

Photoplethysmographic sensors, potential and limitations: Is it time for regulation? A comprehensive review

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ABSTRACT

Healthcare is expected to increasingly shift care out of inpatient settings thanks to wearable monitoring systems. Photoplethysmography (PPG) is an optical technique already integrated into wrist-worn commercial products which presents significant advantages in terms of cost and dimensions. PPG-based devices, despite their ability to detect multiple cardiovascular parameters, are affected by several influencing conditions that depend both on technological or environmental variables, and on intra- and inter-subject variability that influences the whole measurement chain and reliability, hindering an objective characterization of PPG devices. Plus, the lack of standardization for data collection and processing leads to the lack of generalizability and reproducibility of results, preventing the full exploitation of the potential prognostic capacity of this technology. Thus, this review aims not only to summarize the main influencing parameters of PPG technology, which should be addressed when testing the sensor, but also to suggest tentative guidelines for a possible future standardization initiative.

1. Introduction

1.1. Background

In the last decade, national health systems have registered a significant increase in hospitalizations of patients suffering from chronic-degenerative diseases of the cardiovascular system. Although over the years there has been a significant increase in treatment techniques, both from a pharmacological and therapeutic point of view, this paradoxical increase in patients is due to two main reasons: the significant ageing of the world population [1] and the ability to save many more patients from acute events, but not from the related chronic degenerative diseases. This results in the need for assistive technologies for older people living at home, aiming at improving their quality of life (QoL) and well-being perception.

Recent studies [2–4] have shown that carefully monitoring the physiological parameters indicating a possible onset of the conditions that predispose pathologies, would lead to various advantages for the benefit of the patients' QoL and, therefore, in terms of reduction of

hospital admissions and costs held by national healthcare systems. The care of chronic diseases will be increasingly shifted towards home treatment, and involving the use of mobile healthcare monitoring devices (small size, low price, high acceptability by the user and ability to detect multiple parameters) and artificial intelligence (AI) techniques, to provide decision support systems to remotely monitor the clinical progress of the pathology, as long as the measurement accuracy of such devices is appropriate.

1.2. PPG sensors

The scientific community has shown a strong interest in wearable sensors designed to detect various physiological parameters, particularly those related to cardiovascular system, due to the importance of prevention and monitoring. Among the various technologies available on the market, photoplethysmographic (PPG) sensors appear to be one of the most effective technology, thanks to their extremely small size and low costs, as well as the variety of potential physiological parameters that can be derived from the gathered signal [5]. Moreover, PPG sensors

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can be easily integrated into wearable commercial products for large distribution, such as smartwatches and fitness trackers. Indeed, the growing interest of the scientific community in PPG sensors can be observed in Fig. 1, which shows that the related published articles have increased in the last 10 years by 176 % and the trend is still strongly rising.

The simplest PPG sensor is basically constituted by few electrical components: a light source and a photodetector (PD). A PPG sensor can work in transmission mode, with the light source and the PD located in opposite sides with respect to the measurement site, which is capable to provide a good and stable signal [6]; generally, this represents the first choice for the measurement of blood oxygen saturation (SpO₂), usually performed within hospitals. Transmission mode also enables the detection of a wide range of blood components [7,8] through the study of the transmission spectrum of wavelengths in between 550 and 1050 nm [7]. Specifically, some research groups focused on the study of the influence of blood concentration in the optical path, with an “tissue optic” approach, performing a blood component analysis including, for instance, glucose [9], globulin [10], platelets [11] and red blood cell counting [12]. Nevertheless, transmission mode is suitable only for body parts with a low thickness; indeed, most of the commercial devices working this way are usually placed on the fingertip or earlobe, to carry out microvascular assessment, being instead larger arteries more difficult to be inspected lying deeper in the tissue (even if some recent works employ also them on wrist [13,14]). However, the considerations hereinafter presented relate primarily to the reflectance mode configuration, which consists in installing the two components side by side, hence suitable to realize wrist-worn wearable devices based on a PPG sensor. In fact, even if the reflectance mode suffers from motion artifacts with respect to the transmission mode, it eliminates the problems associated with the sensor positioning, which effectively leads to usability and integration into different devices of daily use and therefore to a potential wide effective diffusion of use as a monitoring system, especially for what concerns heart rate (HR), and for SpO₂ as well.

Regardless the specific configuration, the source emits light at a fixed wavelength (usually between 550 and 850 nm), which travels underneath the skin and is partly absorbed and partly reflected by several different biological tissues, including the blood flowing within vessels. The reflected light is then sensed by the nearby PD, which converts it into an electrical signal proportional to its intensity.

The origin of PPG signal underlies on the light-tissue interaction, which is described by the modified Lambert-Beer law that takes into consideration the cumulative effects of both absorbers (e.g. blood, melanin) and scatters (collagen, keratin), which constitute the quite complex biological tissue. Several studies deal with the origin of PPG signal [15–17]; nevertheless, the most accredited theories identify as principal contributor factors the following ones [18]: (1) the different orientation of blood cells during the systolic and diastolic phases, resulting in changes of the overall light attenuation, (2) the volumetric distribution of the absorbers and (3) the mechanical movements of the capillaries and the elastic deformation of the skin during the vascular bed expansion. Beyond the increase of the overall capillary density, this

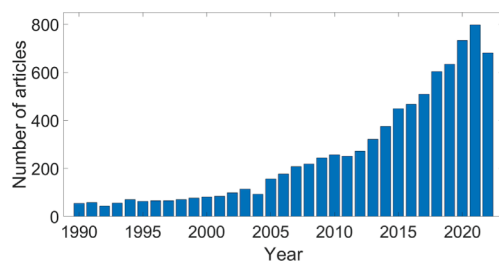


Fig. 1. Report of the number of PPG related articles since 1990. Font: PubMed, October 2022, search query: ((PPG) OR (Photoplethysmography) OR (Photoplethysmographic)).

phenomenon causes variations of the back-reflected light intensity due to local changes of both the scattering and the absorption coefficient of the light.

However, the resulting waveform consists of two superimposed components: the quasi-DC component (direct current) and the AC component (alternating current). The quasi-DC component is generated by all the tissues whose optical properties do not vary significantly or rapidly over time. Possible slow changes of the DC components can be caused by fluctuations of the average blood flow within vessels, by thermoregulation and respiration, vasomotor activities or hydration level [19]. Indeed, PPG DC component represents the total blood volume changes, and thus can be successfully employed in some applications for lower limb venous assessments (approach also referred to as light reflection rheography, LRR) [20–23], since the changes in the total limb blood volume with posture can be derived considering the variations of light absorption in PPG signal. In this context, LRR through PPG has been used for the evaluation of peripheral vascular diseases (PVD), e.g. to evaluate venous reflux in subjects affected by deep venous reflux (also diagnosed using duplex ultrasonography) [24], as an objective diagnostic test suitable for screening of lower limb chronic venous insufficiency (CVI) [25], and as a suitable tool to screen deep vein thrombosis (DVT) in homecare settings through non-invasive devices [26].

Conversely, the AC component is associated to the variation of the blood volume within vessels (information usually of more interest in photoplethysmography): every time the heart beats, it pumps blood through arteries, thus leading to a cyclical variation of the blood volume flowing within different districts (depending on the vessels compliance). The significant absorption of light by the blood, which also depends on the orientation of the erythrocytes [27], leads to a change of the amount of light detected by the PD and therefore to a variation of the electrical output, which can be attributed primarily to the cardiac cycle.

An important index relating the AC and DC components is the so-called perfusion index (PI), which represents the ratio of pulsatile light absorption on continuous light absorption, i.e. the AC/DC ratio [28,29]. PI was initially employed just as the gold standard for assessing PPG signal quality [29]; however, recently it has been shown that PI can be used also for non-invasive haemodynamic monitoring, given that this index assesses the local blood volume variation during systole, and changes according to the systemic and local haemodynamic status [28]. PI measures the local perfusion, is usually low (much lower than 10 %), varies according to the measurement site, and reflects not only the systemic macrohaemodynamic status, but it often especially reveals the local conditions, e.g. local vascular tone, local compression (soft tissues, veins and/or arteries), and outside temperature variations [28].

1.3. PPG signal

A typical PPG waveform varying during time is depicted in Fig. 2. The rising edge of the pulse is the “anacrotic phase”, which is related to systole, while the falling edge of the pulse is the so-called “catacrotic phase”, which is instead related to diastole and wave reflections from the periphery [5]. The “dicrotic notch” is usually seen in catacrotic phase when analysing PPG waveforms acquired from subjects with healthy compliant arteries [5]. The origin of the dicrotic notch has been

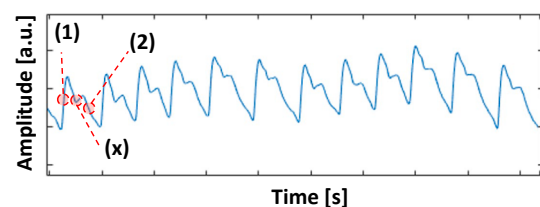


Fig. 2. Typical PPG waveform varying in time: (1) anacrotic phase; (2) catacrotic phase; (x) dicrotic notch.

most explained as caused only by the aortic valve closure, but a recent study by Politi et al. demonstrated that reflected pressure waves could participate as one of the causes of the dirotic notch due to changes in peripheral vascular resistance [30].

Moreover, the slow varying envelope of the PPG waveform represents the well-documented low frequency respiratory-induced intensity variations that include contributions from the venous return to the heart, caused by variations in intra-thoracic pressure and in the sympathetic tone control of cutaneous blood vessels [5]. For this reason, several recent works have focused on algorithms for extracting the respiratory signals starting from PPG waveforms, e.g. using bandpass filters or the Empirical Mode Decomposition (EMD) method [31–33].

The bandwidth of PPG signal is typically lower than 15–20 Hz [34,35]. As an example, Fig. 3 shows the typical frequency content of a wrist PPG waveform with a first peak at approximately 0.2 Hz (corresponding to the respiratory frequency) and a second peak at approximately 1.2 Hz (representing instead the average heart rate).

