the advantage of daily health management.

6. Conclusions

EGG is a technique to measure gastrointestinal electrical activities, which cannot be detected by other examinations of gastrointestinal motility. It is also useful as an examination of the autonomic function controlling gastrointestinal activities.

In the future, aging of the population is expected to advance further in Western countries as well as in Japan. Electrical activities of the gastrointestinal tract reportedly decrease with aging. An adequate diet is indispensable for elderly people to maintain or improve their Quality of life (QOL), and, for this purpose, the maintenance or improvement of the gastrointestinal motor function is important. EGG can be performed safely and easily even in elderly people. Diagnosis or evaluation using EGG is considered to promote not only the preservation or improvement of the gastrointestinal motor function, but also the clarification of biological mechanisms and the development of diagnostic and preventive measures for gastrointestinal disorders. EGG is still in the developmental stage, but will continue to be developed and become applied widely in the future.

Appendix A.

The Wayland algorithm was used to evaluate the determinism of a time series. The conventional methods for estimating the determinism of a time series are the Grassberger-Procaccia algorithm, run-test, and so on. The Wayland algorithm is superior to these other methods because of the following characteristics. It does not need a very large amount of data. It is robust to noise. There is no restriction in relation to the dimensions of the attractor estimated by Wayland algorithm.

In a case where stochastic factors were added to the time series, the visible determinism would be different from that in a case where random variables did not exist. The Wayland algorithm might be used as a mathematical method to evaluate their degrees of freedom. In the Wayland algorithm, the visible determinism can be estimated statistically, with 0.5 as the empirical threshold of the translation error to classify mathematical models as deterministic or stochastic generators.

The procedure for calculating the translation error can be described as follows.

1) The minimum delay in which an autocorrelation function (Eq. (A.1)) is less than $1/e$ (assumed to be 0) is defined as embedding delay τ. Then, time series data are recorded again using the embedding delay as the sampling time. The same numerical value for the embedding delay is employed for the time series regarding time subtraction to compare the smoothness with the orbit of an attractor reconstructed from the original time series data.

$$r(\tau) = \frac{\sum_{k=1}^{N-\tau} x_k x_{k+\tau}}{\sum_{k=1}^{N} x_k^2}. \tag{A.1}$$

2) An attractor is reconstructed from the time series. Now, the linear correlation between adjacent factors of vector $\vec{x}_t$ is eliminated by sampling the time series with respect to each embedding delay defined in 1), and distinguishing the nonlinearity and rulelessness lurking in the dynamics becomes easier.

3) In time series $\{x_i\}$, the K nearest vector $\vec{x}_{t_0}$ series in vector at time t_0 are described as $\vec{x}_{t_i}$ $(i = 0, 1, 2, \ldots, K)$. The variance of each trajectory according to the time is characterized by differential vector $\mathbf{v}(t) = \vec{x}(t_i + \tau_0 \Delta t) - \vec{x}(t_i)$. M onset periods t_0 are chosen at random. The values of

$$E_{\text{trans}}(t_0) = \frac{1}{K+1} \sum_{i=0}^{K} \frac{|\mathbf{v}(t_i) - \bar{\mathbf{v}}|}{|\mathbf{v}|} \tag{A.2}$$

are standardized by the average of the differential vectors at $K + 1$ points, $\{\vec{x}_{t_i}\}_{i=0}^{K}$.

$$\bar{\mathbf{v}} = \frac{1}{K+1} \sum_{i=0}^{K} \mathbf{v}(t_i) \tag{A.3}$$

is obtained at every onset period, where the K points nearest to $\vec{x}_{t_0}$ are selected as $\{\vec{x}_{t_i}\}_{i=1}^{K}$.

The median of the M values of Eq. (A.2) is extracted. Q medians are obtained by repeating the above steps. The translation error is then estimated by the expectation value of the Q medians. The translation error of the attractor generated from the time series is defined as the average of Q median values of $E_{\text{trans}}(t_0)$. $(M, K, Q) = (51, 4, 10)$ was selected in this study (Matsumoto *et al.*, 2002).

4) In general, the threshold of the translation error used to classify the generated time series as a deterministic or stochastic process is 0.5.

