Low-invasive multisensor real-time acquisition system for the assessment of cardiorespiratory and skin conductance parameters

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Abstract— **In recent years, the attention to the health and comfort of the individual, together with the electronic miniaturization progress, have led to an increased interest in the development of biomedical devices that are able to acquire a multitude of biomedical signals. Such devices should be wearable and comfortable during daily use, to be thus suitable for continuously monitoring psychophysical health states. In this context, we have designed and realized a portable biomedical device capable of real-time acquisition of electrocardiographic (ECG), photoplethysmographic (PPG), breathing and galvanic skin response (GSR) signals, for a non-invasive monitoring of multiple physiological parameters. This work shows the architecture of our system, which integrates a Bluetooth module for wireless communication with the central computer and novel analog sensors capable of carrying out breathing and GSR measurements. Preliminary measurements carried out using our system during a controlled breathing protocol illustrated how the simultaneous measurement of ECG, PPG, GSR and respiration allows tracking changes not only in heart rate, but also in epidermal tissue sweating, thus confirming that the device can be successfully employed for monitoring health status and, in perspective, also for assessing the individual's stress level.**

Keywords— Portable biomedical devices, Internet of Medical Things (IoMT), electrocardiography (ECG), photoplethysmography (PPG), galvanic skin response (GSR)

I. INTRODUCTION

In the last years we have witnessed an ever-growing increase in attention to the research and development of portable and wearable biomedical devices capable of assessing individuals' health status and quality of life during daily life situations [1]. Wearable biomedical devices, also known as Wearable Health Devices (WHD), enable continuous home care monitoring of human vital signs with the advantage of minimizing discomfort and interference with normal routine activities [2]. There is a wide range of wearable devices that can be worn on a multitude of body districts (e.g. eyes, ears, arms, wrists, hands, chest) and are specifically designed for extracting the main physiological parameters of interest for a real-time monitoring of the individual [3]. The acquired data can then be preprocessed on site and then stored or shared with other devices through wireless communication (e.g. Bluetooth and Wi-Fi communication protocols), realizing a network of smart biomedical systems nowadays well known as Internet of Medical Things (IoMT) [4]. The real-time sharing of data with clinicians or healthcare workers has been proven to be beneficial for early diagnosis of diseases or for the follow-up and monitoring of ongoing diseases [5].

Nowadays, the increase in human life expectancy together with a highly variable lifestyle among subjects depending on daily-life activities and job type (e.g. hectic activities, sedentary life, prohibitive working day duration [6]), alongside with other unhealthy habits (e.g. abuse of alcohol, tobacco and unhealthy diets), have led to an increase in cardiovascular risk [7] and in particular to heart diseases, which have become one of the leading causes of death [8]. Another factor that affects health and quality of life, which has been underestimated for years and only recently has been considered as a triggering cause of cardiovascular diseases and burdening pre-existing pathological conditions [9] is the chronical stress level [10]. Selye [11] has defined stress as the functional response of the organism to a more or less violent stimulus (*stressor*) of any nature (e.g. physical, mental, emotional). This response of the organism is better known as General Adaptation Syndrome (GAS) [12], during which changes occur in various biomedical parameters, affecting above all the cardiovascular system, the brain and also the sweat glands of epidermal tissue, whose activation is proportional to the activity of the Sympathetic Nervous System (SNS) branch of the Autonomic Nervous System (ANS). For these reasons, the research is nowadays focusing on the realization of low-invasive devices capable of real-time monitoring of health status and stress conditions, taking into account multiple biosignals. Usually, in order to extract cardiovascular parameters, such devices employ photoplethysmography (PPG), which is a simple and low-cost optical technique that detects blood volume changes in the microvascular bed of tissue. A visible or infrared source is used to illuminate a specific area of the body; depending on whether the illumination occurs in transmission or reflection, the portion of light not absorbed or reflected, respectively, is captured by a photodetector, thus obtaining an output signal proportional to the variation of blood flow in the bed tissue [13]. Thanks to its unobtrusive and easy-to-use working principle, PPG has become the most widely used technique for cardiovascular measurements used in biomedical wearable devices, being able to extract important parameters such as

heart rate, heart rate variability, pulse-transit time, oxygen saturation and even estimates of blood pressure [14]. Additional useful information can be extracted monitoring the activity of the sweat glands and extracting the galvanic skin response (GSR) signal. This can be achieved by considering the epidermal tissue as an impedance and carrying out electrical resistance measurements between two areas of the body. Acquiring the GSR signal could therefore be helpful for monitoring the activation level of the sympathetic branch of the ANS, allowing a timely identification of the stressors and assessing the individual's quality of life.

