

REVIEW ARTICLE OPEN

Photoplethysmography based atrial fibrillation detection: a review

Tania Pereira^{1*}, Nate Tran¹, Kais Gadhomi¹, Michele M. Pelter¹, Duc H. Do², Randall J. Lee³, Rene Colorado⁴, Karl Meisel⁴ and Xiao Hu^{1,5,6,7}

Atrial fibrillation (AF) is a cardiac rhythm disorder associated with increased morbidity and mortality. It is the leading risk factor for cardioembolic stroke and its early detection is crucial in both primary and secondary stroke prevention. Continuous monitoring of cardiac rhythm is today possible thanks to consumer-grade wearable devices, enabling transformative diagnostic and patient management tools. Such monitoring is possible using low-cost easy-to-implement optical sensors that today equip the majority of wearables. These sensors record blood volume variations—a technology known as photoplethysmography (PPG)—from which the heart rate and other physiological parameters can be extracted to inform about user activity, fitness, sleep, and health. Recently, new wearable devices were introduced as being capable of AF detection, evidenced by large prospective trials in some cases. Such devices would allow for early screening of AF and initiation of therapy to prevent stroke. This review is a summary of a body of work on AF detection using PPG. A thorough account of the signal processing, machine learning, and deep learning approaches used in these studies is presented, followed by a discussion of their limitations and challenges towards clinical applications.

npj Digital Medicine (2020)3:3; <https://doi.org/10.1038/s41746-019-0207-9>

INTRODUCTION

Atrial fibrillation (AF) is an abnormal cardiac rhythm characterized by a disorganized atrial activity. AF is recognized in the electrocardiogram (ECG) as an irregularly irregular rhythm lasting more than 30 s, with no discernible P-waves preceding the QRS complex.¹ AF prevalence is age, gender, and race dependent.² It is particularly high in the elderly population, reaching 10–17% in subjects 80 years and older.³ In addition, AF is more prevalent in males and in the white population.³ AF is associated with significant morbidity and mortality. One in five strokes is associated with AF and one-third of cardiac arrhythmias hospitalizations are due to AF-related complications. AF has been associated with a twofold increase in the risk of death.⁴ Additionally, the aging population in the US and worldwide is leading to a markedly increasing AF prevalence^{3,5}.

The high prevalence of asymptomatic AF has significant clinical implications on the diagnosis and management of AF.⁶ Intermittent ECG evaluation during clinical visits has a low likelihood of detecting paroxysmal AF. Continuous monitoring would increase the chances of AF detection, thereby allowing appropriate primary and secondary stroke prevention strategies to reduce the high morbidity and mortality of stroke.

For patients with acute ischemic stroke or transient ischemic attack, approximately 10% will have new AF detected during their hospital admission.^{7–9} Continuous ECG monitoring for 30 days is recommended in case of an embolic stroke of undetermined cause (cryptogenic).⁹ Novel non-intrusive approaches for cardiac rhythm monitoring can potentially enable early and accurate detection of asymptomatic paroxysmal AF and create a shift in AF management.^{10,11} Especially for asymptomatic AF cases, new tools

that allow the AF detection will help make the appropriate clinical decisions.¹⁰

Photoplethysmography (PPG) has emerged as a low-cost and non-intrusive modality for continuous monitoring of heart rate. A variety of wearable devices offer PPG-based monitoring, including smartphones and smartwatches. A photoplethysmogram is a pulse pressure signal resulting from the propagation of blood pressure pulses along arterial blood vessels. Measured on the periphery, it carries rich information about the cardiac activity, cardiovascular condition, the interaction between parasympathetic and sympathetic nervous systems, and hemoglobin level.¹² Many physiological parameters can be derived from PPG, including oxygen saturation, heart rate, blood pressure, and cardiac output.¹³ These capacities of PPG open the door to develop new ambulatory diagnosis tools enabling early screening of heart conditions, including arrhythmia.¹⁴

This review provides an account of the approaches used in PPG-based AF detection. A brief overview of the technology behind PPG is first presented, followed by a summary of methods and algorithms developed for PPG-based AF detection. Recognizing the importance of using PPG to detect AF at scale, the motivation of this review is to guide the future development of algorithms towards clinical-grade applications.

PHOTOPLETHYSMOGRAPHY

PPG signal

PPG waveform is generated during a cardiac cycle and typically measured at a peripheral site. Therefore, it is essentially a pulse pressure waveform that originates from the heart contraction and propagates through the vascular tree. As blood flow is controlled

¹Department of Physiological Nursing, University of California, San Francisco, CA, USA. ²David Geffen School of Medicine, University of California, Los Angeles, CA, USA.