References

Alvarez, W. C. (1922) The electrogastrogram and what is shows, *J. Am. Med. Assoc.*, **78**, 1116–1119.

Berne, R. M. and Levy, M. N. (1998) *Physiology 4th edition*, Mosby.

Cajal, S. R. (1911) *Historogie du systeme nerveux de l' homme et des vertebras*, **2**, 942 (in French) (reprinted in English, Cajal S. R., Swanson N. and Swanson L. W. (1995) *Histology of the Nervous System of Man and Vertebrates*, Oxford University Press, U.K.).

Celebi, K. A. and Bor, S. (2007) The acute effect of oral ethanol intake on gastric myoelectrical activity in healthy volunteers, *Turk. J. Gastroenterol.*, **18**(4), 221–224.

Chen, J. D. Z. and Mccallum, R. W. (1993) Clinical applications of electrogastrography, *Am. J. Gastroenterol.*, **88**, 1324–1336.

Chen, J. D. Z. and Mccallum, R. W. (1994) *Electrogastrography: Principles and Applications*, Raven Press, U.S.A.

Cheung, B. and Vaitkus, P. (1998) Perspectives of electrogastrography and motion sickness, *Brain Res. Bull.*, **47**(5), 421–431.

Deborah, L. H., Gwenn, R. S. and Robert, M. S. (2002) Changes in gastric myoelectric activity during space flight, *Digest. Dis. Sci.*, **47**(8), 1737–1745.

Eckmann, J. P., Kamphorst, S. O., Ruelle, D. and Ciliberto, S. (1986) Liapunov exponents from time series, *Phys. Rev. A*, **34**(6), 4971–4979.

Fusamoto, H. (1995) Chronic constipation, *J. Adult Dis.*, **25**, 1506–1507 (in Japanese).

Health and Welfare Statistics Association (2009) *The Trends in Public Health 2009*, Health and Welfare Statistics Association, Tokyo.

Hirota, S., Isozaki, K., Moriyama, Y., Hashimoto, K., Nishida, T., Ishiguro, S., Kawano, K., Hanada, M., Kurata, A., Takeda, M., Muhammad, T. G., Matsuzawa, Y., Kanakura, Y., Shinomura, Y. and Kitamura, Y. (1998) Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors, *Science*, **279**(5350), 577–580.

Homma, S. (1997) Isopower mapping of the electrogastogram (EGG), *J. Auton. Nerv. Syst.*, **62**, 163–166.

Homma, S., Shimakage, N., Yagi, M., Hasegawa, J., Sato, K., Matsuo, H., Tamiya, Y., Tanaka, O., Muto, T. and Hatakeyama, K. (1995) Electrogastrography prior to and following total gastrectomy, subtotal gastrectomy, and gastric tube formation, *Dig. Dis. Sci.*, **40**, 893–900.

Homma, S., Yagi, M., Uchiyama, M., Watanabe, N. and Iwabuchi, A. (1998) Topographic of short bowel syndrome or power electrogastroenterography, *J. Smooth Muscle Res. Japan. sect.*, **2**(1), J-54 (in Japanese).

Hongo, M. and Okuno, H. (1992) Evaluation of the function of gastric motility, *J. Smooth Muscle Res.*, **28**, 192–195 (in Japanese).

Imai, K., Ishimaru, K., Iwa, M., Sasaki, S. and Sakita, M. (1996) Inhibition of abdomainal acupuncture stimulation on electrogastrographic (EGG) study, *Aut. Nerv. Syst.*, **33**(2), 134–139 (in Japanese).

Kaneoke, Y., Koike, Y., Sakurai, N., Washimi, Y., Hirayama, M., Hoshiyama, M. and Takahashi, A. (1992) Electrogastroenterography. I. Analysis of methodology, *Aut. Nerv. Syst.*, **29**, 29–37 (in Japanese).

Kenneth, L. K. and Robert, M. (2004) *Handbook of Electrogastrography*, Oxford University Press, U.K.

Kim, D. W., Ryu, C. Y. and Lee, S. I. (2000) Usefulness of a developed four-channel EGG system with running spectrum analysis, *Yonsei Med. J.*, **41**(2), 230–236.

Kothapalli, B. (1993) Electrogastrogram simulation using a three-dimensional model, *Med. Biol. Eng. Comput.*, **31**(5), 482–486.

