OPTIMISATION IN THE MODELLING OF DIGESTIVE
TRACT ELECTRICAL SIGNALS

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Abstract

Spontaneous electrical rhythms have been recorded in many parts of the digestive tract in animals and humans. The signals contain a low frequency regular oscillation which varies in frequency and waveshape between parts of the tract and between species. A mathematical model postulated for these rhythms comprises a set of mutually coupled Van der Pol oscillators. For the human small and large intestines where signals are nearly sinusoidal the method of harmonic balance is used to obtain analytical results for amplitude, phase and entrained frequency. The non-linear algebraic equations are solved using hill-climbing methods due to Rosenbrock, Powell and Fletcher-Reeves. Algorithms requiring first derivatives of the minimised functions have been found significantly faster than the Rosenbrock method.

1. INTRODUCTION

Since the 1920's it has been known that there exists spontaneous electrical activity in the digestive tract (1). Following the initial recording of signals from the surface wall of the stomach, improvements in electronic recording techniques have led to a great amount of data being obtained throughout the tract and in many species of animals (2). The outstanding feature of the electrical activity is the existence of a spontaneous low frequency oscillation often called the 'basic electrical rhythm' or pacesetter potential (3). This rhythm has been shown to be spontaneously present by the fact that small excised areas of tissue still show regular oscillations.

Although there are considerable differences in the electrical rhythms between species the spontaneous activity has been recorded in the stomach, small intestine, large intestine and rectum (4,5,6,7). In the stomach the rhythm is pulse-like in dogs and rectangular-like in humans. Recordings from stomachs in the resting condition with no mechanical contractions show rhythm frequencies of about 0.05Hz in humans and about 0.08Hz in dogs. In the duodenum the human recordings are nearly sinusoidal, while a typical canine recording is shown in Figure 1. The human duodenal recordings

Figure 1 - Typical canine duodenal recording.

have a small amount of asymmetry which can be allowed for in the mathematical model. The duodenal frequency varies between about 0.2Hz in humans and 0.25Hz in dogs. Over the length of the duodenum there is a constant frequency known as a 'plateau' effect which has been of considerable interest in producing a mathematical model for the tract

(8). From the end of the duodenum to the ileum, the small intestine exhibits a shallow gradient of frequency with the human recording dropping to about 0.17Hz at the ileum. In the colon and rectum however there is a difference in the pattern of behaviour between humans and other species. In humans there are three patterns recorded (9). There are periods of zero activity when no regular rhythms are obtained, interspersed with two oscillations having frequencies of about 0.05Hz and 0.12Hz. These frequencies do not have a precise integer relationship and cannot therefore be viewed as a harmonic phenomenon. There is no obvious gradient of frequency along the length of the colon, but the percentage occurrence of each of the three modes does vary significantly.

Synchronised with the basic electrical rhythms are action potentials which occur whenever there are mechanical contractions in the tract. There are however long periods when no action potentials are present but the low frequency oscillations continue. The nature of the action potentials varies between species and between different parts of the tract. In the canine stomach the whole waveshape of the basic rhythm is altered giving a much larger mark-space ratio as can be seen in Figure 2. In the human duodenum, however, action potentials comprise a burst of high-frequency pulses superimposed on top of the basic rhythm. Recordings made at the Department of Surgery,

Figure 2 - Typical canine gastric recording with action potentials.

Sheffield, in the human colon have so far produced no evidence of any action potentials during mechanical contractions.

Some evidence exists that there is coordination between the stomach and duodenum

which controls the emptying of the stomach contents into the small intestine (10). A further phenomenon in the small intestine comprises a travelling wave of action potential spikes accompanied by a variation in the basic rhythm frequency (11).

Neural and hormonal modulation of the rhythms in intact organs appears to be fairly small, so that changes in frequency of greater than 10% are rare even for large drug stimulations. An exception to this is bombesin which appears to completely stop the electrical activity in the small intestine (12). Similarly, common diseases of the tract seem to have little effect upon the electrical activity except in the case of diverticular disease of the human colon which produces a higher frequency rhythm of about 0.25Hz as seen in Figure 3. Operations such as the cutting of the vagal nerve supply to the stomach produce temporary changes in the electrical patterns but considerable recovery to the normal patterns is often observed (13).