In this study we present an updated version of a multisensor portable electronic system developed for the simultaneous acquisition of different biosignals. A previous prototype was already presented in some previous works ([15]–[19]), demonstrating the effectiveness to carry out synchronous ECG, PPG and breathing measurements. Herein, the system has been integrated with a Bluetooth module to establish wireless communication and data transfer and with the MIKROE-2860 sensor [20] for real-time measurement of GSR. A controlled breathing measurement protocol was carried out to induce changes in ECG, PPG and GSR signals, thus verifying the functioning of our portable device under variable physiological conditions, and showing the potential of integrating a GSR sensor in a synchronous multi-parametric acquisition system for health-status assessment.

II. MATERIALS AND METHODS

A. Portable system architecture

Figure 1 shows the functional schematic diagram of the developed portable biomedical system. It is a microcontroller-based logic electronic system which, assisted by a high-resolution and low noise analog-to-digital converter specially designed for biopotential measurements, manages the biosensors (in terms of alimentation levels, raw data amplitude and others control settings), acquires the sensors signals detected by the converter during the sampling process and sends them to the Bluetooth module which allows wireless communication and data transfer.
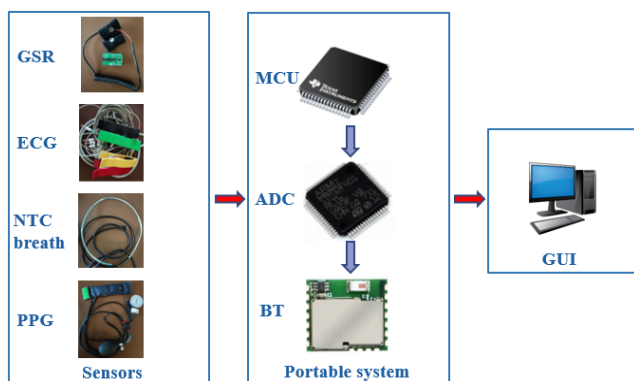

Fig. 1.   Schematic block diagram of our portable biomedical system.

Data collected by the system are then sent to a personal computer which, through an appositely developed graphic-user interface, allows the real-time display of the acquired signals and performs the extraction of the main physiological indices (heart rate, heart rate variability, RR intervals, PP intervals and pulse arrival time).

The core components of the portable system (Fig. 2) are:

- The STM32-F401RE microcontroller with a high-performance ARM Cortex-M4 32-bit RISC core operating at a frequency up to 84MHz;

- The ADS1298 consisting in a multi-channel delta-sigma ($\Delta\Sigma$) analog-to-digital converter with 24-bit resolution and sampling frequency up to 4kHz which is specifically designed for ECG acquisitions;

- The Bluetooth module SPBT3.0DP2, designed for maximum performance in minimal space and includes high speed UART with a transmission speed up to 1.5Mbps.
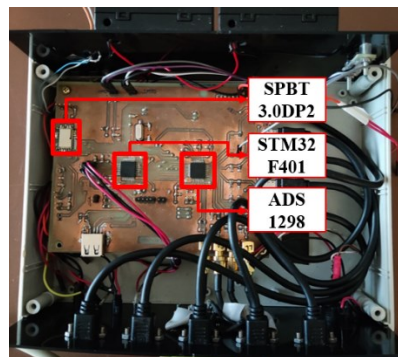

Fig. 2.   Photo showing the details of the core components of the portable system. Highlighted in red, going from left to right, there are the Bluetooth module SPBT3.0DP2, the microcontroller STM32F401RE and the analog-to-digital converter ADS1298.

