Respiratory Monitoring: Current State of the Art and Future Roads

Ian Costanzo*† *Student Member, IEEE,* Devdip Sen*† *Student Member, IEEE,* Lawrence Rhein§, MD, MPH, and Ulkuhan Guler† *Senior Member, IEEE,*

***Abstract*—In this article, we present current methodologies, available technologies, and demands for monitoring various respiratory parameters. We discuss the importance of non-invasive techniques for remote and continuous monitoring and challenges involved in the current "smart and connected health" era. We conducted an extensive literature review on the medical significance of monitoring respiratory vital parameters, along with the current methods and solutions with their respective advantages and disadvantages. We discuss the challenges of developing a noninvasive, wearable, wireless system that continuously monitors respiration parameters and opportunities in the field and then determines the requirements of a state-of-the-art system. Noninvasive techniques provide a significant amount of medical information for a continuous patient monitoring system. Contact methods offer more advantages than non-contact methods; however, reducing the size and power of contact methods is critical for enabling a wearable, wireless medical monitoring system. Continuous and accurate remote monitoring, along with other physiological data, can help caregivers improve the quality of care and allow patients greater freedom outside the hospital. Such monitoring systems could lead to highly tailored treatment plans, shorten patient stays at medical facilities, and reduce the cost of treatment.**

***Index Terms*—Wearables, wireless monitoring, physiological monitoring, vital parameters, biosensors, intensive care unit, ICU, neonatal intensive care unit, NICU, PICU, SICU, respiration parameters, respiration rate, SpO_2, CO_2, O_2.**

I. Introduction

The importance of continuously monitoring the vital signs of at-risk patients and providing improved long-term care has been a driving force for promoting the development of required device technology supported by today's modern digital health care system. Providing medical professionals with the ability to safely monitor vital signs such as temperature, respiration, heart rate, and blood pressure without tethering a patient to a hospital setting would grant freedom and comfort to patients while they recover and return to health [1], [2]. With the availability of robust wireless health monitoring devices, smart long term care in a home environment after a period of hospitalization could reduce the strain on medical resources and the risk of re-admittance [3].

Manuscript received revised ; accepted . This paper was recommended by Associate Editor ..... (Corresponding author: Ulkuhan Guler.)

† Worcester Polytechnic Institute, Department of Electrical and Computer Engineering, MA, USA (e-mail: imcostanzo@wpi.edu, dsen@wpi.edu, uguler@wpi.edu)

§ University of Massachusetts Memorial Medical Center, Division of Neonatology, MA, USA (e-mail:)

* These authors contributed equally to this work

Color versions of one or more of the figures in this paper are available online at http://ieeexplore.ieee.org.

Digital Object Identifier

Among the vital signs of human health, respiration is a key indicator of the physiological status of the human body [4]. Respiratory health is measured by five major parameters: respiratory rate and quality, arterial partial pressure of oxygen (PaO_2), arterial saturation of oxygen (SaO_2), and arterial partial pressure of carbon dioxide ($PaCO_2$). Respiratory rate refers to the number of times an individual inhales and exhales during a given period of time. Respiratory quality describes the effectiveness of each breath, quantified as vital capacity, maximal inspiratory pressure, and expired volume per minute, all of which determine how well individuals inhale and exhale air from their lungs. Partial pressure of blood gases (PaO_2 and $PaCO_2$) describes how well the lungs and the bloodstream exchange gases. Oxygen saturation (SaO_2) is the ratio of hemoglobin loaded with oxygen molecules relative to the total amount of hemoglobin available. SaO_2 is related to PaO_2 through a sigmoid function and is used as a surrogate measurement of the oxygen dissolved in the blood stream. Together, these parameters present a complete view of a patient's respiratory status. By continuously monitoring a person's respiration rate and effort, along with the blood gas content of oxygen and carbon dioxide, we can gain significant insight into that individual's well-being [5]–[7]. A wireless respiratory monitoring system suitable for long-term wear could enhance the health and well-being of individuals of all ages, from neonatal patients with developing lungs to adults with chronic obstructive pulmonary disease (COPD).

Respiration has yet to be sufficiently explored in the context of remote monitoring device technology. Currently, conventional respiratory sensors employed in bedside equipment can monitor individual parameters in a hospital setting, illustrated in Fig. 1. Most of these systems, however, are not convenient for use in a home environment. An unobtrusive, wearable system could significantly improve the quality and safety of long-term care.

In the past decade, the popularity of wearable sensors has grown tremendously in both medical and non-medical applications [8]. Most current commercial wearable sensors, such as Fitbit™ Fitness Tracker [9], Hexoskin® Biometric® Shirt [10], and Garmin® Fitness Tracker [11] focus on the results of physical activity and behavior, such as heart rate, distance traveled, number of steps taken, and calories burned. Although they provide relatively accurate information, they are not considered sufficiently reliable as medical tools. Recent efforts indicate that wearable sensors, initially designed for tracking a person's well-being and physical activity, are now evolving into devices for medical purposes [12].

This momentum has led to several commercially available

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

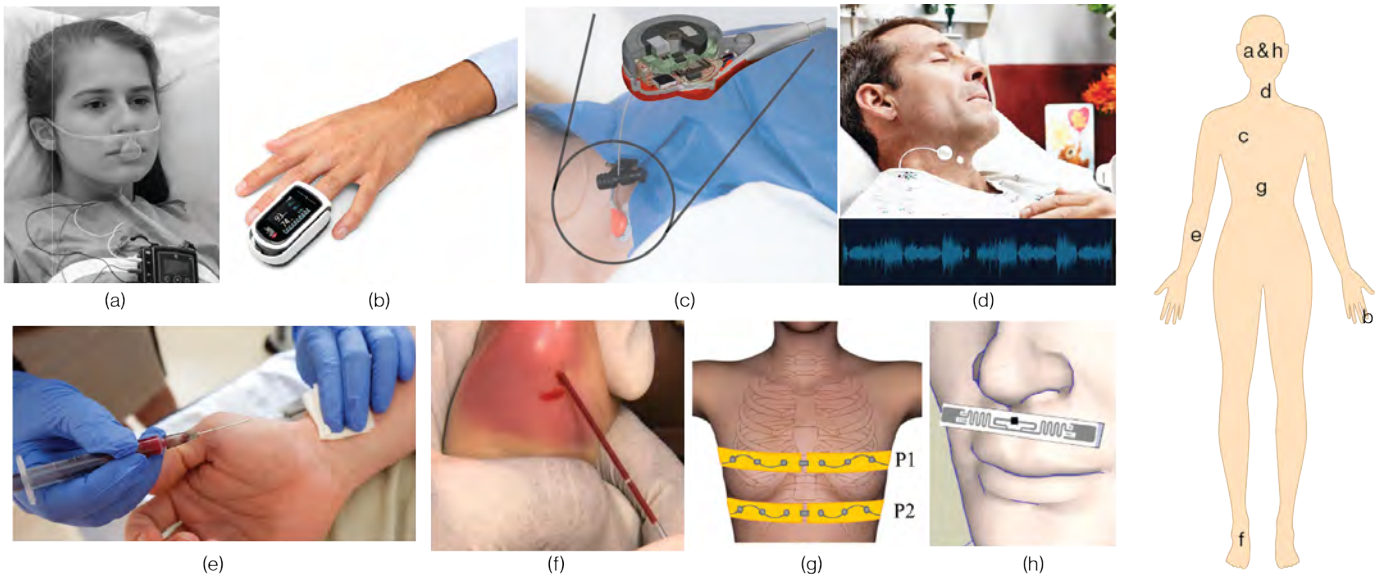

Fig. 1: A sample of respiration monitoring methods: (a) end-tidal CO_2 ($EtCO_2$) [13], (b) pulse oximetry (SpO_2) [14], (c) transcutaneous monitoring [15], (d) neck worn acoustic monitor [16], (e) arterial blood gas analysis (ABG) [17], (f) capillary blood gas (CBG) [18], (g) electrical impedance tomography (EIT) [19], and (h) piezoelectric monitor [20].

wearable devices for the continuous monitoring of patients' vital signs [21]–[23]. SensiumVitals®, an FDA-cleared and CE-marked device, is an end-to-end unobtrusive wearable wireless vital sign monitoring system [21]. The device was developed for the frequent monitoring of the skin temperature, respiration, and heart rate of hospitalized patients after their release from surgical intensive care units (SICUs). Its ability to detect abnormal physiology early will enable clinicians to improve patient care [24], [25]. In addition, the system also allows patients' freedom of movement, and the sense of safety and reassurance of being monitored continuously [21], [26]–[29]. A similar device from Nypro (a Jabil company) also fulfills an identical role of heart rate monitoring [22]. Despite recent developments in medical wearable technology, the breadth and quality of vital information that they generate remain limited, such as respiration. Many devices can only measure two or three parameters, at reduced accuracy and signal to noise ratio (SNR) than their bedside counter parts [21]–[23], [30]–[33].

Hospitals typically record the vital signs of patients at eight-hour intervals, unless the patient has been identified to be at risk [27]. Respiratory failure, however, is unpredictable and can become life threatening in a matter of minutes [34]. The first signs of the onset of patient decline often reveal important markers of a deterioration in health, leading to serious consequences before the deterioration can even be recognized. Frequent alterations to respiration parameters reflect compromised cardiopulmonary and neurological functions [26]. Therefore, quantifying the real-time dynamics and physiological distribution of blood gas is imperative to both clinicians and caregivers, providing them with an understanding of the mechanisms associated with both pathological and normal physiological conditions [35].

In this paper we use two general definitions of care environments; a hospital environment and a home environment. A hospital environment is an established medical care facility with physicians, nurses, and staff on site with appropriate equipment and space to provide definitive medical care. A home care environment would be a location remote from the hospital like a house or an apartment where there is a system to care for a patient under the direction of a physician who may not be on site [36]. Traditionally, care in a home environment is limited in terms of instrument capability and trained care providers. Recent studies have shown that moving from a hospital to home environment can have benefits in patients over-all well being and recovery [3].

The purpose of this paper is to present a comprehensive review of various respiratory monitoring techniques and state-of-the-art noninvasive device technology for monitoring respiratory parameters. The paper also describes the demands on future respiratory monitoring systems associated with digital health transformation. The rest of the paper is organized as follows: Section II presents information about various respiratory diseases and emphasizes the significance of monitoring. Section III discusses contemporary respiratory monitoring methodologies and explores state-of-the-art noninvasive technologies available for respiratory monitoring. Section IV discusses the anticipated technical challenges and demands in the development of wearable sensors for respiratory monitoring, and Section V concludes the paper.

II. Respiratory Diseases and Significance of Respiratory Monitoring

Patients with respiratory disorders, ranging from mild respiratory issues to more severe issues requiring mechanical ventilation, are at risk for complete respiratory failure [44]. Changes in the respiratory rate and blood gas values can be an indication of a critical medical event that may require immediate admission to the intensive care unit (ICU) [45]. Factors that cause abnormal respiratory activity and adversely affect blood gas levels include post-operative respiratory complications, diseases such as COPD , asthma (a

TABLE I
Summary of Respiratory Complications

Complication	Definition	Probable Causes	Signs and Symptoms	References
Hypocapnia	Decrease in the concentration of CO_2	Post-operative complication, drug overdose, use of anesthetic drugs, hyperventilation due to mechanical ventilation treatment	Hemorrhagic infarction, dizziness, blackout muscle cramps and tetany due to decrease in cerebral perfusion	[37], [38]
Hypercapnia	Increase in the concentration of CO_2	Central hyperventilation, encephalitis, meningitis, drug overdose, use of anesthetic drugs, alveolar hyper-ventilation, neuromuscular diseases	Hemorrhagic infarction, seizures, cataphora	[34], [37], [38]
Hypoxemia	Decrease in the concentration of O_2	Diseases like COPD and asthma as well as diseases like heart disease, anemia, and epilepsy	Cyanosis, confusion, headache, shortness of breath, rapid breathing, tachycardia, cardiac arrest	[39], [40]
Hypoxia	Restriction of O_2 delivery to the tissue	Diseases like COPD and asthma as well as diseases like heart disease, anemia, and epilepsy	Cyanosis, cognitive neurological disorders like cerebral palsy, cognitive development disorders like periventiculer leukomalasia and hypoxic ischemic encephalopathy	[39], [40]
Hyperoxia	Increase in the concentration of O_2	Excessive or naive oxygen treatment	Retinoplathy of prematurity, oxidation of tissue (in extreme cases)	[41]–[43]

leading and increasing chronic lung disease in children and adults), bronchitis (inflammation of the lining of the bronchial tubes), respiratory distress syndrome (RDS) in premature births, trauma and severe infections, use of sedation drugs, hyperbaric oxygen treatment in intensive care units and certain psychiatric or psychological conditions such as anxiety and claustrophobia [34]. Common complications arising from respiratory distress lead to blood gas abnormalities such as *hypercapnia*, *hypocapnia*, *hypoxaemia*, *hypoxia*, and *hyperoxia* are outlined in Table I.

Hypercapnia, a common post-operative complication that can arise from over-sedation from the use of anesthesia drugs [34], increases the risk of hypertension and vasodilation which causes an increase in cerebral blood flow, increases the risk of hemorrhagic infarction due to intracranial hemorrhage. Hypercapnia also increases the risk of seizures, and cataphora [37], [38]. During the postoperative period, patients with severe hypercapnia are more likely to have seizures, a higher incidence of re-intubation and mechanical ventilation, and a lower prospective Glasgow Coma Scale [46], [47]. Postoperative complications can last for several days [48].

Hypocapnia directly affects cerebral perfusion. Hypocapnia-induced vasoconstriction, or narrowing of the cerebral arterial blood vessels, can lead to decrease of cerebral perfusion and acute symptoms such as dizziness, blackout, muscle cramp, and tetany may occur.

Hypoxemia can result from a wide range of conditions and diseases that impact the volume of air entering the lungs or the absorption of oxygen from the lung parenchyma. Diseases ranging from respiratory conditions like COPD, asthma, emphysema, bronchitis, pneumonia, and respiratory distress syndrome to heart disease, anemia and epilepsy can also cause hypoxemia [39]. Although mild cases of hypoxemia can lead to problems such as headaches and shortness of breath, more severe cases can impede normal brain and heart functions [40]. Hypoxemia can lead to ischemic white matter injury [37], intraventricular hemorrhage (results from a lack of oxygen to the brain), and periventricular leucomalacia in under-mature brains of premature infant which can evolve to cerebral palsy and auditory deficit [38].

Hypoxemia is closely related to another condition, hypoxia, which arises when insufficient oxygen in the blood perfuses to the tissue. Hypoxia can evolve to cyanosis and in extreme cases, leads to necrosis of cells [40].

Hyperoxia and hypocapnea have similar effects in clinical practice. Additionally, for very young infants, hyperoxia increases the risk of rethinopathy of prematurity (ROP), which is a serious and common morbidity in the neonatal intensive care unit (NICU). ROP is the globally leading cause of youth blindness [42]. Hence, it is important to frequently check the fluctuating levels of PaO_2.

COPD is a common lung disease resulting in shortness of breath, frequent coughing or wheezing, and excess mucus production [49]. COPD, which affects approximately 210 million people in the world, costs approximately $30 billion in direct health care costs in the US alone [50], [51]. COPD is a common condition that mainly affects the middle-aged and the elderly who regularly smoke [49], [51]. COPD has no cure, but it can be managed through treatment and accurate health monitoring [52].

