Non-Invasive Hemoglobin Detection System Based on GMR Sensor

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Abstract. In medical application, hemoglobin meter used to check hemoglobin level in human body as a part of medical checkup. Implementation of the conventional hemoglobin meter requires Invasive test and data analysis separately, which becomes an impediment to obtaining real-time results. This paper presents the design and development of Non-Invasive Hemoglobin detection system based on giant magnetoresistance (GMR) sensor. In this study, hemoglobin containing iron (Fe) atoms was magnetized with a magnetizer composed of 4 permanent magnets. Then the magnetized hemoglobin is detected using a GMR sensor attached to a U-shaped probe where the patient's arm is placed. The sensor output voltage will go through a signal conditioning circuit consisting of an amplifier and a filter. The voltage data obtained then processed and compared with the data from clinical testing using a hemoglobin meter. The result show linear relationship between sensor output and hemoglobin level with the sensitivity of the sensor obtained at 0.0475 V/(g/dL) and coefficient of determination (R^2) of 0.9663 or 96.63%. This system can be modified for a variety uses of medical applications yet still requires further optimization to provide higher precision and wider operating range.

INTRODUCTION

Hemoglobin contained in red blood cell plays a critical function in maintaining the body's health. The purpose of hemoglobin is to bind and carry oxygen from the lung to tissues in the human body [1]. Hemoglobin structure formed by a tetrameric structural and functional unit from a dimer of polypeptide chains called the α- and β-globin’s as shown in the Figure 1. There are four iron atoms (Fe) bonded to a hemoglobin molecule which allows to bind gases such as O2, CO, and NO. These iron atoms can be used to perform magnetic sensor detection when the iron atom is magnetized. The magnetic properties of the iron atom in hemoglobin are affected by whether or not it is bound to oxygen. Oxygenated form of hemoglobin is diamagnetic but deoxygenated one is magnetic due to its four unpaired electrons per Fe atom [2].

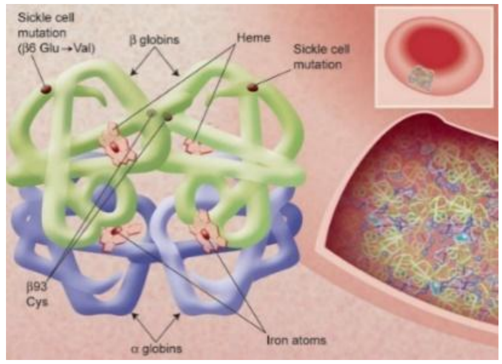


FIGURE 1. Hemoglobin molecule structure [3]

Hemoglobin meter is typically used to measure the hemoglobin levels in blood. If a hemoglobin meter reveals that hemoglobin level is lower than a specific cutoff, then there is a risk of anemia [4]. The use of a hemoglobin meter requires an invasive examination. The patient's condition cannot be monitored in real time for a lengthy period of time due to the delay in collecting and analyzing blood samples. Sensor technology is used in the medical industry to provide inexpensive, portable, and faster analysis medical examinations [5].

Sensor that utilizes magnetoresistive materials or so-called GMR (Giant Magnetoresistance) sensors has been used to measure hemoglobin concentrations [6]. A fluid flow simulator was used to simulate blood flow in the blood vessels. GMR is a magnetic material phenomenon in which the electrical resistance changes in response to an applied magnetic field [7]. The same method also performs using Fe3+-modified Porphyrin in detecting Red Blood Cell [8]. Spin valve type GMR sensor is highly sensitive to detect a very weak magnetic field from magnetic nanoparticles and Fe-hemoglobin inside red blood cells [9]. However, these studies were conduct on lab using flow simulator which the fluids were flow on elastic tube. Hence, we need to developed the convenient system for clinical application. GMR sensors also used for weak field detection applications such as traffic speed monitoring based on earth magnetic field disturbance [10] and AC/DC current measurement [11].

In this study, Giant Magnetoresistance (GMR) sensor is used to detect hemoglobin non-invasively to the human body as shown in Figure 2. By utilizing the iron atom in this hemoglobin molecule, detection using GMR sensor can be carried out when the iron atom is magnetized using a magnetic field source called a magnetizer. The more hemoglobin that is magnetized, the stronger magnetic fields produce that will be detected by the sensor. Thus, the output signal to be read is strong enough for detection. The hemoglobin molecule is a major component of red blood cells while the composition of red blood cells in the blood’s volume contributes 40 - 45% [12].