Figure 3 shows an overview of the portable system including the probes for data acquisition. Commercial peripheral clamp electrodes were used to acquire the ECG signal. The PPG probes were instead made ad hoc to acquire the sphygmic signal using an 850nm light source and a silicon photomultiplier (SiPM) detector which presents higher gain than a normal photodiode, thus allowing to obtain a higher signal resolution [18], [21] and for this reason represents the main innovation introduced by our system. The breathing signal is acquired through a 10kΩ negative thermistor (NTC) in order to acquire a voltage signal that increases during the exhalation phase and decreases in the inhalation phase. Finally, to extract the GSR signal, we integrated into the portable system the MIKROE-2860 (MikroElektronika) module, which detects changes in the electrical conductance that the epidermal tissue offers to the passage of a current between two Ag/AgCl (silver-chloride) electrodes worn on the index and middle fingers of the hand.

Fig. 3.   Overview of the portable biomedical system, alongside with ECG and GSR electrodes, PPG and breathing probes.

B. GSR acquisition

Galvanic skin response is a physiological parameter measuring conductance expressed in Siemens which reflects

autonomic changes in the electrical properties of epidermal tissue [22]. The GSR signal can be decomposed into two components: the skin conductance level (SCL), known as tonic activity, and the skin conductance response (SCR), known as phasic activity. SCL depends on the basal sweat glands activity in the absence of stressors (and thus on the individual's physical characteristics) and it is therefore considered as a reference level to evaluate changes in sweating. On the other hand, SCR is produced by sudden changes in sweating following stressful events, reflecting a fast variation in autonomic arousal. Using a device capable of carrying out skin conductance measurements is therefore essential to assess the activation level of the skin sweat glands and, consequently, to better characterize the activity of the sympathetic branch of ANS, alongside with conventional HRV-based indices [23], [24].

The working principle of the MIKROE-2860 GSR module relies on the volt-amperometric method to obtain skin resistance measurements. Two electrodes are applied on a body area, such as the phalanges of the fingers, characterized by a high concentration of skin sweat glands [15]; by applying an electric potential to the first electrode and detecting the residual potential, knowing the current flowing in the electrodes, it is possible to obtain the value of the resistance offered by the epidermal tissue [16].
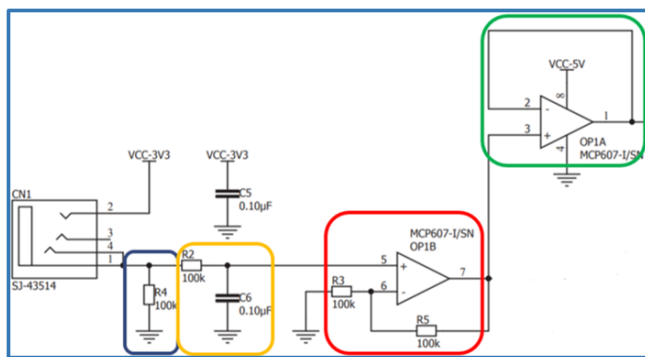

Fig. 4. Electric schematic of MIKROE-2860 GSR module. Figure readapted from the component datasheet [25].

Figure 4 shows the analog front-end of the sweat sensor, reported on the datasheet of the component [25]. A constant voltage is applied to the electrode located on the first finger, resulting in a current flowing from the second one. Knowing the residual potential at the second electrode (i.e. voltage on resistor R4 terminals (blue square)) it is possible to calculate the current flowing on it which is the same that flows on the skin resistance. A passive first-order low-pass filter (yellow square) composed by resistor R2 and capacitor C6, limits the signal response with a cut-off frequency of 15.9 Hz. The detected and filtered potential on R4 is therefore doubled by the op amp non-inverting amplifier circuit (red square) and decoupled from the rest of the front-end by a buffer (green square). Finally, the output of the module (i.e. the buffer output) is connected to the analog-to-digital converter ADS1298 input of our portable system.