³Cardiovascular Research Institute, Department of Medicine, Institute for Regeneration Medicine, University of California, San Francisco, CA, USA. ⁴Department of Neurology, School of Medicine, University of California, San Francisco, CA, USA. ⁵Department of Neurosurgery, School of Medicine, University of California, Los Angeles, CA, USA.

⁶Department of Neurological Surgery, University of California, San Francisco, CA, USA. ⁷Institute of Computational Health Sciences, University of California, San Francisco, CA, USA.

*email: taniapereira10@gmail.com

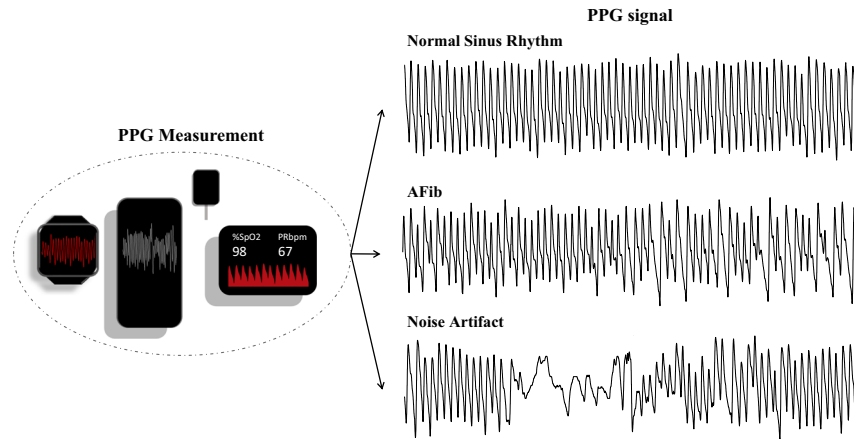


Fig. 1 PPG signal acquired using a wearable device and typical waveforms representing NSR, AF, and noise artifact.

by neural, cardiac, and respiratory interactions, various physiological parameters could theoretically be extracted from analyzing a PPG signal.¹⁵ For this reason, the PPG signal has rich information about physiological conditions.¹³

PPG waveforms have typical morphological components corresponding to landmark events in the cardiac cycle. During the contraction of the left ventricle, blood is ejected out of the heart and propagates along the arterial tree, this corresponds to the initial positive slope of a PPG pulse. The systolic peak marks the maximum of the waveform. A decrease in amplitude following the systolic peak is marked by a local minimum, or the dicrotic notch, which corresponds to the closing of aortic valves separating the systolic and diastolic phases. In some cases, a third peak following the dicrotic notch can be identified. It corresponds to a reflected component of the forward wave from various reflection sites including vessel bifurcations.¹⁶

Clinical parameters

One primary clinical application of PPG is arterial blood oxygen saturation (SpO₂) estimation through pulse oximetry.¹⁷ SpO₂ is defined as the percentage of oxygen saturation in the arterial blood, which can be measured by the ratio of oxygenated hemoglobin concentration to the total hemoglobin concentration, with a normal range between 97% and 98%.¹⁸ Recently, new applications of PPG have emerged for the continuous estimation of valuable cardiovascular parameters in ambulatory settings. Heart rate, blood pressure, and respiratory rate could be closely monitored for fitness or health assessment.¹⁹ Advanced diagnostic applications of PPG were also envisaged. Cardiac function, arterial stiffness, autonomic nervous system (ANS) responses, and apnea are among conditions that could potentially be detected or evaluated using PPG.

Changes in blood volume are synchronous with the heart beats, such synchrony is manifested by the concordance of inter-beat intervals (RR intervals) measured in PPG and time-synchronized ECG.²⁰ Heart rate variability (HRV) is an indirect measurement of ANS, and it has also been considered as a surrogate parameter of the interaction between the brain and cardiovascular system.²¹ HRV metrics can be derived from analyzing RR intervals in time and/or frequency domain as well as using nonlinear dynamic analysis approaches.²² Respiratory rate is one of the fundamental vital signs and can be determined from the time–frequency representation of a PPG signal.²³

Some hemodynamic parameters such as augmentation index (AIx) and pulse wave velocity (PWV) are important biomarkers of arterial stiffness, which is a direct cause of hypertension and a major risk factor for cardiovascular events such as myocardial

infarction and stroke. Both AIx and PWV could be derived from PPG,^{24,25} Subendocardial Viability Ratio (SEVR %) and Ejection Time Index (ETI) are two hemodynamic parameters used in the evaluation of cardiac workload that can be estimated with PPG analysis.²⁵ Additionally, some studies claim that arterial blood pressure could be estimated using advanced analysis of PPG.¹⁷