Accurate, continuous, noninvasive, and real-time monitoring is an essential, valuable tool in assessing patient health in pediatric wards, pediatric intensive care units (PICUs), and NICUs. Admission to a PICU or NICU, which varies based on gestational age and birth weight, often depends on criteria that vary among hospitals [53]–[55]. Significant criteria beyond age and weight are respiratory issues, seizures, sepsis, maternal drug use, maternal age, or abnormal health status [53]–[55]. Every year in the United States $\sim$300,000 neonates among approximately four million newborns are admitted to the NICU [30], [55], [56]. Premature babies have the highest NICU admission rates ($\sim 70\%$). One percent of premature

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

infants are born with compromised health and require long-term care in the NICU [57].

Respiratory distress syndrome of premature infants is one of the most common reasons for infant admission to the NICU [58]. Another common respiratory issue that leads to the hospitalization of children under the age of two years is bronchiolitis, a viral infection [59] that affects approximately 3% of otherwise healthy infants and requires supportive care and respiratory monitoring [59]. Studies have shown that after successful medical treatment in an NICU, early discharge to a more stable home life could improve the chances of survival for these at-risk infants [3], [30]. Certain unresolved medical conditions, however, could undermine the benefits of an earlier release [3].

Unlike healthy-term infants, discharged premature infants following a lengthy stay have a higher rate of readmission and at times even death within the first year. Although the survival rate of the smallest premature infants has increased substantially over time [3], [56], [60], [61], the rate of neonatal morbidity from such conditions as septicemia, chronic lung disease, ROP, and preventricular leukomalacia still remains high [3], [60], [61]. The ability to remotely monitor these babies could increase the likelihood of early discharge and reduce the risk of undiagnosed issues becoming a health threat after hospital release. For example, it is possible to prevent ROP through frequent monitoring of PaO_2. However, taking frequent blood samples from infants can lead to deep anemia and negatively affecting progression of treatment and can lead to delayed discharge. Continuous remote tracking of vital respiratory parameters in a fully wireless and noninvasive manner could provide relevant and accurate data to the caregiver to inform the course of treatment in an home environment setting [34].

III. Respiration Monitoring Methodologies

This section explores the current common practices and recent technologies in respiration monitoring. A classification and comparison of some popular and emerging respiration monitoring methods is presented in Table II. Respiration monitoring methods can be broadly classified into either non-contact or contact monitoring methods. Similar to motion capture or infrared imaging, non-contact methods do not require any intimate contact with patients. Contact systems such as pulse oximetry or transcutaneous measurements directly interact with patients. Contact methods can be further divided into two sub-groups: invasive and noninvasive. Methods that involve penetration of the skin, such as arterial blood gas analysis via phlebotomy, are invasive. Methods in which the skin is kept intact are noninvasive. In terms of clinical significance, the presented methods are described as either high, low, emerging, or in research phase. High clinical significance indicates wide use in clinical practice. Low indicates occasional use in specific circumstances. Emerging means a method is gaining clinical significance. In research phase means these technologies are undergoing development and may be in clinical trial or pre-clinical trial stage and are not yet used in practice. The technical details of these methods are covered in the following subsections.

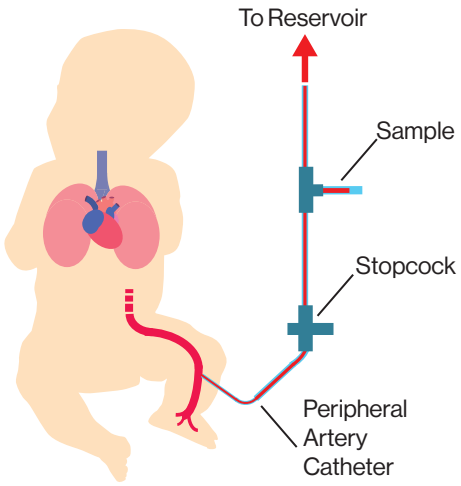

Fig. 2: Peripheral arterial blood gas monitoring.

A. Contact Methods

Contact methods range from invasive blood gas sampling to fairly unobtrusive transcutaneous, end-tidal, and pulse oximetry measurements. A notable advantage of most contact methods over non-contact methods is that they extract blood gas data. Contact methods can be further sub-categorized as invasive and noninvasive as follows.

1) Invasive Contact Methods: Invasive methods involve any procedure that breaks the skin. These methods can accurately assess blood gas concentrations, but only at a single time point. The original method of performing blood gas analysis is blood sampling, the standard by which all other methods are compared [59], [62], [63]. In this method, blood is physically drawn from a patient and tested for oxygen and carbon dioxide. In a solution, as gases behave according to their partial pressures and not their concentrations (Dalton's Law) [64]. Health-care providers measure the partial pressure of blood gases to assess their impact on a patient's physiology.

Blood gas sampling can be done in three ways: arterial blood gas (ABG), venous blood gas (VBG), and capillary blood gas (CBG) analysis. Examples of invasive blood gas sampling are shown in Figures 1e and 1f. Among the three, ABG, is considered the gold-standard for blood gas analysis. The other two methods, VBG and CBG, fail to provide an accurate measure of PaO_2, which is directly related to how well tissues and organs are oxygenated. ABG also assesses the acid-base status and evaluates the efficacy of ventilation [46], [62], [63], [65]. An illustration of a peripheral ABG monitoring system on an infant appears in Fig. 2.

Unfortunately, ABG is an invasive and painful procedure requiring the skills of a professionally trained person [62], [66]. As the procedure is difficult to perform on infants because of their size and low blood volume, placement of the arterial line has a 10-25% rate of failure [67]. Invasive ABG monitoring involves significant risks, including tissue necrosis, nerve damage, thrombus formation, infection, circulatory impairment, and hemorrhage [62], [68]. Moreover, when performed at night, it can disrupt the sleep cycle of patients [69]. Not only is ABG sampling invasive and painful, but it is also a highly selective, momentary account of the potentially varying

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

TABLE II
Classification of Respiration Monitoring Methods

	Contact											
	Invasive			Noninvasive								
Name	Arterial Blood Gas (ABG)	Venous Blood Gas (VBG)	Capillary Blood Gas (CBG)	Transcutaneous CO_2 ($PtcCO_2$)	Transcutaneous O_2 ($PtcO_2$)	Pulse Oximetry (SpO_2)	End-tidal CO_2 ($EtCO_2$)	Electrocardio blue-gram (ECG)	Acoustic	Airflow	Chest Wall Movement
Device	Phlebotomy	Phlebotomy	Phlebotomy	Severinghaus Electrode	Clark Electrode	LEDs and Photodiodes	Colorimetry / Spectroscopy	Electrodes	Microphone on patient	Sensor in / near airway	Electrodes or bands on abdomen
Pros	Accurate measurement of CO_2 and O_2	Accurate measurement of CO_2	Accurate measurement of CO_2	Good estimation of arterial CO_2	Good estimation of arterial O_2	Immediate information, no heating of skin	Identifies apnea, airway obstruction	Cardiac behavior, respiration rate	Does not need external excitation	Determine respiration profile, detect apnea, airway obstruction	Accurate measurement of respiration rate
Cons	Painful, difficult to perform	Painful, inaccurate O_2 measurement, difficult to perform	Painful, inaccurate O_2 measurement, difficult to perform	Heating of the skin, inherent offset	Heating of the skin, inherent offset	Surrogate method, no accurate co-relation outside of limited range	Not very accurate in non-intubated patient	Susceptible to noise, multiple leads necessary	Susceptible to noise, complex to design	Affected by time resolution and distance	Susceptible to motion artifacts, skin irritation
References	[62], [63], [65], [70]	[62], [63], [70]	[62], [63]	[6], [15], [71]–[73]	[6], [35], [73]	[74]–[77]	[37], [78], [79]	[30], [31]	[80], [81]	[20], [82]–[84]	[85]–[90]
Reliability	High for O_2 and CO_2	High for CO_2, Low for O_2	High for CO_2, Low for O_2	High	High	High under certain conditions	High for intubated patients	High for multiple leads	Low	Low	Medium
Precision	High	High	High	High	High	High	Medium	Medium	Low	Low	Medium
Training Required	Advance	Advance	Advance	Advance	Advance	Basic	Advance	Intermediate	Basic	Basic	Basic
Clinical Significance	High	Low	Low	Emerging	Emerging	High under certain conditions	High for intubated patients	High for multiple leads	In research phase	Yes	Yes
Home Care Use	No	No	No	Not feasible	Not feasible	Yes	Not feasible	Yes	Not feasible	Not feasible	Yes
Monitoring duration	Momentary	Momentary	Momentary	Hours	Hours	Days/Weeks	Days/Weeks	Days/Weeks	Days/Weeks	Days/Weeks	Days/Weeks
Accuracy	High	High	High	Medium	Medium	Medium	Medium/Low	Medium	Medium/Low	Medium/Low	High
Comfort	Low	Low	Low	Medium	Medium	Medium/High	Medium/Low	Medium/Low	Medium/High	Medium	Medium
Continuous	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	Noncontact			
Name	Acoustic	Radar	Optical	Thermal
Device	Microphones and speakers in the room	Radar arrays in the room	Camera	IR cameras
Pros	Unobtrusive, monitors respiration and heart rate	Unobtrusive, measure respiration and heart rate	Unobtrusive, can detect breathing patterns	Unobtrusive, monitors respiration rate
Cons	Susceptible to environmental factors	Cannot distinguish between short and deep breaths	Susceptible to lighting, temperature variation, motion artifacts	Susceptible to lighting and motion artifacts, dependent on sensor placement and requires additional calibration
References	[91]	[85], [92], [93]	[45], [94]–[96]	[97], [98]
Reliability	Low	Low	Low	Low
Precision	Low	Low	Low	Low
Training Required	Intermediate	Intermediate	Intermediate	Intermediate
Clinical Significance	In research phase	In research phase	In research phase	In research phase
Home care Use	Yes	Yes	Yes	Yes
Monitoring duration	Days/Weeks	Days/Weeks	Days/Weeks	Days/Weeks
Accuracy	Medium	Medium	Medium	Medium
Comfort	High	High	High	High
Continuous	Yes	Yes	Yes	Yes

Blood Gas Data | Blood Gas and Respiration Rate Data | Respiration Rate Data

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

ventilatory status of critically ill patients [46], [69], a significant drawback of this procedure.

2) Noninvasive Contact Methods: The last two decades has witnessed an innovative shift towards continuous, noninvasive monitoring methods, capable of analyzing oxygen and carbon dioxide measurements continuously and generating real-time data on respiratory changes in patients [62], [63], [65], [70], [99]. These methods use a large variety of sensing mechanisms. A representative selection is discussed in this subsection.

a) Transcutaneous CO_2 Monitoring: A noninvasive technique used for measuring $PaCO_2$ that is growing in popularity is monitoring the transcutaneous partial pressure of carbon dioxide ($PtcCO_2$). $PtcCO_2$ estimates $PaCO_2$ by measuring the gas diffused through the skin. Changes in $PtcCO_2$ can be directly correlated with changes in $PaCO_2$ [46], [100].

$PtcCO_2$ was originally introduced in intensive medical care, particularly for neonates and polio patients [6], [46]. The technique, however, is now used for infants, children, and adults in a wider variety of medical applications. The monitoring of $PtcCO_2$ is especially beneficial in estimating $PaCO_2$ in neonates and children after cardiothoracic surgery [101], in patients at risk of developing post-operative hypercapnia after neurosurgery [102], and in pregnant women at risk of developing hypercapnia during laparoscopic surgery resulting from CO_2 insufflation [103]. $PtcCO_2$ monitoring is used in spontaneously breathing children with respiratory and airway issues such as status asthmatics and croup. It is also used during the treatment of acidosis, which is related to diabetic ketoacidosis [46]. $PtcCO_2$ may also be useful in apnea and other sleep study testing and bronchoscopic examinations [72]. Instead of measuring only the respiratory rate, $PtcCO_2$ monitoring also measures the consequences of abnormal ventilation [45].

Many modern transcutaneous measurement devices use electrochemical sensors to measure gas diffusion through the skin [15]. The Stow-Severinghaus electrode, originally developed in the mid-1950s [6], is the most common electrode for measuring CO_2. This glass electrode, surrounded by a bicarbonate solution and a membrane permeable to CO_2, measures the pH of the bicarbonate solution based on the presence of CO_2 [6]. An illustration of the transcutaneous measurement of the partial pressure of arterial blood gas appears in Fig. 3.

Transcutaneous measurement is further improved by heating the skin to approximately 42°C, which induces local hyperemia (excess of blood) [46], [71]. The heat induces vasodilation of the dermal capillary bed below the sensor, which results in increased arterial blood flow. Vasodilation also facilitates the diffusion of CO_2 [46], [71]. Although applying heat is necessary for the transcutaneous CO_2 measurement to work, the external application of heat has the tendency to alter the solubility of CO_2 in the blood. It also increases the metabolic rate of the tissue by ∼5% for every °C [46], resulting in a $PtcCO_2$ reading that is consistently higher than that of $PaCO_2$. The offset is further affected by local CO_2 production in the epidermal cells [46]. Factors affecting the accuracy of this technique include improper placement, trapped air bubbles, inappropriate calibration techniques, and a damaged membrane [46]. Additionally, proper care should be taken to avoid burning the skin, particularly sensitive neonatal skin [45]. Another concern in the continuous monitoring of $PtcCO_2$ is overnight drift of the $PtcCO_2$ signal [104]. Modern systems, however, are less prone to errors caused by overnight drift [69], [99], [104]. The measurement of $PtcCO_2$ is influenced by skin thickness and temperature, the amount of contact gel, and the state of peripheral perfusion [77].

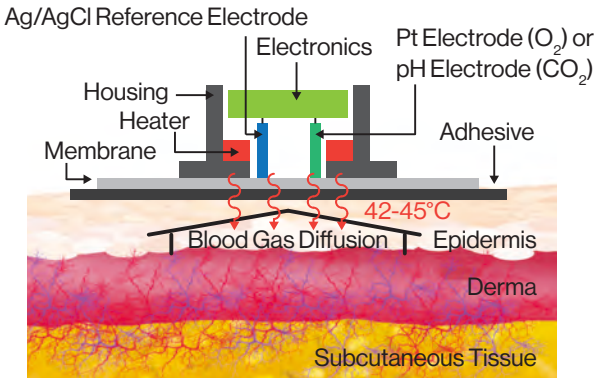

Fig. 3: Transcutaneous measurement of the partial pressure of arterial blood gas.