1.4. PPG strengths and applications

PPG technology has two main advantages that make it such a highly effective technology in the clinical setting. The first advantage is that PPG is an extremely simple and relatively inexpensive technology, whose main components can be contained in particularly small wearable devices, such as smartwatches, whose popularity (as mentioned above) is constantly increasing. According to the Pew Research Center, 21 % of Americans wear a smartwatch or a smart band, mostly aged between 18 and 49 years [36]. Indeed, smartwatches are the new trend [37] nowadays, being their global market valued at \$20.64 billion in 2019 and projected to reach \$96.31 billion by 2027 [38,39]. Smartwatches are very appealing since they also allow immediate access to the digital world, including internet browsing, messages and notifications; at the same time, IoT-enabled devices simplify remote monitoring by sharing data on cloud-based services [40], thus potentially playing an important role in telemedicine. Plus, rapid advancements in miniaturization are expected to propel further growth in the market. In addition to that, these devices are not perceived by users as medical devices, favouring a continuous use over the day and, thus, the possibility to be continuously monitored without perceiving it, hence obtaining measurement results that better represent the real-life conditions of the user. This increases even further the capability not only in detecting acute events, but also in monitoring the progression of a particular clinical condition over time, making it possible to establish thoughtful targeted actions, but also to identify anomalous patterns and prevent developing issues. The second reason that gives this technology such high potential is the great variety of relevant physiological parameters it can provide. In addition to the HR, which can be derived from the cyclical variation of the blood volume over time, further information can be extracted from a PPG signal and its derivatives [41,42], such as pulse rate variability.

(PRV) [43–51], atrial fibrillation events [52–58], cardiac output [59–64], breathing rate [31,65–67], blood oxygenation [68], general vascular health and the risk for cardiovascular diseases [69].

Among the others, the Pulse Transit Time (PTT) exploiting PPG

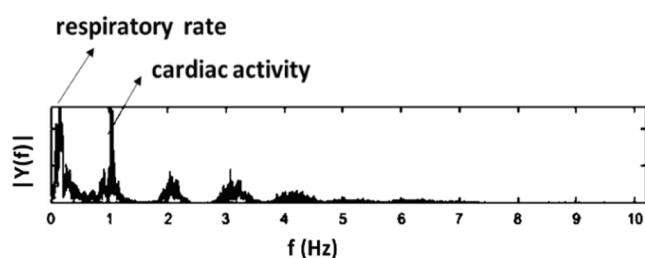


Fig. 3. Typical frequency content of a PPG waveform. The peaks corresponding to the respiratory rate and cardiac activity are indicated in the figure.

signals recorded at two different sites can also be used to determine the Pulse Wave Velocity (PWV) and to continuously estimate, without any cuff [70–75], the Blood Pressure (BP), which can also be measured via PPG sensors with other different techniques [76]. PTT has been defined as the time it takes for a pulse wave to travel a known distance (along a given artery) and is inversely proportional to PWV, which is the speed of the pulse wave along the arterial vessel [72]. Some recent works have highlighted the feasibility of using the reflective PTT (named R-PTT) to estimate the blood pressure [77–80]. R-PTT can be extracted computing the time duration between the first PPG peak (i.e. the percussion) and the second one (reflected) in a cardiac pulsation cycle. Physiologically, the R-PTT measured on the wrist represents the time required for the pulse wave to propagate from the radial artery in forward direction to the end of the arm, and then reflected back to the radial artery as a back-propagating pulse [77]. Even if PTT and R-PTT methods usually still require individual calibration processes using conventional cuff type devices, recent works have shown encouraging results, with errors in BP estimations lower than 8 mmHg, defined as “Grade A” devices by the Advancement of Medical Instrumentation (AAMI) and British Hypertension Society (BHS) standards [79–81].

Besides, the combination of the parameters measured using PPG signals can subsequently give indications on other physiological conditions reflected by them, such as the level of stress or fatigue of a worker [82–85] (also in the Industry 4.0 context), the quality of sleep [86,87] or if the attention threshold falls below certain limits during specific activities [88] or, recently, even in the early detection of COVID-19 symptoms [89,90].

Despite this capability in detecting multiple physiological conditions related to the cardiovascular system, the PPG signal is affected by several influencing parameters [6,69], described in the following section. Such parameters prevent the PPG technology from being extensively used in a clinical environment, which is the reason why its clinical use is limited only to few parameters, such as HR and peripheral oxygen saturation, mainly in a transmission mode configuration. Thus, due to the great inter- and intra-subject variability and to several sources of uncertainty [69,91], PPG technology is mainly used for general health status assessment and for fitness purposes.

Therefore, the PPG-derived HR, which represents a powerful *trans*-diagnostic biomarker that could be used in a clinical environment, and which could potentially be continuously monitored during normal daily life, cannot be used for a clinical health assessment as the accuracy of the acquisitions is often inadequate in the general population. Several studies have investigated the feasibility of using PRV indices, extracted starting from pulse-pulse interval (PPI) time series, as a surrogate of HRV computed from gold standard electrocardiogram (ECG) [92–94]. Usually, short-term measurement norms are based on ~ 5 min time series, and time-domain and frequency domain indices are more often considered. Among the time-domain indices, the MEAN PPI can be used to detect alterations of heart rhythm (e.g. tachycardia, bradycardia); the standard deviation of the inter-beat interval of normal sinus beats (SDNN) represents the HR variability, while the root mean square of successive differences between normal heartbeats (RMSSD) is used to estimate the vagally mediated changes reflected in HRV [95]. In the frequency domain, the main bands considered are the Low Frequency (LF) band (0.04–0.15 Hz), mainly related to sympathetic activity of the Autonomous Nervous System (ANS), and the High Frequency (HF) band (0.15–0.4 Hz), instead reflecting more the parasympathetic activity and the respiration. The ratio of LF to HF power (LF/HF ratio) has been widely employed to estimate the ratio between sympathetic and parasympathetic nervous system activity, i.e. the sympatho-vagal balance, under controlled conditions, although this index has been recently debated [95,96]. Some recent studies investigating the feasibility of using PPG for assessing HRV found an overall good agreement of most time and frequency-domain short-term measures during rest, which however decreases during postural or mental stress [50,93,94].

Other studies are currently focusing on which extent it is possible to

decrease time series length (i.e. the so called ultra-short term HRV) for reliably assessing heart rate variability also from PPG recordings in daily life situations [97–100].

It is worth mentioning that many research groups are nowadays also focusing on the so called “non-contact PPG”, also exploiting machine learning approaches, which represents a possible alternative to the conventional PPG technique (with several potential advantages) [101–104] to detect physiological parameters, such as HR. Specifically, the measurements rely on digital cameras; the frames sequence is analyzed within a region of interest (usually the face) to detect the color variation of the frames pixels. However, since non-contact PPG substantially differs from the contact one and also has different influencing parameters and criticalities, it is beyond the scope of this paper.

1.5. PPG vs ECG

If PPG and ECG are compared, several differences can be identified in both measurement procedure and accuracy. For example, ECG recording requires a preliminary phase, where skin must be adequately prepared, and the measurement circuit needs to be closed for signal acquisition. On the other hand, PPG-based devices allow an immediate measurement, and this is undoubtedly advantageous for wearable sensors commonly used for own health monitoring. Moreover, ECG suffers from baseline wandering, that is not the case of PPG, even if it presents a baseline drift requiring an initial stabilization period. For sure, the most evident weakness of PPG sensors is represented by motion artifacts, still leaving a lot of room for research and improvement, from hardware development to measurement procedure optimization (even through proper artifact rejection algorithms). Furthermore, ambient light conditions can also influence PPG measurement, and this requires particular attention in LED and PD positioning, needing a very good sensor-skin contact. Skin color can also affect the results, but multi-wavelength PPG (e.g. green, red, blue, IR, etc.) seems to be powerful to this aim [105]. Conversely, the flexibility of PPG-based sensors with respect to ECG should be highlighted; in fact, whereas ECG requires a standard electrode positioning (generally on the thorax and on the limbs, but sometimes the loop closes through electrodes embedded in a smartwatch, such in the case of Samsung Galaxy Watch3 [106]), PPG sensors can be placed wherever a quite superficial vessel is available (not only a finger and the wrist, but, just as an example, also on the temple (e.g. OH1 sensor by Polar [107]) or earlobe).

Different wearable commercial products have been proposed in the recent years [108], but very few of them achieved the U.S. Food and Drug Administration (FDA) clearance. It is worth mentioning that different smartwatch companies are catching in the field with their products. While Apple cleared the FDA status for irregular rhythm notification by using the electrocardiogram in its Apple Watch, the Samsung Gear S2 achieved the approval to monitor the HR when used in combination with the LIVMOR Halo™ detection system [69]. Hence, despite the significant improvement in terms of monitoring of the main physiological parameters allowed by these typologies of devices (i.e. PPG-based smartwatches and chest straps), the full exploitation of the prognostic capacity is still lacking due to the sources of disturbance.

1.6. Aim of the work

Several recent articles describe all the main potential sources of inaccuracy of PPG-based devices [41,69,109,110]. This is an important first step for a kind of research that aims to achieve a careful and conscious planning of experimental tests, thus leading to improve the accuracy of these devices and allowing them to be used in a clinical setting. However, the mere knowledge of the influence parameters is not a sufficient condition for this step to take place. Indeed, due to the intrinsic

nature of these parameters of influence which does not allow their control, traditional guidelines for the evaluation of uncertainty are not

adequate [108], as it is difficult to control many of the individual influence parameters, resulting in a great amount of physiological variability. Therefore, the scope of this work is not limited to describe the possible sources of influence, but also to disseminate a series of suggestions and standardized methodologies proposed by the scientific community that, if collectively adopted, could lead to an easier comparison and correlation of different results from various experiments thanks to some common guidelines that should be followed in the metrological evaluation of these devices. This could also accelerate the process that may lead to the adoption of PPG-based devices in the clinical practice, thus enhancing the efficacy of the national healthcare systems and increasing the patients QoL by reducing hospitalizations. In the following paragraphs, special attention is paid to the ANSI/CTA-2065 standard [127] (hereafter mentioned as CTA-2065), proposed and released in 2018 by the Consumer Technology Association, since it aims to define the process to test and validate the accuracy of a device for HR monitoring under different conditions.