Modes of PPG measurement

A PPG signal has two main components: a quasi-static direct current (DC) component, which represents light reflected/transmitted from static arterial blood, venous blood, skin and tissues; and pulsatile alternate current (AC) component which arises from modulation in light absorption due to changes in arterial blood volume. PPG measurement can be carried out using two modes: transmission and reflectance. In transmission mode, the light transmitted through the medium is detected by a photodetector (PD), which is positioned in the opposite site of the light source. The sensor must be located on the body at a site where transmitted light can be detected. The measurement site is limited to the extremities of the body, such as the fingertip or earlobe. The greatest disadvantage of the transmission mode is the location of the device that can interfere with daily routine movements.²⁶ In reflectance mode, the PD detects light that is back scattered or reflected from tissues, bone, and/or blood vessels, which means the light source and PD are positioned on the same side. Unlike the transmission mode, the measurement sites are not restricted to any particular location, which facilitates a user-friendly monitoring approach. The wrist, forearm, ankle, and forehead are common measurement sites.²⁷

Since the basic form of PPG technology requires only a few optoelectronic components (a light source and a PD: to measure the variations on the light reflected/transmitted by the tissues), it can be easily and inexpensively incorporated in various digital devices such as watches, smartphones, or wearables.²⁸ The ubiquitous availability of PPG in a wide range of wearable digital devices has motivated the search for new applications and the development of novel biomedical solutions.

PPG-BASED AF DETECTION

In a PPG signal, AF is manifested as varying pulse-to-pulse intervals and pulse morphologies. On the other hand, a normal sinus rhythm (NSR) is recognizable through regularly spaced PPG pulses with similar morphologies between consecutive pulses. Recognizing an arrhythmia in a PPG signal can sometimes be challenging in the presence of artifacts. Common sources of artifacts are motion and poor sensor contacts. Artifacts can be misinterpreted as

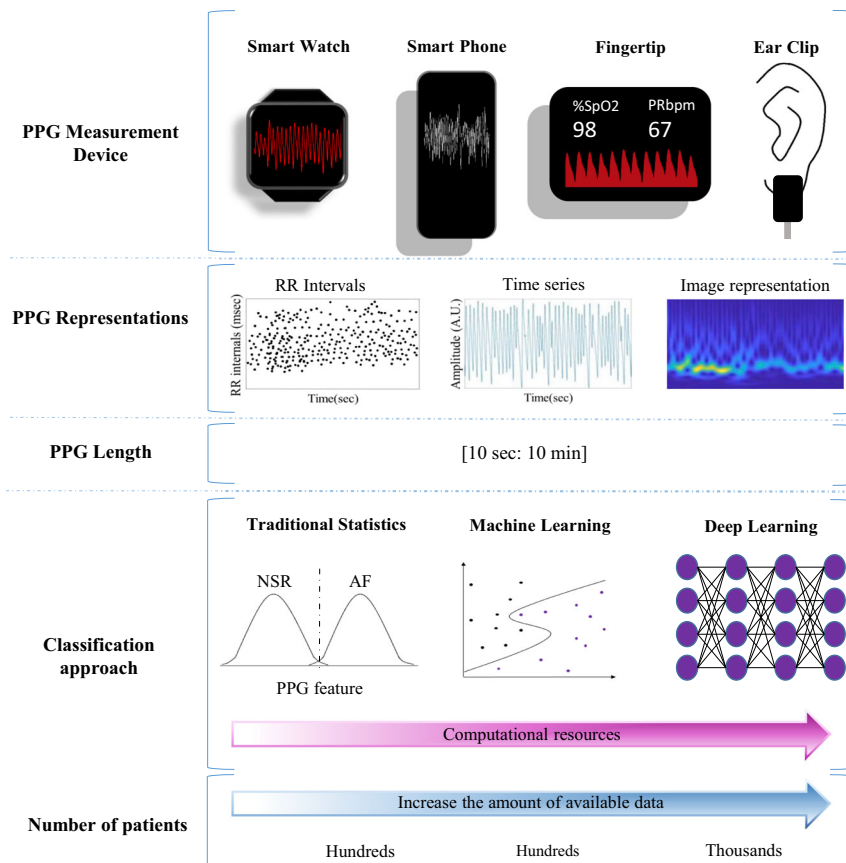


Fig. 2 Overview of the main features extracted from PPG signals used in the studies reviewed (see Tables 1–3). SpO2 oxygen saturation, PRbpm pulse rate (beats per minute).

physiological abnormalities. Motion artifacts can be identified using accelerometry data. Most modern wearable devices include accelerometry sensors that measure acceleration forces along different spatial directions. It is a common practice to discard PPG contaminated with an artifact. Figure 1 depicts samples of PPG with NSR, AF, and artifact.