A rate-based transcutaneous CO_2 monitor was developed in [105]. An illustration of the measurement system is displayed in Fig. 4. The system measures the rate of the diffusion of CO_2 through the skin, which is linearly correlated with the arterial partial pressure of CO_2. This methodology overcomes the limitations of conventional transcutaneous monitors that track the steady-state concentration of gas and require the heating of the skin. The system consists of a sampler chamber, a CO_2 sensor, a four-way valve, and a fan, the latter of which facilitates the circulation of gases through the monitoring system. The sampler chamber is flushed with nitrogen after it has been placed on the skin with light pressure. This ”zeros” the instrument and allows the sensor to measure the rate of change in carbon dioxide. Then the four-way valve is flipped, and CO_2 that diffuses through the skin is recirculated through the sensor unit. Using a single path, the dual wavelength infrared detection system, the sensor unit, measures the CO_2 concentration [106]. The sampler chamber can be sized to fit any patient. Although this system overcomes the heating requirement, it is still too bulky and power hungry for a wireless, wearable device.

b) Transcutaneous O_2 Monitoring: A technique similar to measuring transcutaneous CO_2, can be used to measure the partial pressure of O_2 with the use of Clark electrodes. Clark electrodes, consisting of a platinum cathode covered by an oxygen-permeable membrane, were invented as a means for measuring ambient oxygen concentrations in the blood during cardiac surgery [73]. Later, they were used in a wide range of medical applications. Transcutaneous oxygen is a useful parameter in measurements as it is directly related to the arterial partial pressure of oxygen and overcomes some of the limitations of surrogate methods such as SpO_2 in assessing PaO_2. In addition, $PtcO_2$ has a linear relationship with PaO_2 [108].

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

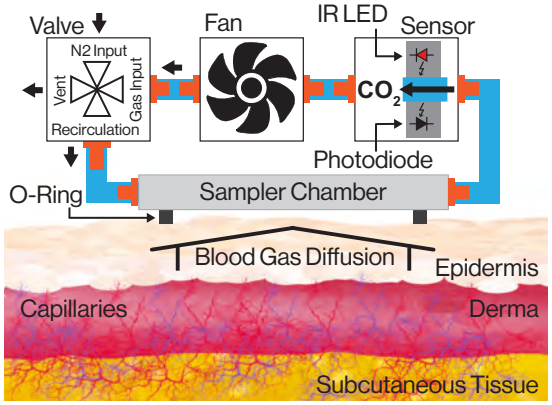

Fig. 4: Rate-based $PtcCO_2$ measurement system, reproduced from [105].

Fig. 5: Sampler heads for the rate-based monitor, reproduced from [105].

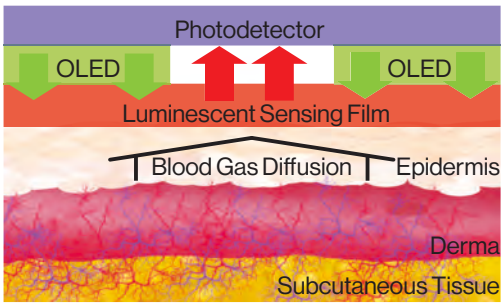

Fig. 6: Fluorescence-based $PtcO_2$ measurement system using organic photodiodes and LEDs, reproduced from [35].

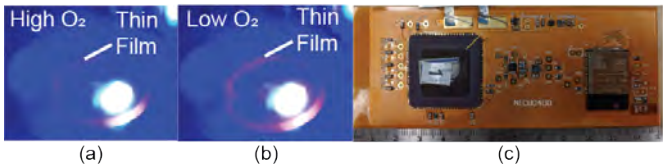

Fig. 7: Changing intensity of the emitted red light of the Pt-porphyrin thin film with a) high and b) low O_2 concentration and c) prototype $PtcO_2$ wearable. Adapted from [107].

Emerging as an effective approach to monitoring transcutaneous oxygen are fluorescence-based oxygen sensors [35], [99], [107]. These systems use a film embedded with a fluorescent dye, typically platinum porphyrin or rubidium. When excited by shorter wavelength light such as blue or green, the films emit a red or orange light. The intensity and lifetime of the emitted light are inversely proportional to the partial pressure of oxygen around the film. This technique is illustrated in Fig. 6. The sensing mode is fluorescent and photo physical instead of photo-chemical, and the sensor consumes no O_2. This technique does not require an electrolytic solution, allowing for a more comfortable dry electrode. Some early experiments suggest this technique may not require a heating element [35], [107], [109].

A $PtcO_2$ sensor using the fluorescence-based method is presented in [110], [111]. These studies show the sensitivity of the platinum porphyrin die to oxygen and its use in conjunction with an optical readout circuit to create an effective oxygen sensor. A custom-integrated analog front end for a $PtcO_2$ sensor is presented in [107] as a prototype low-power design to be used in a medical wearable device. One study in [111] showed that as the fluorescent lifetime of these dies is solely dependent on oxygen concentrations, the time-domain fluorescent lifetime measurements are more robust to changes in the optical path [112]–[114]. Fig. 7a and 7b show the change in the intensity of emitted red light as the concentration of O_2 changes. The wearable prototype of the $PtcO_2$ monitor is shown in Fig. 7c.

c) Pulse Oximetry: Pulse oximetry measures peripheral saturation of oxygen (SpO_2) is a surrogate measurement of SaO_2. As SpO_2 can be correlated with PaO_2 under certain conditions, it provides an alternative way of measuring PaO_2. The relationship between SpO_2 and PaO_2 is described by the oxy-hemoglobin dissociation curve, shown in Fig. 8c. Measurements of SpO_2 and PaO_2 in a healthy person closely agree; from 75 mmHg to 100 mmHg or 95% to 100% saturation. However, SpO_2 is less accurate at assessing PaO_2 at the extremes (hyperoxia and hypoxia events) [74]–[77], [115]. SpO_2 is particularly poor at detecting hyperoxia events, which can be dangerous for some classes of patients, like neonates. Other parameters like temperature and blood pH can shift the dissociation curve [77].

Pulse oximetry involves comparing the photoplethsymograms (PPG), or optically obtained changes in the peripheral tissue, of two wavelengths of light. A transmissive SpO_2 measurement is displayed in Fig. 8a and an illustration of the waveform components is shown in Fig. 8b. In Fig. 8b, AC refers to the time-variant small signal component of the PPG signal generated by the pulsating blood and DC refers to the bias in the signal generated by the tissue and non-pulsating blood. A typical pulse oximeter sensor consists of two light-emitting diodes (LEDs) - red and infrared (IR).

A spectrum relating the extinction coefficient of different hemoglobin types to wavelengths is shown in Fig. 8d. Light travels though the blood vessel or tissue to a photo-detector (PD). The measurement can be transmissive or reflective. In a transmissive measurement, the PD is placed on the opposite side of the finger, the foot, the toe, or the earlobe from the light source. In a reflective measurement, the light source and detector are next to each other, and light can be reflected by bone or other structures to measure the SpO_2 [74]–[77], [115]. As oxygenated hemoglobin (oxyhemoglobin) absorbs more IR than red light at high saturation values, the detection of red light by the PD is more influential than that by the IR. Deoxygenated hemoglobin (reduced hemoglobin), however, absorbs more red light than IR. The PD detects IR better than red light at low saturation values. Saturation levels are thus derived from the ratio of red and IR absorption [116]–[118].

There are other types of hemoglobin that can interfere with SpO_2 measurements and are related to serious conditions. Carboxyyhemoglobin is when carbon monoxide bonds with hemoglobin. In this state, the carbon monoxide can not unbind

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

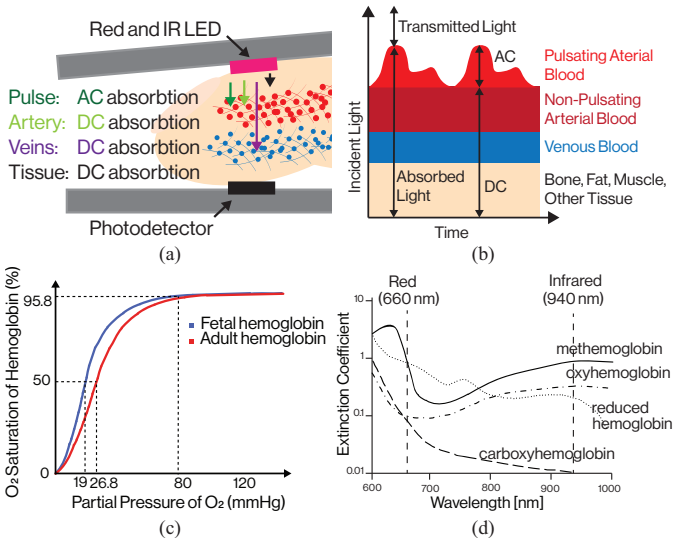

Fig. 8: SpO_2 measurement details (a) transmissive SpO_2, (b) SpO_2 waveform, reproduced from [74], (c) oxy-hemoglobin dissociation curve, reproduced from [119], (d) absorbed light spectra for a variety of hemoglobin types, reproduced from [115].

from the hemoglobin quickly, rendering the hemoglobin unable to oxygenate the tissue. Methemoglobin is when the iron atom in the heme group is in the Fe^{3+} state instead of the Fe^{2+} state. This causes the methemoglobin to be unable to bind to oxygen and carry it to the tissue. Both cases result in poor oxygenation and can be difficult to assess with some pulse oximeters [115].

Easier to use than transcutaneous monitors, SpO_2, a common metric for assessing respiratory health, is often used in conjunction with $PtcCO_2$ or end-tidal carbon dioxide concentration ($EtCO_2$) [77]. The skin, which does not need to be heated, has the ability to provide immediate important information about arterial oxygen saturation. SpO_2 does not measure the concentration of dissolved oxygen in plasma, but instead, measures the proportion of hemoglobin molecules that are loaded with oxygen. One of the important requirements of pulse oximeters is that sensors be carefully placed so that they do not interfere with optical shunts but still maintain adequate pulse pressure. In addition, SpO_2 is affected by motion artifacts, which can lead to false alarms and readings. It also exhibits erroneous readings in those with high skin pigmentation [74]–[77].

Flexible substrates and organic devices are well suited for use in wearable medical devices. An all-organic optoelectronic sensor for pulse oximetry, presented in [74], uses green and red OLEDs in combination with an OPD. Green OLEDs were selected over infrared OLEDs because infrared OLEDs are neither stable in air nor efficient. In addition, the absorptivity of green light in oxygenated and deoxygenated hemoglobin is comparable to that of infrared light [74].

A low-power vitals monitoring system-on-chip (SoC) is presented in [32]. This SoC integrates a PPG sensor, a bioimpedance sensor and an electrocardiogram into a compact and flexible package for continuous physical-logical monitoring. The goal of this device is to provide medical grade signal quality in a compact and disposable form factor. The

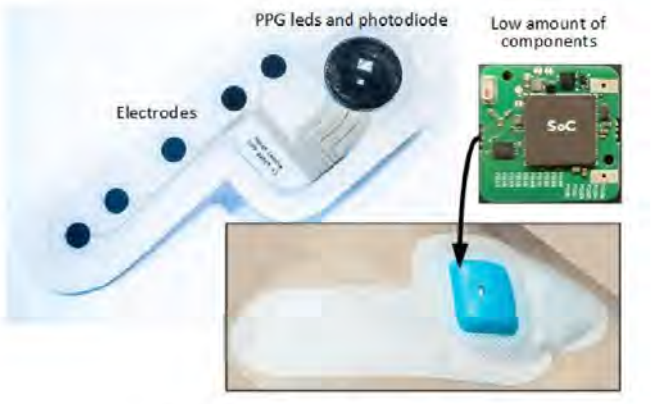

Fig. 9: Vitals monitoring wearable presented in [32].

wearable sensor systems consumes 1 mW of power and can transmit the encrypted patient data securely to a basestation over a Bluetooth Low Energy link. The front-end circuits have each have a dynamic range of approximately 90 dB and on chip digital signal processing The high level of integration in this device make is practical for production and use as a disposable health patch. The prototype of this state-of-the-art wearable is shown in Fig. 9.

d) Electrocardiography-derived Respiration Monitoring: Electrocardiography (ECG) is commonly considered as a tool to access cadiac electrical activity. However, it can also be extended to monitor pulmonary behavior. ECG-derived respiration (EDR) monitoring involves deriving respiration data, such as respiration rate and breathing morphology, from an ECG signal [23], [30], [31]. There is a range of techniques to extract respiration data from an ECG waveform suitable for compact single- or dual-lead wearable ECG devices [23], [30], [31]. Many EDR monitors take advantage of a phenomenon known as respiratory sinus arrhythmia (RSA); respiration modulates the heart rate, shortening the time between peaks during inspiration and lengthening during expiration [31], [120]. However, direct measurement of RSA can have limitations with older patients or active movement [31], [121]. Newer methods like ECG filtering, $R_{amplitude}$ and $RS_{amplitude}$ measurements, and QRS areas have been shown to be more robust [31], [122]. A design challenge for ECG wearables is that these single- or dual-lead systems are susceptible to interference and the sensitive front end is vulnerable to large common-mode currents that can develop in a wearable environment [33].

A multi-mode sensor using a PPG sensor and ECG sensor to measure heart rate, respiration rate, oxygen saturation, heart rate variability and a surrogate of systolic blood pressure is presented in [30]. The system is intended for neonate patients. The sensor system is implemented on two stretchable and flexible patches; one attaches to the chest and the other to the foot. Trials indicate fairly good agreement with gold standard tests and the system is an excellent example of the future of wearable medical devices. An illustration of the wearable system is shown in Fig. 10.

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

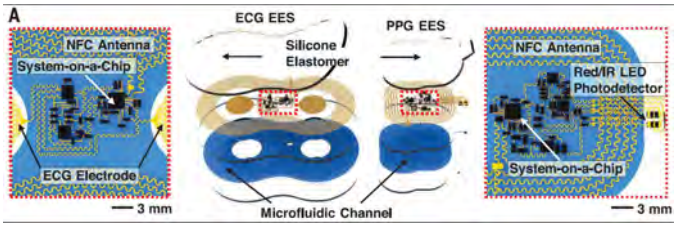

Fig. 10: An illustration of the battery free, wireless module for the ECG and PPG sensors presented in [30]. From left to right, a close up of the ECG readout circuit and communication electronics, an exploded view of the ECG assembly, an exploded view of the PPG assembly, a close up of the PPG readout and communication electronics.

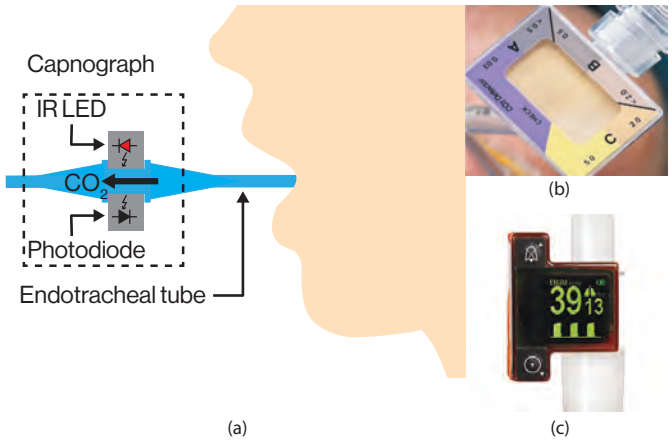

Fig. 11: (a) End-tidal CO_2 with endotracheal intubation, (b) a qualitative colorimetric readout [78], (c) a quantitative readout from an infrared capnograph [123].

e) End-tidal CO_2 Monitoring: Another noninvasive alternate for measuring the partial pressure of arterial CO_2 is $EtCO_2$. End-tidal capnography, illustrated in Fig. 11a with endotracheal intubation, is the measurement of the partial pressure of exhaled carbon dioxide [78]. It is commonly employed when a patient has a cannula and is considered the standard of care wherever endotracheal intubation takes place [46]. Capnographic assessments may be qualitative or quantitative. A qualitative capnographic measurement uses a colorimetric scale (typically litmus paper) to show the approximate range of $EtCO_2$ values, shown in Fig. 11b. A quantitative measurement, typically taken by spectroscopy, provides a more accurate numerical readout of $EtCO_2$ than the colorimetric scale, shown Fig. 11c [78], [79], [124].