The rest of the article is organized as follows: the first part (Section 2) reviews and analyzes the main influencing parameters. The second part (Section 3) describes and summarizes the principal standards that have been proposed by the scientific community. Finally, in Section 4 the authors provide their considerations and conclusion.

2. Accuracy and potential influencing parameters

The great potential of PPG sensors is to enable monitoring of different physiological parameters via a small practical wearable device. Table 1 illustrates an overview of PPG wearable devices and the related measured parameters. As shown in Table 1, PPG wearable devices allow HR monitoring. Moreover, many other parameters can be derived from PPG, such as HRV, SpO₂, PTT, BP and Blood Volume Pulse, perfusion index, respiration rate, glucose concentration. Besides, Table 1 reports also the positioning and the typology of the device (commercial or prototypal).

However, PPG-based wearable devices are not intended as medical devices. Indeed, in clinical environments, the detection of a specific physiological parameter should be accurate for a heterogeneous

Table 1
Comparison of PPG wearable devices.

Name	Position	Typology	Measured parameters
AIO Smart Sleeve [111]	arm	commercial	HR, HRV, SpO ₂
Aktiia [112]	wrist	commercial	HR, HRV, BP
Apple Watches [113]	wrist	commercial	HR, HRV, SpO ₂
Asus VivoWatch SP [114]	wrist	commercial	HR, PTT, BP, SpO ₂
BP with prototypal PPG-based device [76]	wrist	prototypal	HR, PTT, BP
CareUp [115]	wrist	prototypal	HR, PTT, BP, SpO ₂
Cosinuss Two [116]	ear	commercial	HR, BP, SpO ₂ , perfusion index
Dream Sock [117]	ankle	commercial	HR, average SpO ₂
Empatica EmbracePlus [118]	wrist	commercial	Blood Volume Pulse, HR, HRV, SpO ₂ , respiration rate
Fitbit Smartwatch [119]	wrist	commercial	HR, HRV, SpO ₂ , respiration rate, glucose
Garmin Smartwatches [120]	wrist	commercial	HR, SpO ₂ , respiration rate
Jabra Elite Sport [121]	ear	commercial	HR
Oura Ring [122]	finger	commercial	HR, SpO ₂
Polar OH1 [123]	arm/temple	commercial	HR
PPG-based Smart Wearable Device [124]	wrist	prototypal	HR, glucose
Samsung Galaxy Watch [125]	wrist	commercial	HR, BP
Scosche Rhythm [126]	wrist	commercial	HR

population both in the short term, that is in a specific limited time interval within a single day, as well as in a longer time interval, which can be either days or weeks. This implies that also physiological variability should be managed by the measuring technology itself, to provide reliable results.

PPG technology is characterized by a significant sensitivity to various influencing factors that affect acquisitions, especially in normal daily life conditions. Specifically, Fig. 4 highlights how the output signal is not a function of the single input quantity, but instead of a combination of multiple influencing factors, which in many cases cannot be controlled or isolated. Hence, these aspects should be considered within the measurement uncertainty, to correctly interpret the results also in function of the target application requirements.

When following a scientific approach aimed to the metrological characterization of PPG sensors, if these influencing parameters are not properly accounted with a standardized protocol, different research groups could end up with inhomogeneous results, which implies a general poor reproducibility and replicability of tests and, consequently, the impossibility to use PPG sensors in a clinical environment.

Among other things, the lack of a univocal approach mainly regards the planning of the tests, including the choice of the reference device (i.e. the gold standard) to compare the PPG output. Indeed, during the evaluation of the metrological performances of a PPG-based device during HR measurements, a common practice is to compare the measurements between the tested device (i.e. PPG-based device) and a reference device (usually an ECG-based device [128]) to determine if results are within fixed limits of agreements [129,130] based on the specific target clinical application.

While there are recommendations that specify whether a HR measuring device can be considered accurate or not (e.g. ANSI/AAMI/IEC 60601-2-27:2011/(R)2016 considers accurate a HR monitoring device if the mean absolute percentage error is $\leq 10\%$ of the input rate or ± 5 bpm), on the other hand there is not a general adoption of univocal characteristics of the reference device. Some research groups have adopted different devices used as reference, among which ECG [129,131] devices, chest straps [82,132,133], and pulse oximeters [134–136]. Thus, it should be considered that even before describing the possible influencing factors, a first discrepancy in obtaining the actual accuracy of any optical sensor lies on the choice of the reference device, which can introduce itself an additional error and lead to poor reliability of the results. Moreover, it should be also considered that the agreement between the reference and tested device (which obviously has its own measurement accuracy) may also depend on how the reference device is used and on the characteristics of the protocol chosen, especially in the case of physical activity execution (commonly, higher the activity intensity, higher the measurement uncertainty of wearable devices) [137]. For instance, ECG patches perform badly when the skin is stretched or excessively wet, whereas ECG straps are inaccurate when the skin is too dry (due to the different electrodes technology), when the strap loosens up, or for specific anatomical shapes of the chest [138].

Another important choice when planning a test protocol is the specific physical activity to be performed by the test population. Wang and

colleagues [139] recruited 50 healthy adults to test simultaneously for each subject a standard ECG, the Polar H7 ECG-based chest strap, and four wrist worn PPG-based commercial products. They found that the wrist-worn devices decrease their performance with physical exercises, showing a difference in HR acquisition up to -39 and $+33$ bpm, respectively, if compared to the standard ECG; none of them achieved the accuracy of the chest-strap. Indeed, as it will be discussed in the next section, the accuracy of HR measurements varies significantly under different conditions of physical activity. Specifically, several studies agree that wearable wrist-worn optical sensors tend to underestimate HR values with an overall negative bias [134,139–141].

In a controlled laboratory setting, different commercial devices have proven to adequately measure the HR under different physical activities within an acceptable error range of 5% [131,142]. However, different physical activities replicated in the laboratories do not fully reflect daily life situations, including small simple actions, such as specific rhythmic movements or cyclic motion of the wrist [143,144], that can lead to different additional errors. In a recent study [110] the accuracy of a PPG-based wristband was assessed under different actions (e.g. keyboard typing) and physical activities (e.g. slow walking). Authors found that the accuracy decreases significantly in dynamic conditions not only for hand movement, but also during speaking activities, cognitive and emotional stress, which indicates the presence of influencing factors different from physical disturbances.

In addition to the reference device and physical activity choice, there are many other influencing parameters that affect the output of the sensor; the main ones are reported in Table 2. All these influencing parameters should suggest considering suitable precautions to mitigate their effects during the performance evaluation of a PPG-based device.

Nevertheless, without any standardization process and any capability to detect all the possible influencing parameters affecting the output of the sensor, any evaluation of the accuracy is not possible, and, thus, the clinical validation of PPG technology.

2.1. Contact pressure

The contact pressure between the sensor and the individual’s skin can significantly affect the quality of the PPG signal, leading to a peak distortion and a decrease in amplitude that prevent the straight-forward usage of the sensor, resulting in errors in the HR determination [133,145–147]. During PPG acquisition on a subject at rest, the amplitude of PPG signal increases with increasing contact pressure up to a maximum and then decreases again [146], as qualitatively shown in Fig. 5.

Specifically, there are two main reasons which cause the contact pressure to affect the PPG signal: the former concerns the stability of the adhesion of the sensor to the skin. Indeed, if the sensor is not firmly attached to the skin, relative movements may create additional motion artifacts. Moreover, if the displacement of the sensor is perpendicular and far enough from the skin, this could lead to the complete loss of the AC component of the PPG signal. The latter reason is that an excessive

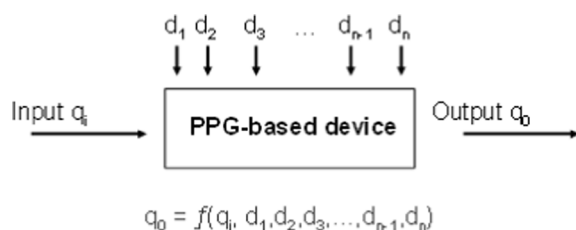


Fig. 4. Schematic representation of different influencing parameters which are part of the output function. Specifically, q_i and q_o represent the input and output quantity, respectively, while d_1, \dots, d_n represent different influencing variables.

Table 2
Principal influencing parameters of PPG signal.

Sensor design and positioning	Subject specificity	External factor
Emitting light intensity	Oxygen concentration	Ambient light
Wavelength	Microcirculation volume	Room temperature
Photodiode sensitivity	Arterial stiffness and blood volume	
Sensor skin interface	Interstitial fluids	
Contact pressure	Skin tone	
Motion artifacts	Body mass index and wrist circumference	
Body location	Body temperature	
Sensor design	Venous pulsation	

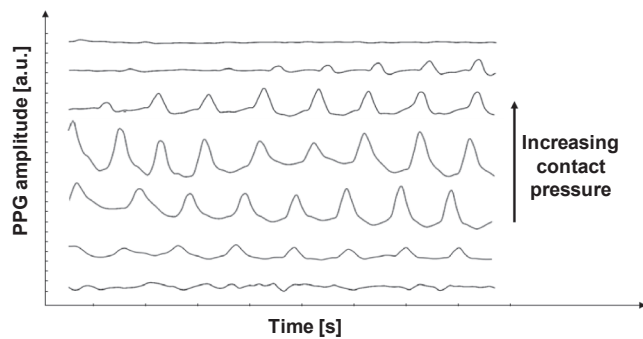


Fig. 5. Variation of PPG signal amplitude for increasing contact pressure [137].

contact pressure on the skin may be transferred through the subcutaneous tissues to the blood vessels, altering and deforming the arterial geometry and the subcutaneous perfusion, and, therefore, the acquired PPG signal. Ideally, the best PPG waveform can be obtained when the contact pressure is equal to the pressure difference between the inside and outside of the blood vessel (i.e. transmural pressure) [6]. When the pressure exerted by the probe exceeds the transmural pressure, the vessel wall starts collapsing and fluttering, thus the AC amplitude starts decreasing as the arterial pulsation is locally partially inhibited to expand. Despite the significant influence of this parameter, no generally accepted standards have been adopted, neither the CTA-2065 standard provides any specific indication in this sense.