Figure 3 - Human colonic recording showing higher frequency rhythm characteristic of diverticulitis.

2. DATA RECORDING AND ANALYSIS

The electrical signals are normally recorded from stainless steel electrodes placed on either the inside or outside wall of the tract. Electrodes implanted on the outside wall are placed during an operation and the leads taken out through a drain in the abdominal wall. Six electrodes are usually implanted and removed after about two weeks. To make recordings from normal humans swallowed tubes are used which contain one or two electrodes 0.1mm. in diameter. The electrodes are surrounded by suction caps so that they can be secured to the inside wall of the gut with a negative

pressure of 20cm. of mercury. A third method of recording employs surface electrodes placed over the stomach region for non-invasive measurement of gastric activity (14).

All the signals are mvolts in amplitude and are amplified before recording onto 6 channel ultraviolet paper in parallel with a 4 channel analogue FM tape recorder. Large amounts of data have been recorded from humans and dogs in this way and it has been found desirable to select visually from the ultraviolet recordings suitable 8 minute stretches of data for subsequent interactive analysis. These stretches are compressed onto another FM analogue tape by playing back the original tapes 16 times faster than real time. In this way 1000 8-minute stretches of data can be compressed onto one 1200ft. analogue tape.

The logging and analysis program used for the gastro-intestinal research forms part of a general systems analysis and identification package which has grown out of the medical application (15). There are 41 options currently available each of which can be conversationally selected by a three letter code.

The LOG option is used to continuously log the compressed data via a high speed ADC onto the 1M word disc of a GE4020 process control computer. Various display options allow for 'paging' and expansion of the data base. Amongst the analysis programs the fast Fourier transform is most commonly used for accurate measurement of the digestive rhythm frequencies. An example of this is shown in Figure 4 which is a canine duodenal transform also containing a gastric component, made evident by using a logarithmic transform. Use is also being made of a fast Walsh transform (16) and Figure 5

Figure 4 - Log transform of canine duodenal recording containing an additional gastric spectral peak.

is an example of this applied to a human colon with diverticular disease. The normal low frequency mode together with the higher frequency mode characteristic of diverticulitis can be clearly seen.

Figure 5 - Fast Walsh transform of data from a human colon with diverticulitis.

3. DIGESTIVE TRACT MODELLING

A mathematical model which reproduces all the known physiological phenomena recorded from the gastro-intestinal tract comprises a set of mutually-coupled oscillators. For the small and large intestines which have a tubular structure, a one-dimensional 'chain' of oscillators has been utilised (8), while for the stomach a two-dimensional plane is necessary (17). The simplest model for the individual oscillator units consists of a non-linear second order differential equation of the Van der Pol type

$$\ddot{x} - \epsilon(a^2 - x^2)\dot{x} + \omega^2 x = 0$$

where frequency, waveshape and amplitude are determined by the parameters ' ω ', ' ϵ ' and ' a '. The interactive analysis techniques described briefly in the previous section are being used to set these parameters in analogue and digital simulations of the tract. Various forms of mutual coupling can be used but the normal structure employed in this work corresponds to linear resistive, capacitive and inductive coupling as shown in the equivalent circuit of Figure 6.

Figure 6 - Equivalent circuit of two mutually-coupled Van der Pol oscillators.

Investigation of the basic phenomena produced by this model has been done by analogue simulation of up to 8 cells. It has been found that two stable limit cycles are obtainable from mutually coupled Van der Pol oscillators for particular forms and values of coupling. This enables the human colonic data to be modelled by a ring structure of oscillators. Summation of two adjacent cells to give the model output reproduces the three modes as shown in Figure 7. The three modes in this figure were

Figure 7 - A human colonic model comprising a ring of 4 Van der Pol oscillators showing three solutions.

obtained by switching on the simulation from different initial conditions. Switching between the modes can be caused by injection of sinusoidal and random disturbances or perturbations to the basic oscillator cells (18).

