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ORIGINAL RESEARCH

Using generalized additive models to decompose time series and waveforms, and dissect heart–lung interaction physiology

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Abstract
Common physiological time series and waveforms are composed of repeating cardiac and respiratory cycles. Often, the cardiac effect is the primary interest, but for, e.g., fluid responsiveness prediction, the respiratory effect on arterial blood pressure also convey important information. In either case, it is relevant to disentangle the two effects. Generalized additive models (GAMs) allow estimating the effect of predictors as nonlinear, smooth functions. These smooth functions can represent the cardiac and respiratory cycles' effects on a physiological signal. We demonstrate how GAMs allow a decomposition of physiological signals from mechanically ventilated subjects into separate effects of the cardiac and respiratory cycles. Two examples are presented. The first is a model of the respiratory variation in pulse pressure. The second demonstrates how a central venous pressure waveform can be decomposed into a cardiac effect, a respiratory effect and the interaction between the two cycles. Generalized additive models provide an intuitive and flexible approach to modelling the repeating, smooth, patterns common in medical monitoring data.

Keywords Hemodynamic monitoring · Central venous pressure · Mechanical ventilation · Signal processing · Statistical modelling

1 Introduction

Medical waveforms of physiological measurements, like electrocardiogram (ECG), invasive arterial blood pressure (ABP), photoplethysmogram (pleth) and central venous pressure (CVP), are ubiquitous in settings with closely monitored patients, notably in intensive care units and operating rooms. While waveforms of these signals are often displayed on a bedside monitor, they are rarely interpreted directly by the clinician (the ECG being a notable exception). Instead, simple summary characteristics, e.g. heart rate, respiratory rate and standard blood pressure features, are automatically calculated by the bedside monitor and presented beside the waveforms.

The main signal in these waveforms comes from the heart. In addition, respiration impacts the waveform, and the cyclic respiratory effect can convey important information about patient physiology. This is especially recognised in fluid responsiveness research where "dynamic" fluid responsiveness indicators such as the pulse pressure variation (PPV) have repeatedly outperformed "static" indicators [1, 2]. However, the details of the cyclic respiratory effects can be difficult to disentangle, illustrated by the ventilation-related limitations to PPV such as tidal volume, respiratory rate and respiratory system compliance [3].

Researchers have developed several, methods for analysing medical waveforms and derived time series: e.g. pulse pressure variation (PPV), cardiac output estimation, hypotension prediction index, etc. While many of these measures are useful and often implemented in commercial monitors, they do not always reflect what the clinician expects them to (e.g. a high PPV from a patient with a subtle arrhythmia). Generally, these complicated algorithms are difficult to understand and typically proprietary. This makes it difficult

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