In different studies the optimal contact pressure was tested for different subjects under different conditions. Teng and colleagues [146] evaluated the change in pulse amplitude (AC) of reflective PPG signals with increasing contact force, from 0.2 to 1.8 N; authors found that the pulse amplitude peaked at different contacting forces, from 0.2 to 1.0 N, for different subjects, with most of subjects achieving their maximum of AC/DC ratio between 0.2 and 0.4 N. They concluded that the actual force exerted at the artery wall would be different for each subject due to the specific subject's characteristics (i.e. physiological inter-subject variability). In another study [148], the finger PPG waveform was analysed under different contact pressure values, finding the highest amplitude at 60 mmHg. Similarly, in a recent study [137], authors tested the performance of a wrist-worn HR-PPG sensor for different contact pressures during different physical activity rates; they found that 54 mmHg provided the best HR results (compared with an ECG-based chest strap) among the whole cohort of subjects, and that the contact pressure produces stronger effects on the PPG signal quality than those deriving from the intensity of the physical activity. Furthermore, authors concluded that, by considering the specific optimal contact pressure of each subject, it is possible to reduce the mean average percentage error up to 47%. However, assessing the optimal range of the contact pressure is challenging due to the wide variability of the biological characteristics of subjects in terms of tissues features and arterial stiffness [146,149].

Based on the recent studies on the effect of contact pressure in PPG measurements, a device which can carefully control the contact pressure and vary it with respect to the specific characteristics of the user, to get the best AC/DC ratio, would bring a potential benefit in terms of signal quality and reliability. Nevertheless, this represents an important parameter that should be taken into consideration when testing the performances of PPG sensors, to achieve a standardization of PPG measurements.

2.2. Skin tone and wavelength

Skin colour and light wavelength are two interconnected aspects to be addressed together; indeed, the penetration depth of the light beam and the optical response of the skin tissue vary with wavelength and subjective characteristics.

Regardless of the specific body location, the first tissue encountered

by the light beam is the skin, whose characteristics play an important role in light absorption and scattering (Table 3, readapted from [77,150]). The epidermis is quite thin and basically a light-absorbing layer, whereas the dermis is a thick layer where light scattering plays an important role [151]. For instance, it has been calculated that the air-skin interface causes about 5% of the light provided by the LED to be reflected away from the skin and this percentage can be even higher for oblique angles of incidence [151]. Nevertheless, this aspect could be reduced with a proper contact pressure, minimizing the thickness of the air-skin interface. As above mentioned, cutaneous optical properties vary among different subjects; specifically, there is a significant variation in melanin content among human races, accounting for different skin colours. Fig. 6 shows the absorption spectra of melanin, water, and oxygenated and deoxygenated haemoglobin for different wavelengths.

As reported in the figure, melanin is a highly light absorber, hence it can significantly attenuate the incident light provided by the PPG sensor. While for wavelengths higher than 1200 nm, the percentage of melanin (and, therefore, the skin colour) no longer influences the absorption, at shorter wavelengths (i.e. 530 nm - which is commonly used in PPG-based commercial devices) it strongly affects the PPG output. Conversely, shorter wavelengths as the green light have been demonstrated to be less susceptible to motion artifacts. Indeed, blue and green radiations do not penetrate through the skin (Fig. 7) as deeply as the red and the infrared [152,153] ones, thus the signal is also less prone to disturbances [154].

Lee and colleagues [156] compared the HR during physical activity measured through a PPG sensor equipped with different PPG wavelength values. They concluded that green light ensured relative freedom from motion artifacts if compared with red, so the authors concluded that it is more suitable for monitoring the HR in normal daily life [157]. Moreover, Shchelkanova et al. [158] compared blue and green wavelengths for PPG acquisition in normal and cold temperatures evidencing that, despite the fact that blue light has received little attention until now due to the employment of photodetectors with inherently lower sensitivity, it could be convenient to combine blue light-based treatments with simultaneous PPG acquisition for cardiovascular parameters monitoring.

There are several articles in literature [159–161] demonstrating that PPG sensors used on darker skins provide inaccurate HR measurements up to 15% more frequently if compared with lighter skin [109]. Given the dependency between the subject's characteristics and the wavelength, the possibility of having different wavelengths in the same sensor, to choose from time to time the one that best suits the individual subject characteristics, is the condition that could provide the best accuracy on a heterogeneous cohort of subjects, opening a new path for multiple applications. Towards this direction, different studies [162–164] adopted multi-wavelength sensors to investigate the performances of different light colours in various conditions. Most of these studies used a configuration in which a single PD is placed in the centre of the sensor, and a plurality of LEDs are placed around it, with different configurations, but always keeping the same distance between the PD and the LEDs with the same wavelength. This configuration can ensure a higher probability that at least one of the LEDs is in a proper contact with the skin in case of unwanted relative shifts/rotations between PPG and skin, besides being able to rely on different wavelengths. Yan et al. [152] used an advanced multi-wavelength patch sensor (i.e. green, orange, red, and infrared - IR) able to select a suitable illumination and LED illumination intensity based on the skin colour. They found the compatibility of that particular PPG sensor if compared with three-lead ECG regardless the skin colour. Similarly, in a recent study, Han and colleagues [155] developed a sensor with a plurality of LEDs (i.e. blue, green, red, and IR) arranged in two concentric circumferential paths with radius of 4.75 and 9.75 mm, respectively. The aim of this specific sensor layout was to reduce the problems of directionality between the light and the PD, as well as to test different distances between the LEDs and the PD. Authors found that the blue light provided the worst

Table 3
Tissue depth and optical parameters.

Materials	Thickness [mm]	Refractive index	Absorption [1/mm]	Scattering anisotropy	Scattering coefficient [1/mm]	Wavelength [nm]
Air	–	1.00	–	–	–	–
Epidermis	0.14	1.40	0.50	0.8	31.3	530
			0.26		22.1	660
			0.12		17.4	850
			0.06		16.0	940
Dermis	2.6	1.50	0.28	0.8	19.2	530
			0.15		14.4	660
			0.10		10.5	850
			0.08		9.7	940
Subcutis	4	1.44	0.28	0.8	16.3	530
			0.40		12.3	660
			0.13		9.6	850
			0.08		8.9	940
Arteries	2 (DC)	1.40	1.80	0.95	709	530
			1.88	0.98	849	660
	2.2 (AC)		4.65	0.98	804	850
			5.87	0.97	710	940

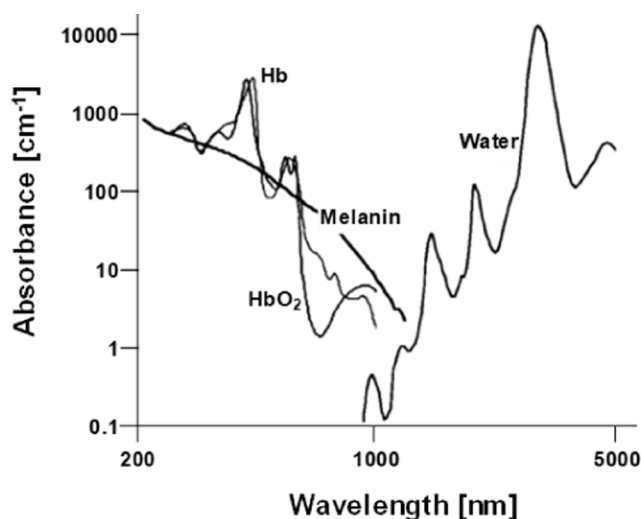


Fig. 6. Absorption spectra of skin [151].

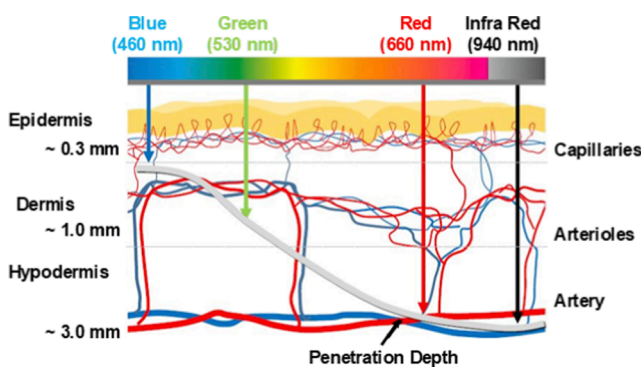


Fig. 7. Different mean light penetration depth at different wavelengths [155].

performance if compared to the other wavelengths, attributing the low signal quality to the poor depth penetration within the epidermis [165]. Besides, they confirm the feasibility of measuring PPG while using a multi-wavelength circular optical sensor, foreseeing the circular configuration in future wearable commercial devices.

Given the high number of articles describing skin colour as a parameter that influences the quality of the PPG signal, with some exceptions [109,166], it is important that future studies aiming at

evaluating the metrological performance of the PPG sensor take this influencing parameter into account, by possibly using distinct wavelengths for different applications, and by enrolling people with different skin colours. In this direction, the von Luschan’s chromatic scale and Fitzpatrick scale are widely used for skin classification [167–169]. Table 4 shows the classification of each skin type in corresponding regions.

The CTA-2065 standard provides indications on the characteristics of the cohort of subjects to be enrolled. Specifically, it advises that at least 25 % of the participants should have a skin colour within the range of I to III and at least 25 % should be within the range of IV to VI based on the Fitzpatrick Scale.

Moreover, the standard suggests to place the optical sensor away from wounds, tattoos, or other kinds of skin conditions that may affect the signal, such as high density wrist hair and sweat, which have been found to influence the measurement results [108].

2.3. LED-PD distance and configuration

As previously described, the most important information of a PPG signal is contained within a very small AC component, which is superimposed to a noisy and drifting DC component, leading the PPG signal to be prone to noise and, thus, inaccuracy when extracting physiological parameters. Recent studies focused on the improvement of the quality of PPG sensors through the optimization of three constructive parameters, namely: a) the distance between the LED and the PD, b) the area including LED and PD, and c) the relative position of the LED and PD [170]. This optimization aims at maximizing the AC/DC components ratio to achieve a better reliability of the PPG sensor. This is achieved through the assessment of the optical model that simulates the light within the skin, based on the Lambert-Beer law [171,172]. Specifically, the path travelled by the light, which is often defined as “banana shaped”, changes according to the path length within the skin, which acts as a medium that gradually deteriorates the light as it travels back to the PD.