C. Experimental protocol

Measurements were recorded on a normotensive healthy 22-years old female while sitting on a chair. Four ECG electrodes were positioned on the wrists and legs in accordance with Einthoven's triangle [26] for up to 3-lead electrocardiographic signal acquisition. The PPG probes were worn on the left wrist and forearm for pulse sphygmic detection, while breathing and sweating probes were worn respectively on the nose and on the index and middle fingers of the hand (according to [27]). All the signals were sampled at 24-bit resolution with a 500 Hz sampling frequency. Data were transferred wirelessly via Bluetooth using the appositely developed GUI into a Personal computer, which also allows to plot the signals in real-time, in order to visually detect any artifacts due to incorrect probes positioning (we refer to [17], [19] for further information).

In order to evoke physiological changes both in cardiovascular parameters and sweat glands activity during the real-time acquisition, the following experimental protocol was implemented:

- Rest 1 (R1): 360 seconds in which the subject was breathing spontaneously in a resting condition;

- Controlled breathing (CB): a 360-s recording in which the subject was instructed to carry out a paced breathing with period of 6 seconds, in which each cycle consisted of 3-seconds inhale and 3-seconds exhale phases;

- Rest 2 (R2): another 360-s recording in which the subject breathes spontaneously analogously to R1.

An initial preparation procedure lasting around 150 seconds was carried out, recorded but not used for the analysis, in order to check the correct functioning of the system and installation of the probes and to allow acquiring data in stationary conditions. During all phases, the subject was instructed not to make any movement. During the paced breathing phase, the subject followed a visual metronome appositely developed to support the correct execution of controlled breathing (we refer the reader to [19] for further information).

D. Data processing

Filtering procedures are usually needed to extract physiological information from the raw signals and to reduce the external noise typically picked up by the sensors. The ECG raw data was pre-processed using a zero-phase fourth order bandpass Butterworth digital filter to extract the signal between 0.1 Hz and 20 Hz (respectively low cut-off and high cut-off frequencies), also rejecting the 50 Hz line voltage frequency component. The Pan-Tompkins algorithm was employed to do detect R peaks [28] and extract the R-R interval (RRI) time series. In order to remove undesired optical components captured by the SiPM at higher frequencies (e.g. 100 Hz emitted by the lighting of our laboratory), the PPG raw signal was also filtered with the same Butterworth filter but with a high cut-off frequency set to 15 Hz (given the lower power content of PPG signals). A threshold-based peak detection algorithm was employed to find the PPG minima and extract the pulse-to-pulse interval (PPI) time series. An 11-point moving average (i.e. smoothing) digital filter has been applied to the breathing signal to better visualize the inhalation and exhalation phases. Skin resistance offered by the epidermal tissue was estimated by applying Ohm's law once the voltage across finger electrodes and the voltage divider current were known. Finally, Ohm-to-Siemens conversion was carried out in order to obtain the GSR signal as a function of skin conductance. The MATLAB-based software LEDALAB was employed to analyse GSR activity, firstly under-sampling raw data at 20 Hz and then separating SCL and SCR components with

continuous decomposition analysis based on a standard deconvolution method [29].

