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A peak detection method for identifying phase in physiological signals

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ABSTRACT

Introduction: To understand the integrated behavior of biological systems, the interactions between their constituent parts are often studied. For example, the interaction between blood pressure and heart rate reveals information about the cardiac baroreflex. For the purpose of characterizing relationships between physiological signals, it is useful to identify phase either as a primary outcome or as an intermediate step to obtain other relevant secondary indices. Existing methods for phase estimation in physiological signals often suffer from a lack of thorough description and standardization, which renders reproducibility and interpretation difficult. A relatively simpler peak detection algorithm was compared to the gold standards of wavelet and Hilbert transforms for its ability to obtain phase.
Methods: The accuracy and computation time of the peak detection algorithm was compared to the gold standard methods *in silico* by applying all three to data of known phase, and signal-to-noise ratios from −20 to 5 dB. We then compared the performance of the peak detection method to the Hilbert and wavelet methods by applying each to four different types of *in vivo* data.
Results: The peak detection technique is less susceptible to noise and over 10 times faster, computationally, than the wavelet technique. Application to *in vivo* physiological data shows that equivalent results are obtained from each technique.
Conclusions: The peak detection method can be used to obtain phase in physiological signals, provide a clearer and more direct interpretation, and be more easily reproducible. Because of its design features, peak detection could also be used to identify individual oscillations in relevant signals, as well as to obtain amplitudes and direct time delays.

1. Introduction

Homeostasis is an integral feature of biological systems and is maintained in part by negative feedback loops. The presence of these loops contributes to the creation of oscillations in the corresponding physiological signals. For example, oscillations exist in heart rate [17], spontaneous vasomotion of arteries [18,10], electrical activity of skeletal muscle [23], and circadian rhythms in hormone levels [5]. The key variables that characterize an oscillation are its amplitude, frequency, and phase. In particular, phase is used to determine the relative progress of one oscillatory cycle at a particular time.

Phase analysis is also applied to the study of the relationship between a pair of associated signals, which can aid understanding of the integrated function of multiple parts of a given system. There are multiple techniques that are routinely employed for estimating the phase of signals, most commonly relying on either a wavelet or Hilbert transform. Both of these techniques are regarded as gold-standards and have been shown to return statistically similar results for signals that have a previously defined narrow frequency band of interest [16,20].

The term "phase" is general and can be applied to a wide variety of situations. Since the phase of an *in vivo* signal can represent the physical state of the system being measured, it is interpreted differently depending on context. For example, in the case of a blood pressure time-series, phase can be used as a normalized indicator of arterial contraction and relaxation while in the case of the position of the foot of a pedaling cyclist, phase indicates which part of a particular pedal cycle occurs at any given time. The same type of analysis can be performed on any signal presenting cyclical behav-

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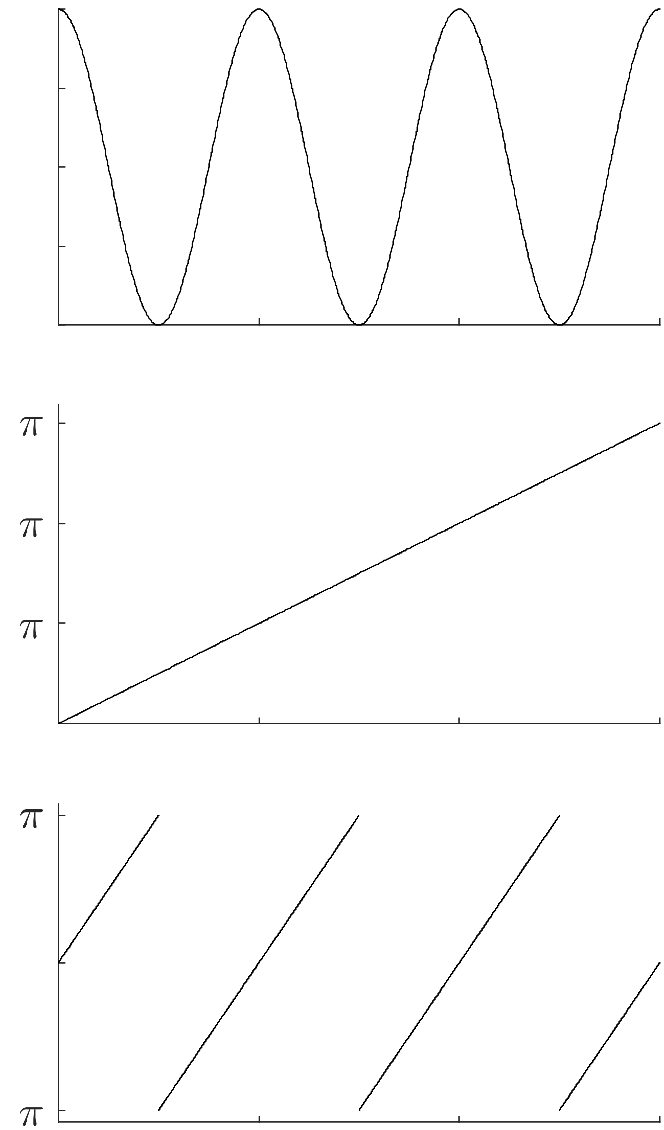

