# Frontiers in Physiology: Computational Physiology and Medicine

# Advances in Basic and Applied Research in Photoplethysmography

Editors: John Allen1 and Panicos A Kyriacou2

**Author affiliations**

1 Research Centre for Intelligent Healthcare, Coventry University, Coventry UK

2 Research Centre for Biomedical Engineering, City, University of London, London UK

Email for correspondence: ad5325@coventry.ac.uk

**ORCID IDs of Editors:**

John Allen: <http://orcid.org/0000-0002-7263-0533>

Panicos A Kyriacou: <http://orcid.org/0000-0002-2868-485X>

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**Figure 1.** Beat-to-beat pulse amplitudes of multi-site PPG recordings for a healthy subject compared to those from a patient with systemic sclerosis (SSc). Time-frequency type images of the various measurement phases including a reactive hyperaemia testing phase can automatically be classified using a pre-trained convolutional neural network (CNN) system. PPG sensing and advanced analytics offer new ways in to assess cardiovascular patients.

***Background***

Welcome to this Frontiers in Physiology Research Topic Collection on the Advances in Basic and Applied Research in Photoplethysmography.

Photoplethysmography (PPG) is a vascular optics technique that can be used to detect blood volume changes in the microvascular bed of tissue with each heartbeat (Allen 2007, Kyriacou and Allen 2021). In recent decades there has been a significant increase in the number of published articles describing basic and applied research in PPG, hailing it as a non-invasive, low cost, and simple optical measurement technique applied at the surface of the skin to measure a whole host of physiological parameters. The popularity of this topic can be attributed to the realization that PPG has important implications for a wide range of applications including cardiovascular system assessment, vital signs monitoring including non-invasive blood pressure estimation and heart rate, and the study of pain. In addition, the recent significant contributions of PPG to wearable devices have had a major impact on the popularity and usability of PPG. There is currently a large body of literature contributing new knowledge on the relation of the PPG pulse morphology, pulse wave analysis and pulse features extraction with the physiological status of peripheral blood vessels, such as vascular ageing and stiffness, blood pressure and compliance, microvascular disease, autonomic function, amongst others. There are also significant efforts in the utilization of the PPG for the detection of heart arrhythmias such as Atrial Fibrillation (AF). Researchers are continuing to strive in combining the PPG sensory capabilities of wearables, such as smartwatches, with Artificial Intelligence (AI) machine learning approaches in delivering ubiquitous health monitoring solutions that go beyond the current available consumer devices. The motivation and aim of this Research Topic is to bring together the latest cutting edge basic and applied research in the field of Photoplethysmography. The Research Topic for Frontiers in Physiology: Computational Physiology and Medicine showcases 16 original research papers covering a diverse range of contributions in the broad field of PPG measurement and analysis.

***Summary of published papers in the Collection***

Cardiovascular disease continues to be the leading cause of death globally, this is one of the very important areas where PPG has considerable potential to help impact on disease burden by allowing us to understand better vascular ageing and also to enable low-cost accessible monitoring of cardiovascular status. Žikić et al (2023) in ‘*Using the photoplethysmography method to monitor age-related changes in the cardiovascular system*’ collected single site PPG measurements from above the left common carotid artery in 117 healthy adult participants (up to 70 years of age) and analysed the data using a non-linear technique (detrended fluctuation analysis, DFA) to produce a ratio of scalar coefficients which were found to decrease exponentially with age – giving a biomarker for monitoring ageing. Age-related changes in PPG shape have also been reported in the literature including classifying the pulse into one of four classes based on the dicrotic notch position (Dawber et al 1973). Zanelli et al (2023) in ‘*Clustered photoplethysmogram pulse wave shapes and their associations with clinical data*’ noted however that when working with real data, labelling waveforms with one of these four classes was no longer straightforward but the correct identification of the PPG shape could enhance precision and reliability of extracted biomarkers. Using a PPG data set of 300 subjects (aged 19-83 years) they employed unsupervised machine learning and deep learning approaches to overcome the data labelling limitations (including K-medoids based clustering, similarity matrix computed with Derivative Dynamic Time Warping, PPG features extracted with CNN AutoEncoder). The results indicated that PPG wave shapes do differ due to their dicrotic notch characteristics. However, there are additional differences such as width of the systolic peak and the strength of a secondary systolic wave and by investigating the optimal number of clusters they found 7 clusters of PPG wave shapes instead of the aforementioned 4 classes.