A schematic representation of the light path travel is shown in Fig. 8

Table 4
Fitzpatrick and von Luschan’s skin classification.

Fitzpatrick type	von Luschan	Description
I	0–6	Very light or white
II	7–13	Light
III	14–20	Light intermediate
IV	21–27	Dark intermediate
V	28–34	Dark or brown
VI	35–36	Very dark or black

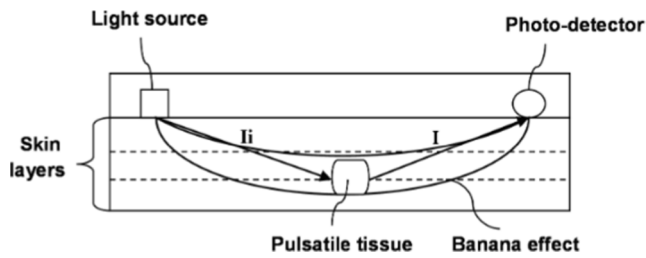


Fig. 8. Banana shape effect on reflection mode PPG [173].

[173]. The light incident on the skin surface is denoted as I_i , while I is the intensity of light emerging from the tissue following the “banana shaped” path. According to Lambert-Beer law, the light intensity passing through different layers of skin decays in an exponential manner [173].

Kao and colleagues [77,174] simulated an optical model to determine the optimal distance between the PD and LED for different wavelengths within the range from 1.65 mm to 3.65 mm with increments of 0.1 mm. The authors concluded that the best AC/DC ratio occurs for different distances based on the wavelength, and specifically of 1.85, 2.35, 2.75 and 2.75 mm for wavelengths of 530, 660, 850, and 940 nm, respectively. Nevertheless, other aspects (e.g. current, PD surface) or configurations may lead to different results [170]. Indeed, several existing multi-wavelength sensors have non-uniform distances between each single wavelength and the photodetector [155].

As concerns the LED-PD distance, another parameter which may influence the PPG sensor performance is the number of LEDs and PDs, as well as the specific arrangement layout. Indeed, placing multiple LEDs around a photodetector in a single sensor can improve the quality of the PPG signal [175], thanks to two main reasons: a) to capture more light reflected back to the PD and b) to increase the chance that at least one LED or PD remains properly in contact with the skin, in case of sensor movement.

Different configurations have been adopted in both commercial and academic research implementations (Fig. 9) and the general common layout is the circular one, where the other components (in a variable number) are mounted on circumferences of increasing radius with respect to a central LED or PD [152,155,175].

In a configuration with the LEDs arranged on external circumferences it is important to not exceed the distances to be able to effectively get the pulsatile flow [155] (it is suggested to be less than 6 mm for multiple wavelengths [176]). Baek and colleagues [175,177] employed two configurations: triple LEDs with centred photo-detector, for enhancing light intensity, and multiple PDs with centred light source configuration. They conclude that a multiple PDs configuration intends to detect more reflected light (with respect to the emitted portion), whereas multiple light source configuration aims at the emission of enhanced light intensity to make more reflected photons towards a given detection area. Therefore, thresholds for adaptive light intensity control should be determined differently according to the sensor type.

In conclusion, the sensor configuration should be properly selected according to the specific target application. Moreover, adopting more wavelengths can be useful to monitor more physiological parameters (e.g. SpO₂), as well as to improve the quality of the PPG signal, making it more suitable for different users’ biological characteristics.

2.4. Motion artifacts and signal crossover

Other significant sources of inaccuracy in PPG-based wearable devices are caused by i) motion artifacts (MA), which result in a low signal quality, and ii) cyclical wrist motions/physical activities, which cause signal crossover. These potential sources of inaccuracy are more intense when the PPG signal is acquired from the wrist if compared to the finger [143], due to the flexibility of the wrist and the extensor digitorum tendons. MA, which can be periodic, quasi-periodic, or non-periodic [178,179], are caused by subject-sensor relative movements and result in a signal distortion with an amplitude much larger than the pulsatile

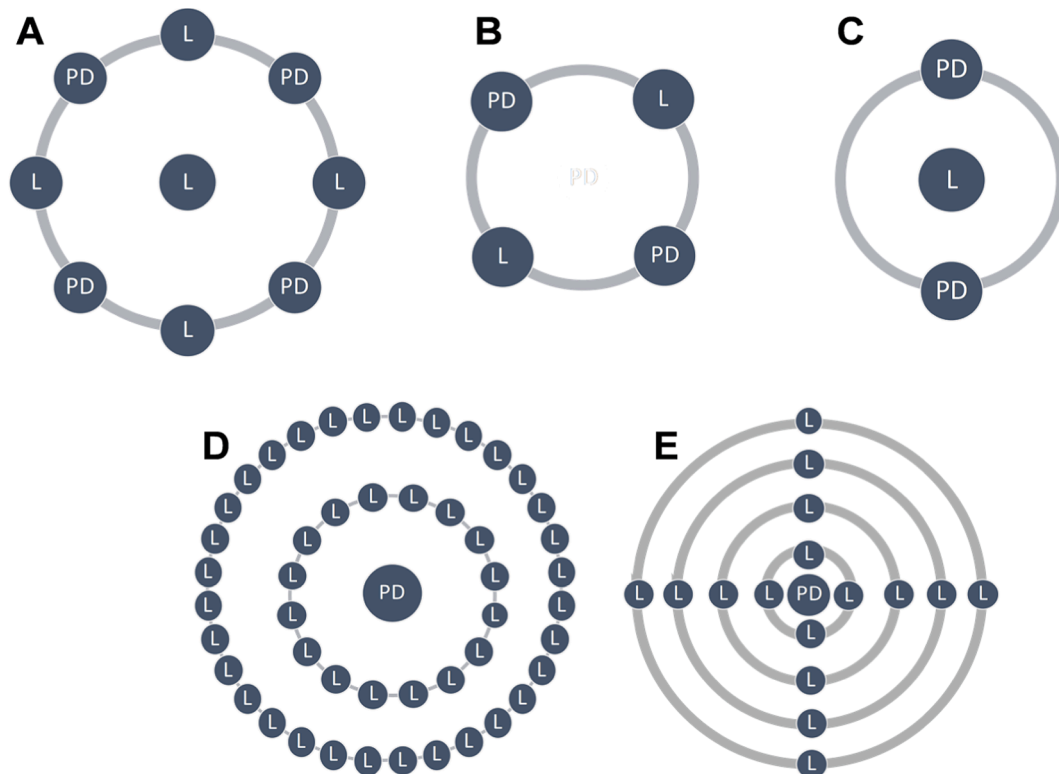


Fig. 9. Different configurations of LEDs (L) and PDs (PD) layout and design for both commercial and research purposes. A = Apple Watch series 6, B = Huawei Watch GT 2, C = Fitbit Inspire HR, D = configuration from Han et al. [155], E = configuration from Yan et al. [152].

component [143] and a very low signal-to-noise ratio (SNR), especially during intense physical activity. Plus, MA, whose frequency band usually ranges from 0.1 to 20 Hz [180], can overlap to HR frequency range (commonly from 0.9 to 3 Hz). Indeed, MA generated by repetitive actions like walking and jogging tend to lock on the HR signal generated by the cardiovascular cycle. Thus, common filtering strategies cannot effectively remove this problem without distorting the useful signal [180] and algorithms may mistake the step rate as the HR cadence. In a recent study, Bent et al. [109] explored HR and PPG data from consumer-grade and research-grade devices under different activities. They found that wearable PPG-based devices reported a higher error during physical activity, varying with the specific activity type. The overall results showed to over-report the HR during low-intensity physical activity, and the consumer-grade devices were found to be more accurate than research-grade devices at rest. They also stated that repetitive motion (e.g. walking), which can lead to signal crossover effect, led to significant errors. Plus, repetitive actions which involve the wrist (e.g. typing) produced an error in HR higher if compared with results achieved at rest and as high as during walking (i.e. repetitive motion). In this context, Umair and colleagues [98] compared the data quality of six common wearable heart rate monitoring biosensors (ECG: Firstbeat Bodyguard 2, Polar H10 chest strap; PPG devices: Empatica E4, Samsung Gear S2, and Polar OH1) in resting and physical/mental stress sessions. Their results highlighted that ECG chest strap obtained the lowest number of artifacts, followed by the PPG wristband, ECG sensor board kit, and PPG smartwatch. Although MA can be minimized by choosing specific wavelengths (e.g. green [6,181]), or acquiring the signal from specific body locations [181], or using soft flexible sensors better adhering onto the skin [182], they cannot be entirely eliminated for the specific working principle of the PPG sensor and for the susceptibility of the opto-mechanical coupling between the sensor and the skin. Thus, there is the need for suitable signal processing algorithms steps for removing the motion interferences to correctly trace the HR. Several research groups have proposed different effective strategies for minimizing the effect of MA, including the use of the moving average, Wiener and Kalman filtering, independent component analysis, and artificial neural network analysis [163,183–193]. The use of these algorithms has already proved a good efficacy. Sukor and colleagues [194] carried out different acquisitions of a PPG and a simultaneous ECG signal; in order to improve the overall quality of the PPG acquisitions, they extracted specific morphology features from the signal, achieving a mean error of 0.49 ± 0.66 bpm, compared to 7.23 ± 5.78 bpm without using the artifact detection algorithm. Other positive results were achieved by Karlen and colleagues [195], who created an algorithm based on Gaussian filters and cross-correlation with 96.2 % sensitivity and 99.2 % positive predictive values with a capability to detect MA even between two heartbeats. Li and colleagues [196] proposed a MA removal algorithm based on the optical difference in frequency domain of the acquired signals to suppress irregular disturbances. They not only simulated their method, but also designed and fabricated a wearable optoelectronic device to monitor the PPG signal, demonstrating that the proposed method reduces the average error in HR estimation from 13.04 to 3.41 bpm in motion and deformation situations [196].

Another common technique increasing the capability in identifying the part of the PPG signal corrupted by MA is to use a secondary sensor working in conjunction with the optical sensor; its specific task is to detect and quantify the movement, to isolate the correspondent specific portion of the PPG signal and to increase the capability to interpret it with more awareness and effectiveness through adaptive filters. The most commonly used sensors for this scope are accelerometers [197–199], gyroscopes [200,201], and piezoelectric transducers [202]. Although secondary sensors are not capable of discerning small movements (e.g. typing on a keyboard), their contribution is important in reconstructing and restoring the original PPG signal.