Lin, H. H., Chang, W. K., Chu, H. C., Huang, T. Y., Chao, Y. C. and Hsieh, T. Y. (2007) Effects of music on gastric myoelectrical activity in healthy humans, *Int. J. Clin. Pract.*, **61**(7), 1126–1130.

Lyapunov, A. M. (1892) The general problem of the stability of motion, *Comm. Soc. Math. Kharkow* (in Russian) (reprinted in English, Lyapunov, A. M. (1992) The general problem of the stability of motion, *Int. J. Control*, **55**, 531–534).

Martin, B. C. and Barghout, V. (2004) National estimates of office and emergency room constipation-related visits in the United States, *Am. J. Gastroenterol.*, **99** (Suppl. 11), S7–S26.

Matsumoto, M. and Nishimura, T. (1998) A 623-dimensionally equidistributed uniform pseudorandom number generator, *ACM Trans. Model. Comp. Simul.*, **8**(1), 3–30.

Matsumoto, T., Tokunaga, R., Miyano, T. and Tokuda, I. (2002) *Chaos and Time Series Prediction*, pp. 49–64, Baihukan, Tokyo (in Japanese).

Matsushita, M. and Okazaki, K. (2009) Constipation, *Med. Pharm. Sci.*, **61**(6), 831–837 (in Japanese).

Matsuura, Y. (2009) Quantitative Evaluation of Electrogastrography Based on Nonlinear Stochastic Model, Doctoral dissertation, Nagoya City University, Graduate School of Natural Sciences (in Japanese).

Matsuura, Y. and Takada, H. (2009) A study of stochastic resonance as a mathematical model of stationary electrogastrography, *NOLTA 2009 Proceedings*, 348–351.

Matsuura, Y., Iwase, S., Takada, H., Watanabe, Y. and Miyashita, E. (2003) Effect of three days of consecutive hot wet pack application to the epigastrium on electrogastrography in constipated young women, *Aut. Nerv. Syst.*, **40**, 406–411 (in Japanese).

Matsuura, Y., Yokoyama, K., Takada, H., Iwase, S. and Shimada, K. (2007) Frequency analysis of electrogastrography of healthy women during sleep, *Trans. Japan. Soc. Med. Biol. Eng.*, **44**(4), 560–566 (in Japanese).

Matsuura, Y., Takada, H., Yokoyama, K. and Shimada, K. (2008) Proposal for a new diagram to evaluate the form of the attractor reconstructed from electrogastrography, *Forma*, **23**(1), 25–30.

Matsuura, Y., Takada, H. and Yokoyama, K. (2009) Dependence of Lyapunov exponents on embedding delay in electrogastrography analysis, *IEEJ Trans. Electron., Inf. Syst.*, **129**(12), 2243–2244 (in Japanese).

Nakamura, E., Kito, Y., Fukuta, H., Yauchi, Y., Hashitani, H., Yamamoto, Y. and Suzuki, H. (2002) Cellular mechanism of the generation of spontaneous activity in gastric muscle, *Folia Phamacologica Japonica*, **123**(3), 141–148.

Naruse, T., Inoue, H. and Inomata, H. (2000) *Power Spectral—Time Analysis of Electrogastrography, Proceedings of the Society of Instrument and Control Engineers Tohoku Chapter*, **189-1**, 1–9 (in Japanese).

Nelsen, T. S. and Becker, J. C, (1968) Simulation of the electrical and mechanical gradient of the small intestine, *Am. J. Physiol.*, **214**, 749–757.

Okuno, Y., Hongo, M. and Ujiie, H. (1988) Percutaneous recording of gastric electrical activity (electrogastrography): Its technique and analysis, *J. Smooth Muscle Res. Japan. sect.*, **24**(6), 392–394 (in Japanese).

Ozawa, S. and Fukuda, Y. (2009) *Medical Physiology 7th edition*, Igaku-Shoin, Tokyo (in Japanese).

Pezzolla, F., Riezzo, G., Maselli, M. A. and Giorgio I. (1989) Electrical activity recorded from abdominal surface after gastrectomy or colectomy in humans, *Gastroenterology*, **97**, 313–320.