The advantage of $EtCO_2$ monitoring is that it identifies apnea or airway obstruction immediately. $EtCO_2$ monitoring is valuable during cardiopulmonary resuscitation, the confirmation of endotracheal tube position, and procedural sedation-analgesia. Since CO_2 readily absorbs IR light, a common working method is to use an IR LED and a PD. The reduction in IR detection confirms the presence of CO_2 in exhaled air [78], [79], [124]. Unfortunately, with non-intubated patients, the accuracy of $EtCO_2$ may be compromised since expired gas by mouth breathing, room air, and oxygen delivered through the ipsilateral nasal cannula may be contaminated. In addition, because of alterations in ventilation-perfusion ratios and patient positioning, the correlation between $PaCO_2$ and $EtCO_2$ can be affected [46]. Other factors that can severely

Fig. 12: Acoustic respiration monitor from Masimo [16].

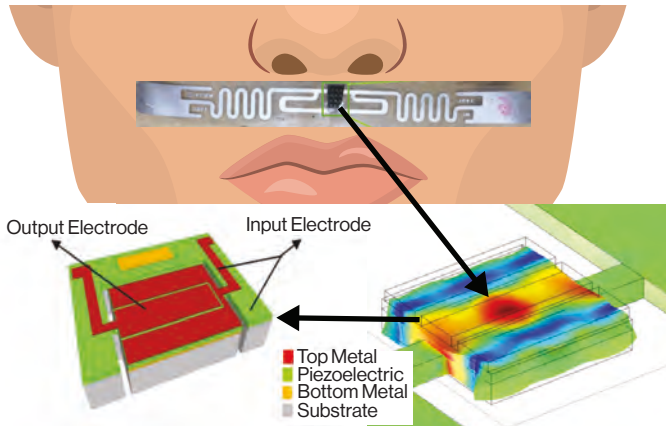

Fig. 13: Piezoelectric flow sensor, reproduced from [20].

reduce the accuracy of $EtCO_2$ are smaller tidal volumes, as seen in infants and children [37], variation in the mechanical ventilation type, and the site of $EtCO_2$ sampling.

f) Acoustic: Another noninvasive technique and a common indicator of respiration quality is sounds from the breath and lungs [80], or acoustic monitoring. Acoustic sensors can be either contact, as in [16], [81] or non-contact, as in [91]. Most acoustic respiration monitors use microphones to record sounds of air moving in and out of a patient's body and common measure respiration by placing a microphone over the trachea, which emits sound directly related to air flow. Breath sounds can also be monitored from the upper abdomen with a stethoscope, common in routine doctor visits. An illustration of a commercial acoustic respiration monitor is shown in Fig. 12.

As many respiratory sounds have unique frequency ranges and waveform shape, which contribute to identifying specific conditions, acoustic monitoring is useful. Acoustic signals from the body provide an accurate assessment of respiration quality without the need for an external excitation signal, as in pulse oximetry and thoracic impedance measurement. Thus, acoustic monitoring is suitable for a low-power wearable sensor [16], [81]. Unfortunately, it is susceptible to noise, such as a patient's speech, environmental vibrations, ambient noise, and internal body sounds. Interference from these sources of noise adds to the complexity of the design [16], [81]. That is, the noise figure drives the detection and alarm algorithm and consequently the complexity of the electronics. A neck-mounted microphone system that measures the turbulence created by breathing is demonstrated in [16] and [81].

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

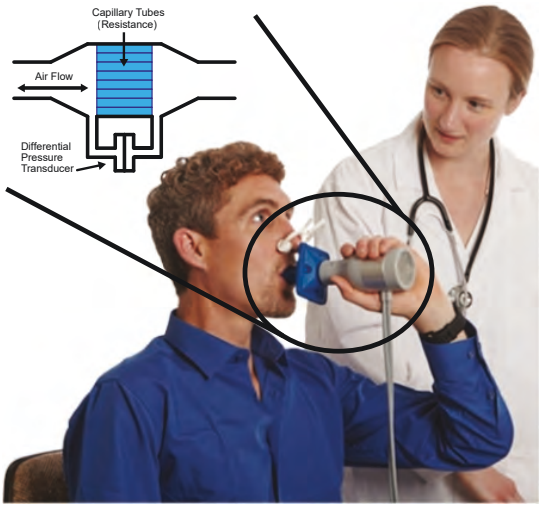

Fig. 14: A simplified schematic of a pneumotachograph. Adapted from [127].

g) Airflow: Sensors measure the flow rate or volume of air inhaled and exhaled respiration. Traditionally, these devices are often included as part of larger mechanical ventilation systems or spirometers for pulmonary function tests [125]. These traditional airflow sensors can be categorized into differential meters, turbine meters, hot wire meters, and optical meters. Nevertheless, many of these airflow measurement systems are not suitable as wearable technology because they are bulky; newer technology such as piezo- and pyroelectric materials, however, are making wireless, wearable airflow meters feasible.

A pneumotachograph is a differential flow meter that uses resistance in the airflow to create a pressure drop for a given flow rate. A drop in pressure can then be measured with a differential pressure sensor. Resistance is typically developed using a bundle of capillary tubes or a series of meshes, as shown in Fig. 14. Although pneumotachographs can measure tidal respiratory relatively accurately, care must be given in their design to avoid excessive resistance or dead space, which can alter normal breathing patterns [126], [127].

Another method for measuring air flow, similar to a pneumotachnograph, is the use of a small turbine in a cylinder. As air moved by respiration turns the turbine, a phototransistor counts the number of revolutions. Since the dimensions of the turbine are known, the volume flow rate can be determined from the number of counts within a certain time frame. While these devices can give accurate measures of respiration rate and effort, they are bulky and require a sealed path from the patients mouth to the sensor (i.e. a mouth piece) and are not suitable for long-term continuous monitoring.

Emerging techniques for air flow monitoring are micro-electromechanical systems (MEMS) and nano-electromechanical systems (NEMS). A thin film piezoelectric on a substrate (TPoS) device that monitors respiration is shown in Fig. 13 [20]. Variation in inhaled and exhaled airflow changes the resonant frequency of the TPoS resonator. A wireless frequency detector measures the shift in order to plot the respiration profile. The efficiency of the device, however, is affected by the distance between the antenna and the body, which are strongly dependent on time resolution.

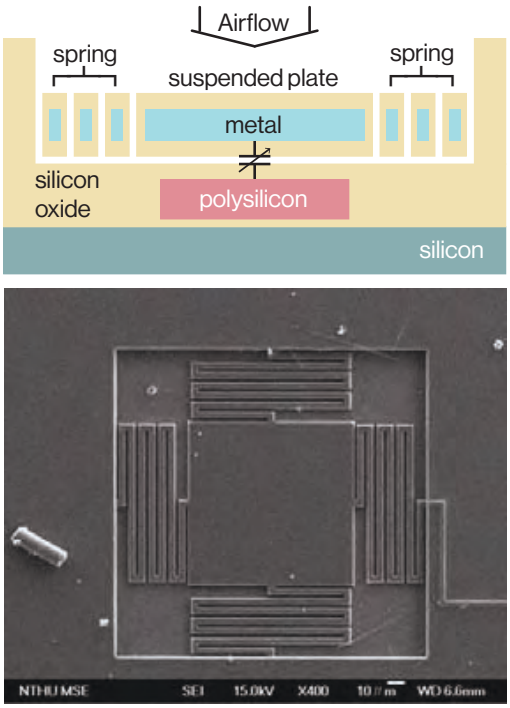

Fig. 15: MEMS capacitive flow sensor, reproduced from [82].

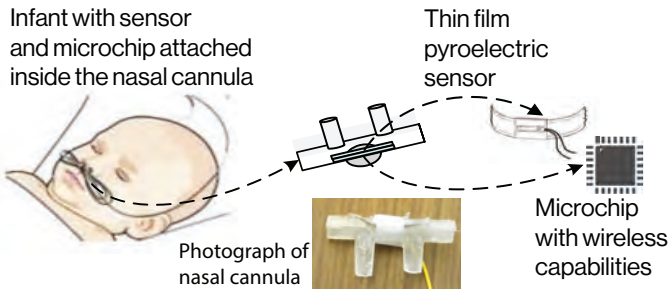

Fig. 16: Pyroelectric airflow sensor in a nasal cannula, reproduced from [128].

Unfortunately, owing to the high cost of fabrication, these types of devices are commercially challenging.

Another type of airflow sensor is the CMOS MEMS capacitive flow sensor, shown in Fig. 15. Airflow from respiration induces a pressure change on the floating plate, resulting in a change in capacitance with respect to the bottom electrode. The change in capacitance is measured to determine the respiration profile. A CMOS MEMS capacitive flow sensor is demonstrated in [82]. After CMOS processing, however, an additional micro-machining process is required, greatly increasing the cost of the system.

Pyroelectric transducers can convert variations in temperature into electrical signals [83]. Since exhaled air is usually warmer than atmospheric air owing to body heat, this transducer, placed near the nose or mouth, detects variation in temperatures caused by breathing [83]. Fig. 16 demonstrates an airflow measurement system with pyroelectric sensors. In a recent study, the authors instrumented the transducer so that it detected apnea in neonatal patients [83], [84], [128] and mounted it in the nasal cannula of a patient. They also simulated apnea in adult volunteers holding their breath. In

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

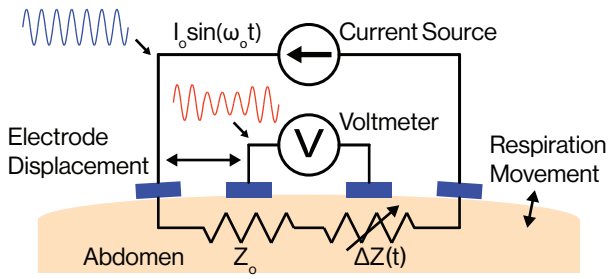

Fig. 17: Chest wall movement bio-impedance measurement, reproduced from [86].

the limited number of tests (20 events), the instrumented pyroelectric sensor successfully detected all events.

A noninvasive, continuous respiratory rate monitoring system is presented in [129]. The respiratory rate is inferred by changes in the heat transfer between the breathing airflow and the temperature sensor placed between the mouth and the nose. The sensor is a lightweight wearable that can stick to the skin between the nose and the upper lip.

The sensor is attached to the skin through a medical-grade adhesive sticker. The dimensions of the sensor are 30 X 16 X 20 mm^3 and weighs approximately 8 grams. The thermal collectors made of copper were installed inside a housing surface facing towards the oral and the nasal airflow. These thermal collectors transfer the heat from exhaled air to the temperature sensors. A change in respiratory rate causes a change in temperature in the copper thermal collectors. This temperature change is detected by a proportional change in the resistance of the thermal sensor. This change in resistance is transformed into electrical signals which are further processed at the base station. The respiration rate is estimated by adding the oral and the nasal signals and employing a mean crossing algorithm, which leads to accurate estimation for both high and low frequencies. While the system was tested with volunteers, future studies need to be conducted with patients in a clinical setting.

h) Chest Wall Movement: The variation in impedance across the skin of the thorax can be used to monitor the respiration quality of a patient. In this method, sometimes referred to as thoracic impedance measurement, electrodes are placed on the thorax, illustrated in Fig. 17. As the volume of gas in the thorax changes, the distance between the electrodes changes, causing the impedance value to change. The change in the signal can be correlated with the respiration rate of the patient. The high frequency of the test signal restricts the current to the outermost layers of the skin, forcing a path along the surface rather than through the epidermis and deeper tissues [85], [86], [88]–[90].

Another way to determine the rate and quality of respiration in a patient is electrical impedance tomography (EIT). EIT uses an array of electrodes around the body part being analyzed, in this case the thorax. The difference in conductivity of the internal tissues of the human body allows an image to be reconstructed based on the electrical signals. As lung tissue has significantly lower conductivity than the other tissue in the abdomen, it produces a high-contrast image [87], allowing the accurate measurement of lung volume and movement.

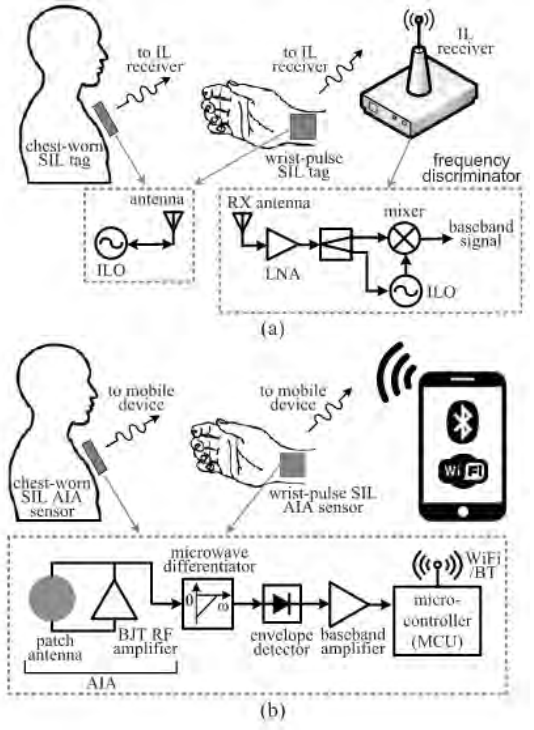

Fig. 18: System diagram of a wearable radar system for measuring chest wall movement from [130].

The drawbacks of these bio-impedance measurements are motion artifacts and skin irritation caused by the electrodes. In addition, the device also requires multiple electrodes for accurate measurements, and electrodes require accurate placement to minimize false alarms.

A wearable antenna system is presented in [130]. Using a small microwave patch antenna, this system measures respiration by taking advantage of the Doppler effect to detect small movements of the chest wall. The system also measures pulse, and its measurements closely agree with those of the pulse oximeter. A system diagram illustrating the operation of the wearable radar system is shown in Fig. 18.

Optoelectronic plethysmography measures chest wall movements using reflective markers placed on the chest. Cameras monitor the motion of the markers, detecting changes in volume resulting from respiration. A single optical fiber chest wall movement sensor is presented in [131]. This method, which takes advantage of the fact that light propagation through a fiber will change after a stain is applied to the fiber, measures chest wall movements. In one study, subjects were measured while lying down, and an optical fiber encapsulated in silicon rubber was placed on the right side of the chest to minimize the influence of the heart beat on the measurement. Reference measurements were made using a pheumotachograph. A system diagram of their experimental setup is shown in Fig. 19. While the fiber optic sensor and the pheumochograph show reasonable agreement, all measurements showed a standard deviation of about 50%. Even when great care was taken in positioning the sensor on the body, the patient's heartbeat and movements significantly impacted the sensor readout.