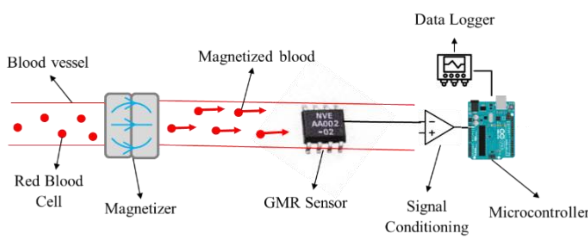


FIGURE 2. Simplified diagram of the proposed system

METHODS

Principle of Detection

The proposed system utilizes GMR sensor as a magnetometer by measuring the magnetic field produced by the magnetized hemoglobin flowing in a blood vessel. We use simplified analogy from the Biot-Savart Law commonly applied to calculate the magnetic field produced by a long straight current-carrying wire. Based on Biot-Savart Law, the magnetic field (B) produced by long straight wire is given by [13]:

$$\boldsymbol{B} = \frac{\mu_0}{4\pi} I \int \frac{dl \times \hat{r}}{r^2} \quad (1)$$

The magnetized hemoglobin will be assumed as a collection of current loops, where each loop represents a single hemoglobin molecule. For the purposes of this analogy, we consider each infinitesimal length dl of the current loop to be a tiny section of blood vessel carrying magnetized hemoglobin. The current I represents the magnetic moment of the hemoglobin molecule and is aligned with the blood flow direction which in the x-axis. The vector pointing from the element of length dl to the point P where we placed the GMR Sensor is denote as r as shown in the Figure 3. By integrating the contributions of each segment, we obtain the total magnetic field at a point in space due to all the segments of blood vessel:

$$\boldsymbol{B} = \frac{\mu_0 I}{2\pi a}\hat{\boldsymbol{x}} \tag{2}$$

We can predict that the magnetic field strength will increase with decreasing distance to the sensor. This is consistent with the fact that the magnetic field is inversely proportional to the distance from the source as stated in Eq. 2. The direction of the magnetic field at point P is aligned with the blood flow direction in the x-axis.

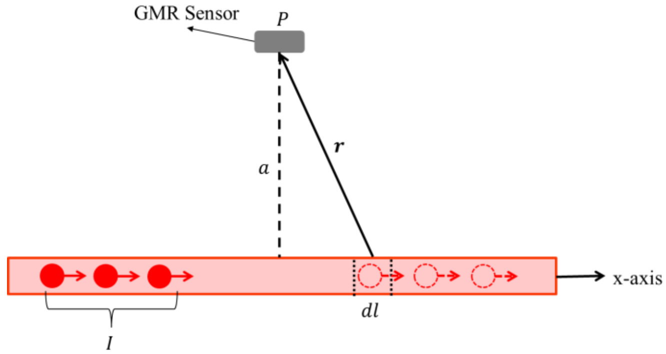


FIGURE 3. Analytical model for proposed method

The GMR sensor used is a sensor manufactured by NVE Corporation with the AA0002-02 series. According to the working principle of the GMR material, this GMR sensor operates with a change in the applied magnetic field and then causes a change in the resistance. The magnitude of the reduction in resistance is generally 4% to 20%, depending on the material structure of the GMR layer. Most sensor products from NVE that rely on GMR materials show a reduction in resistance of 14% to 16% [14]. The direction of sensitivity of GMR sensors is in the plane of the package which is also the plane of the flux concentrator as shown in the Figure 4. According to the previous analytical assumption, then the GMR sensor must be positioned so that the direction of sensitivity is parallel to the direction of blood flow.

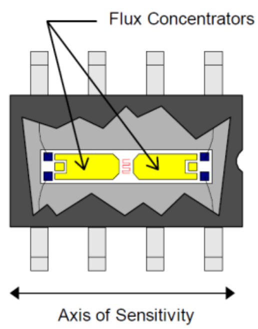


FIGURE. 4. Sensitivity direction of GMR Sensor

The Magnetizer

The magnetizer is used to magnetize hemoglobin which will be detected by the GMR sensor. The magnetic field produced by this magnetizer must be large enough to optimally magnetize hemoglobin so that the resulting magnetic field is strong enough to be detected and can last long enough to be detected by the sensor. It consists of 4 magnets are used which are arranged in a way that two magnets are combined and then mounted on an iron plate and two other magnets are installed next to it bounded by plates made of insulating material so that a magnetic field is produced in a planar direction (see Figure 5). This iron plate is also used so that the magnetic field flux is concentrated on the iron plate and does not spread in various directions. The type of magnet used is a neodymium magnet with dimension of 50×50×20 mm grade N42 each can produce a magnetic field of 0.46 T on its surface.

