Breathing Pattern and PCO_2 Analysis for Diagnosing Asthma

Sophia Benkirane
Department of Bioengnineering (University of Calforina, San Diego)
La Jolla, USA
sbenkirane@ucsd.edu

Sameera Chandrasekhar
Department of Bioengnineering (University of Calforina, San Diego)
La Jolla, USA
sachandrasekhar@ucsd.edu

Li Gong
Department of Bioengnineering (University of Calforina, San Diego)
La Jolla, USA
l3gong@ucsd.edu

Sharfa Pital
Department of Electrical and Computer Engineering (University of Calforina, San Diego)
La Jolla, USA
spital@ucsd.edu

Shubham Singh
Department of Bioengnineering (University of Calforina, San Diego)
La Jolla, USA
shs008@ucsd.edu

***Abstract*—There is no gold standard for the diagnosis of asthma. As a result, asthma is frequently under and over diagnosed. To reduce the likelihood of misdiagnosis, we propose a dual-diagnostic system for asthma consisting of a Severinghaus electrode to be used in conjunction with a strain gauge, to best inform clinicians in making a diagnosis. The Severinghaus electrode measures the partial pressure of CO_2 (pCO_2) in the patient's blood sample, which if lower than an acceptable range, is indicative of hyperventilation, a symptom of asthma. As pCO_2 levels are not determinant of asthma, we complement this metabolic test with a neuromuscular assessment of breathing pattern using a strain gauge. A strain gauge worn around the patient's chest is sensitive to subtle, abnormal changes in pressure exerted by the torso that are characteristic of hyperventilation or irregular breathing. In the model that we propose, the voltage signal transduced from the pressure exerted on the gauge passes through a comparator which generates a square wave pattern of the patients' breathing that will be analyzed for irregular breathing patterns that are associated with asthma. In this study we will model and simulate a circuit in LTspice to show how our strain gauge system can be implemented to give a more accurate diagnosis of asthma.**

I. Introduction

Asthma is a widespread chronic respiratory condition associated with overbreathing [1]. Despite advancement in technology, the current estimates suggest that as high as 73% of true asthma patients go undiagnosed because there is no golden standard to diagnose asthma [2]. An effective diagnosis of asthma requires evaluation of a broad range of symptoms. Given the need for a maximally informed diagnosis of asthma, a bioinstrument that can characterize asthma symptoms would result in accurate identifications, leading to improved patient care. To do this, we propose a dual-verification complimentary system that is capable of identifying breathing patterns and pCO_2 analysis in order to accurately diagnose asthma. For these functions, we utilize two instrumentations: a ***Severinghaus Electrode*** that measures pCO_2 levels and a ***Strain Gauge/Comparator*** System that outputs voltage of breathing pattern.

A. Severinghaus Electrode

Asthma is a disorder associated with overbreathing, which results in an excessive loss of CO_2 [3]. The body's attempt to reduce CO_2 loss results in secreting mucus that blocks airways [3]. In respiratory medicine it is common to measure arterial CO_2 for conditions such as hyperventilation, and a Severinghaus electrode is one way to measure CO_2 concentration [4]. The arterial partial pressure of CO_2 (pCO_2) controls how many liters of air is exchanged in the lungs per minute [5].

$$P_aCO_2 = K \times \frac{VCO_2}{V_e - V_d} \quad (1)$$

Where VCO_2 is the rate of CO_2 production, V_e is the minute ventilation and V_d is the dead space, or the volume of ventilated air that does not participate in gas exchange. If minute ventilation increases, P_aCO_2 is expected to decrease assuming VCO_2 and V_d stay constant.

A Severinghaus electrode measures blood CO_2 levels through the use of a pH meter. Dissolved CO_2 reacts with water to form carbonic acid (H_2CO_3) which dissociates, giving rise to a surplus of H^+ ions. PH is a measure of the concentration of H^+ concentration.

$$CO_2(aq) + H_2O(l) \rightarrow H_2CO_3(aq) \rightarrow H^+(aq) + HCO_3^-(aq) \quad (2)$$

The Severinghaus electrode has two compartments, the sample chamber and the chamber with the electrodes separated by a membrane permeable to only CO_2 [6]. The Severinghaus electrode measures the pH as a voltage, which can be used to find pCO_2. One way to diagnose asthma is by comparing patients' pCO_2 obtained from the Severinghaus electrode to healthy pCO_2 values from medical data. The normal pCO_2 range is from 35 to 45 mmHg, and asthma patients have pCO_2 values that are below normal [5].