Fig. 1. Example cosine function and its corresponding phase. There are three cycles of the cosine wave (**top**), resulting in a total increase of 6π radians of phase (**middle**). The bottom panel shows the same phase wrapped from −π to π.

ior, in which each individual cycle (Fig. 1, top) increases phase by 2π radians (Fig. 1, middle). Since the circumference of a unit circle is 2π, phases that differ from one another by a multiple of 2π represent the same physiological state. In this study, the convention by which phase is visualized by wrapping it from −π to π (Fig. 1, bottom) was used.

When two parts of a physiological system interact (as they do, for example in negative feedback loops), oscillations in the signals arising from each system adjust in response to changes in the other system. This has been shown in networks in the brain [8], the physiological origin of pathological human tremors [15], the relationship between blood pressure and sway patterns in human standing [11], blood flow in adjacent nephrons [21], and glycolytic oscillations in cells that receive a periodic nutrient supply [3]. In these cases, phase and phase difference can be used either themselves or as a means to obtain phase lock index, time delay, or other measures of synchrony. Monitoring free-running physiological signals without externally perturbing them, however, cannot distinguish between coincidental synchrony and physical coupling [19].

Although the wavelet and Hilbert transforms have been used for decades to study physiological oscillations, methodologies can differ significantly and there remains a lack of clear and detailed guidelines as to their use in various fields. Analyses often rely on 3rd-party software with inconsistent degrees of explicit description. Particularly, imprecise reported methods of filtering and smoothing, either as pre- or post-processing can dramatically alter their output. Because of this, studies are often burdened by lack of reproducibility, and results become difficult to interpret.

The goal of this study was to test the ability of a basic peak detection method to return accurate phase when applied to a variety of *in silico* and *in vivo* signals. The aim is that the important simplifications in the proposed methodology would reduce the barriers to transparency and clarity. Because measurement noise and physiological noise are the primary sources of interference with phase estimators, the wavelet, Hilbert, and peak detection techniques were tested for their robustness to noise on simulated signals with known phase. The computing times of these three techniques were also compared. In addition to *in silico* testing, the phase in signals comprising four physiological systems were estimated in order to determine phase difference between related pairs of signals. The results obtained with the peak detection method were then compared to those obtained with the wavelet and Hilbert transforms.

2. Methods

Each signal, whether *in silico* or *in vivo*, was filtered using a 6th order Butterworth bandpass filter prior to analysis. This filter design was chosen for its flat frequency response in the passband, a required characteristic when comparing the powers of different frequencies. Filter orders between 6 and 20 had no distinguishable effect on phase relative to each other, and thus the minimum of 6 was chosen to minimize computing time. Signals were first filtered forward then backward to undo any phase alterations that could have been incurred. The passband of the filter was determined case-by-case to isolate relevant signal morphology and is described in detail in the respective sections.

Because phase is defined on a circle, applying arithmetic statistics to it is erroneous. This fact is illustrated using the following example: the mean of the angles π/4 and 7π/4, calculated arithmetically, is π. However, since 7π/4 is the same as −π/4 when plotted on a circle, the mean is 0. For this reason, circular statistics were used when dealing with phase. A good resource for circular statistics is found in [2]. When phase difference was shown in figures as a time-series, phase slips of ±2π radians, *i.e.* regions where phase jumped from π to −π only because of wrapping, were removed for clarity of presentation.

All data synthesis and analysis were performed using Matlab (r2014b, The Mathworks, Natick, MA, USA) and statistical comparisons were performed using SPSS (v22, IBM, Armonk, NY, USA). Results are expressed as mean ± standard deviation unless otherwise indicated, and differences were considered significant if $p < 0.05$.

2.1. Estimating phase

This section describes the wavelet transform, Hilbert transform, and peak detection techniques. To allow comparisons between the techniques on an even playing field, their pre- and post-processing methods were unified as much as possible. To eliminate edge effects, $3/f_L$ s were removed from both ends of all phase time-series, where f_L was the low-frequency bound of the filter passband.

i) *The Morlet wavelet* transform is a Gaussian-windowed sinusoid. The Morlet wavelet of order six, used in this study, is a cosine wave modulated by a Gaussian of such width that six periods fit in 95% of its area. The wavelet transform returns power, a measurement of how well a wavelet represents the given signal on