ECG remains the gold standard for the electrophysiological definition and recognition of arrhythmias,¹ including AF diagnosis.²⁹ In a recent study, new deep learning approaches achieved cardiologist-level AF detection of 12 types of arrhythmia (F1 score = 0.84 vs F1 score = 0.78) when 91,232 single-lead ECGs from 53,549 patients were analyzed.³⁰ Compared to ECG, PPG-based AF detection is more challenging but also rewarding in situations where longer monitoring time and lower cost beyond what ECG offers is needed, e.g., screening AF at scale.

Recent advances in sensor technologies and wearable devices have increased the role that a PPG-based solution could play in the assessment of health status. Electronics capable of recording PPG signals with relatively high signal-to-noise ratio (SNR) may warrant reliable PPG monitoring and screening of arrhythmia.^{11,31}

In a typical AF detection algorithm, features (temporal, spectral, or morphological) are extracted from the acquired PPG signal and analyzed by the detection algorithm to inform if an AF rhythm is detected. In some approaches, image representation of the temporal waveform has been considered. The derived image would then be analyzed using conventional image processing or artificial intelligence-based methods (Fig. 2).^{32–34} Traditionally, prominent features were derived from the tachogram (RR intervals) since it is a reliable measure of heart beats.³⁵ Realizing that PPG waveforms may carry physiological information beyond heart rate, new features beyond RR intervals were derived.³⁶ The use of PPG time series and their images representation (e.g. raw

plot of the signal, fast Fourier transform spectrum, or wavelet spectrogram—represented in the Fig. 2 in PPG representation part) were used with promising results in the detection of physiological events,^{32,37,38} Images for PPG representation in Fig. 2 is a general depiction of the format types of information used by the different algorithms.

In the following sections, we review studies of PPG-based AF detection. A body of white papers and peer-reviewed works indexed by PubMed, Scopus, IEEE Xplore, and Web of Science up to June 2019 was selected based on the following search expression: (PPG “OR” Photoplethysmography) “AND” (atrial fibrillation “OR” AF “OR” AFib) “AND” (detection “OR” recognition). Each study is reviewed with respect to the size, the number of patients, and recording settings of data analyzed, the PPG device and site of recording, the AF detection algorithm, and its performance. Figure 2 summarizes the main features examined in these studies, described with more details in Tables 1–3.

Performance metrics

AF detection algorithms can be evaluated using several performance metrics. It is common for many studies to report sensitivity, specificity, and accuracy. Sensitivity is defined as the probability to detect true AF events, while the specificity measures the proportion of actual Non-AF instances correctly identified as such. Accuracy is a balanced metric of sensitivity and specificity. The accuracy of an AF detection algorithm is its ability to differentiate between AF and Non-AF cases.³⁹ Generally, accuracy is the most common reported metric, along with the area under the curve (AUC) of the receiver operating characteristic (ROC). A ROC for differentiating AF vs Non-AF is generated by plotting sensitivity vs (1-specificity) at different classification thresholds. AUC is a

Table 1. Studies on photoplethysmography-based AF detection using statistical analysis approaches.