B. Strain Gauge/Comparator System

Since pCO_2 values may be inconclusive in diagnosing asthma, we propose a second test be conducted to confirm the patient's diagnosis. A strain gauge and comparator system is designed to detect the patient's breathing patterns. A strain gauge is a sensor that is highly sensitive to changes in displacements, which will be advantageous to detect small changes in breathing [7]. The strain gauge will be worn by the patient around their chest. The movement in the chest as a result of breathing in and out will be detected by the strain gauge. The resulting measured movement, a sine wave, will pass through a series of components like an op-amp voltage buffer, high-pass filter, and inverting hysteretic comparator to be translated into a square wave. The frequency and duration of the trigger of the square wave will be analyzed to determine if the patient is experiencing hyperventilation or irregular breathing. If a patient exhibits irregular breathing through the strain gauge system coupled with low pCO_2 levels, a strong asthma diagnosis can be given due to the reduced risk of under or over diagnosing asthma since a dual diagnostic system is being employed.

II. Methods: Severinghouse Electrode

A. Assumptions

VCO_2 and V_d stay constant. Changes to these variables are indicative of other conditions. V_d or dead space can increase with airway obstruction [8].

B. Overall Sensor Design

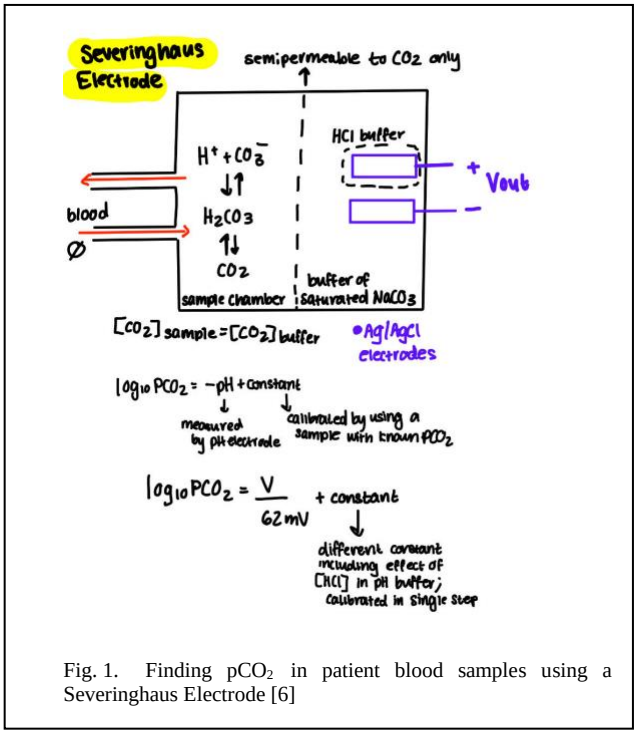


Fig. 1. Finding pCO_2 in patient blood samples using a Severinghaus Electrode [6]

C. Overall Sensor Design

In a Severinghaus electrode, the concentration of CO_2 is equalized in both chambers. Both the sample chamber and the chamber with the electrodes have the following chemical reaction taking place:

$$H^+ + CO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 \quad (3)$$

Two relevant equations relate pH and $\log10pCO_{2,\text{ and}}$ output voltage and $\log10pCO_2$:

$$\log10pCO_2 = -pH + \text{constant} \quad (4)$$

(constant calibrated by using a sample with known pCO_2) [6].

$$\log10pCO_2 = V_{out}/62\ \text{mV} + \text{constant} \quad (5)$$

(a different constant that includes the effect of HCl in the buffer, and can be found from calibration in a single step) [6]. From these equations, output voltage or pH can be used to determine $\log10pCO_2$, which can then be used to find pCO_2, and below than average values can be used to help diagnose asthma.