For simulation of large sections of the digestive tract a digital simulation comprising 100 interconnected cells is being used (8). The major phenomenon recorded from the small intestine is a frequency 'plateau' throughout the duodenum. This 'plateau' occurs in spite of the fact that measurements on small excised tissue indicate a steady frequency gradient along the whole length of the small intestine. An example of the plateau effect reproduced by the digital simulation is given in Figure 8 which also indicates a secondary plateau introduced by an 'incision' in the model matching known physiological data in dogs (19).

Figure 8 - 100 oscillator digital simulation showing two frequency 'plateaux' caused by an 'incision' in the model.

4. ANALYTICAL TECHNIQUES APPLIED TO THE DIGESTIVE TRACT MODEL

In the case of nearly-sinusoidal electrical signals it has been possible to use analytical methods to solve the equations of the coupled oscillator model. The particular areas of current interest have been the human small intestine and colon. In both the duodenum and colon of humans, the signals are nearly sinusoidal in nature and both areas exhibit frequency entrainment. The phenomenon of frequency entrainment of a single Van der Pol oscillator by an external forcing function has been known for many years (20). In this work the case of mutually-coupled Van der Pol oscillators

is considered and the method of harmonic balance is employed to obtain approximate analytical solutions (21).

For two coupled oscillators under entrainment the harmonic balance method assumed a sinusoidal solution for each cell given by

$$x_1 = A_1 \cos(\omega_e t + \beta)$$

$$x_2 = A_2 \cos(\omega_e t + \alpha)$$

Differentiation of these solutions and ignoring second derivative terms in amplitude because of the assumption of slowly varying coefficients gives

$$\dot{x}_1 = -A_1(\omega_e + \dot{\beta})\sin(\omega_e t + \beta) + \dot{A}_1\cos(\omega_e t + \beta)$$

$$\dot{x}_1 = -A_1(\omega_e + \dot{\beta})^2\cos(\omega_e t + \beta) - 2(\omega_e + \dot{\beta})\dot{A}_1\sin(\omega_e t + \beta)$$

etc.

Substitution of these expressions into the governing equations and simplification of the circular functions is followed by ignoring all the harmonic terms and retaining only the fundamental component. By equating the sine and cos terms in each equation, time is eliminated and 4 algebraic equations result. When there are 'n' interconnected oscillators, '2n' non-linear algebraic equations are obtained whose solution gives directly the values of entrained frequency, 'n' amplitudes and 'n-1' phases (the phase of the first oscillator is taken to be 0°). For the 'nth' oscillator the equations have the following typical form which here represents inductive coupling for a 'chain' model

$$(\omega_n^2 - \omega_e^2)A_n \cos \alpha_n - \lambda_n \omega_e A_{n+1} \sin \alpha_{n+1} - \lambda_{n-1} \omega_e A_{n-1} \sin \alpha_{n-1} + \xi_n \omega_e A_n \sin \alpha_n -$$

$$\xi_n \lambda_n A_{n+1} \cos \alpha_{n+1} - \xi_n \lambda_{n-1} A_{n-1} \cos \alpha_{n-1} + \xi_n A_n^2/2 \left\{ -A_n/2 \cdot \omega_e \sin \alpha_n + \lambda_n A_{n+1} \right.$$

$$\cos \alpha_{n+1} + \lambda_{n-1} A_{n-1} \cos \alpha_{n-1} + \lambda_n A_{n+1}/2 \cos(2\alpha_n - \alpha_{n+1}) + \lambda_{n-1} A_{n-1}/2 \cos$$

$$(2\alpha_n - \alpha_{n-1}) \left. \right\} = 0$$

For some types of coupling between two oscillators it has been found that the algebraic equations can be solved directly when the uncoupled frequencies are equal.