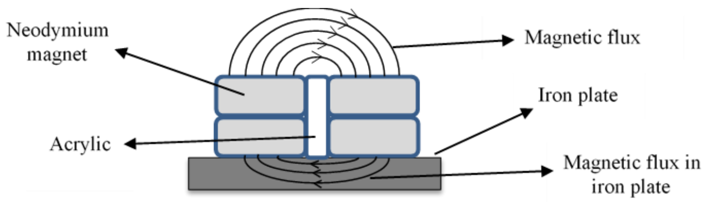
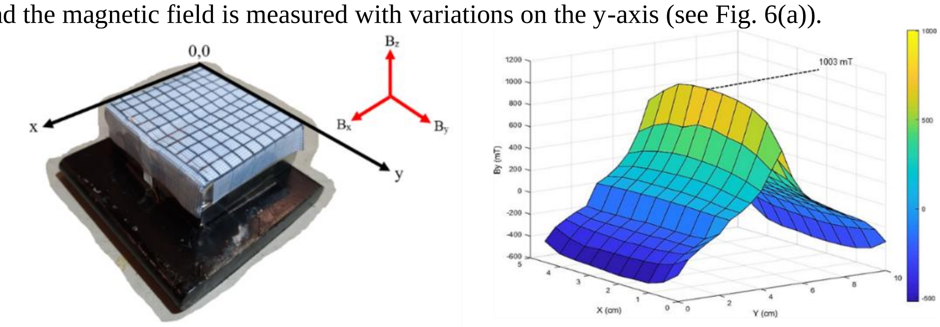


FIGURE 5. Magnets arrangement of magnetizer

Mapping of the magnetic field flux from the magnetizer is carried out to deter-mine the strength and direction of the maximum planar magnetic field on the surface of the magnetizer. So that we can know the location to place the arm or flow of hemoglobin to be magnetized. The instrument used in mapping the magnetic field from this magnetizer is the Teslameter F.W. Bell 5180®. Magnetic field mapping is only carried out in the x-y plane on the surface of the magnetizer and the magnetic field is measured with variations on the y-axis (see Fig. 6(a)).



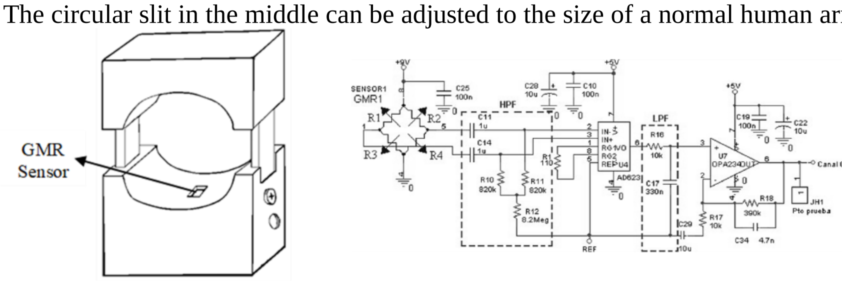
(a) (b)

FIGURE 6. (a) Directions of the coordinate axes on the magnetic field flux mapping and (b) Magnetic field mapping in the y direction

Data was collected at a height (z-axis) of 0 cm from the magnetizer. Figure 6(b) shows the magnetic field mapping data acquired on the magnetizer for the magnetic field in the y-direction. the maximum magnetic field for the y-direction is 1.003 T at coordinate (2.5,5) cm. So that the arm to be magnetized is placed at the point x = 2.5 cm and y = 5 cm and aligned in the direction of the y axis.

Signal Conditioning

In general, this system consists of two parts, namely a detector and a signal conditioning unit as shown in the Figure 6. The detector consists of a GMR sensor system mounted on a U-shaped probe to mount the arm. The sensor probe is made of metal which functions as a shield that protects the sensor from the strong magnetic field generated by the magnetizer. The circular slit in the middle can be adjusted to the size of a normal human arm.