III. Methods: Strain/Comparator System

A. Assumptions

In our model we are assuming all active circuit components are ideal, and that the elastic band strains proportionally to the change in pressure exerted outwardly by the torso during breathing. We further assume nominal resistance of the strain gauge and minimal effect of variance of environmental conditions such as humidity and temperature.

For our simulation, we assume a regular respiratory rate to be between 12-20 breaths per minute, about 0.2-0.33 Hz and strain from a normal breathing pattern to be characterized by a roughly sinusoidal waveform. As such, we model the breathing detected by the strain gauge using a voltage input as a constant sine wave of between 0.2 and 0.33 Hz. The input voltage wave is assumed to have no noise, despite components like the high-pass filter being able to attenuate noise.

B. Simulation Design

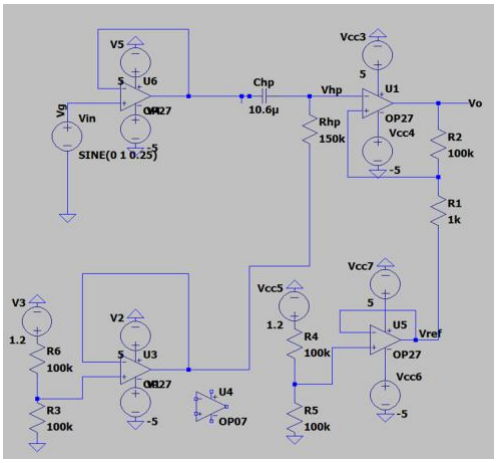
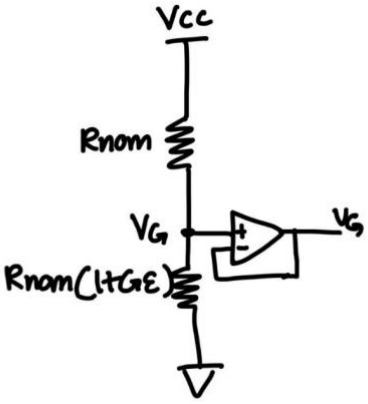


Fig. 2. Simulated circuit in LTSpice. The input sine wave represents normal breathing of a person not having asthma.

C. Design Aims

Assuming nominal resistance of strain gauge and minimal effect from variance of environmental conditions, the strain gauge is designed to maximize sensitivity for very small displacements. As the resistance of the strain gauge changes, the value for V_G changes as well.



D. Equations

Voltage division across the strain gauge

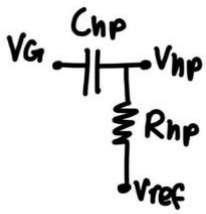
Set conditions: $V_{cc} = 5\,V,\ R_{nom} = 100k\,\Omega$

$$V_G = \frac{1+G\varepsilon}{2+G\varepsilon}V_{cc} \tag{6}$$

Sensitivity $S = \frac{\delta V_G}{\delta \varepsilon} = \frac{1}{4}GV_{cc}$ (7)

High pass filter with a corner frequency of 0.1 Hz

The corner frequency for the high pass frequency is chosen based on regular breathing patterns. We want to tune in to signals above 6 breaths per minute (0.1 Hz).



Corner frequency f_c=0.1 Hz (or 6 breaths per min)

$$R_{hp}C_{hp} = \frac{1}{\omega} = \frac{1}{2\pi \cdot 0.1} \tag{8}$$

$$R_{hp} = 150\ k\Omega$$

$$C_{hp} = 1.06 \times 10^{-5}\ F$$

E. Overall Circuit

Figure 3 shows the entire Strain Gauge/Comparator System. A strain gauge is utilized to quantify the breathing in and out of the patient in the form of voltage. The strain gauge flexing due to the patient's breathing in and out, generates a sinusoidal waveform which gets fed into the op-amp voltage buffer through a voltage divider. The buffer circuit mitigates the noise that can be reduced because of a low impedance source and a high impedance load. Next, the signal passes through a high pass filter which filters the waveform that is not of interest, for example noise. Next, the comparator converts the sinusoidal analog signal into a digital signal which helps us determine when the patient is breathing in or breathing out. The generated square wave can be analyzed to determine the frequency and regularity of the patient's breathing. Additionally, a potentiometer is utilized to vary the sensitivity of the device so that it can be used across different patients.