III. RESULTS AND DISCUSSION

In this section, we show the results of the offline processing carried out using MATLAB on the data acquired as described in the previous section. For data analysis, the ECG lead 1 and the PPG acquired on the left wrist were considered, in addition to the signals obtained by NTC and GSR sensors. Fig. 5(a) and Fig. 5(b) show the heart rate trend computed respectively from the R-R interval (RRI) and pulse to pulse interval (PPI) time series extracted from ECG lead 1 signal and from the PPG signal. Fig.5(c) depicts the trend of the raw GSR signal during the measurement protocol from the R1 phase (0s – 360s), followed by the CB phase (360s – 720s) to the end of the R2 phase (720s – 1080s).
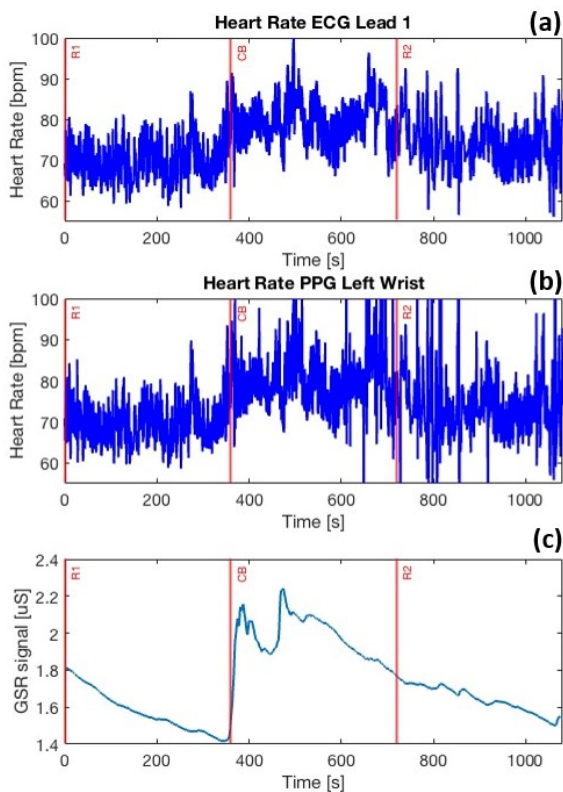
Fig. 5. Complete view of the whole acquisition time window; (a) heart rate ECG 1 lead, (b) left wrist PPG heart rate, (c) GSR signals during the execution of the measurement protocol. The vertical red lines denote the transition between different breathing conditions according to the adopted experimental protocol.

Figure 6 reports a 25-seconds detail of recordings from second 150 to 175 s, i.e. across the transition between the spontaneous to the paced breathing conditions occurring at the second 150. The low values of the GSR signal (Fig. 6(c)) together with lower values of heart rate (see Fig. 5(a) and (b)) (typical for resting conditions [30]) suggest that the subjects is relaxed during the R1 phase. GSR in the first phase moreover gradually decreases, indicating that the subject under test becomes more and more relaxed. A sudden change in the GSR signal occurs from the beginning to about the middle of the CB phase, indicating an increase of the skin conductance (or decrease of skin resistance) which may be due to a shift of the sympathovagal balance to the sympathetic side. Although a slower breathing rate (the so-called "deep breathing") typically induces a relaxation response [31], [32], the transient sympathetic activation reported during the transition from R1

to CB may be related to the temporary response of the organism to the different and non-spontaneous breathing pattern, probably misinterpreted as "a stressor" or anyway as an external trigger.

During the CB phase, a slight increase of the heart rate can also be observed, which may be related to the fact that the subject was not used to breath in a non-spontaneous way and thus appeared a bit troubled at the beginning. Moreover, the change of the heart rate due to respiration could be related to the widely known phenomenon of Respiratory Sinus Arrhythmia (RSA) [33], [34]. The transition between controlled breathing and the second rest phase did not show any abrupt variations of GSR, which continues to gradually decrease towards the values observed during the first spontaneous breathing condition.
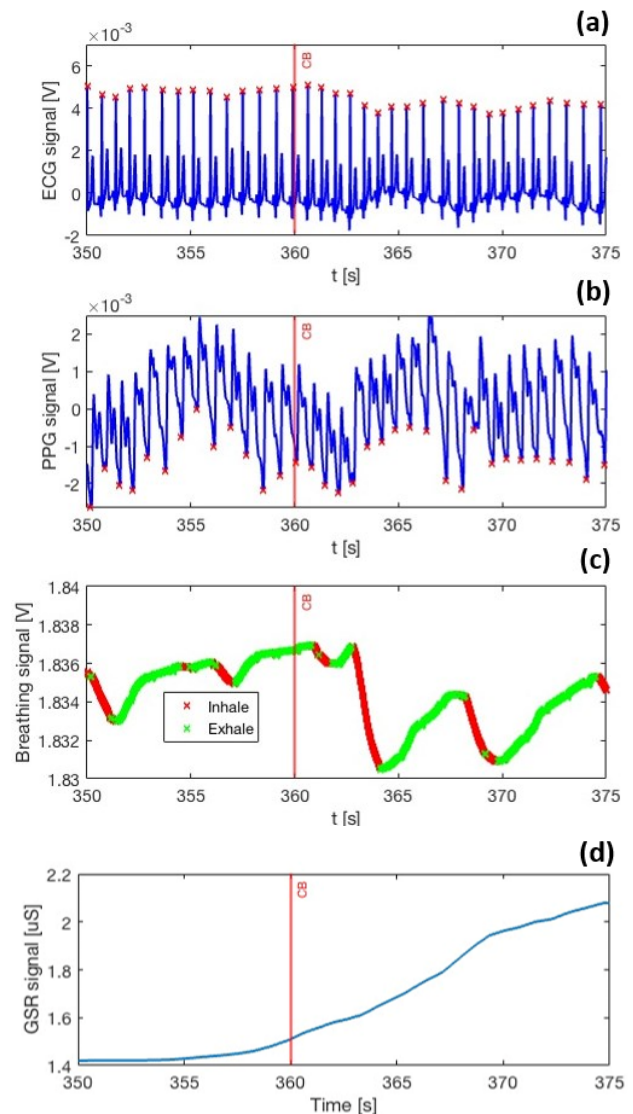
Fig. 6. A 25-seconds recording detail of (a) ECG 1 lead, (b) left wrist PPG, (c) breathing and (d) GSR signals during transition from spontaneous to controlled breathing phases. In (a) red crosses indicate ECG R peaks; in (b) red crosses indicate PPG minima; in (c) the inhale period is indicated in red, while the exhale period in green. The vertical red line denotes the transition between spontaneous and controlled breathing.

