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Detection of the Recovery Phase of in vivo Gastric Slow Wave Recordings

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Abstract

Gastric motility is coordinated by bio-electrical events known as slow waves. Abnormalities in slow waves are linked to major functional and motility disorders. In recent years, the use of high-resolution (HR) recordings have provided a unique view of spatiotemporal activation profiles of normal and dysrhythmic slow wave activity. To date, in vivo studies of gastric slow wave activity have primarily focused on the activation phase of the slow wave event. In this study, the recovery phase of slow waves was investigated through the use of HR recording techniques.

The recovery phase of the slow wave event was detected through the use of the signal derivative, computed via a wavelet transform. The activation to recovery interval (ARi) metric was computed as a difference between the recovery time and activation time. The detection method was validated with synthetic slow wave signals of varying morphologies with the addition of synthetic ventilator and high frequency noise. The methods was then applied to HR experimental porcine gastric slow wave recordings. Ventilator noise more than 10% of the slow wave amplitude affected the estimation of the ARi metric. Signal to noise ratio below 3 dB affected the ARi metric, but with minor deviation in accuracy. Experimental ARi values ranged from 3.7–4.7 s from three data sets, with significant differences across them.

I. INTRODUCTION

Gastic motility is governed by an underlying bio-electric activity known as slow waves. These slow waves are generated and propagated through a network of specialized cells known as the interstitial cells of Cajal (ICC), which are present in the smooth muscle musculature [1]. Damage to the structure and function of ICC have been implicated in major functional motility disorders such as gastroparesis and functional dyspepsia [2], [3]. Recent in vivo high-resolution (HR) recordings, along with mathematical modeling have provided a comprehensive view of the propagation characteristics of the activation phase of slow wave activity in the gastrointestinal (GI) tract [4], [5]. A recent HR mapping investigation has revealed the presence of dysrhythmic slow waves in gastroparetic patients, who have reduced ICC counts [6].

The recovery phase of in vitro slow waves has been studied extensively [7] but to date, has seldom been analyzed in in vivo recordings. This is due to a combination of factors ranging from a lack of an effective method to detect the recovery phase of the slow wave which contains varying signal morphology of the recovery phase, low signal to noise ratio (SNR) recordings [8], and inappropriate use of signal filters [9]. In cardiac electrophysiology, the detection of the recovery phase of the bio-electrical activity, along with calculation of the activation-to-recovery interval (ARi) is routinely performed and has become a significant clinical indicator [10]. It is anticipated that defining the ARi of the slow wave event in the GI field will allow for an improved mechanistic understanding of the functional consequences of dysrhythmic slow wave activity in motility disorders.

Currently, automated and real time techniques exist to analyze and define the activation phase of the slow wave [11], [12], [8]. In this study, we have developed a novel approach to detect the recovery phase of the slow wave using the wavelet transform to calculate the ARi of the slow wave event. It was validated using synthetic slow wave signals generated from experimental data, and also applied to HR experimental data.

II. METHODS

A. Detection Method

The recorded signals were first pre-processed and filtered according to previous methods [13], after which the activation time of the slow wave events were automatically marked and clustered into their propagating wavefront [8], [14]. The recovery of the slow wave event corresponds to the time of maximum upstroke of the signal, a short period after the activation time [15]. In this study, the wavelet transform was used to compute a derivative estimate of the slow wave signal to detect the point of maximum upstroke. The method was applied to synthetic slow wave signals, followed by application to HR gastric slow wave recordings.