Another approach to measure chest wall movements is a

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/RBME.2020.3036330, IEEE Reviews in Biomedical Engineering

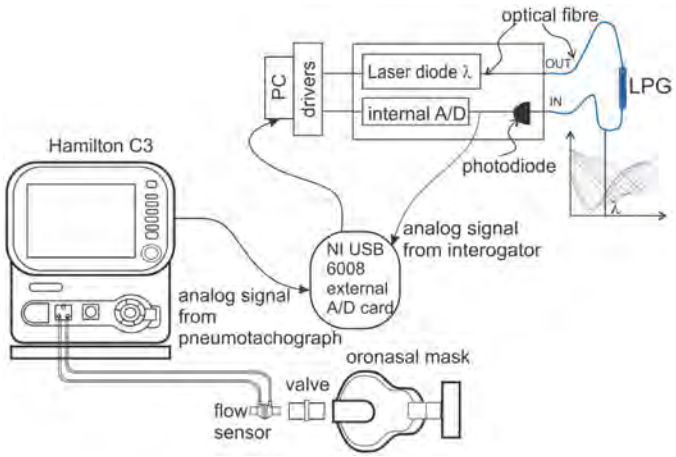

Fig. 19: Optical fiber chest wall movement measurement experiment system from [131].

wearable wireless sensor that senses the variation of the abdominal wall as the person breathes, shown in [132]. The sensing system is based on triboelectric nanogenerators (TENGs). The TENG sensor is built with a polytetrafluoroethylene (PTFE) film which has a thickness of 100 μm. A nylon film, whose thickness is 30 μm, is used as the positive and negative tribo-material. The conductive electrodes are made up of copper with a thickness of 50 μm, while acrylic sheets are used as support structures.

The device is a smart belt with the TENG sensor, used to sense the abdominal circumference of the patient during breathing. The periodic variation is transformed into a repeatable oscillation in the TENG, which outputs an electrical signal corresponding to the respiration information.

B. Non-contact Methods

A non-contact respiration monitoring system does not entail any actual contact between the device and the patient; therefore, it also falls under the category of a noninvasive method, shown in Table II. Non-contact methods include acoustic-based, optical-based, radar-based, and thermal-based systems, which are explained in the following sub-sections.

a) Acoustic: A non-contact acoustic system, demonstrated in [91], takes advantage of Doppler shifts in acoustic signals from exhaled breaths. The exhaled air causes turbulence, triggering ultrasonic signals. Standard microphones and a speaker can be implemented in a simple sonar system in which the speaker transmits a continuous, ultrasonic frequency and the microphone detects disturbances created in the presence of exhaled air. Environmental factors and patient movements, however, can severely affect the accuracy of the acoustic system.

b) Radar: The concept of detecting small physiological movements such as heartbeat and respiration using microwaves dates back to the 1970s [133]. Phase information in received radar signals is detected. Radar physiological sensing has widespread applications such as motion detection based the monitoring of security, searching for survivors under earthquake rubble, and identifying potential abnormalities in sleeping people [134]. A study in [135] uses radar with a frequency-modulated continuous wave (FMCW) to obtain a periodic signal by modulating the frequency of a continuous signal mixed with an echo. The proposed FMCW radar system, mounted to the ceiling above the bed, operates at a frequency of 9-10 GHz. Electromagnetic radio waves with a frequency of 9.5 GHz propagate to the patient, reflect, and return with a time difference of Δt, resulting in a frequency difference between a received and emitted signal. The frequency shift over time (Δf) is used to measure the distance between the patient and the radar. Breathing by the patient changes the amount of energy reflected to the radar and the distance to the patient. The system accurately measures respiratory rate in mechanically ventilated patients. Its accuracy, however, is compromised because of spontaneous breathing.

Ultra-wideband (UWB) radar, presented in [93], is another emerging contact-less method for respiration monitoring. The time and phase delay between the transmitted pulse and the echo can be post-processed to evaluate the patient's breathing patterns. The technique, unfortunately, encodes only phase information; it cannot distinguish between deep and shallow breaths. In addition, exposure to radio frequencies, along with high-power systems, is a concern for neonatal infant care [85], [93]. A study in [92] introduced a non-contact respiration and heart rate monitoring system using Doppler radar and employing a time-domain peak detection algorithm to achieve fast respiration and heart rates, an advantage over earlier frequency domain methods. The results of the study correlate closely with commercial ECGs and respiration bands [92].

A non-contact vital sign monitoring system for use in ambulances was presented in [136]. The system was designed to limit patient exposure to contamination and cross-contamination from catastrophic events, toxic environments, and infectious organisms under bio-chemical hazard conditions. The system consists of two microwave radars: a 10-GHz respiratory monitoring radar positioned 20 cm away from the isolator and a 24-GHz cardiac-monitoring radar positioned just below the stretcher underneath the isolator. While the 10-GHz isolator receives reflected microwaves modulated by the motion of the pulmonary chest wall, the 24-GHz radar monitors reflected microwaves modulated by the dorsal-side cardiac motions of a patient.

c) Optical: Optical-based respiratory monitoring can be used to detect respiration patterns in a noninvasive fashion. A camera is used to detect movement of the chest walls in order to monitor respiration. A study presented in [137] introduces an optical method of simultaneously assessing the heart rate and respiration by measuring chest wall movements, associated with inhalation/exhalation activities of the lungs and by the mechanical pumping of the heart. The study uses a laser Doppler vibrometer (LDVi) pointed towards the left ventral thoracic surface of the patient's heart. The left location on the chest was chosen so that both cardiac and respiratory motions could be detected and measured using a single-point laser. Nevertheless, as the cost of installation and operation of such a unique piece of equipment is prohibitive and it is usable on only bedridden patients, this approach is limited

and not cost-effective for the general medical market.

A study presented in [138] aimed at detecting and measuring the rate and timing parameters of the respiratory cycle of a sleeping baby using video imaging. The study applied a technique that used motion magnification on wavelet decomposition and an elliptic filter to magnify breathing movements that were difficult to observe with the naked eye. The study involved an experiment using a Nikon D5300 DSLR camera with a CMOS focal plane. The camera lens was approximately 1 m away from the baby. The technique successfully measured the respiratory rate remotely, despite the varying positions of the baby and presence of a blanket. The technique, however, produced no real-time measurements.

A high-speed camera can be used to detect movement that can be post-processed and analyzed to monitor respiration. Video photoplethymography can also capture the heart rate, and motion analysis can capture the respiration rate [94], [95]. Furthermore, a fiber-grating vision sensor can be used to project a set of bright spots on a patient [96]. The moving distances of bright spots can be captured using a charge-coupled device camera. Each image can be post-analyzed to monitor respiration. The drawbacks of using this technique are environmental factors such as lighting and temperature variations, which can induce errors in measurements; and the initial cost of implementing the system is high. In addition, motion artifacts can play a crucial role in the accuracy of the system [45], [94].

d) Thermal: Compared to inhaled air, exhaled air contains more CO_2, is significantly warmer, and consists of more humidity. These variations can be detected and the value of respiration rate can be estimated. A study involving 20 children at a local hospital, presented in [139], developed a thermal imaging method that automatically monitored the respiration rate. The technique determined changes in the skin surface temperature on the nose tip and tracked the region. The duration of the thermal video recording was two minutes per child at an image capture rate of 50 frames per second. The captured thermal images were post-processed, filtered, and segmented in order to correctly identify the nasal region. To automatically track and identify the nasal area, the authors developed an algorithm. While the respiration rate values they obtained using this technique were closely correlated with conventional contact-based methods, the method presented a number of issues. The time it took to process the images of each subject was relatively long, approximately 15 minutes. The method identified respiration only through the nose, not through the mouth. In addition, it was not able to handle major head movements.

If an object has a temperature above absolute zero Kelvin (-273.15°C), it emits radiation at a particular rate with a distribution of wavelengths. The wavelength distribution is directly dependent on the object's temperature. The use of special cameras that detect and measure IR thermal radiation is the basis of non-contact respiratory monitoring using thermography imaging. Based on the Debauches wavelet function, continuous wavelet transformation for sensing and detecting breathing signals within an image stream is presented in [140], which examined seven premature infants in an NICU with a median gestational age of 29 weeks. The results of this study showed a clear change in temperature over the infant's nasal region and successfully monitored a 0.3°C to 0.5°C temperature change between the inhaling and exhaling process. Even though the study had a limited number of participants, the preliminary results provided a reasonable basis for the use of this technique. However, the technique involves installation of special cameras for each neonate in the NICU and involves individual post-processing and calibration.

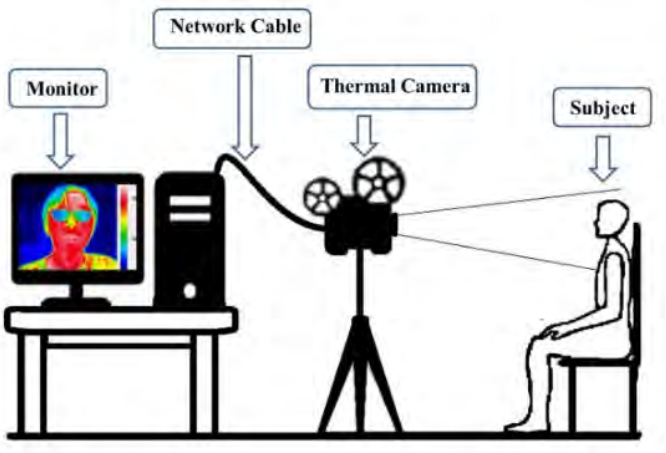

Fig. 20: An illustration of the basic thermal imaging system from [98] to monitor respiration.

A thermal-based sensor can be used to monitor the respiration rate by detecting changes in a patient's temperature caused by respiration [97]. The IR imaging-based respiration monitoring method, combined with feature recognition, has shown to be a robust noninvasive monitoring system [98]. Figure 20 shows the basic setup of the thermal imaging respiration monitoring system. Tracking algorithms follow facial features, which relate to respiration. Features are selected manually from a reference image, usually the first image in the video. The drawback of this non-contact method is that the thermal sensors need to be placed extremely close to the patient's head, and turning the head in another direction could reduce the accuracy of the sensor. Additionally, feature selection has be to manual and requires individual calibration.

IV. Technical Demands and Challenges

While multiple emerging techniques and technologies have shown considerable promise, they also come with multiple challenges such as hardware and software constraints, weight and form factor requirements, available power limitations, encapsulation to name a few. There is also a demand to have a vision beyond the regulatory requirements to improve the end user experience. The details of these demands and challenges and ideas how to overcome them are discussed in the following subsections.

A. Safety, Comfort, and Efficacy

The Food and Drug Administration (FDA) classifies biomedical devices as Class I, II, and III, depending on the amount

of risk, where Class I devices are deemed as lowest risk. The requirements for safety and efficacy should go beyond those that are mandatory by regulatory boards and should also meet the needs of the everyday user.

There is a range of demands associated with the development of wearable respiratory monitoring systems in the age of digital health transformation. These concerns include but are not limited to the following: Wearables must perform with a certain level of accuracy to reduce the rate of false positives or even worse, false negatives, [34], [141]. Although the comfort and wearability of the device are important factors for long-term monitoring, they should not compromise the accuracy of measurements. The device's usage on patients should not cause any additional damage and should have the ability to be work comfortably by all patients [30]. The device should also allow unprovoked and natural patient movement and behavior and it should have the ability to be tolerated by critically ill patients. The device should be user friendly and easy to understand such that it does not require the interpretation or intervention of a medically trained professional. An ideal respiratory wearable should have the capability to detect and indicate the cause of the respiratory issue, leading to prompt corrective actions [34].

B. Standardization

After the development phase, the next challenge will be standardization and regulation. All developers of wearable sensors refer to particular standards specific to their products. The design and testing of wireless medical devices, however, should also adhere to FDA-recognized standards. Major organizations that provide FDA-recognized standards are the Association for the Advancement of Medical Instrumentation (AAMI) [142], the International Organization of Standardization (ISO) [143], the Institute of Electrical and Electronics Engineers (IEEE) [144], the International Electrotechnical Commission (IEC) [145], and the American National Standards Institute (ANSI) [146].

C. Security and Privacy

Privacy and security are particularly difficult given the low power and computation capabilities of wearable, wireless devices. However, privacy and security must be at the forefront of device development in this digital health era. Wearables will accumulate large quantities of personal data, which must be encrypted and minimize the risk of lost and hacked data.

Despite the significant advancements in the designing of wearable technology and the device functionality, very little thought is given to security. Wireless wearables are incredibly vulnerable to privacy and security threats. Moreover, they are known to have highly reduced computing capabilities, storage, area, weight, and power [147]. These limitations also determine the security features that are available for these devices. Yet, they grasp sensitive, private information and need a source of trust as they directly affect the health of the patient.

Work presented in [148] proposed a model of lightweight implementation of data security for wireless next-generation biomedical devices including wearables. The model consists of three layers. The first layer consists of data integrity and mutual authentication, the second layer involves data privacy, and the third layer brings in data confidentiality. Each layer is built on top of another. Wearable wireless devices should deploy protection mechanisms providing, at least, basic security properties, to mitigate and prevent attacks.

D. Next-generation Materials for Wearable Devices

In the past few years, there has been significant progress in making materials and developing packaging techniques suitable for long-term medical wearables [21], [30], [149]. Historically, wearable devices have either been in large bandages with bulky electronics and batteries attached to them, or they were simply a watch or an armband with an electronic device attached to it [32], [150]. New stretchable and flexible substrates and printable electronic circuits have enabled a new wave of devices that are lighter weight and more comfortable [30], [151]. New devices like organic diodes and transistors can be printed on these new flexible substrates, reducing the requirement for traditional rigid electronic components [35], [74]. One of the significant barriers to the wide adoption of these flexible devices is their sensitivity to humidity and temperature [74]. However, many of these concerns are mitigated with proper encapsulation and material choices. Another significant hurdle is forming reliable connections between flexible devices and more rigid components [152].

E. Miniaturization and Power

Miniaturizing accurate measurement methodologies has been a significant hurdle in transforming conventional bulky instruments into smart, wearable devices. For one, as smart, miniaturized, and wearable medical devices should not be tethered to wall outlets or bulky batteries. Therefore a critical challenge that must be addressed is the powering of these next-generation wireless wearable devices.

Powering wearable devices is a key aspect of an effective design. Many groups have proposed different solutions, such as wireless links [30], batteries [32], and super capacitors [153]. Flexible batteries are not yet widely available and multiple wearables such as hearing aids use small coin cells. Semi-rigid lithium polymer cells available, but they are not durable to the stress and the strain of everyday movements. Wireless power links offers a possible solution for patients with limited mobility (bedbound individuals or infants) were the wearable system can be closely linked with a base station [30]. Other energy harvesting techniques may be deployed for wearables in energy-restricted environments.

F. Wireless Communication

Today, there are a range of popular wireless communication protocols, such as Zigbee, Bluetooh, NFC and etc. Designers can choose the protocols that best match their design specifications and target audience. In this subsection, we cover some popular choices seen in commercial devices today.

Zigbee is an open wireless standard that uses the 2.4 GHz (international), 915 MHz (Americas and Australia) and 868 MHz (Europe) industrial, scientific, and medicine (ISM) bands. Zigbee has an operating range of 10-20 m indoors and over 1000 m with clear line-of-sight. Zigbee uses binary phase-shift keying for the lower frequency bands and quadrature phase shift keying for the high frequency international band. The advantage of Zigbee is the flexibility in how its networks can be setup; Zigbee is capable of peer-to-peer, mesh, tree, or star networks. Additionally, it also has a low-power requirement which is advantageous for wearable devices [154].