(a) (b)

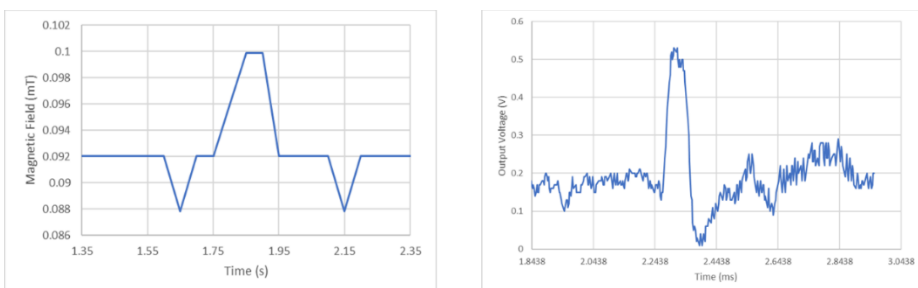
FIGURE 7. (a) Detector and (b) Signal conditioning circuit [10]

The signal conditioning unit consists of a signal conditioning circuit and microcontroller. The output signal from the GMR sensor will be a very small voltage because the magnetic field generated by the magnetization of hemoglobin is very weak. For this reason, required a signal conditioner circuit which consists of a signal amplifier and filter so that the data obtained can be analyzed.

The GMR output signal first passes through a high pass filter circuit to remove the DC signal from the GMR sensor. So that the signal that is passed is only an AC signal or a signal originating from a magnetic field disturbance that varies with time and eliminates measurement noise from the magnetizer. Even though the magnetizer is placed near the sensor and produces a strong magnetic field, the magnetizer is static so it doesn't produce a response signal to the circuit.

The signal conditioning circuit is tested using a slider that moves a neodymium magnet. The slider is driven by two DC motors which are controlled by the micro-controller so that the sliding speed of the slider is adjustable. The speed of the slider was adjusted to approach the velocity of blood flow in the arteries around 20 cm/s to 45 cm/s [15]. Slider speed was measured using the Tracker software. This software analyzes the motion of an object via video based on the frame rate per second. We obtained speed of the slider under normal circumstances is 28.058 cm/s to 44.056 cm/s which still in range of blood flow velocity in the arteries.

The sensor probe along with the signal conditioning circuit is tested using a mag-net mounted on a slider. The sensor probe tip is positioned parallel to the Vernier® Teslameter probe tip at the same distance along the slider track. The graph in Figure 7 shows that a output voltage produced with a peak voltage of 0.53 V resulted from a difference in the magnetic field disturbance (ΔB) applied of 7.874 μT. The signal peak on this graph shows the state when the detected magnet moves toward the sensor while the signal valley formed indicates the state when the detected magnet moves away from the sensor.



(a) (b)

FIGURE 8. (a) Magnetic field disturbance and (b) Signal response from GMR Sensor

RESULTS AND DISCUSSION

Testing of proposed system was performed in the Clinical Laboratory. This system is tested on patients who carry out medical check-up which include hemoglobin levels check. The instrument used to check hemoglobin levels in the Clinical Laboratory is Sysmex XP-300™ Automated Hematology Analyzer. The measurement results from this instrument will be used to compare the measurement results from the developed system.

The sample output voltage signal from the measurement results from one of the patients is shown in the graph in Figure 9. From this graph it can be seen that the area from the 14 ms to 27 ms has higher signal peaks than the other areas. This area was the time where the detection process occurs. Then data processing is done by calculating the RMS (Root Mean Square) voltage in the detection area so that the voltage value is obtained for each patient who performs the examination.

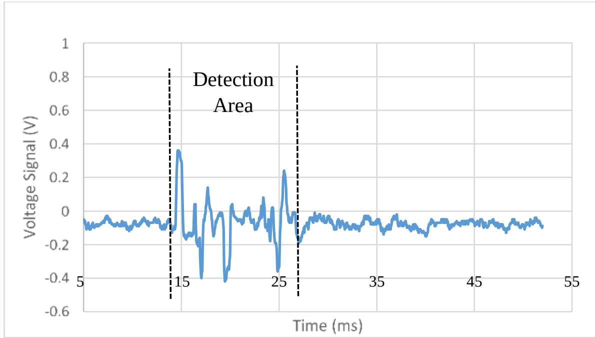


FIGURE 9. Sample of output voltage

The processed data then compared with the results of laboratory tests using a hemoglobin meter. Figure 10 shows the relation of between the output voltage to the hemoglobin concentration level. The equation of the curve of relation between output voltage (V) and hemoglobin levels (g/dL) is:

$$V = 0.0475\mathrm{H} - 0.5498 \tag{3}$$

From Eq. 3, the GMR sensor's sensitivity could be obtained at 0.0475 V/(g/dL) and the coefficient of determination (R^2) of this model is 0.9663 or 96.63%.