For example, Lee and colleagues [200] evidenced that signals acquired using accelerometers are often not suitable for MA reduction,

while gyroscope-assisted approach exhibited better performance, especially during an exercise involving walking, at the expense however of a higher power consumption. Even better results can be achieved using an adaptive MA reference selection approach implemented by Lee et al. [203], that exploits both acceleration and gyroscope signals. The results reported in [203] showed that such an approach, which compares the dominant frequencies from PPG, acceleration and gyroscope signals selecting the most appropriate one, is capable of further improving HR estimation accuracy.

Some commercial products, such as Empatica E4, rely on two LEDs, one of which (i.e. red light) is used as a reference light to reduce motion artifacts [204]. Although this approach may result in some data gap, an approach to mitigate the effect of the artifact correction method has already been proposed [205].

The use of a secondary sensor to reduce MA is not limited to accelerometers. Indeed, instead of a motion sensor, an additional PD has also been used to reduce MA [143], demonstrating also a good capability in capturing micro-motions artifacts, which mainly derive from the relative motion between the skin and the vessels underneath [206,207]. In this direction, Pandey and colleagues [207] implemented an additional organic PD able to significantly reduce MA and ambient light interference, containing the DC drift within 1 % of its average. Specifically, the authors used the additional PD as a motion reference to enhance the capability of recovering the corrupted PPG signal, also reducing the ambient light noise by controlling the emitter intensity and PD bias. Similarly, to overcome some limitations of accelerometers as motion reference, such as the poor performances in detecting specific motions (e.g. finger tapping), a recent approach [208] explored the use of a secondary PPG sensor (with a different wavelength), finding a highest correlation between the main PPG sensors with the secondary one rather than an accelerometer. Although the study focused only on specific wrist motions, without performing a complete motion characterization, this approach is promising and can lead to signal improvements both on time and frequency domains. Finally, to overcome SNR degradation of PPG signal due both to motion and changes in ambient light, some studies, rather than using an additional sensor, designed a specific low-current and high dynamic range analog front-end [209,210], achieving good results in terms of noise reduction and power consumption.

2.5. Other potential influencing parameters

The influencing parameters described in the previous paragraphs are only a part of them all, and represent those most discussed and examined in the literature. In this section, other potential influencing parameters will be briefly discussed; under certain conditions, they could significantly limit the overall quality of the PPG signal.

First, the room/body temperature is an important factor that should be considered during PPG acquisitions, as it can activate the biological mechanism of vasoconstriction or vasodilatation, which results in a different blood perfusion within the capillary bed underneath the sensor. Although the level of perfusion is significantly variable across human populations and it depends on many factors, low temperature could reduce perfusion even further, especially in the body extremities (where usually PPG sensors are located), reducing SNR and lowering the reliability of PPG signal. Khan and colleagues [211] investigated the effect of temperature on the PPG signal quality and on the SpO₂ estimation from the hand in three different conditions: i) normal digit temperature, ii) after 5-minute immersion of the hand in a 0–4 °C ice-water bucket, and iii) after keeping the hand in hot water at 55 °C. The authors concluded that the warm condition significantly improved the quality of the acquired PPG signal, whereas under cold condition the quality was reduced.

In similar studies [212,213], the relationship between ambient and skin temperature while deriving different cardiovascular parameters (i.e. pulse wave velocity, BP, HR) from a PPG signal was evaluated. Results demonstrated the inter-dependency of temperature and signal quality,

suggesting that room and peripheral temperature should be considered when using PPG sensors. Also the exposure to mild cold has proven to affect the circulation, altering the PPG reproducibility and decreasing the AC components amplitude [214]. Thus, temperature has been proven to affect the accuracy of PPG signal [69]. Specifically, if temperature rises, the PPG amplitude increases [215,216], while when temperature falls both PPG amplitude and PTT decrease [214,217,218]. Also Shchelkanova and colleagues [158] found that PPG estimated precision tended to degrade upon a significant drop in the skin temperature, evidencing that such a decrease of precision is more evident for shorter heart beat intervals (i.e. higher HR), being instead less affected for lower HR. Therefore, temperature is a parameter to keep under control not only in terms of peripheral body temperature, but also as an external environmental parameter.

Finally, Evdochin and colleagues [219] investigated the behaviour of PPG signals for two different external stimuli, namely the external temperature and pressure. They concluded that the vasomotor mechanism, caused by an external temperature, results in a significant effect on the signal, thus affirming that the information about the external temperature could be used to feed an algorithm that consequently switches on a wavelength (e.g. IR) able to reach deeper tissues.

Another important aspect that influences the PPG signal is the specific body location where PPG sensor is placed [220]. In particular, there are two aspects to consider: the first is due to the specific anatomical constitution of the body site. In fact, in presence of a thick layer of skin, fat or poor vascularity can lead to a decrease in sensor performance by increasing the absorbed light and thus decreasing the amount of light backscattered to the PD. The second aspect is due to the susceptibility of that site to cause MA due either to the presence of muscles and tendons or to body accelerations (e.g. wrist).

As previously briefly introduced, most PPG probes work in reflectance mode, since this modality allows to place the sensor potentially anywhere on the body. Instead, PPG sensors in transmission mode are usually employed on the fingers and earlobes, since in other body locations it is difficult for light to penetrate human tissues. However, some recent works [13,63] proposed a PPG transmission wristband with USB communication data transfer within a combo ECG/PPG portable system aimed at low invasive acquisition for real-time monitoring of cardiovascular and respiratory parameters. This has been made possible also thanks to the employment of a novel typology of photodetectors, i.e. the silicon photomultipliers (SiPMs) (provided by STMicroelectronics) with high responsivity, gain and Signal to Noise Ratio (SNR) [221,222].

Both in transmission and reflectance modes, on one side forehead, fingertips, and earlobe are excellent measurement sites [223–225] thanks to the high density of blood vessels near the surface of the skin; therefore, these are typical PPG sensors locations in a clinical environment. Plus, during physical activities the ear is less susceptible to MA, thus reducing the optical noises corrupting the PPG signal. On the other hand, despite the high signal quality that can be achieved from these locations, another aspect to consider is the user’s comfort, since the optical device should not hinder the normal daily life gestures. Thus, favouring this aspect, the wrist is generally considered the most appropriate spot, having increased its popularity due to its adoption by the vast majority of commercial devices (e.g. smartwatches and wristbands). Nevertheless, the wrist location suffers from a high degree of variability in vascular structures underneath the skin and from optical noises originated by the movements of tendons, muscles, and fingers.

Ambient light represents yet another influencing parameter [226,227], which interferes with the PPG signal both with regard to the DC and the AC components. Therefore, it is important that the PD is exposed only to the light provided by the LED that has already travelled through the subcutaneous tissues. In this direction, some useful precautions consist in i) encasing the PD in a shield able to avoid the direct light coupling [228], or ii) to use PDs integrating a light filter [229], or iii) to implement filters outside the PPG bandwidth [69].

Finally, there are also further influencing parameters, which depend

on specific user’s biological and physiological characteristics. Among these, the most significant ones are the body mass index (BMI), the respiration rate, and the venous pulsation. Specifically, the BMI indirectly affects the PPG signal by varying the dermal capillary density [230–232] and its depth, as well as varying the skin thickness [233,234] and the trans-epidermal water loss [235], which results in a variation of the path and of the properties of the tissues encountered by the light. Similarly, the respiration rate and the venous pulsation indirectly affect the optical signal due to their mechanical effects on the vascular system, both resulting in a variation of the PPG amplitude of DC and AC components [236–239].

Recently, Fine and colleagues [69] carried out a detailed review of several influencing parameters of the PPG technology, summarizing them in a very effective and schematic table (partially reported in Table 5), where they also report the impact of each influencing parameter and provide a potential mitigation technique.

Due to the widespread use of PPG sensors in commercial products (e.g. smartwatches), which could represent a significant step forward in physiological monitoring during normal daily life, it is interesting to mention the main influencing parameters considered by the smartwatch manufacturers, thus going beyond the scientific production.

Among the commercial products that adopt the PPG sensors to acquire HR and other physiological parameters, the Apple Watch results from numerous studies [109,240,241] to be the one providing the highest quality HR in different conditions, when compared with other commercial products considered as reference. Nevertheless, Apple Inc. states that “Even under ideal conditions, Apple Watch may not be able to get a reliable heart rate reading every time for everybody. And for a small percentage of users, various factors may make it impossible to get any heart rate reading at all” [242]. Thus, it is interesting to recall the main influencing factors that could play a role on the signal quality (Table 6), as reported by Apple Inc. [243] on its official website. Apple Inc. does not directly report the skin colour as a possible parameter of influence, despite numerous scientific articles confirm such correlation, as described in the paragraph 2.2. However, it should also be considered that the current Apple Watch on the market employs three different wavelengths (i.e. green, red, and IR) that have a different degree of absorption by melanin, as already discussed and shown in Fig. 6. A very recent study assessing the reliability of commercially available smartwatches and devices (Withings Move ECG lead I, Apple Watch series 5 - lead I, Kardia Mobile 6L - six leads) (lead II) for electrocardiogram-based detection of atrial fibrillation indicated very high sensitivity/specificity values (91 %–99 %); Kardia resulted the most sensitive device, but less

Table 5
Summarized influencing parameters, impact and mitigation technique; re.

Influencing parameter	Impact	Mitigation technique
Skin tone	Decrease signal intensity	PPG wavelength selection
Obesity/BMI	Decrease signal intensity, modified PPG waveform	Not found in literature
Age	Change in signal intensity, modified PPG waveform	Calibration
Gender	Change in signal intensity	Calibration
Respiratory rate	Modified PPG waveform	High pass filter
Venous Pulsation	Modified PPG waveform	High pass filter/contact pressure
Local body temperature	Change in signal intensity	Calibration
Body site	Change in signal intensity, modified PPG waveform	Calibration
Motion artifacts	Change in SNR	Filters and secondary sensors
Ambient light	Change in SNR	Optical shielding and selective filters
Contact pressure	Change in SNR, modified PPG waveform	Apply optimal pressure for high SNR

adapted from [69]

Table 6
Influencing parameters reported by Apple Inc. [242].