Bluetooth is another popular wireless communication protocol that is widely used in mobile electronics. It also uses the 2.4 GHz ISM band and uses frequency hopping spread spectrum (FHSS) to enable a robust connection between paired devices (in either a peer-to-peer or a star configuration). Bluetooth typically has a range of 1 m to 10 m indoors. There is ultra-low power version of Bluetooth known as Bluetooth Low Energy (BLE) is targeted at power constrained applications like wearables and IoT devices [154]. However, the FDA warns against using BLE for medical devices due to a security security flaw in the protocol [155].

Short range communication protocols like radio frequency identification (RFID) and near field communication (NFC) are popular as they can be implemented simply with low power and area requirements. Additionally these short range techniques can be inductively coupled with wireless power links [30]. However, a short range of 10 cm to 1 m can be limiting in some applications.

A major concern with wireless communication is power consumption. The deciding factors for the power consumed is the amount of data that needs to be transmitted, the distance of the link, and how often. Zigbee and Bluetooth have shown similar energy consumption in some applications [156]. However, in different applications there can be an order of magnitude difference in power consumption [154]. Zigbee can have an energy per bit of 100nJ/bit to 10 uJ/bit with data rates around 250 kbps. BLE can have an energy per bit ranging from 75 nJ/bit to 200 nJ/bit with data rates up to 1 Mbps. RFID and NFC can range from 50 nJ/bit to 500 nJ/bit width data rates ranging from 400 kbps to 600 kbps [154], [156], [157]. Designers need to consider what type of network they require, along with how much data they need to send, and what type of power source they have available and choose the protocol accordingly.

G. Signal Processing and Artificial Intelligence

As every human body is unique, another challenge is to ensure that each wearable is individually calibrated to achieve a high degree of accuracy. Analysis based on machine learning coupled with personalized calibration, will enable relevant and accurate monitoring of an individual. Also, if the alignment of components (i.e., LEDs and PDs in pulse oximetry) on a wearable is improper, it may lead to inaccurate data measurement and subsequent treatment. Robust design with an ability to tolerate misalignment and human error is required. Wearables need to be capable of operating under various conditions, enabling the independent monitoring of a patient's activities [158]. Another major requirement is the ability to accurately measure parameters in noisy and dynamic environments and transmit them via a wireless communication link over long periods. Artificial intelligence can overcome many of the challenges that wearables face in terms of signal acquisition processing.

Collecting bio-signals from a multitude of patients for long periods has multiple challenges. Sensors need regular and, at times, individual calibrations. Drift in the measured parameters over time can lead to compounding errors. Signal acquisition is also prone to instability in acquisition techniques and the measured signals. Such issues can negatively affect the accuracy of the device. Recent advancements in deep learning algorithms have the potential to enable a trained data set, with a feedback system to enable robust and accurate operation. These new algorithms can considerably reduce false positives and negatives. Integrated algorithms on the wearable device can correct human-to-human variations, long-term drifts, and detect critical features to assist caregivers by providing the highest quality analysis.

V. Conclusion

This article presents a review of contemporary techniques for respiration monitoring, recent developments in methods and devices, and technical challenges associated with each. It aims to provoke thinking about the next generation of respiration monitors for medical use in the context of "smart and connected health." The development of new sensing methods, along with the use of existing techniques, should help health care providers make more accurate and timely predictions promoting a more positive quality of life for patients.

Acknowledgment

The authors would like to thank Dr. Ebru Akar, medical doctor at the Pediatrics Clinic of the Izmir Municipal Hospital, Turkey, for her valuable feedback and advice.

References

[1] H. White, A. Berenson, J. Mannan, H. Feldman, L. Rhein, and RHO Group, "Utilization trends of respiratory medication in premature infants discharged on home oxygen therapy," *Pediatr. Pulmonol.*, vol. 55, no. 4, Apr 2020.

[2] K. I. Mohammed, A. A. Zaidan, B. B. Zaidan, O. S. Albahri, M. A. Alsalem, A. S. Albahri, A. Hadi, and M. Hashim, "Real-Time Remote-Health Monitoring Systems: a Review on Patients Prioritisation for Multiple-Chronic Diseases, Taxonomy Analysis, Concerns and Solution Procedure," *J. Med. Syst.*, vol. 43, no. 7, pp. 223–21, Jun 2019.

[3] K. Bockli, B. Andrews, M. Pellerite, and W. Meadow, "Trends and challenges in United States neonatal intensive care units follow-up clinics," *Journal Of Perinatology*, vol. 34, pp. 71–74, Oct 2013.

[4] J. Mcbride, D. Knight, J. Piper, and G. B. Smith, "Long-term effect of introducing an early warning score on respiratory rate charting on general wards," *Resuscitation*, vol. 65, no. 1, p. 41–44, 2005.

[5] S. R. Braun, *Respiratory Rate and Pattern*, 3rd ed. Butterworths, 1990, p. 226–230.

[6] J. W. Severinghaus, P. Astrup, and J. Murray, "Blood gas analysis and critical care medicine," *American Journal of Respiratory and Critical Care Medicine*, vol. 157, p. S114–S122, Apr 1998.

[7] U. Guler, I. Costanzo, and D. Sen, "Emerging Blood Gas Monitors and How They Can Help with COVID-19," *IEEE Solid-State Circuits Magazine*, vol. 12, no. 4, 2020.

[8] A. Nag, S. C. Mukhopadhyay, and J. Kosel, "Wearable Flexible Sensors: A Review," *IEEE Sensors Journal*, vol. 17, no. 13, pp. 3949–3960, July 2017.

[9] Fitbit, "Fitbit Fitness Tracker," [accessed 15-February-2019]. [Online]. Available: https://www.fitbit.com/home

[10] Hexoskin, "Hexoskin Biometric Shirt," [accessed 15-February-2019]. [Online]. Available: https://www.hexoskin.com/

[11] Garmin, "Garmin fitness tracking," [accessed 15-February-2019]. [Online]. Available: https://buy.garmin.com/en-US/US/cIntoSports-c571-p1.html

[12] M. Haghi, K. Thurow, and R. Stoll, "Wearable devices in medical internet of things: Scientific research and commercially available devices," *Healthcare Informatics Research*, vol. 23, no. 1, pp. 4–15, 2017.

[13] K. M. Miller, A. Y. Kim, M. Yaster, S. R. Kudchadkar, E. White, J. Fackler, and C. L. Monitto, "Long-term tolerability of capnography and respiratory inductance plethysmography for respiratory monitoring in pediatric patients treated with patient-controlled analgesia," *Paediatr. Anaesth.*, vol. 25, no. 10, pp. 1054–1059, Oct 2015.

[14] "Masimo - MightySat Rx," Jul 2020, [Online; accessed 17. Jul. 2020]. [Online]. Available: https://www.masimo.com/products/monitors/spot-check/mightysatrx

[15] SenTec, "Digital Transcutaneous Blood Gas Monitoring," 2018. [Online]. Available: https://www.sentec.com/fileadmin/documents/General_Brochure____EN___RF-007857-b_.pdf

[16] Masimo, "Rainbow Acoustic Monitoring," 2018. [Online]. Available: http://www.masimo.com/siteassets/us/documents/pdf/plm-11467a-brochure-rainbow-acoustic-monitoring-us.pdf

[17] "Arterial Blood Gases (ABG) · Cardiovascular · OSCE Skills · Medistudents," Nov 2020, [Online; accessed 3. Nov. 2020]. [Online]. Available: https://www.medistudents.com/en/learning/osce-skills/cardiovascular/arterial-blood-gases

[18] Global Health Media Project, "Newborn Care Series: Taking a Heel Blood Sample," Jul 2012, [Online; accessed 2. Nov. 2020]. [Online]. Available: https://www.youtube.com/watch?v=MieKJa5YJd4

[19] S. A. Santos, A. Robens, A. Boehm, S. Leonhardt, and D. Teichmann, "System Description and First Application of an FPGA-Based Simultaneous Multi-Frequency Electrical Impedance Tomography," *Sensors (Basel).*, vol. 16, no. 8, Aug 2016.

[20] S. Moradian and R. Abdolvand, "Mems-based passive wireless respiration profile sensor," *2016 IEEE SENSORS Conf.*, pp. 1–3, Oct 2016.

[21] SensiumVitals®, [accessed 31-January-2019]. [Online]. Available: https://www.sensium.co.uk/

[22] Y. A. Bhagat, P. Vcrdon, S. Avuthu, D. Parsons, M. Sussman, G. Wable, and R. Hugeneck, "Like kleenex for wearables: A soft, strong and disposable ECG monitoring system," *2018 IEEE Biomedical Circuits and Systems Conference (BioCAS)*, pp. 1–1, 2018.

[23] I. Tomasic, N. Tomasic, R. Trobec, M. Krpan, and T. Kelava, "Continuous remote monitoring of COPD patients-justification and explanation of the requirements and a survey of the available technologies," *Med. Biol. Eng. Comput.*, vol. 56, no. 4, pp. 547–569, Apr 2018.

[24] T. Watkins, L. Whisman, and P. Booker, "Nursing assessment of continuous vital sign surveillance to improve patient safety on the medical/surgical unit," *J Clin Nurs*, vol. 25, no. 1-2, pp. 278–281, Jan 2016.

[25] J. L. Vincent, S. Einav, R. Pearse, S. Jaber, P. Kranke, F. J. Overdyk, D. K. Whitaker, F. Gordo, A. Dahan, and A. Hoeft, "Improving detection of patient deterioration in the general hospital ward environment," *Eur J Anaesthesiol*, vol. 35, no. 5, pp. 325–333, 05 2018.

[26] M. Hernandez-Silveira, K. Wieczorkowski-Rettinger, S. Ang, and A. Burdett, "Preliminary assessment of the sensiumvitals®: A low-cost wireless solution for patient surveillance in the general wards," *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 4931–4937, 2015.

[27] M. Hernandez-Silveira, K. Ahmed, S.-S. Ang, F. Zandari, T. Mehta, R. Weir, A. Burdett, C. Toumazou, and S. J. Brett, "Assessment of the feasibility of an ultra-low power, wireless digital patch for the continuous ambulatory monitoring of vital signs," *BMJ Open*, vol. 5, no. 5, pp. 1–9, 2015.

[28] A. C. W. Wong *et al.*, "Sensium: An Ultra-Low-Power Wireless Body Sensor Network Platform: Design & Application Challenges," *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 6576–6579, Sep. 2009.

[29] M. A. Hernandez-Silveira, S. S. Ang, and A. Burdett, "Challenges and trade-offs involved in designing embedded algorithms for a low-power wearable wireless monitor," *The 15th International Conference on Biomedical Engineering*, pp. 416–419, 2014.

[30] H. U. Chung *et al.*, "Binodal, wireless epidermal electronic systems with in-sensor analytics for neonatal intensive care," *Science*, vol. 363, no. 6430, pp. 1–12, 2019.

[31] C. Varon, J. Morales, J. Lázaro, M. Orini, M. Deviaene, S. Kontaxis, D. Testelmans, B. Buyse, P. Borzée, L. Sörnmo, P. Laguna, E. Gil, and R. Bailón, "A Comparative Study of ECG-derived Respiration in Ambulatory Monitoring using the Single-lead ECG," *Sci. Rep.*, vol. 10, no. 5704, pp. 1–14, Mar 2020.

[32] S. Song, M. Konijnenburg, R. van Wegberg, J. Xu, H. Ha, W. Sijbers, S. Stanzione, D. Biswas, A. Breeschoten, P. Vis, C. van Liempd, C. van Hoof, and N. van Helleputte, "A 769 w battery-powered single-chip soc with ble for multi-modal vital sign monitoring health patches," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 13, no. 6, pp. 1506–1517, 2019.

[33] Y. Shu, Z. Chen, Y. Lin, S. Wu, W. Huang, A. Y. Chiou, C. Huang, H. Hsieh, F. Liao, T. Zou, and P. Chen, "26.1 a 4.5mm2 multimodal biosensing soc for ppg, ecg, bioz and gsr acquisition in consumer wearable devices," in *2020 IEEE International Solid- State Circuits Conference - (ISSCC)*, 2020, pp. 400–402.

[34] M. Folke, L. Cernerud, M. Ekström, and B. Hök, "Critical review of non-invasive respiratory monitoring in medical care," *Medical & Biological Engineering & Computing*, vol. 41, no. 4, p. 377–383, 2003.

[35] C. J. Lim, S. Lee, J. H. Kim, H. J. Kil, Y. C. Kim, and J. W. Park, "Wearable, luminescent oxygen sensor for transcutaneous oxygen monitoring," *ACS Applied Materials & Interfaces*, vol. 10, no. 48, p. 41026–41034, Jul 2018.

[36] C. H. Ellenbecker, L. Samia, M. J. Cushman, and K. Alster, "Patient Safety and Quality in Home Health Care," in *Patient Safety and Quality: An Evidence-Based Handbook for Nurses*. Agency for Healthcare Research and Quality (US), Apr 2008. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK2631

[37] L. M. L. Dix, L. C. Weeke, L. S. D. Vries, F. Groenendaal, W. Baerts, F. V. Bel, and P. M. A. Lemmers, "Carbon dioxide fluctuations are associated with changes in cerebral oxygenation and electrical activity in infants born preterm," *The Journal of Pediatrics*, vol. 187, pp. 66–72, 2017.

[38] M. Chatterjee *et al.*, "A novel approach toward noninvasive monitoring of transcutaneous CO_2," *Medical Engineering & Physics*, vol. 36, no. 1, pp. 136–139, 2014.

[39] M. Sarkar, N. Niranjan, and P. Banyal, "Mechanisms of hypoxemia," *Lung India*, vol. 34, no. 1, pp. 47–60, Jan 2017.

[40] "Hypoxemia (low blood oxygen)." [Online]. Available: https://my.clevelandclinic.org/health/diseases/17727-hypoxemia

[41] J. L. Cousins, P. A. Wark, and V. M. McDonald, "Acute oxygen therapy: a review of prescribing and delivery practices," *Int. J. Chron. Obstruct. Pulmon. Dis.*, vol. 11, p. 1067, 2016.

[42] S. J. Kim, A. D. Port, R. Swan, J. P. Campbell, R. V. P. Chan, and M. F. Chiang, "Retinopathy of Prematurity: A Review of Risk Factors and their Clinical Significance," *Surv. Ophthalmol.*, vol. 63, no. 5, p. 618, Sep 2018.

[43] D. S. Martin and M. P. W. Grocott, "Oxygen therapy and anaesthesia: too much of a good thing?" *Anaesthesia*, vol. 70, no. 5, pp. 522–527, May 2015.

[44] "Respiratory failure." [Online]. Available: https://www.nhlbi.nih.gov/health-topics/respiratory-failure

[45] F. Al-Khalidi, R. Saatchi, D. Burke, H. Elphick, and S. Tan, "Respiration rate monitoring methods: A review," *Pediatric Pulmonology*, vol. 46, no. 6, p. 523–529, 2011.

[46] J. D. Tobias, "Transcutaneous carbon dioxide monitoring in infants and children," *Pediatric Anesthesia*, vol. 19, no. 5, pp. 434–444, 2009.

[47] A. Amaddeo and B. Fauroux, "Oxygen and carbon dioxide monitoring during sleep," *Paediatric Respiratory Reviews*, vol. 20, pp. 42–44, 2016.