The cardiovascular system is complicated but PPG does give a valuable way in to study its dynamics and key physiological variables such as blood pressure (BP) and heart rate (HR). Xing et al (2023) in ‘*Temporal complexity in photoplethysmography and its influence on blood pressure*’ used the Higuchi fractal dimension (HFD) and autocorrelation function (ACF) to assess temporal complexity of the PPG and interpreted the stochastic patterns with a model-based simulation which has potential to help optimise BP estimation algorithms. They adapted the classic four-element Windkessel model incorporating BP dependent compliance profiles and simulations generated PPG responses at various timescales. Importantly, the relationship between complexity and haemodynamics, as predicted by their model, aligned well with the experimental analysis in data collected from 40 healthy subjects. HFD and ACF had significant contributions to BP, displaying stability even in the presence of high cardiac output fluctuations. Temporal complexity patterns are essential to single-site PPG-based BP estimation and understanding the physiological implications of these patterns can aid in the development of such algorithms. A cardiovascular variability study was also reported by Mejía-Mejía et al (2022) with ‘*Spectral analysis for pulse rate variability assessment from simulated photoplethysmographic signals*’. Pulse rate variability (PRV) has been used as a surrogate of heart rate variability (HRV, measured via ECG) although there have been shown to be differences which could arise from physiological processes or from technical aspects of extraction of PRV from PPG. They extracted frequency-domain information from PRV in order to establish the best performing combination of parameters and algorithms to obtain the spectral representation of PRV. They found that with specific interpolation methods the Fast Fourier Transform (FFT) and multiple signal classification (PMUSIC) algorithms gave the best results, and considering the lower complexity of FFT over PMUSIC, recommended that FFT should be considered as the appropriate technique to extract frequency-domain information from PRV signals.

The use of PPG for clinical monitoring was also covered in several leading-edge papers. Stockwell et al (2023) in ‘*Forehead monitoring of heart rate in neonatal intensive care*’ described pioneering R&D in PPG sensor development for heart rate monitoring in critically unwell infants, with the reflection mode measurements made advantageously at the forehead site rather than peripherally on a limb. They reported data comparing heart rates measured with a forehead-based PPG sensor against a wrist-based PPG sensor in 19 critically unwell infants in neonatal intensive care collecting 198 hours of data, with good agreement between techniques (Bland-Altman limits of agreement of 8.44 bpm, bias 0.22 bpm) showing that the forehead is a reliable alternative location for measuring vital signs using the PPG. Roldan et al (2023) in ‘*Non-invasive monitoring of intracranial pressure changes: healthy volunteers study*’ aimed to evaluate the possible association between pulsatile near infrared spectroscopic waveform features at the forehead and induced changes in intracranial pressure (ICP) in healthy volunteers. They reported data from 16 healthy volunteers with measurements acquired during body position changes and with Valsalva manoeuvre, the classification model features were extracted and analyses carried out to compare the 2 signals. The results revealed significant differences in the features extracted from these signals, demonstrating a correlation with ICP changes induced by positional changes and Valsalva manoeuvre. The classification models were capable of identifying changes in ICP using features from optical signals from the brain, with a sensitivity ranging from 63 to 80% and specificity ranging from 60 to 70%, this work representing a first step towards the non-invasive monitoring of intracranial pressure. Pettit et al (2024) in ‘*Photoplethysmogram beat detection using symmetric projection attractor reconstruction*’ presented a novel method which uses the Symmetric Projection Attractor Reconstruction (SPAR) method to generate an attractor in a two-dimensional phase space from the PPG signal. A line is defined through the origin of this phase space to be a Poincaré section, beats are detected when the attractor trajectory crosses an optimally defined section. The method was assessed on the Wearable Stress and Affect Detection (WESAD) dataset, achieving median F1 scores of 74.3% in the Baseline phase, 63.0% during Stress, 93.6% during Amusement, and 97.7% during Meditation phases and comparable to one of the best algorithms identified in a recent benchmarking study of 15 beat detection algorithms. Iqbal et al (2023) in ‘*Deep learning classification of systemic sclerosis from multi-site photoplethysmography signals*’ described a pilot study assessing a novel approach to identify patients with the autoimmune connective tissue disease systemic sclerosis (SSc) using deep learning analysis of RGB scalograms of multi-site PPG waveforms (example traces and illustrative analysis approach in Figure 1). Two different convolutional neural networks (CNNs, namely GoogLeNet and EfficientNetB0) were trained and evaluated, with EfficientNetB0 giving overall improved performance (accuracy 87.3%) compared to GoogLeNet (83.1%) but both CNNs were superior to traditional ML methods.