Fig. 7 shows the analysis carried out on the GSR signal by LEDALAB, which performs the decomposition of the signal in tonic (SCL) and phasic (SCR) activities. This analysis evidences the phasic activity, whose trend is shown at the

bottom of the figure, only during the transition between R1 and CB (up to the center of this phase), confirming the previous interpretation and remarks.
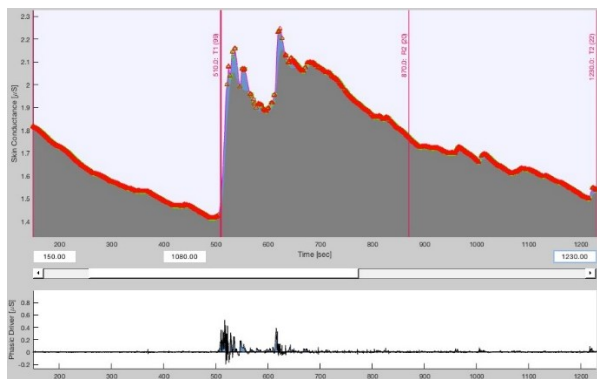

Fig. 7. Analysis of GSR signal carried out using LEDALAB: (a) GSR signal with both tonic and phasic (in blue) components. In red the peaks of the signal are highlighted. (b) Phasic component of GSR signal.

IV. CONCLUSION

A mini-invasive portable biomedical system capable of performing synchronous and real-time multi-parametric biosignal acquisition has been realized and presented. The synchronous acquisition of ECG+PPG+breathing+GSR signals allows to carry out a thorough assessment of physiological states. The system is compact and portable, the wireless-communication allowed by SPBT3.0DP2 Bluetooth module permits also to exchange acquired data without the use of cables. Thanks to these features the system, belonging to IoMT devices, has a very high potential to be used not only for real-time monitoring of cardiovascular parameters, but also for multilevel stress assessment.

The preliminary results presented in this work highlighted the effectiveness of this device in detecting cardiovascular parameters, but also variations of GSR due to alterations in the physiological state caused by different breathing phases. The possibility of simultaneously extracting 3-Lead ECG, PPG signal on 2 different locations (e.g. left wrist-left arm, left wrist-left ankle, left wrist-right wrist), respiration activity and GSR makes our system suitable also for the analysis of cardiorespiratory interactions, to be explored as a future activity. The implementation of other acquisition protocols aimed at causing orthostatic and mental stress could be useful to assess the responses of the organism and further test our system. Future works could regard the implementation, within the firmware of the portable system, of linear algorithms for estimation of dynamic information measures to assess physiological activity and the stress level [35], [36]. Finally, a future upgrade of the system foresees the realization a novel prototype completely wearable, to be easily and comfortably employed for a continuous daily monitoring of health-status and quality of life.