[48] N. Gill, B. Wright, and C. Reilly, "Relationship between hypoxaemic and cardiac ischaemic events in the perioperative period," *British Journal of Anaesthesia*, vol. 68, no. 5, pp. 471–473, 1992.

[49] "Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach," 2007. [Online]. Available: https://www.who.int/gard/publications/GARD_Manual/en/

[50] A. Guarascio, S. Ray, C. K. Finch, and T. H. Self, "The clinical and economic burden of chronic obstructive pulmonary disease in the USA," *ClinicoEconomics and Outcomes Research*, vol. 5, pp. 235–245, 2013.

[51] "Chronic Obstructive Pulmonary Disease (COPD)," Feb 2018. [Online]. Available: https://www.cdc.gov/copd/infographics/copd-costs.html

[52] A. Qaseem *et al.*, "Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease: A Clinical Practice Guideline Update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society," *Annals of Internal Medicine*, vol. 155, no. 3, pp. 179–191, Aug 2011.

[53] K. A. Ziegler, D. A. Paul, M. Hoffman, and R. Locke, "Variation in NICU Admission Rates Without Identifiable Cause," *Hospital Pediatrics*, vol. 6, no. 5, pp. 255–260, 2016.

[54] W. Harrison and D. Goodman, "Epidemiologic trends in neonatal intensive care, 2007-2012," *JAMA Pediatrics*, vol. 169, no. 9, pp. 855–862, 2015.

[55] W. N. Harrison, J. R. Wasserman, and D. C. Goodman, "Regional variation in neonatal intensive care admissions and the relationship to bed supply," *The Journal of Pediatrics*, vol. 192, pp. 73–79, 2018.

[56] J. Martin, B. Hamilton, M. Osterman, A. Driscoll, and P. Drake, "Births: Final Data for 2016," *National Vital Statistics Reports*, vol. 67, no. 1, pp. 1–55, Jan 2018.

[57] C. Ferre, W. Callaghan, C. Olson, A. Sharma, and W. Barfield, "Effects of Maternal Age and Age-Specific Preterm Birth Rates on Overall Preterm Birth Rates — United States, 2007 and 2014," *Morbidity and Mortality Weekly Report*, vol. 65, no. 43, pp. 1181–1184, Nov 2016.

[58] S. Reuter, C. Moser, and M. Baack, "Respiratory distress in the newborn," *Pediatrics in Review*, vol. 35, no. 10, p. 417–429, Oct 2014.

[59] S. Gal *et al.*, "Transcutaneous PCO_2 monitoring in infants hospitalized with viral bronchiolitis," *Eur J Pediatr*, vol. 174, pp. 319–324, 2015.

[60] Committee on Fetus and Newborn, "Hospital discharge of the high-risk neonate," *American Academy of Pediatrics*, vol. 122, no. 5, pp. 1119–1126, Nov 2008.

[61] J. Xu, S. L. Murphy, K. D. Kochanek, B. Bastian, and E. Arias, "Deaths: Final data for 2016," *National Vital Statistics Reports*, vol. 67, no. 5, pp. 1–76, 2018.

[62] A. Goenka, R. Bhoola, and N. McKerrow, "Neonatal blood gas sampling, methods," *South African Journal of Child Health*, vol. 6, no. 1, pp. 1–18, 2012.

[63] R. T. Brouillette and D. H. Waxman, "Evaluation of the newborn's blood gas status," *Clinical Chemistry*, vol. 43, no. 1, pp. 215–221, 1997.

[64] R. N. Pittman, *Chapter 3: The Respiratory System and Oxygen Transport*. Morgan & Claypool Life Sciences, 2011.

[65] S. Awasthi, D. Malviya, and R. Rani, "Peripheral venous blood gas analysis: An alternative to arterial blood gas analysis for initial assessment and resuscitation in emergency and intensive care unit patients," *Anesthesia: Essays and Researches*, vol. 7, no. 3, pp. 355–358, 2013.

[66] S. Ballesteros-Peña, G. V.-D. L. Hoz, and I. Fernández-Aedo, "Pain scores for intravenous cannulation and arterial blood gas test among emergency department patients," *Enfermería Clínica (English Edition)*, vol. 28, no. 6, pp. 359–364, 2018.

[67] R. N. G. B. Tan *et al.*, "Monitoring oxygenation and gas exchange in neonatal intensive care units: current practice in the Netherlands," *Front. Pediatr*, vol. 3, no. 94, pp. 1–5, 2015.

[68] D. Fraser and D. Fraser, *Blood Gas Analysis*. NICU Ink Book Publishers, 2012.

[69] J. H. Storre, F. S. Magnet, M. Dreher, and W. Windisch, "Transcutaneous monitoring as a replacement for arterial PCO_2 monitoring during nocturnal non-invasive ventilation," *Respiratory Medicine*, vol. 105, no. 1, pp. 143–150, 2011.

[70] E. Zeserson *et al.*, "Correlation of Venous Blood Gas and Pulse Oximetry With Arterial Blood Gas in the Undifferentiated Critically Ill Patient," *Journal of Intensive Care Medicine*, vol. 33, no. 3, pp. 176–181, 2018.

[71] S. E. Huttmann, W. Windisch, and J. H. Storre, "Techniques for the measurement and monitoring of carbon dioxide in the blood," *Annals of the American Thoracic Society*, vol. 11, no. 4, pp. 645–652, 2014.

[72] M. Hirabayashi, C. Fujiwara, N. Ohtani, S. Kagawa, and M. Kamide, "Transcutaneous PCO_2 monitors are more accurate than end-tidal PCO_2 monitors," *Journal of Anesthesia*, vol. 23, no. 2, pp. 198–202, 2009.

[73] J. W. Severinghaus, "The invention and development of blood gas analysis apparatus," *Anesthesiology*, vol. 97, no. 1, pp. 253–256, Jul 2002.

[74] C. M. Lochner, Y. Khan, A. Pierre, and A. C. Arias, "All-organic optoelectronic sensor for pulse oximetry," *Nature Communications*, vol. 5, no. 1, pp. 1–7, 2014.

[75] M. Tavakoli, L. Turicchia, and R. Sarpeshkar, "An ultra-low-power pulse oximeter implemented with an energy-efficient transimpedance amplifier," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 4, no. 1, pp. 27–38, Feb 2010.

[76] A. Madan, "Correlation between the levels of SpO_2 and PaO_2," *Lung India*, vol. 34, pp. 307 – 308, 2017.

[77] C. F. Poets, "Pulse oximetry vs transcutaneous monitoring in neonates: practical aspects," Oct 2003. [Online]. Available: https://acutecaretesting.org/-/media/acutecaretesting/files/pdf/pulse-oximetry-vs-transcutaneous-monitoring-in-neonates--practical-aspects.pdf

[78] R. Ortega, C. Connor, S. Kim, R. Djang, and K. Patel, "Monitoring ventilation with capnography," *New England Journal of Medicine*, vol. 367, no. 19, p. e27, 2012.

[79] "Emerging uses of capnography in emergency medicine," 2013. [Online]. Available: http://www.masimo.com/siteassets/us/documents/pdf/lab7849a_whitepaper_emerging_uses_of_capnometry_in_emergency_medicine.pdf

[80] A. Ray, "Auscultation of the respiratory system - some additional points," *Annals of Thoracic Medicine*, vol. 10, no. 4, pp. 296–296, Dec. 2015.

[81] P. Corbishley and E. Rodriguez-Villegas, "Breathing Detection: Towards a Miniaturized, Wearable, Battery-Operated Monitoring System," *IEEE Transactions on Biomedical Engineering*, vol. 55, no. 1, pp. 196–204, Jan 2008.

[82] S. Liao, W. Chen, and M. S. C. Lu, "A CMOS MEMS Capacitive Flow Sensor for Respiratory Monitoring," *IEEE Sensors Journal*, vol. 13, no. 5, pp. 1401–1402, May 2013.

[83] I. Mahbub, M. S. Hasan, S. A. Pullano, F. Quaiyum, C. P. Stephens, S. K. Islam, A. S. Fiorillo, M. S. Gaylord, V. Lorch, and N. Beitel, "A low power wireless apnea detection system based on pyroelectric sensor," *2015 IEEE Topical Conference on Biomedical Wireless Technologies, Networks, and Sensing Systems (BioWireleSS)*, pp. 1–3, Jan 2015.

[84] S. Shamsir, S. H. Hesari, S. K. Islam, I. Mahbub, S. A. Pullano, and A. S. Fiorillo, "Instrumentation of a pyroelectric transducer based respiration monitoring system with wireless telemetry," *2018 IEEE International Instrumentation and Measurement Technology Conference (I2MTC)*, pp. 1–6, May 2018.

[85] S. A. Pullano, I. Mahbub, M. G. Bianco, S. Shamsir, S. K. Islam, M. S. Gaylord, V. Lorch, and A. S. Fiorillo, "Medical devices for pediatric apnea monitoring and therapy: Past and new trends," *IEEE Reviews in Biomedical Engineering*, vol. 10, pp. 199–212, 2017.

[86] W. Lee and S. Cho, "Integrated all electrical pulse wave velocity and respiration sensors using bio-impedance," *IEEE Journal of Solid-State Circuits*, vol. 50, no. 3, pp. 776–785, March 2015.

[87] E. Bahns, *The Breathing Book: Spontaneous breathing during artificial ventilation*. Drager Medical GmbH, 2015.

[88] A. K. Gupta, "Respiration rate measurement based on impedance pneumography," *Texas Instrumentation Application Report*, pp. 1–11, 2011.

[89] S. Kira, Y. Hukushima, S. Kitamura, and A. Ito, "Transthoracic electrical impedance variations associated with respiration," *Journal of Applied Physiology*, vol. 30, no. 6, pp. 820–826, 1971.

[90] A. Barker and B. H. Brown, "Simple impedance pneumograph and volume integrator," *Medical & Biological Engineering*, vol. 11, no. 3, pp. 352–353, 1973.

[91] T. Wang, D. Zhang, L. Wang, Y. Zheng, T. Gu, B. Dorizzi, and X. Zhou, "Contactless respiration monitoring using ultrasound signal with off-the-shelf audio devices," *IEEE Internet of Things Journal*, pp. 1–1, 2018.

[92] X. Yang, G. Sun, and K. Ishibashi, "Non-contact acquisition of respiration and heart rates using doppler radar with time domain peak-detection algorithm," *2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 2847–2850, July 2017.

[93] D. Zito, D. Pepe, M. Mincica, F. Zito, A. Tognetti, A. Lanata, and D. De Rossi, "SoC CMOS UWB Pulse Radar Sensor for Contactless Respiratory Rate Monitoring," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 5, no. 6, pp. 503–510, Dec 2011.

[94] G. Capraro *et al.*, "'no touch' vitals: A pilot study of non-contact vital signs acquisition in exercising volunteers," *2018 IEEE Biomedical Circuits and Systems Conference (BioCAS)*, pp. 1–4, Oct 2018.

[95] P. S. Addison *et al.*, "Video-Based Physiologic Monitoring During an Acute Hypoxic Challenge: Heart Rate, Respiratory Rate, and Oxygen Saturation," *Anesth. Analg.*, vol. 125, no. 3, pp. 860–873, Sept 2017.

[96] H. Aoki *et al.*, "Development of non-restrictive sensing system for sleeping person using fiber grating vision sensor," *MHS2001. Proceedings of 2001 International Symposium on Micromechatronics and Human Science (Cat. No.01TH8583)*, pp. 155–160, Sep. 2001.

[97] C. H. Hsu and J. C. Chow, "Design and Clinical Monitoring of a newly developed non-attached infant apnea monitor," *Biomedical Engineering Applications, Basis & Communications*, vol. 17, no. 3, pp. 126–134, 2005.

[98] Z. Zhu, J. Fei, and I. Pavlidis, "Tracking human breath in infrared imaging," *2005 IEEE Symposium on Bioinformatics and Bioengineering (BIBE)*, pp. 1–6, 2005.

[99] W. van Weteringen, T. G. Goos, T. van Essen, C. Ellenberger, J. Hayoz, R. C. J. de Jonge, I. K. M. Reiss, and P. M. Schumacher, "Novel transcutaneous sensor combining optical tcPO2 and electrochemical tcPCO2 monitoring with reflectance pulse oximetry," *Med. Biol. Eng. Comput.*, vol. 58, no. 2, pp. 239–247, Feb 2020.

[100] B. S. Nassar and G. A. Schmidt, "Estimating Arterial Partial Pressure of Carbon Dioxide in Ventilated Patients: How Valid Are Surrogate Measures?" *Ann Am Thorac Soc*, vol. 14, no. 6, pp. 1005–1014, Jun 2017.

[101] J. D. Tobias *et al.*, "Transcutaneous Monitoring of Carbon Dioxide Tension After Cardiothoracic Surgery in Infants and Children," *Anesth Analg*, vol. 88, no. 3, pp. 531–534, Mar 1999.

[102] K. J. Drummond *et al.*, "Transcutaneous Carbon Dioxide Measurement after Craniotomy in Spontaneously Breathing Patients," *Neurosurgery*, vol. 41, no. 2, pp. 361–365, Aug 1997.

[103] K. Bhavani-Shankar *et al.*, "Transcutaneous PCO_2 monitoring during laparoscopic cholecystectomy in pregnancy," *Can J Anaesth*, vol. 45, no. 2, pp. 164–169, 1998.

[104] S. Aarrestad *et al.*, "Validity of transcutaneous PCO_2 in monitoring chronic hypoventilation treated with non-invasive ventilation," *Respiratory Medicine*, vol. 112, no. 3, pp. 112–118, 2016.

[105] M. Chatterjee, X. Ge, Y. Kostov, P. Luu, L. Tolosa, H. Woo, R. Viscardi, S. Falk, R. Potts, and G. Rao, "A rate-based transcutaneous CO_2 sensor for non invasive respiration monitoring," *Physiological Measurement*, vol. 36, no. 1, pp. 883–894, 2015.

[106] LI-COR, "The LI-820 CO_2 Gas Analyzer," 2009. [Online]. Available: https://www.licor.com/documents/kt3l5jl3b2fcrxcn5zri

[107] I. Costanzo, D. Sen, and U. Guler, "An integrated readout circuit for a transcutaneous oxygen sensing wearable device," in *2020 IEEE Custom Integrated Circuits Conference (CICC)*, Mar 2020, pp. 1–4.

[108] D. C. Hutchison, G. Rocca, and D. Honeybourne, "Estimation of arterial oxygen tension in adult subjects using a transcutaneous electrode," *Thorax*, vol. 36, no. 6, pp. 473–477, Jun 1981.

[109] D. Sen, I. Costanzo, and U. Guler, "Contemporary and nascent techniques for monitoring of oxygenation as a vital sign," in *2020 IEEE 63rd International Midwest Symposium on Circuits and Systems (MWSCAS)*, 2020, pp. 647–650.

[110] I. Costanzo, D. Sen, and U. Guler, "A prototype towards a transcutaneous oxygen sensing wearable," in *2019 IEEE Biomedical Circuits and Systems Conference (BioCAS)*, Oct 2019, pp. 1–4.

[111] I. Costanzo, D. Sen, B. Giri, N. Pratt, P. Rao, and U. Guler, "Fluorescent intensity and lifetime measurement of platinum-porphyrin film for determining the sensitivity of transcutaneous oxygen sensor," in *2020 IEEE International Symposium on Circuits and Systems (ISCAS)*, 2020, pp. 1–5.