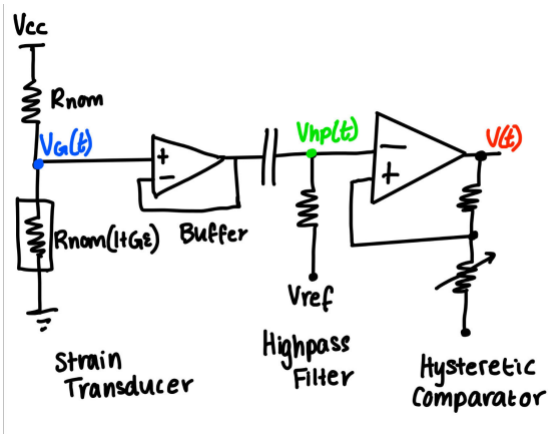


Fig. 3. The entire Strain Gauge/Comparator device that is designed to detect breathing pattern

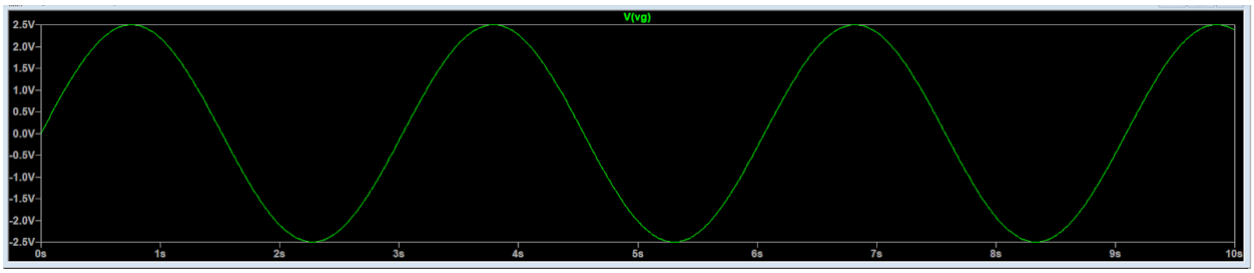
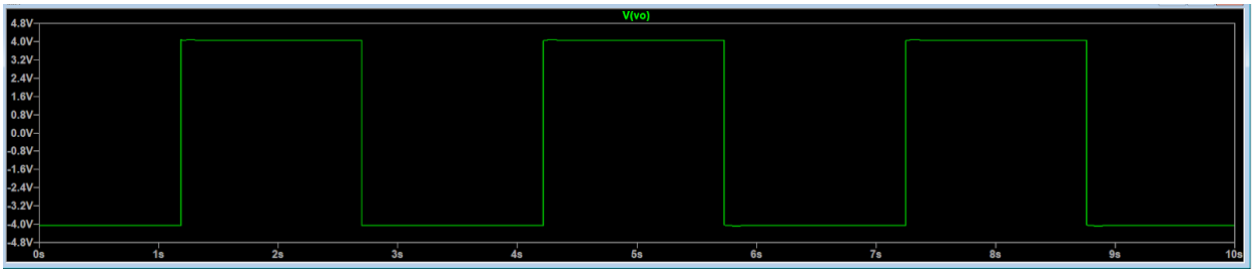


Fig. 4. A. The breathing of the patient is represented by a sine wave of amplitude of 2.5 V and frequency of 0.33 Hz (20 breaths per min).