Influencing parameter	Description
Skin perfusion	Skin perfusion varies significantly from person to person and can also be impacted by the environment. If you're exercising in the cold, for example, the skin perfusion in your wrist might be too low for the HR sensor to get a reading
Skin tattoos	Permanent or temporary changes to your skin can impact HR sensor performance. The ink pattern and saturation of some tattoos can block light from the sensor, making it difficult to get reliable readings.
Motion artifacts	Rhythmic movements, such as running or cycling, give better results compared to irregular movements, like tennis or boxing
Contact pressure	Wearing Apple Watch with the right fit – not too tight, not too loose, and with room for your skin to breath – keeps you comfortable and lets the sensors do their job

useful to rule out atrial fibrillation, whereas Apple had the highest specificity [244].

To summarize what has been discussed in this section, Table 7 reports the relevant recent approaches and results that have been proposed by different research groups in regard to the evaluation of each influencing parameter.

3. Lack of homogeneity in assessing the metrological performance of wrist-worn PPG-based devices

Literature reports that there is often a lack of homogeneity in the evaluation of the metrological performance of optical wearable sensors for the measurement of HR due to various factors (e.g. the choice of the sample, which is often too homogeneous, or the omission of significant information or an inappropriate setting for the intended use). The lack of standardization, hindering a proper comparison of the results from different or similar studies, reduces the effectiveness of a study and jeopardizes the overall quality of results. Specifically, many validation studies on wrist-worn PPG-based devices are also considered to provide inconclusive evidences for different reasons, such as for the approach in comparing different variables [245] or for methodological issues [138]. For instance, for clinical applications, the most popular method (around 85 %) to present the results and to assess the agreement of two different measurement systems is the Bland-Altman plot [246,247]. However, in the medical literature there is still inappropriate application of other

statistical methods to assess agreement [246]. Pearson's correlation coefficient and Student's *t*-test or the corresponding non-parametric Wilcoxon test in case of small sample size with not normally distributed data [248,249] are also largely used by researchers but are not considered exhaustive [250], as well as the concordance correlation coefficient. All this inevitably leads to confusion in reporting results when comparing a PPG sensor with a reference device.

Aside the data analysis and reporting, from a methodological point of view, the effect of the skin colour or of the sensor placement, strap tightness, contact pressure, room temperature, BP, or wrist circumference are often not reported; plus, many physical activities, performed to verify the sensor accuracy, do not reflect real daily life actions. Thus, the authors agree with Sartor and colleagues [138], that the lack of regulation in the commercialization of non-medical HR monitoring devices should not justify the lack of standard requirements for validating this technology. The above considerations lead to side effects on both scientific and commercial point of view. From a scientific point of view, the diffusion of inhomogeneous results creates contradictory findings, which cannot be interpreted, replicated, reproduced, and generalized [251]. This not only leads to a waste of energy that does not increase awareness on the behaviour of the device under different conditions, but also to a lack of support in the quantification of the accuracy and, therefore, in their adoption in the healthcare context. Similarly, from a commercial point of view, the lack of clear and well-defined methods of benchmarking sensor accuracy can cause several companies to enter the market with low-cost and low-quality products. Thus, on the one hand there will be inexpensive products accessible to a larger part of the population, but on the other hand this will lead to a generalized distrust on the performance and reliability of these devices. It is crucial to establish what are the optimal conditions of use of PPG-based devices, and, above all, what are those biological behavioural or environmental conditions that cause a reduction in metrological performance, making the devices no longer suitable for a specific sporting or clinical use. Only with this information it would be possible to implement all those appropriate strategies for shielding or compensating the different undesired influence parameters as much as possible.

Promoting a standardization and good scientific practices [245,251–254] in order to characterize wearable technology means enhancing the safety of the end-users, as well as exploiting an extraordinary opportunity to drastically improve the effectiveness of wearable devices for physiological health status monitoring but also, in perspective, for the assessment of many different conditions [84,98,255,256].

Table 7
Influencing parameters affecting the quality of PPG signal and optimal approaches to improve the data acquisition.

Influencing parameter	Technique investigated to mitigate the issue	Result	Challenge	Relevant work
Contact pressure	Optimal contact pressure	Wrist-worn device: [0.2–0.4] N and 54 mmHg, finger device: 60 mmHg	Tissues and arterial stiffness	[137,146,148]
Skin tone and wavelength	Optimal light colour	Green light, blue light multi-colour light	Skin conditions (e.g., wrist hair and sweat)	[152,155–158,162–164]
	Optimal skin colour	Light skin		[109,159–161]
LED-PD distance and configuration	Optimal LED-PD distance	< 6 mm if multiple wavelengths	Sensor type and target application	[155]
	Optimal configuration	Multiple LEDs or PDs around a LED or PD		[152,155,177,181]
Motion artifacts and signal crossover	Reduced MA in data collection	Wavelength selection, sensor body location, sensor adherence on the skin	Physical activity type	[6,181–182]
	Reduced MA in signal processing	Moving average, Wiener and Karman filtering, independent component analysis, ANNs		[163,183–193]
Other potential influencing parameters	Quantified movements to interpret MA	Additional sensors (e.g., accelerometer and gyroscope) or double LEDs	Blood perfusion	[197–202,204,205]
	Optimal SNR and reliability	Warm skin and ambient temperature		[158,211–218]
	Optimal light transmission	Photomultipliers and location with high density of blood vessels		Constitution of body site
Reduced interferences from ambient light	Reduced interferences from ambient light	PD in a shield, light filter integrated or implemented	BMI, respiration rate and venous pulsation	[69,226–229]
	Reduced interferences from others physiological features	High pass filter (except for BMI influence)		[230–239]

4. Necessity of a technical standard

As mentioned in the previous paragraph, in recent years a general request has arisen from the scientific community [108,109,245,251,257] to adopt a standardized methodology at a global level in the evaluation of the performance of HR measurement devices, and specifically of PPG sensors. In addition to increasing the transparency, the repeatability, the consistency, and the interpretability of results, this would allow to give a specific weight to the various influencing parameters and finally to quantify the measurement uncertainty. Thus, the adoption of a single standard could make it possible to compare results of different PPG sensors (also typically tested under different conditions).

Table 8 summarizes different aspects that should be taken into consideration during the design phase of any comparative PPG test, including any aspect which may influence the measured quantity.

Currently, the Guide to the Expression of Uncertainty in Measurement (GUM) [258] would not seem adequate to meet the required needs. For this reason, in this paragraph, some interesting methodological proposals reported by the scientific community will be summarized and presented, with the hope that a single and profitable way of testing these devices can be adopted by the widest participation. Among different sources [245,251], particular consideration will be given to the standard ANSI/CTA-2065 [127]. It provides not only directions on the different characteristics that are desirable for the test sample and test methods and procedures, but also detailed indications (time and intensity) on different indoor test protocols. In the next paragraphs the following aspects will be discussed: study participants, device characteristics and setup, and, finally, analysis and results.

4.1. Study participants

Table 9 summarizes the three main steps that should be followed in selecting the potential candidates for the experimental study.

The sample size should be carefully determined based on the characteristics and the objective or application of the study [259,260]. Indeed, on the one hand the sample size should have sufficient statistical power to provide reliable and significant results, on the other hand it should minimize the costs and the time of the tests. The CTA-2065 standard suggests 20 participants as the minimum number for a generic study to evaluate the performance of a device. However, as the data acquired from some subjects could be damaged or unusable, once the target number has been set, it should be still increased by at least 10 % to prevent it from being undersized. For instance, in a study aimed at

Table 9

Descriptive participant’s characteristics which should be reported.

Participant selection and characteristics
Selection of the most appropriate number of participants
Verify the heterogeneity of the sample in terms of age, gender, skin tone, weight, height, BMI, wrist circumference, blood pressure
Interview with all the participants before starting any tests

evaluating wearable technology for physiological acquisitions, Van Lier and colleagues [245], after having determined the sample size in 55 subjects through a power analysis, recruited 40 % more subjects to ensure the right amount of available data. In addition to the number of participants, it is essential that the sample is representative across biological and physiological differences among the population, as such characteristics could have a significant influence on PPG signal, as described in the previous sections. Table 5 reports a list of potential covariates, which are generally recognized to be relevant in the selection of the sample for bio-behavioural research purposes [251]. In this direction, the CTA-2065 standard prescribes specific percentages of the sample composition in terms of skin tone, BMI, and gender balance. Specifically, basing on the Fitzpatrick scale, at least 25 % of participants should fall within a skin colour between 1 and 3 and another 25 % should have a skin colour between 4 and 6. Plus, the sample, which should have a minimum percentage of 40 % for both men and women, must also contain a 10 % of subjects with a BMI below 20 kg/m² and a 10 % with a BMI above 25 kg/m².

Arterial BP is not reported in the CTA-2065 standard. However, also this parameter should be taken into consideration, as it can affect the PPG signal amplitude by changing the variation of the volume of blood vessels at each heartbeat, depending on the specific arterial compliance of the subject. Plus, it can provide also useful information when setting the optimal contact pressure of the sensor against the skin, as it depends on the transmural pressure, which is linked to the actual BP of each participant.

The wrist circumference of each participant should be measured, as it can potentially affect the PPG signal [251], reporting whether some participants perceive a particular cooling sensation in the extremities of the limbs, which could be associated with a severe peripheral vasoconstriction. Kleckner and colleagues [261] proposed a framework for selecting and benchmarking mobile devices in psychophysiological research, evidencing the fundamental importance to employ well-used and validated tasks (e.g. those indicated by Menghini and colleagues [110]), to enable the researcher to attribute the validation failure to the

Table 8

Proposed strategy to evaluate the metrological performance of PPG sensor.