Rosenstein, M. T., Collins, J. J. and De Luca, C. J. (1993) A practical method for calculating largest Lyapunov exponents from small data sets, *Physica D*, **65**, 117–134.

Sarna, S. K., Daniel, E. E. and Kingma, Y. J. (1971) Simulation of the electrical activity of the stomach by an array of relaxation oscillators, *Am. J. Dig. Dis.*, **17**, 299–310.

Sagami, Y. and Hongo, M. (2007) Electrogastrogram, in *Clinical Examination of the Autonomic Nervous System*, 4th ed., Bunkodo, Tokyo (in Japanese).

Sato, C. (1970) *Nonlinear Oscillation Theory*, Asakura Publishing, Tokyo (in Japanese).

Sato, S., Sano, M. and Sawada, Y. (1987) Practical methods of measuring the generalized dimension and the largest Lyapunov exponent in high dimensional chaotic systems, *Prog. Theor. Phys.*, **77**, 1–5.

Shen, H., Ichimaru, Y. and Kobayashi, M. (2003) Development of electrogastrographic (EGG) analysis system and its pplication for nutritional physiology, *Japan. J. Physiol. Anthropol.*, **8**(1), 9–16 (in Japanese).

Smout, A. J., Van Der Schee, E. J. and Grashuis, J. L. (1980) What is measured in electrogastrography?, *Dig. Dis. Sci.*, **25**(3), 179–187.

Sonnenberg, A. and Koch, T. R. (1989) Physician visits in the United States for constipation: 1958 to 1986, *Dig. Dis. Sci.*, **34**(4), 606–611.

Thomsen, L., Robinson, T. L., Lee, J. C. F., Farraway, L., Hughes, M. J. G., Andrews, D. W. and Huizinga, J. D. (1998) Interstitial cells of Cajal generate a rhythmic pacemaker current, *Nat. Med.*, **4**, 848–851.

Thor, P., Lorens, K., Tabor, S., Herman, R., Konturek, J. W. and Konturek, S. J. (1996) Dysfunction in gastric myoelectric and motor activity in Helicobacter pylori positive gastritis patients with non-ulcer dyspepsia, *J. Physiol. Pharmacol.*, **47**(3), 469–476.

Tokumaru, O., Mizumoto, C., Takada, Y., Tatsuno, J. and Ashida, H. (2003) Vector analysis of electrogastrography during motion sickness, *Dig. Dis. Sci.*, **48**(3), 498–507.

Torihashi, S. (2005) Structure and function of interstitial cells of Cajal, *Pediatric Surg.*, **37**(4), 467–472 (in Japanese).

Takayama, I., Horiguchi, K., Daigo, Y., Mine, T., Fujino, M. A. and Ohno, S. (2002) The interstitial cells of Cajal and a gastroenteric pacemaker system, *Arch Histol. Cytol.*, **65**(1), 1–26.

Takens, F. (1981) Detecting strange attractors in turbulence, in *Dynamical Systems and Turbulence, Lecture Notes in Mathematics*, vol. 898 (eds. D. A. Rand and L.-S. Young), pp. 366–381, Springer-Verlag.

Tokmakçi, M. (2007) Analysis of the electrogastrogram using discrete wavelet transform and statistical methods to detect gastric dysrhythmia, *J. Med. Syst.*, **31**(4), 295–302.

Van Der Schee, E. J. and Grashuis, J. L. (1987) Running spectrum analysis as an aid in the representation and interpretation of electrogastrographic signals, *Med. Biol. Eng. Comput.*, **25**, 57–62.

Wayland, R., Bromley, D., Pickett, D. and Passamante, A. (1993) Recognizing determinism in a time series, *Phys. Rev. Lett.*, **70**, 580–582.

Yoneda, H., Ishizaki, N., Imai, K., Ono, K., Yano, T. and Yamamura, Y. (2002) Influence of water road test on electrogastrograms of diabetes mellitus patients, *Aut. Nerv. Syst.*, **39**(1), 80–86 (in Japanese).

Zhishum, W., Zhenya, H. and Chen, J. Z. (1997) Blind EGG separation using ICA neural networks, *Proceedings of the 19th Annual International Conference of the IEEE*, 1351–1354.