REFERENCES

[1] D. Dias and J. P. S. Cunha, "Wearable health devices—vital sign monitoring, systems and technologies," *Sensors (Switzerland)*, vol. 18, no. 8, 2018.

[2] M. Di Rienzo, F. Rizzo, G. Parati, M. Ferratini, G. Brambilla, and P. Castiglioni, "A textile-based wearable system for vital sign monitoring: Applicability in cardiac patients," *Comput. Cardiol.*, vol. 32, pp. 699–701, 2005.

[3] R. S. Bisht, S. Jain, and N. Tewari, "Study of Wearable IoT devices in 2021: Analysis Future Prospects," *Proc. 2021 2nd Int. Conf. Intell. Eng. Manag. ICIEM 2021*, pp. 577–581, 2021.

[4] R. Suvarna, S. Kawatkar, and D. Jagli, "Internet of Medical Things [IoMT]," *Int. J. Adv. Res. Comput. Sci. Manag. Stud.*, vol. 4, no. 6, pp. 173–178, 2016.

[5] A. Kos and A. Umek, "Wearable sensor devices for prevention and rehabilitation in healthcare: Swimming exercise with real-time therapist feedback," *IEEE Internet Things J.*, vol. 6, no. 2, pp. 1331–1341, 2019.

[6] S. Koldijk, M. A. Neerincx, and W. Kraaij, "Detecting Work Stress in Offices by Combining Unobtrusive Sensors," *IEEE Trans. Affect. Comput.*, vol. 9, no. 2, pp. 227–239, 2018.

[7] N. A. Rigotti and C. Clair, "Managing tobacco use: The neglected cardiovascular disease risk factor," *Eur. Heart J.*, vol. 34, no. 42, pp. 3259–3267, 2013.

[8] P. Kakria, N. Tripathi, and P. Kitipawong, *A Real-Time Health Monitoring System for Remote Cardiac Patients Using Smartphone and Wearable Sensors*, vol. 2015. 2015.

[9] S. J. Bunker *et al.*, "'Stress' and coronary heart disease: Psychosocial risk factors: National Heart Foundation of Australia position statement update," *Med. J. Aust.*, vol. 178, no. 6, pp. 272–276, 2003.

[10] W. J. Chen, "Work-related stress and depression susceptibility for the sanitarian manpower in country," *3rd Int. Conf. Bioinforma. Biomed. Eng. iCBBE 2009*, pp. 12–14, 2009.

[11] H. Selye, "Forty years of stress research: principal remaining problems and misconceptions," *Can. Med. Assoc. J.*, vol. 115, no. 1, pp. 53–56, 1976.

[12] A. J. Cunanan *et al.*, "The General Adaptation Syndrome: A Foundation for the Concept of Periodization," *Sport. Med.*, vol. 48, no. 4, pp. 787–797, 2018.

[13] J. Allen, "Photoplethysmography and its application in clinical physiological measurement," *Physiol. Meas.*, vol. 28, no. 3, p. R1, 2007.

[14] Y. Maeda, M. Sekine, and T. Tamura, "The advantages of wearable green reflected photoplethysmography," *J. Med. Syst.*, vol. 35, no. 5, pp. 829–834, 2011.

[15] D. Oreggia *et al.*, "Physiological parameters measurements in a cardiac cycle via a combo PPG-ECG system," in *2015 AEIT International Annual Conference (AEIT)*, 2015, pp. 1–6.

[16] V. Vinciguerra *et al.*, "PPG/ECG Multisite Combo System Based on SiPM Technology," in *Sensors. CNS 2018. Lecture Notes in Electrical Engineering book series (LNEE), vol. 539*, Andò B. et al. (eds), Ed. Springer, Cham, 2019, pp. 353–360.

[17] R. Pernice, A. Parisi, G. Adamo, S. Guarino, L. Faes, and A. Busacca, "A portable system for multiple parameters monitoring: towards assessment of health conditions and stress level in the automotive field," in *2019 AEIT International Conference of Electrical and Electronic Technologies for Automotive (AEIT AUTOMOTIVE)*, 2019, pp. 1–6.