[112] M. Quaranta, S. M. Borisov, and I. Klimant, "Indicators for optical oxygen sensors," *Bioanalytical Reviews*, vol. 4, no. 2-4, p. 115, Dec 2012.

[113] C. McDonagh, C. Kolle, A. McEvoy, D. Dowling, A. Cafolla, S. Cullen, and B. MacCraith, "Phase fluorometric dissolved oxygen sensor," *Sensors Actuators B*, vol. 74, pp. 124–30, 2001.

[114] M. Y. Berezin and S. Achilefu, "Fluorescence Lifetime Measurements and Biological Imaging," *Chem. Rev.*, vol. 110, no. 5, p. 2641, May 2010.

[115] A. Jubran, "Pulse oximetry," *Crit Care*, vol. 19, p. 272, Jul 2015.

[116] P. E. Bickler, J. R. Feiner, and J. W. Severinghaus, "Effects of Skin Pigmentation on Pulse Oximeter Accuracy at Low Saturation," *Anesthesiology*, vol. 102, no. 4, pp. 715–719, Apr 2005. [Online]. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1942319

[117] "The Effects of Dark Skin Pigmentation and Low Saturation in Oximetry | Nonin," Aug 2020, [Online; accessed 4. Aug. 2020]. [Online]. Available: https://www.nonin.com/resource/effects-of-skin-pigmentation-in-oximetry

[118] E. D. Chan, M. M. Chan, and M. M. Chan, "Pulse oximetry: Understanding its basic principles facilitates appreciation of its limitations," *Respir. Med.*, vol. 107, no. 6, pp. 789–799, Jun 2013.

[119] J. G. Betts *et al.*, *Transport of Gases*. OpenStax, 2017.

[120] F. Yasuma and J.-i. Hayano, "Respiratory Sinus Arrhythmia: Why Does the Heartbeat Synchronize With Respiratory Rhythm?" *Chest*, vol. 125, no. 2, pp. 683–690, Feb 2004.

[121] A. Schäfer and K. W. Kratky, "Estimation of breathing rate from respiratory sinus arrhythmia: comparison of various methods," *Ann. Biomed. Eng.*, vol. 36, no. 3, pp. 476–485, Mar 2008.

[122] D. Widjaja, J. Taelman, S. Vandeput, M. A. Braeken, R. A. Otte, B. R. Van den Bergh, and S. Van Huffel, "Ecg-derived respiration: Comparison and new measures for respiratory variability," in *2010 Computing in Cardiology*, 2010, pp. 149–152.

[123] Masimo, "Emma^{TM}capnograph," 2017. [Online]. Available: http://www.masimo.com/siteassets/us/documents/pdf/plm-10642a_product_information_emma_capnograph_us.pdf

[124] L. Rhein, C. Greco, and K. Matthes, *Measures of Carbon Dioxide*. Cambridge University Press, 2018, p. 38–44.

[125] F. Montecchia, S. Luciani, R. Cicchetti, R. Grossi, F. Midulla, C. Moretti, and P. Papoff, "Pharyngeal and esophageal pressure measurements to evaluate respiratory mechanics in infants on high flow nasal cannula: A feasibility study," in *2015 IEEE International Symposium on Medical Measurements and Applications (MeMeA) Proceedings*, May 2015, pp. 234–239.

[126] C. M. A. Reinaux, A. Aliverti, L. G. M. d. Silva, R. J. d. Silva, J. N. Gonçalves, J. B. Noronha, J. E. C. Filho, A. D. d. Andrade, and M. C. d. A. Britto, "Tidal volume measurements in infants: Opto-electronic plethysmography versus pneumotachograph," *Pediatric Pulmonology*, vol. 51, no. 8, pp. 850–857, 2016.

[127] "Vitalograph - The Fleisch Pneumotachograph," Aug 2020, [Online; accessed 15. Aug. 2020]. [Online]. Available: https://vitalograph.com/education/fleisch

[128] I. Mahbub, T. Oh, S. Shamsir, S. K. Islam, S. A. Pullano, and A. S. Fiorillo, "Design of a pyroelectric charge amplifier and a piezoelectric energy harvester for a novel non-invasive wearable and self-powered respiratory monitoring system," *2017 IEEE Region 10 Humanitarian Technology Conference (R10-HTC)*, pp. 105–108, Dec 2017.

[129] H. E. Hurtado *et al.*, "Non-invasive continuous respiratory monitoring using temperature-based sensor," *Journal of Clinical Monitoring and Computing*, vol. 34, pp. 223–231, 2019.

[130] C. Tseng, L. Yu, J. Huang, and C. Chang, "A wearable self-injection-locked sensor with active integrated antenna and differentiator-based envelope detector for vital-sign detection from chest wall and wrist," *IEEE Transactions on Microwave Theory and Techniques*, vol. 66, no. 5, pp. 2511–2521, May 2018.

[131] M. D. Ivanovic, J. Petrovic, A. Savi?, G. Gligoric, M. Mileti?, M. Vukcevic, B. Bojovic, L. Hadzievski, T. Allsop, and D. J. Webb, "Real-time chest-wall-motion tracking by a single optical fibre grating: a prospective method for ventilator triggering," *Physiol Meas*, vol. 39, no. 4, p. 045009, 04 2018.

[132] Z. Z *et al.*, "A Portable Triboelectric Nanogenerator for Real-Time Respiration Monitoring," *Nanoscale Res Lett*, vol. 14, no. 354, pp. 1–11, 2019.

[133] J. C. Lin, "Noninvasive microwave measurement of respiration," *Proceedings of the IEEE*, vol. 63, no. 10, pp. 1530–1530, Oct 1975.

[134] C. Gu and C. Li, "From tumor targeting to speech monitoring: Accurate respiratory monitoring using medical continuous-wave radar sensors," *IEEE Microwave Magazine*, vol. 15, no. 4, pp. 66–76, June 2014.

[135] K. Loon *et al.*, "Wireless non-invasive continuous respiratory monitoring with FMCW radar," *J Clin Monit Comput*, vol. 30, pp. 797–805, September 2016.

[136] S. Suzuki, T. Matsui, H. Kawahara, H. Ichiki, J. Shimizu, Y. Kondo, S. Gotoh, H. Yura, B. Takase, and M. Ishihara, "A non-contact vital sign monitoring system for ambulances using dual-frequency mocrowave radars," *Med Biol Eng Comput*, vol. 47, pp. 101–105, 2009.

[137] P. Marchionni, L. Scalise, I. Ercoli, and E. P. Tomasini, "An optical measurement method for the simultaneous assessment of respiration and heart rates in preterm infants," *Review of Scientific Instruments*, vol. 84, no. 12, p. 121705, 2013.

[138] A. Al-Naji and J. Chahl, "Remote respiratory monitoring system based on developing motion magnification technique," *Biomedical Signal Processing and Control*, vol. 29, pp. 1 – 10, 2016. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1746809416300441

[139] F. AL-Khalidi *et al.*, "An Evaluation of Thermal Imaging Based Respiration Rate Monitoring in Children," *American Journal of Engineering and Applied Sciences*, vol. 4, no. 4, pp. 586–597, 2011.

[140] A. Abbas *et al.*, "Neonatal non-contact respiratory monitoring based on real-time infrared thermography," *BioMed Eng OnLine*, vol. 93, no. 10, pp. 1–17, October 2011.

[141] P. J. Soh, G. A. E. Vandenbosch, M. Mercuri, and D. M. M. . Schreurs, "Wearable Wireless Health Monitoring: Current Developments, Challenges, and Future Trends," *IEEE Microwave Magazine*, vol. 16, no. 4, pp. 55–70, May 2015.

[142] AAMI (Assoc. Adv. Med. Instrum.), [accessed 17-January-2019]. [Online]. Available: http://www.aami.org

[143] ISO (Intl. Org. Stand.), [accessed 17-January-2019]. [Online]. Available: http://www.iso.org/iso/home.html

[144] IEEE Stand. Assoc., [accessed 17-January-2019]. [Online]. Available: http://standards.ieee.org

[145] IEC (Intl. Electrotech. Comm.), [accessed 17-January-2019]. [Online]. Available: http://www.iec.ch
[146] ANSI (Am. Natl. Stand. Inst.), [accessed 17-January-2019]. [Online]. Available: http://ansi.org
[147] P. A. Williams and V. McCauley, "Always connected: The security challenges of the healthcare internet of things," in *2016 IEEE 3rd World Forum on Internet of Things (WF-IoT)*. IEEE, 2016, pp. 30–35.
[148] P. S. Vladimir Vakhter, Betul Soysal and U. Guler, "Minimum on-the-node data security for the next-generation miniaturized wireless biomedical devices," in *2020 IEEE International Midwest Symposium on Circuits and Systems (MWSCAS*. IEEE, 2020.
[149] J. Kim *et al.*, "Advanced materials for printed wearable electrochemical devices: A review," *Advanced Electronic Materials*, vol. 3, no. 1, p. 1600260, 2017. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/aelm.201600260
[150] R. G. Haahr, S. Duun, E. V. Thomsen, K. Hoppe, and J. Branebjerg, "A wearable "electronic patch" for wireless continuous monitoring of chronically diseased patients," in *2008 5th International Summer School and Symposium on Medical Devices and Biosensors*, 2008, pp. 66–70.
[151] H. Kim, Y.-S. Kim, M. Mahmood, S. Kwon, N. Zavanelli, H. S. Kim, Y. S. Rim, F. Epps, and W.-H. Yeo, "Fully integrated, stretchable, wireless skin-conformal bioelectronics for continuous stress monitoring in daily life," *Advanced Science*, vol. 7, no. 15, p. 2000810, 2020. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/advs.202000810
[152] e. a. Lall, Pradeep, "Folding-reliability of flexible electronics in wearable applications." *Proceedings of the ASME 2019 International Technical Conference and Exhibition on Packaging and Integration of Electronic and Photonic Microsystems. ASME 2019 International Technical Conference and Exhibition on Packaging and Integration of Electronic and Photonic Microsystems.*, 2019.
[153] Y. Zheng, Y. Yang, S. Chen, and Q. Yuan, "Smart, stretchable and wearable supercapacitors: prospects and challenges," *CrystEngComm*, vol. 18, no. 23, pp. 4218–4235, Jun 2016.
[154] S. Mujumder, T. Mondal, and M. J. Deen, "Wearable Sensors for Remote Health Monitoring," *Sensors*, vol. 17, no. 1, pp. 1–45, 2017.
[155] "FDA Informs Patients, Providers and Manufacturers About Potential Cybersecurity Vulnerabilities in Certain Medical Devices with Bluetooth Low Energy," Mar 2020, [Online; accessed 19. Aug. 2020]. [Online]. Available: https://www.fda.gov/news-events/press-announcements/fda-informs-patients-providers-and-manufacturers-about-potential-cybersecurity-vulnerabilities-0
[156] C. Del-Valle-Soto, L. J. Valdivia, R. Velázquez, L. Rizo-Dominguez, and J.-C. López-Pimentel, "Smart Campus: An Experimental Performance Comparison of Collaborative and Cooperative Schemes for Wireless Sensor Network," *Energies*, vol. 12, no. 16, p. 3135, Aug 2019.
[157] P. Mannion, "Comparing Low Power Wireless Technologies (Part 2)," *Digi-Key's North American Editors*, Dec 2017. [Online]. Available: https://www.digikey.com/en/articles/comparing-low-power-wireless-technologies-part-2
[158] H. C. Koydemir and A. Ozcan, "Wearable and Implantable Sensors for Biomedical Applications," *Annual Review of Analytical Chemistry*, vol. 11, no. 1, pp. 127–146, 2018.

Ian Costanzo received his B.Sc. degree in Mechanical Engineering, with a minor in Electrical Engineering from Worcester Polytechnic Institute (WPI), Worcester, Massachusetts in 2015. He received his M.S. degree in Electrical Engineering in 2017, also from WPI. He is currently a Ph.D. candidate in the New England Center for Analog and Mixed Signal IC Design (NECAMSID) and the Integrated Circuits and Systems Lab (ICAS). Ian's research interests cover a broad range of circuits and systems, from kW RF subsystems to mW data converters. During his Master's, Ian worked on solid-state, high-power RF matching networks and RF amplifiers for semiconductor processing applications. His Ph.D. research focuses analog and mixed-signal design for a wearable wireless sensor patch for monitoring of respiratory functions in premature infants.

Devdip Sen received the B.E. degree in Electronics Engineering from the University of Mumbai, Mumbai, India, in 2015, and the M.S. degree in Electrical and Computer Engineering from Worcester Polytechnic Institute, Worcester, MA, USA in 2017. He is currently a Ph.D. candidate in the New England Center for Analog and Mixed-Signal IC Design (NECAMSID) and the Integrated Circuits and Systems (ICAS) lab at Worcester Polytechnic Institute. His research interests include biomedical sensors and instrumentation, low power analog/mixed-signal circuits systems, and low power data converters. His Ph.D. research includes development of wearable wireless sensors for monitoring of respiratory functions in premature infants and wearable, wireless alert systems that would prevent painful pressure ulcers (bedsores). He serves as a reviewer for the American Society for Engineering Education (ASEE), various IEEE conferences such as ISCAS, BioCAS, MWSCAS, and the IEEE Transactions on Biomedical Circuits and Systems.

Lawrence Rhein, MD, MPH Lawrence Rhein received his B.S. degree in Biology from Harvard University, Cambridge, MA, USA in 1992; his M.D. from the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA in 1996, and his MPH degree from Harvard University School of Public Health, Boston, MA, USA in 2015. He did his residency in Pediatrics at the Boston Children's Hospital. He is dual board-certified in Newborn Medicine and Pediatric Pulmonology. He is an associate professor at the UMass Medical School and the Department Chair of Pediatrics at UMass Memorial Medical Center (UMMMC) and the Chief of the Division of Neonatology. Additionally, he is the Director of the Center for Healthy Infant Lung Development (CHILD Clinic) at UMMMC, and his research interests include chronic lung disease of prematurity and long-term outcomes of preterm infants.

Ulkuhan Guler Ulkuhan Guler received the B.Sc. degree in Electronics and Telecommunication Engineering from the Istanbul Technical University, Istanbul, Turkey, the M.E degree, in Electronics Engineering from the University of Tokyo, Tokyo, Japan, and the Ph.D. degree in Bogazici University, Istanbul, Turkey. She worked at the National Research Institute of Electronics and Cryptology, TUBITAK, Turkey from 2006 until 2015 as a principal design engineer. In 2015, she joined Georgia Institute of Technology as a post-doc research fellow. In August 2018, she joined Worcester Polytechnic Institute (WPI) where she is currently working as an Assistant Professor in the department of Electrical and Computer Engineering. She is the founding director of the Integrated Circuits and Systems (ICAS) Lab at WPI. Her research interests lie in the area of circuits and systems, with a focus on analog/mixed-signal integrated circuits for sensing interfaces, bioelectronics, and security for healthcare applications. Particularly, she is interested in developing wearable and implantable biomedical devices. Dr. Guler is a senior member of IEEE and serves as a reviewer and committee member in various societies including Circuits and Systems, Biomedical Circuits and Systems, and Solid-State Circuits. She has also served as a panel member for the National Science Foundation (NSF) and the European Research Council (ERC).