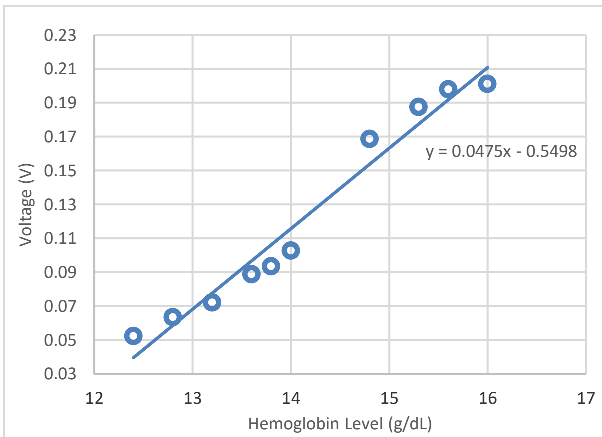


FIGURE 10. Output voltage of sensor GMR versus Hemoglobin level

CONCLUSION

We have successfully designed and developed a non-invasive hemoglobin detection system based on the GMR sensor. The magnetizer used to magnetize hemoglobin can produce a maximum magnetic field in the y-axis direction of 1003 mT. The clinical test result show directly proportional relation between sensor output and hemoglobin level with the sensitivity of the sensor obtained at 0.0475 V/(g/dL) and coefficient of determination (R^2) of 0.9663 or 96.63%. From this result it was concluded that the developed system has the potential to be used in many applications related to medical uses. For further works, the magnetizer should utilize the electromagnet instead of permanent magnet to produce stronger magnetic field and provide safety. Also enhanced by machine learning algorithm for more powerful data processing.

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REFERENCES

1. M. H. Ahmed, M. S. Ghatge and M. K. Safo, Subcell. Biochem **94**, 345-382 (2020).
2. K. L. Bren, R. Eisenberg and H. B. Gray, Proceedings of the National Academy of Sciences **112,** 13123–7 (2015).
3. A. N. Schechter, Blood **112,** 3927–38 (2008).
4. S. Y. Hess, A. Owais, M. E. D. Jefferds, M. F. Young, A. Cahill and L. M. Rogers, Ann N Y Acad Sci **1523,** 11–23 (2023).
5. Ramli R, Haryanto F, Khairurrijal K and Djamal M, Biosensors for Health, Environment and Biosecurity (InTech), (2011).
6. A. Aminudin, M. Djamal and D. H. Tjahyono D, Journal of Chemical and Pharmaceutical Research **8,** 922-928 (2016).
7. I. Ennen, D. Kappe, T. Rempel, C. Glenske and A. Hütten, *Sensors (Switzerland)* **16(6),** 904 (2016)
8. A. Aminudin, D. H. Tjahyono, Suprijadi, M. Djamal, R. Zaen and A. B. D. Nandiyanto, IOP Conf. Ser.: Mater. Sci. Eng. **180,** 012137 (2017)
9. S. H. Park, K. S. Soh, D. G. Hwang, J. R. Rhee and S. S. Lee, Journal of Magnetics **13,** 30–3 (2008).
10. J. Pelegrí Sebastiá, J. Alberola Lluch and J. R. Lajara Vizcaíno, Sens Actuators A Phys **137,** 230–5 (2007).
11. C. Mușuroi, M. Oproiu, M. Volmer and I. Firastrau, Sensors (Switzerland) **20**, (2020).
12. K. Almezhghwi and S. Serte, Comput Intell Neurosci **2020,** 1–12 (2020).
13. D. J. Griffiths, Cambridge University Press, (2023).
14. NVE Corporation, (2019).
15. E. N. Marieb and K. Hoehn, Benjamin Cummings, (2010).