[18] V. Vinciguerra *et al.*, *Progresses towards a processing pipeline in photoplethysmogram (PPG) based on SiPMs*. 2017.

[19] R. Pernice *et al.*, "Low invasive multisensor acquisition system for real-time monitoring of cardiovascular and respiratory parameters," *20th IEEE Mediterr. Electrotech. Conf. MELECON 2020 - Proc.*, pp. 306–310, 2020.

[20] A. M. Qualifying and P. Report, "Wearable Health Monitoring Devices," *Encycl. Gerontol. Popul. Aging*, pp. 5388–5388, 2021.

[21] G. Adamo *et al.*, "Signal to Noise Ratio of silicon photomultipliers measured in the continuous wave regime," in *2014 Third Mediterranean Photonics Conference*, 2014, pp. 1–3.

[22] J. J. J. Braithwaite *et al.*, "A Guide for Analysing Electrodermal Activity (EDA) & Skin Conductance Responses (SCRs) for Psychological Experiments," …, pp. 1–42, 2013.

[23] F. Shaffer and J. P. Ginsberg, "An Overview of Heart Rate Variability Metrics and Norms," *Front. public Heal.*, vol. 5, p. 258, Sep. 2017.

[24] R. Pernice *et al.*, "Reliability of Short-Term Heart Rate Variability Indexes Assessed through Photoplethysmography," in *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2018, pp. 5610–5613.

[25] MikroElektronika, "GSR CLICK," 2022. .

[26] J. Hohl and S. Rush, "The complete heart-lead relationship in the einthoven triangle," *Bull. Math. Biophys.*, vol. 30, no. 4, pp. 615–623, 1968.

[27] M. van Dooren, J. J. G. G. J. de Vries, and J. H. Janssen, "Emotional sweating across the body: Comparing 16 different skin conductance measurement locations," *Physiol. Behav.*, vol. 106, no. 2, pp. 298–304, 2012.

[28] H. Sedghamiz, "Matlab Implementation of Pan Tompkins ECG QRS," pp. 1–3, 2014.

[29] M. Benedek and C. Kaernbach, "A continuous measure of phasic electrodermal activity," *J. Neurosci. Methods*, vol. 190, no. 1, pp. 80–91, 2010.

[30] R. L. Burr, S. A. Motzer, W. Chen, M. J. Cowan, R. J. Shulman, and M. M. Heitkemper, "Heart rate variability and 24-hour minimum heart rate.," *Biol. Res. Nurs.*, vol. 7, no. 4, pp. 256–267, Apr. 2006.

[31] K. Deepak, "The Role of Autonomic Nervous System in Rapid Breathing Practices.," *Proc. Sci. Breath,. Int. Symp. Sudarshan Kriya, Pranayam Conscious.*, pp. 42–45, 2002.

[32] B. W. Kromenacker, A. A. Sanova, F. I. Marcus, J. J. B. Allen, and R. D. Lane, "Vagal mediation of low-frequency heart rate variability during slow yogic breathing," *Psychosom. Med.*, vol. 80, no. 6, pp. 581–587, 2018.

[33] J. A. Hirsch and B. Bishop, "Respiratory sinus arrhythmia in humans: how breathing pattern modulates heart rate," *Am. J. Physiol. Circ. Physiol.*, vol. 241, no. 4, pp. H620–H629, 1981.

[34] M. Javorka *et al.*, "Respiratory Sinus Arrhythmia Mechanisms in Young Obese Subjects," *Front. Neurosci.*, vol. 14, p. 204, 2020.

[35] R. Pernice, G. Volpes, J. C. Krohova, M. Javorka, A. Busacca, and L. Faes, "Feasibility of Linear Parametric Estimation of Dynamic Information Measures to assess Physiological Stress from Short-Term Cardiovascular Variability," in *2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*, 2021, pp. 290–293.

[36] R. Pernice *et al.*, "A validity and reliability study of Conditional Entropy Measures of Pulse Rate Variability*," in *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2019, pp. 5568–5571.