Author (year) [ref.]	Number of patients	Dataset features	Age of population	Length PPG segments	Measurement device	Acquisition conditions	Input data	Methodology	Performance results for rhythms detection
Lee et al. (2013) ⁹¹	74	74 prior and after cardioversion + Public databases (MIT-BIH AF + MIT-BIH NSR + MIT-BIH Arrhythmia Database)	–	2 min	Video camera of smartphone	Inpatient	RR times series features Time varying coherence functions and Shannon entropy	Derived threshold values of features for best ROC	Acc = 0.9645, Sen = 0.9716, Sp = 0.9539
Nemati et al. (2016) ⁵²	46	15 with AF 31 non-symptomatic	–	3.5 to 8.5 min	Wrist-worn device Samsung Simband	Inpatient	RR times series features sample entropy with the embedding dimensions $m = 1$, and 2 (SampEn1 and SampEn2), standard deviation, robust standard deviation	Elastic Net logistic model	Acc = 0.95, Sen = 0.97, Sp = 0.94, AUC = 0.99
Bonomi et al. (2016) ⁵⁰	16	4 with AF, 1 atrial flutter, 11 NSR	65.2 ± 14.0	30 s	Wrist-wearable sensor—Philips Cardlo and Motion Monitoring Module	Outpatient—continuous measurement	RR times series features	First-order 11-state Markov model	Sen = 0.97 ± 0.02, Sp = 0.99 ± 0.03
J. Eckstein et al. (2016) ⁹²	80	40 with AF 40 Non-AF	80 ± 8 75 ± 7	5 min	Video camera of smartphone	In- and outpatient checkpoint	RR times series features RMSSD and SD1/SD2 index extracted from the Poincare plot	Derived threshold values of features for best ROC	AUC = 0.931, Sen = 0.950, Sp = 0.950
D. McManus et al. (2016) ⁹³	121	98 with AF 15 with PAC 15 with PVC	66	2 min	Video camera of smartphone	Inpatient	RR times series features RMSSD, Shannon Entropy, Poincare plot	Derived threshold values of features for best ROC	AF: Acc = 0.951, Sen = 0.970, Sp = 0.935. PAC: Acc = 0.955, Sen = 0.667, Sp = 0.980. PVC: Acc = 0.960, Sen = 0.733, Sp = 0.976
Shashikumar et al. (2017) ⁵¹	98	45 with AF, 53 with other rhythms (ARR)	–	30 s	Wrist-worn device Samsung Simband	Inpatient	PPG image spectral representation of wavelet transform—features obtained from the CNN + RR times series features (sample entropy, standard deviation, robust version of the standard deviation, min and the max of the sample entropy features)	Elastic net logistic model	Acc = 0.918, AUC = 0.95
T. Conroy et al. (2017) ⁹⁴	77 Test: 34	44 healthy subjects, 33 with AF 13 healthy subjects, 21 with AF	38 ± 12, 64 ± 11, 45 ± 17, 68 ± 11	5 min	Single earlobe PPG sensor	Inpatient	RR times series features. Coefficient of variation, standard deviation, average of	Derived threshold values of features for best ROC	Acc = 0.952, Sen = 0.909, Sp = 0.909

Table 1 continued

Author (year) [ref.]	Number of patients	Dataset features	Age of population	Length PPG segments	Measurement device	Acquisition conditions	Input data	Methodology	Performance results for rhythms detection
Tang et al. (2017) ⁴⁸	666 stroke patients	150 with AF, 516 Non-AF	74.5 ± 12.8, 66.3 ± 14.8	1 min, 2 min, 10 min	Bedside monitor	Inpatient	the difference in beat-to-beat: pNN35 RR times series features. Time domain: mean, standard deviation, and RMSSD. Frequency domain: low-frequency range (LF), power in the high-frequency range (HF), and the ratio of LF and HF. Nonlinear analytical methods: Shannon entropy, and turning point ratio	Logistic regression analysis	1-min: AUC = 0.949, 2-min: AUC = 0.972, 10-min: AUC = 0.973
Bashar et al. (2018) ⁶⁴	200	–	Older than 45 years old	30 s	Video camera of smartphone	Outpatient—checkpoint	Noise/movement detection: Variable frequency complex demodulation. AF detection: RR times series features (RMSSD, Shannon entropy and sample entropy)	Noise/movement detection: thresholds. AF detection: Support vector machines	Acc = 0.9116
Chong et al. (2018) ⁶⁵	99	88 patients with AF prior and after cardioversion 11 health subjects	–	2 min	Video camera of smartphone	Outpatient—checkpoint	Noise/movement detection: Signal slope changes, turning point ratio changes, and kurtosis change. AF detection: RMSSD and Shannon Entropy (ShE)	Noise/movement detection: thresholds. AF detection: thresholds	Acc = 0.9667, Sen = 0.9765, Sp = 0.9714
Tarniceriu et al. (2018) ⁴⁹	29	15 NSR, 14 with AF	67.5 ± 10.7, 74.8 ± 8.3	20 consecutive RR	Wrist-worn device PulseOn Ltd.	Inpatient	RR times series features	Markov model	Sen = 0.9845, Sp = 0.9913
H.M. de Morree et al. (2018) ⁷⁴	27	8 AF 19 non-AF	69 ± 101, 67 ± 13	120 s	Wrist-worn device Philips Cardio	Outpatient—continuous measurement	RR times series features Shannon entropy, RMSSD, normalized RMSSD, pNN40, pNN70, sample entropy, and coefficient of sample entropy	Derived threshold values of features for best ROC	Acc = 0.981, Sen = 0.984, Sp = 0.980

RR R to R interval, NSR normal sinus rhythm, ARR other arrhythmias, VA ventricular arrhythmias, AUC area under the curve, Acc accuracy, Sen sensitivity, Sp specificity, PVC premature ventricular contractions, PAC premature atrial contraction, pNN35/pNN40/pNN70 percentage of differences of successive RR that exceeded 35 or 40 or 70 ms by the total number of RR intervals

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.