The wavelet transform is a signal processing technique to decompose the signal $f(t)$ according to the mother wavelet ψ as such.

$$W_f(a, b) = \int_{-\infty}^{\infty} f(t) \psi_{a,b}(t) dt \quad (1)$$

where W_f is the wavelet transform of the signal $f(t)$, $\psi_{a,b}(t) = \frac{1}{\sqrt{a}} \psi\left(\frac{t-b}{a}\right)$ and a and b are the scale and translation parameter. The wavelet can be defined as the derivative of the smoothing function $\phi(t)$, which has a fast decay and a non-zero constant integral K as previously described [16], [17].

$$K = \int_{-\infty}^{\infty} \phi(t) dx \neq 0 \quad (2)$$

Given that the wavelet has combined properties of data smoothing and differentiation [16], [17], it can be shown that the first derivative of the signal $f(t)$ can be computed as [16].

$$\frac{df(t)}{dt} = \lim_{s \rightarrow 0} \frac{W_f}{Ks^{3/2}} \quad (3)$$

A spline wavelet was used with a scale parameter of 6. The discrete wavelet transform was used via the ‘trous algorithm’ to avoid sub-sampling [17], [16]. The upstroke of the signal was found using the maximum derivative after the site of the activation time (2 s to 7 s after the activation time) as shown in Fig. 1.

B. Synthetic slow wave data

Synthetic slow wave signals were derived from HR mapping data from pigs using previously described techniques [13] (See II-C for experimental methods). In brief, the slow wave signal events were aligned and stacked from an electrode. A singular value decomposition was then performed on the stack to acquire the first principal component, which represents the average morphology. In particular, fifteen different representative morphologies of extracellular slow wave were taken from three pigs, with five different slow wave morphologies from each pig.

The main source of noise for detection of the recovery phase of the slow wave event are ventilator artifact and high frequency noise from other electrical interference. Synthetic ventilator noise was applied at a frequency of 12 cpm using a sinusoid with a random shift of $\pi \pm \frac{\pi}{2}$ (from a normal distribution) to simulate experimental conditions. The amplitude of the ventilator varied from 0 to 100% of the slow wave amplitude. For high-frequency noise, white Gaussian noise was added to the signals. The SNR was varied from 60 to -5 dB. Fig. 2 shows an example of two different synthetic signal morphologies of slow wave activity with synthetic noise. The ARi metric was calculated for each noise level for the 15 different morphologies. Due to the random nature of synthetic noise, the metrics were computed 50 times at each noise level to acquire an average metric.

C. Experimental Pig Data

Ethical approval for experimental studies was granted by University of Auckland Ethics Committee. HR slow wave mapping studies were undertaken in pigs (n=3). The experimental method used to acquire the datasets are described previously [18], [19]. In brief, the pig was anesthetized, after which a mid-line laparotomy was performed to gain access to the serosal of the stomach. Flexible printed circuit electrodes (up to 256 recordings sites) were then placed on the gastric serosa and packed with warm saline gauze prior to recording [5]. The data was recorded at 512 Hz using an ActiveTwo data acquisition system (Biosemi, the Netherlands) modified for passive recordings for period of 2–4 min. ANOVA was performed on the slow wave interval to quantify the significance of variation across datasets.

III. RESULTS

A. Synthetic Data

The ARi was successfully computed in 15 synthetic slow wave signals with a median of 4.3 s. With the addition of ventilator noise, from 0 to 100% of slow wave amplitude, the estimation of ARi of the slow wave decreased from a median value of 4.3 to 3.1 s (Fig. 3). When ventilator noise was less than 10% of slow wave amplitude of the ventilator, the estimates were stable, after which they became less reliable. With a decrease in SNR from 60 to -5 dB of the slow wave morphology, the ARi decreased from a median value of 4.3 to 4.2 s (Fig. 4). The estimation of ARi was steady until about 3 dB after which the estimate had a minor deviation in accuracy. The results suggest that the ARi metric computed using the derivative wavelet is resistant to high-frequency noise, but is potentially under estimated with the presence of ventilator artifact. Ventilator artifact can distort the recovery phase morphology making its detection inaccurate due to the upstroke of ventilator and the slow wave recovery phase being similar.