Aspect to consider	Proposed strategy	Reference	Comments
Study participants	Sample size	Min 20 participants + 10 % more subjects than target number + 40 % more subjects than target number	ANSI/CTA-2065 [127] Van Lier et al. [245]
	Sample type	Specific percentages for skin tone, BMI and gender Representative across biological and physiological differences (age, gender, skin, tone, weight, height, BMI, wrist circumference, and blood pressure)	ANSI/CTA-2065 [127] Nelson et al. [251]
	Survey before experiment	Collect information on the health status, explain and sign the protocol, verify presence of tattoos	Nelson et al. [251]
Device characteristics and setup	Reference device	EKG or electrode-based device	ANSI/CTA-2065 [127]
	Testing device	Commercial product, prototype, or lab device	ANSI/CTA-2065 [127]
	Measurement setup	Report room temperature and ambient lighting; sensor position; characteristic of eventual straps used, and contact pressure measured between skin and sensor	ANSI/CTA-2065 [127]

given device under test rather than to problems associated with the specific novel task). A good practice should also envisage preventive interviews with the subjects who will participate in the study. This is recommended for several reasons: i) to ensure the correct heterogeneous composition of the sample, ii) to collect any relevant information such as any particular pathology, medical treatment, or use of medications, which could potentially exclude the subject from being enrolled in the study, iii) to explain the subjects each protocol step and to inform them on the proper behaviours to be maintained (e.g. make natural movements and not talk during the test), iv) to let them sign any relevant document if needed, v) to verify the presence of any possible tattoo or skin spots in the measurement site, and vi) to ask the participants not to take any drugs or stimulants (e.g. coffee) that may affect the measurements in the hours preceding the study, if needed.

4.2. Device characteristics and setup

First, a reference device should be considered, such as an ECG or an electrode-based device accordingly to the CTA-2065 standard. Specifically, a chest strap for ECG could be used, allowing ease of use and robust stability even during different and intense physical activities.

In general, hardware and software characteristics should be reported to describe the PPG-based testing device, if it is a commercial product. Thus, the manufacturer, the model, and the firmware update, as well as main information from the datasheet of the reference device, such as sampling rate, should be described in the study, as specified in Table 10. Then, the raw data provided by the device should be explained. Otherwise, if the testing device is a prototype, generic information as sampling rate could not be enough and hardware information should be provided in more detail, i.e. electronic components (such as filters) and the general layout of LED-PD disposition, as well as their characteristics (such as LED wavelengths). For completeness, exhaustive images should be illustrated to allow a deep understanding of the tested measurement device. Moreover, a detailed description of the data transmission modality should also be reported. This includes specifying the type of protocol used in case of wireless transmission, or the presence of any cables that may affect the stability and adherence of the sensor to the skin, especially during physical activity, as well as any adopted precautions to reduce this effect.

In addition to report the devices characteristics, it is also important to describe the environmental conditions in which the test takes place. Specifically, it is recommended to report the room temperature and the type of ambient lighting, as well as any solutions adopted to shield the PD from ambient light.

Another aspect that should be described is the fastening solution adopted to fix the sensor to the selected body location. This is particularly important when the sensor is placed on the terminal part of the limbs, such as on the wrist. Both the characteristics of the strap (e.g. width and elasticity), and the contact pressure with which the sensor is fastened to the subject, should be contemplated. While wearing the

Table 10
Descriptive device characteristics and testing information that should be reported.

Device characteristics and testing condition
Reference device
Sensor type and specification, producer, model and firmware version
Data provided (e.g. raw data, R-R interval) and sampling rate
Testing device
Sensor's producer, model and firmware version (if commercial product)
Detailed hardware and software description (if a prototype or lab version)
Sampling rate and data transmission
Testing conditions
Room light and temperature
Sensor placement and fastening solution
Contact pressure between the sensor and the skin

device, it is a good practice to avoid skin spots or tattoos, and to ask participant not to move any muscles, as it could cause a significant oscillation in the contact pressure.

Once a thorough description of hardware and sensor positioning is provided, also a detailed description of the physical activity to be performed should be reported. The exercise program, which could be at rest or during a specific physical activity, should be designed by the experimenter accordingly to the expected aim of the study. Regardless the specific physical activity, it is important that the test recreates the normal daily life conditions as much as possible, asking the participants to perform all movements in the most natural way.

A timetable could be a useful tool in the description of the specific physical activity, allowing to detail and quantify the active phases of the test and the breaks.

A detailed example is reported in Table 11, where a walking and a jogging activity lasting a total of 12 min are described. During the activities, subjects should refrain from using mobile devices, music players, books, or any external stimuli unless it is foreseen in the test protocol itself.

4.3. Analysis of results

Before proceeding with the analysis of the results, regardless of the signal processing strategy, a first step should be a visual inspection of the data provided by the reference ECG device and the device under test. Indeed, a purely qualitative analysis could provide indications about the quality of the data, highlighting any spike, damage, or loss of the signal that could lead the experimenter to exclude part of the dataset. The exclusion of data values must always be considered a delicate process, since removing non-legitimate values can lead even to significant variations in the results, compromising their validity and interpretation. In any case, it should be reported the probable causes of data missing (e.g. non-adherence, device failure, connections, battery life) and how corrupted data were handled; it should also be reported the percentage of data availability for each participant and for all the participants for both reference and tested devices. All the remaining acquisitions should be included even if this reduces the agreement with the reference device. Once the dataset is considered suitable, it is possible to proceed, based on the collected data, with all the appropriate preprocessing steps (e.g. band-pass filtering, MA removal) to estimate the investigated parameter (e.g. HR) and determine whether or not the tested device is capable to produce physiological signals compatible to the reference device. To assess such an agreement, there are several approaches that may be adopted; however, it is not possible to be too prescriptive in considering a single approach as a standardized methodology, since each one is based on considerations and assumptions which are dependent on the specific type of test and on the boundary conditions.

Nevertheless, the CTA-2065 standard suggests using the Mean Ab-

Table 11
Dynamic walking and jogging protocol reported in the CTA-2065 standard [127].

Walking and jogging protocol
1 min (0:00–1:00) standing quietly on treadmill
1 min (1:00–2:00) walking at comfortable pace
3 min (2:00–5:00) self-selected running speed of at least moderate intensity with minimal incline but not less than 0 % (i.e. between 0 % and 1 %)
1 min (5:00–6:00) walking at comfortable pace
2 min (6:00–8:00) at a running speed resulting in vigorous intensity
2 min (8:00–10:00) at a running speed resulting in vigorous intensity at a higher speed than the previous stage
1 min (10:00–11:00) walking at comfortable pace
1 min (11:00–12:00) standing quietly on treadmill
After 12 min has elapsed, data collection should end

*During this test the participants shall be running/jogging in a natural style. Treadmill speed shall be brought from zero to the chosen speed while the participant is on the treadmill belt.

solute Percentage Error (MAPE) to determine how the physiological parameter extracted from the testing and reference device are close to each other, which can be calculated as follows [73]:

$$MAPE = \frac{100}{N} \sum_{i=1}^N \left(\left| \frac{R_{test} - R_{ref}}{R_{ref}} \right| \right)$$

where R_{test} is the physiological parameter resulting from the testing device, R_{ref} is the physiological parameter obtained from the reference device and N is the total number of samples across participants.

The standard also suggests reporting the mean and standard deviation of the physiological parameter for each (both from the testing and reference device) and for all the participants. Other metrics widely used are the absolute error and its standard deviation, the average relative error, and the Pearson's correlation coefficient [262].

Kottner and colleagues [257] affirm that a single measure agreement provides only limited information; thus, they recommend to report a combination of coefficients and a graphical method which could be a powerful approach to provide useful information about the distribution score. In this direction, the Bland-Altman plot [130] is widely used and preferred to the Pearson's correlation coefficient, being sensitive to a linear movement of all the observations [245]. Plus, the Bland-Altman plot can highlight both under and overestimation, considering both the mean overall difference among individuals and participants and showing any possible missing data. Using Bland-Altman plots, the limits of agreement and the ratio between half the 95 % confidence interval for the difference and the mean of the averaged values have also been employed as metrics for agreement between two measures [263].

Although a tested device is generally considered accurate if the MAPE is ≤ 10 % [264], caution must be taken in defining a device as accurate for a given parameter in a specific context of use (given that the test conditions undoubtedly influence the measurement results). Specifically, it must always be considered that it is not easy to recreate tests that perfectly match spontaneous gestures in normal daily life. The results should be compared with those of different studies under similar test conditions, to check whether different groups of experts come to the same conclusions, providing justifications and considerations in the conclusion of a study. Moreover, based on the topics covered in this article, an important effort from the authors should be to interpret the data in relation and in terms of the different influencing parameters, trying to correlate the results to each possible variable and providing indications on how a given parameter may have influenced the results and which action would be appropriate to improve the results for future studies. Also, sensitivity analysis could help in understanding which factors have a higher impact on the measurement results. Finally, it would be helpful to make data and algorithms available in publicly accessible databases [265,266].

5. Conclusion

The recent growth of interest in wearable technologies has led to a significant increase in scientific studies aimed at evaluating the performance of PPG sensors in the detection of different physiological parameters for health status monitoring, contributing to prevent the worsening of health conditions and adverse events. However, the high sensitivity of these optical sensors to various external influencing parameters, both environmental and subject dependent, highlights a poor reproducibility and comparability of the results and a lack of validity and reliability of the protocols chosen for their testing and validation. This may depend on different reasons, such as the lack of procedural information, the improper planning of the tests, or the inadequate selection of the test population. Nevertheless, the main reason is the poor consideration of the different influencing parameters, whose can still be partly shielded or compensated, even if a large part cannot be controlled or discharged from the signal.

The lack of a standardized methodology and the unsuitability of the

GUM has emphasized this issue, which therefore does not allow the performance of these sensors to be uniquely defined, thus limiting their application for clinical use. Indeed, it is necessary to be able to properly assess the agreement and reliability of different tests and to have a unique classification method.

This review follows the request of the scientific community to promote behavioural indications in evaluating the performance of PPG sensors in different conditions, hence highlighting a series of best practices and recommendations to be adopted in PPG-based sensors metrological characterization. Thus, based on different proposals that are emerging both from literature and manufacturers, this work summarizes and reports a general set of guidelines to allow uniformity and comparability of different results. Specifically, the clear steps and precautions mentioned in this work are relatively easy to adopt and can be used in a large variety of studies. For these reasons, a methodological rigor in the execution of the tests should be encouraged, to prevent ambiguous or incorrect quantifications of the performance of the PPG sensors. Indeed, as the future of (tele)medicine lies in the metrological quality of the measurements, this is an issue that needs to be addressed in the short term.

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