A number of papers in the collection have been published on non-invasive blood pressure (BP) measurement: ‘*Intensive care photoplethysmogram datasets and machine-learning for blood pressure estimation: generalization not guarantied*’ (Weber-Boisvert et al 2023) studied the differences between the MIMIC waveform dataset and PPG-BP dataset (an alternative public dataset obtained under controlled experimental conditions) and suggested that BP estimation models based on the MIMIC dataset have reduced predictive power on the general population; ‘*The identification of blood pressure variation with hypovolemia based on the volume compensation method*’ (Chen et al 2023) to identify the blood pressure variation, which is important in continuous blood pressure monitoring, especially in the case of low blood volume, and which is critical for survival; ‘*Towards continuous non-invasive blood pressure measurements - Interpretation of the vasculature response to cuff inflation*’ (Loureiro et al 2023) investigated BP surrogates (e.g. pulse transit or arrival time) giving results to provide promising directions to improve the calibration process featuring cuff inflation towards accurate and robust non-invasive blood pressure estimation; ‘*Filtering-induced changes of derived pulse transmit time across different ages: A neglected concern in photoplethysmography-based cuffless blood pressure measurement*’ (Liao et al 2023) showed the filtering-induced PTT changes are significantly influenced by age and PTT definition. These factors deserve further consideration to improve the accuracy of PPG-based cuffless blood pressure measurement using wearable sensors.

A number of papers have been published related to pain and its objective assessment: ‘*Induced pain affects auricular and body biosignals: from cold stressor to deep breathing*’ (Rapalis et al 2023) investigating targeted biofeedback parameters to close the loop in active pain therapy via auricular vagus nerve stimulation - personalising pain therapy and increasing patient compliance; ‘*Photoplethysmography upon cold stress - impact of measurement site and acquisition mode*’ (Fleischhauer et al 2023) systematically investigated the impact of the cold pressor test (CPT), i.e. a painful stimulus, on the morphology of PPG signals in 39 healthy volunteers and compared contact PPG recorded at the finger / earlobe and non-contact PPG (imaging PPG, iPPG) recorded at the face. Their findings underlined the importance of recording setup and physiological as well as metrological differences that relate to the measurement protocol; ‘*Morphological features of the photoplethysmographic signal: A new approach to characterize the microcirculatory response to photobiomodulation*’ (Ovadia-Blechman et al 2023) indicated that post-acquisitional analysis of morphological features of the PPG waveform can provide new measures for the exploration of microcirculation responsiveness to photobiomodulation such as in the study of peripheral vasodilatation, wound healing and pain; ‘*Contactless photoplethysmography for assessment of small fiber neuropathy*’ (Marcinkevics et al 2023) also considers the pain caused by small fiber neuropathy, looking to develop objective noninvasive assessment methods. The team developed a modular prototype contactless (imaging) photoplethysmography system with three spectral bands (420 nm, 540 nm, and 800 nm) for assessing peripheral neuropathy patients via a skin topical heating test and spectral analysis of cutaneous flowmotion in 30 subjects, with results showing that neuropathic patients had a significantly lower vasomotor response (50%), flare area (63%), flare intensity index (19%), and neurogenic component (54%) of cutaneous flowmotions compared to the control group. iPPG showed potential as a cost-effective alternative for the objective and non-invasive assessment of neuropathic patients, but further research is needed to enhance PPG signal quality and to establish diagnostic criteria.

***Concluding remarks***

We, the Editors, hope this Research Topic Collection will give you a deeper appreciation and understanding of the PPG technology and its application in a diverse range of clinical physiological measurements. We also hope this will help spark fresh ideas and new research collaborations across the specialisms including with biomedical engineering, scientific and clinical colleagues. With the current trends of PPG based technologies, sensing and analytics techniques, and clinical applications we can forecast with great confidence that PPG will continue to grow and enable the development of further disruptive technologies used in healthcare and wellbeing applications.

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