Simple relationships between entrained frequency and coupling factor have been found (22) and similarly for amplitude. It has also been found that prediction of two stable limit cycles can be obtained from the harmonic balance method. Thus Figure 9 shows the good agreement between analytical and simulated results giving the minimum coupling

Figure 9 - The minimum coupling coefficient required to produce 2 stable limit cycles as a function of waveshape parameter.

values of waveshape factor 'E' which produce two stable limit cycles. The analytical relationship is given by

$$\text{Minimum Coupling} = \frac{-(\omega^2 - 2\varepsilon^2) + \sqrt{[(\omega^2 - 2\varepsilon^2)^2 - 8\omega^2\varepsilon^2]}}{2\omega^2}$$

In the majority of cases the non-linear algebraic relationships cannot be solved directly and methods of hill-climbing have to be used. Provided the waveshape factor 'E' is less than unity good correlation has been obtained between simulated and hill-climb results as can be seen in Figure 10a and b. These figures show the effect of coupling changes on entrained frequency, amplitude and phase. These results were obtained using a Rosenbrock constrained optimisation technique requiring function evaluation only (23). For realistic simulation of the human duodenum a chain of oscillators is required and Figure 11 shows the amplitudes obtained for an 18x1 chain solved with the Rosenbrock algorithm. The open-ended chain is not representative of a section of the intact organ and the large end - effects can be clearly seen in Figure 11. To make the chain represent a section of the organ, end-effect correction

(a) in-phase mode

(b) anti-phase mode

Figure 10 - Variations of entrained frequency, amplitudes and phase for two coupled oscillators.

has been attempted so that the first and last oscillators have an additional input predicted from knowledge of the conditions along the chain. Figure 11 shows the result obtained by linear extrapolation of amplitude and phase from the first and last

Figure 11 - Entrained amplitudes for an 18x1 chain using a Rosenbrock algorithm.

two oscillators in the chain. In this example an amplitude of 2.0 units would be expected for the whole chain since there is no gradient of uncoupled frequency.

For hill-climbing on more than 10 oscillators the Rosenbrock algorithm was found to be too slow using an ICL 1907 computer. The problem is basically unconstrained and the first partial derivatives of the functions to be minimised can be evaluated, albeit with considerable tedious algebraic manipulation. Two algorithms suited to this approach and implemented on the NAG library of the ICL 1900 series have been tried. The first is a Powell routine (24) which commences the hill-climb using steepest descent and then curves to terminate at the Newton-Raphson point. This algorithm has been found generally reliable and fairly fast. A line-printer output from this method is shown in Figure 12 which represents a tube simulation having 5 oscillators along the length and 4 around the periphery. In the graph plot the oscillators around the tube are numbered 1 to 4 and the absence of a number indicates that higher number(s) occupy the same point on the graph. For this 40 variable example 61 iterations were performed in 100 second of machine time and gave a hill-value of $2.6 \cdot 10^{-2}$. The uncoupled oscillators had equal frequencies and values of amplitude and phase around the tube should have been identical. The second algorithm is a Fletcher-Reeves routine (25) which uses 'n' one-dimensional searches based on steepest descent to a local minimum. When a local minimum is located the conjugate direction is found and another one-dimensional search is commenced. This algorithm has been found to give better results both in terms of hill-values and speed. Figure 13 is the amplitude result obtained

Figure 12 - Entrained amplitudes and phases for a
5 x 4 tube using a Powell algorithm.

for an 18x1 chain using the Fletcher-Reeves algorithm. 41 iterations of the 36 one-dimensional searches were obtained in 40 seconds and gave a hill-value of $2.6 \cdot 10^{-2}$. This example did not employ any form of end-correction and clearly shows the non-uniform amplitude if end-effects are not considered.

Figure 13 - Entrained amplitudes for an 18x1 chain
using a Fletcher-Reeves algorithm.

5. CONCLUSIONS

A mathematical model comprising linked oscillators based on Van der Pol's equation is capable of reproducing the known phenomena recorded electrically from the surface walls of the mammalian digestive tract. For the human small and large intestines nearly-sinusoidal electrical signals are recorded and analytical solutions have been obtained using the method of harmonic balance. For the case of 'n' oscillators in a condition of frequency entrainment '2n' non-linear algebraic equations are obtained from the harmonic balance method. Solution of these equations requires hill-climbing methods and gives directly the most important variables of frequency, amplitudes and phases. For small numbers of oscillators a Rosenbrock algorithm is satisfactory and simple to programme. For large numbers of oscillators the Rosenbrock method is too slow and hence optimisation algorithms requiring first derivatives of functions have been used. Both Powell and Fletcher-Reeves routines have been satisfactory for up to 50 variables with the later algorithm being considerably faster.

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