B. The square wave output waveform. The output goes low (-4V) when breathing in and high (+4V) when breathing out.

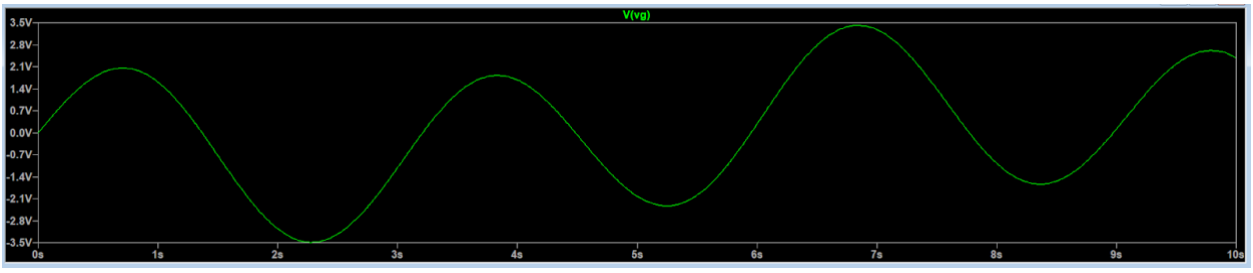


Fig 5. A. The input waveform represents the irregular breathing of a patient having asthma.

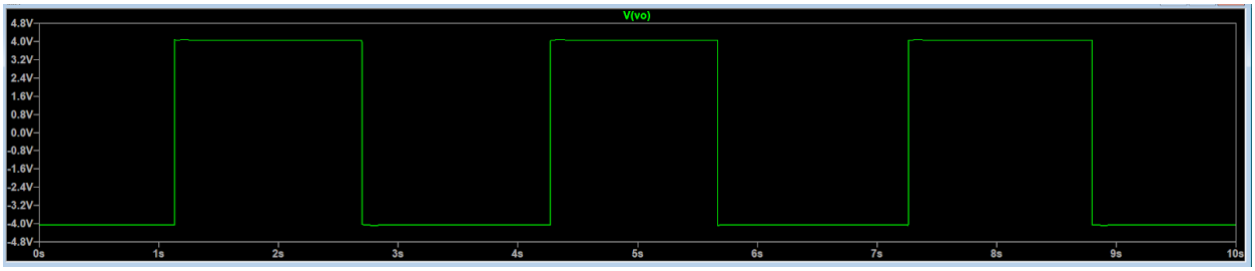


Fig 5. B. The square output waveform of the sinusoidal irregular breathing. The frequency and the duration for which the toggle is on for can be calculated from the output.

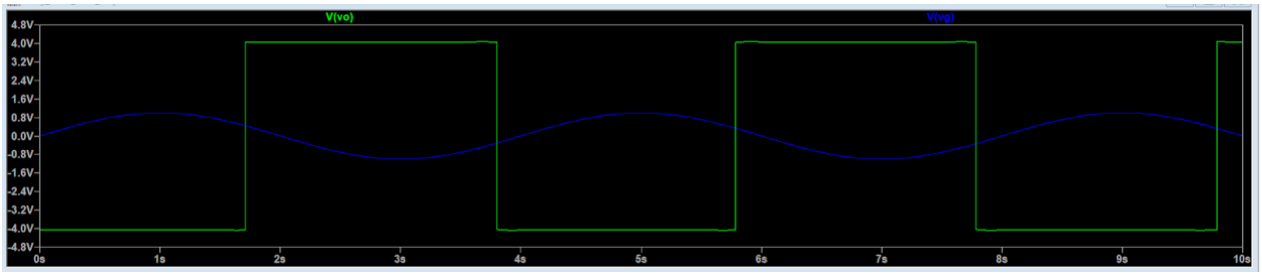


Fig 6. The blue graph represents normal breathing of a person not having asthma. The green waveform represents the output square waveform.

IV. RESULTS

A. Hyperventilation Simulation

In order to verify the circuit shown in Figure 3, we simulated it in LTspice. We first simulated hyperventilation by setting the voltage input as a sine wave of an amplitude of 2.5V and a frequency of 0.33 Hz, as shown in figure 4a. The output is a uniform square wave that is -4V at low and +4V at high, as shown in figure 4b. Hyperventilation can be determined by analyzing the output waveform's frequency. If the frequency of the output waveform is higher than that of normal breathing (Fig 6), then the patient is suffering from hyperventilation.