B. Experimental Data

Fig. 5 shows the boxplot of the ARi of the slow wave event from three pig subjects along with corresponding activation propagation profiles. The data set selected from Pig 1 has a normal stable antegrade propagation profile [19], while Pig 2 had an unstable dysrhythmic propagation profile with circumferential wavefronts [20], and Pig 3 had a stable ectopic pacemaker. Analysis of variance (ANOVA) was performed on the slow wave interval to determine whether subject was a factor in accounting for the variation between data sets. The F-statistic (value of 528) was used to calculate the p value ($p < 0.05$), which showed a significant difference in means across the three subjects, which warrants further investigation. These results demonstrate practical validity of the novel methods, and show proof-of-principle that ARi metric may be important in gastric dysrhythmia analysis, with potential alteration to the kinetics of ICC ion channels during aberrant propagation (difference and larger variation). Another possible factor is that intracellular recordings have shown different region of the stomach have varying ARi [21] and this will need to be analyzed in future trials. However, the range of ARi from experimental data from this study (3.7–4.7 s) are in general agreement with previous intracellular studies [21].

IV. CONCLUSIONS

HR in vivo mapping of the activation phase of the slow wave activity has been a vital advance to uncover spatiotemporal characteristics of GI dysrhythmias in motility disorders such as gastroparesis [6]. Investigating the recovery phase of the slow wave activity, introduced here, could aid in understanding mechanisms that are responsible for initiating and maintaining slow wave dysrhythmias. This approach is supported by the significance of ARi as a metric in cardiac electrophysiology.

Now that these methods are established, future physiological studies will aim to assess the differences in recovery spatiotemporal profiles to the activation profile. Multi-layer ICC and smooth muscle tissue studies may also be carried out using experimental and or

mathematical modeling techniques to define the accuracy of the slow wave recovery morphology. Further work may include assessment of the choice of wavelet and the scale parameters in wavelet, and whether it could be related to the SNR of an experimental signal. In this study, a ventilator frequency of 12 cpm was used, as this is a common setting, but other ventilator frequency parameters could be investigated to assess the change in ARi. Techniques to minimize the effect of ventilator noise will be investigated such as the use of bipolar recordings and/or analysis, averaging techniques or blind source separation techniques.

In conclusion, a new method to detect the recovery of the slow wave event is presented, along with validation and application in experimental data. It is anticipated that its use will aid in improving our knowledge of GI electrophysiology through understanding mechanisms that are responsible for initiation and maintenance of dysrhythmias.

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Figure 1.

Detection of the recovery phase of the slow wave event. (a) shows a typical slow wave event with the red cross marking the activation time. (b) shows the derivative calculated by a wavelet transform, with the maximum defined as the point of recovery (shown as a green cross). This is then denoted in the signal in (a) as a green plus.

Figure 2.

Synthetic slow wave events generated using experimental data. (a) and (b) are two synthetic signal with different morphologies without any noise. (c) shows the signal (a) corrupted with 20% of ventilator noise at 12 cpm, while (d) is corrupted with high-frequency noise yielding a signal-to-noise ratio of 5dB.

Figure 3. Effect of ventilator noise on the ARi of the slow wave event. The median slow wave intervals are plotted against ventilator noise. The ARi estimates drop from 4.3 s to 3.1 s.

Figure 4.

Effect of high-frequency noise on the ARi of the slow wave event. The median slow wave intervals are plotted against the signal to noise ratio of the slow wave signals. The ARi estimates drop from 4.3 s to 4.2 s.

Figure 5.

(a) Boxplot of ARi of slow wave activity across three pig subjects along with their activation propagation profiles in (b, c and d). Pig 1 with normal antegrade propagation (b) had an ARi of 4.9 ± 0.4 s ($n=423$), while Pig 2 with dysrhythmic circumferential propagation (c) had an ARi of 3.8 ± 0.7 s ($n=706$), while Pig 3 with ectopic pacemaker propagation (d) had an ARi of 4.0 ± 0.7 s ($n=1220$). ANOVA showed a significant difference across all three pig subjects.