B. Irregular Breathing Simulation

Next, we simulate asthmatic irregular breathing patterns which can include forced abdominal expiration and thoracic-abdominal asynchrony [9] by superimposing two sine waves of unequal amplitude and frequency as the input voltage, see figure 5a. Both abdominal expiration and thoracic-abdominal asynchrony are characterized by the abdominal expansion being out of sync with expansion of the chest, which can be measured by transducing strain inputs from two elastic bands, one around the chest, and the other around the abdomen area. Thus, the two overlaid waves represent the two inputs. The output of these waves is a single squarewave of nonuniform period, see figure 5b. Similar to hyperventilation, the frequency of the square wave can be determined. Additionally, as seen in figure 5b, the duration for which the outputs stay high and low varies throughout the output because the patient is not breathing consistently. Therefore, the frequency and the duration of the trigger can be analyzed to determine if the patient is breathing irregularly. Additionally, it's important to note that the output for both hyperventilation and irregular breathing is visibly different from the output of healthy breathing (Fig 6).

V. DISCUSSION

A. Advantages

Our simulation results revealed that our model can allow us to distinguish potentially asthma-associated irregular breathing patterns from regular breathing using square-wave voltage outputs. Therefore, there exists a clear advantage for using a strain gauge alongside a Severinghaus electrode to diagnose asthma, as the clinician has a broader symptom basis for making their diagnosis.

B. Limitations

The disadvantages of this pair are that neither irregular breathing patterns, nor low PCO_2 levels are determinative of asthma, and are associated with a wide range of other conditions. Furthermore, collecting blood samples to input into the electrode is an invasive process and may cause patient discomfort. Minimally invasive methods such as an FeNO test for measuring nitric oxide levels in the lungs, which is indicative of inflammation, exist as alternatives.

C. Future Directions

Some future directions include seeking feedback from clinicians on what information they find most useful in making a diagnosis and performing physical simulations using a prototype that provides more realistic signal inputs compared to sine waves. Additionally, we can make the device more user-friendly by incorporating a microcontroller equipped with an LED indicator. This LED turns on when hyperventilation or irregular breathing is detected by the device, thereby serving as a visual cue for the physician.

VI. ACKNOWLEDGMENTS

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VII. REFERENCES

[1] D. D. Deenstra et al., "Prevalence of hyperventilation in patients with asthma," *Journal of Asthma*, vol. 59, no. 8, 6 Aug. 2021, pp. 1560–1567, https://doi.org/10.1080/02770903.2021.1959926.

[2] J. Kavanagh et al., "Over- and under-diagnosis in asthma," *Breathe*, vol. 15, no. 1, Mar. 2019, https://doi.org/10.1183/20734735.0362-2018.I. S. Jacobs and C. P. Bean, "Fine particles, thin films and exchange anisotropy," in Magnetism, vol. III, G. T. Rado and H. Suhl, Eds. New York: Academic, 1963, pp. 271–350.

[3] H. Golan, "Asthma and allergies," breatheon.com, http://www.breatheon.com/asthma-and-allergies/ (accessed Mar. 8, 2024).R. Nicole, "Title of paper with only first word capitalized," J. Name Stand. Abbrev., in press.

[4] A. Umeda et al., "Recent insights into the measurement of carbon dioxide concentrations for clinical practice in Respiratory Medicine," *Sensors*, vol. 21, no. 16, 2021, https://doi.org/10.3390/s21165636.

[5] Z. Messina, "Partial pressure of carbon dioxide," StatPearls [Internet]., https://www.ncbi.nlm.nih.gov/books/NBK551648/ (accessed Mar. 17, 2024)

[6] G. Cauwenberghs. (2024). "Electrochemical biosensors for blood-gas and acid-base physiology. pH, PO2, and PCO2," [Lecture Notes]. Available: https://isn.ucsd.edu/courses/beng186b/lectures/beng186b-lecture15-notes.pdf

[7] G. Cauwenberghs. (2024). "Displacement, strain, and pressure transducers. Potentiometers, voltage dividers, and Wheatstone bridges," [Lecture Notes]. Available: https://isn.ucsd.edu/courses/beng186b/lectures/beng186b-lecture3-notes.pdf

[8] A. A. Kerr, "Dead space ventilation in normal children and children with Obstructive Airways Disease," Thorax, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC470363/

[9] G. J. Connett and M. Thomas, "Dysfunctional breathing in children and adults with asthma," *Frontiers in Pediatrics*, vol. 6, 20 Dec. 2018, https://doi.org/10.3389/fped.2018.00406.