



Hemoglobin concentration measurement based on magnetic sensor

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ABSTRACT

The paper presents the measurement system of hemoglobin concentration using giant magnetoresistance (GMR) sensor. Hemoglobin was magnetized by a strong magnetic field $1,1T$. The hemoglobin was influenced by an external magnetic field. Then, the magnetic field of hemoglobin was detected by GMR sensor. GMR sensor circuit was developed using wheatstone bridge. The results of tests are obtained using sensitivity parameter of GMR sensor. Responses of the voltage of GMR sensor versus the concentration of hemoglobin have been obtained the linear equations. A strong correlation between the voltage of GMR sensor and the concentration of hemoglobin was revealed. The sensitivity of GMR sensor were $20.22 \frac{mV}{g/dL}$, $20.34 \frac{mV}{g/dL}$, $20.45 \frac{mV}{g/dL}$, $20.59 \frac{mV}{g/dL}$ and $20.95 \frac{mV}{g/dL}$ for the flow rate 0.29 cm/s , 0.31 cm/s , 0.33 cm/s , 0.35 cm/s and 0.37 cm/s respectively. The sensitivity of GMR sensor increased with increase of flow rate and concentration of hemoglobin. Increasing the flow rate, rising the unbalance of the bridge circuit and increasing the zero drift of GMR sensor. The prototype of hemoglobin concentration measurement has developed successfully.

Key words: Hemoglobin Concentration, GMR sensor, Sensitivity, Magnetization, Flow rate

INTRODUCTION

The Blood in the human body has a highly essential. In the human body consists of 55% of blood fluid and 45% of blood cells, if summed overall in adults about 4-5 liters. Blood cells consist of erythrocytes (99%), thrombosit (0.6 to 1.0%), and leukocytes (0.2%). Erythrocytes contain hemoglobin which serve to circulate oxygen. This means, blood cells are dominated by the hemoglobin. Hemoglobin is a protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and carbon dioxide from the tissues to the lungs. Hemoglobin has four protein molecules (chain globulin) are connected together. Each chain globulin contains important central structure called heme molecules. Iron-containing heme molecule that transports oxygen and carbon dioxide in the blood. This iron is what gives the red color of blood.

Heme consists of the porphyrin and the iron atom. The porphyrin is composed of four pyrrole rings. Her fourth bonded to one another via a bridge methenyl, forming a ring tetrapirrol. The iron atom in heme binds four nitrogen atoms centered protoporphyrin ring. The iron atoms can take the form of ferrous (Fe^{2+}) or ferric (Fe^{3+}) so hemoglobin is also known as ferohemoglobin and ferihemoglobin or methemoglobin. Only when iron in ferrous form, the compound can bind oxygen. Under normal circumstances the 100 ml of blood contains 15 grams of hemoglobin capable of carrying oxygen 0.03 gram[1]. The oxygen is bound together with blood through the lungs. Heme structure consists of porphyrin dan Fe is shown in Figure 1.

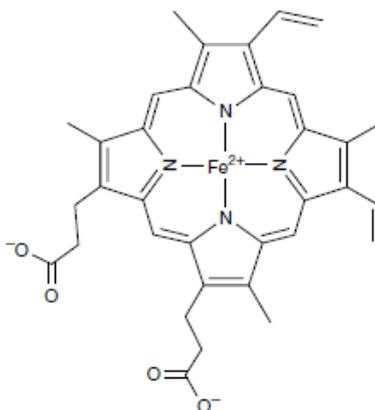


Figure 1. Heme structure consists of porphyrin dan Fe[2]

Magnetic properties of hemoglobin are obtained from oxyhemoglobin, carbonmonoxyhemoglobin, and ferrohemoglobin to fill four unpaired electrons per heme. Carbonmonoxyhemoglobin molecule has a zero magnetic moment and there are no unpaired electrons. Oxyhemoglobin molecules much like carbonmonoxyhemoglobin, zero magnetic moment and there are no unpaired electrons. Ferrohemoglobin, in contrast to oxyhemoglobin and carbonmonoxyhemoglobin, hemoglobin itself contains unpaired electrons, magnetic susceptibility shows paramagnetic contributions. Magnetic data interpretation can be made only in relation to the nature and magnitude of their mutual interaction of the four heme molecule. One possibility is that the heme-heme interaction is strong enough for a few moments all the electrons in the molecule becomes resultant moment, with the same value for all molecules. Magnetic data in this way result the value, = 10.92 Bohr magnetons [2]. The paramagnetic molar of deoxyhemoglobine susceptibility (HHb) is 3,000 mol/ml [3] and by determining a magnetisation curve for erythrocytes the magnetic dipole moment of HHb is estimated to be $8\mu_B$ or $\mu_{HHb} = 7.42 \times 10^{-23} Am^2$ [4]. In a strong static magnetic field an erythrocyte responds in such way that its disk plane is oriented parallel to the direction of the magnetic field, independently of the hemoglobin state, *i.e.*, oxygenated (diamagnetic HbO₂) or deoxygenated (paramagnetic HHb) [5].

Magnetic properties of hemoglobin is very weak. To be able to detect the magnetic properties of magnetic sensors hemoglobin needed working weak magnetic field. One of the sensors that can detect weak magnetic field sensor is giant magnetoresistance (GMR). GMR sensor is a sensor that works based on the effect of changes very big obstacle on metallic materials when in an external magnetic field. GMR sensors have several advantages when compared to other sensors, such as having high sensitivity, high temperature stability, low power consumption, size is relatively small, and a fairly cheap price as well as the magnetic properties can be varied within a very wide range [6]. Comparative characterization in some field sensor with GMR sensors can be shown in Table 1.

Table 1. Characteristics different in magnetic field sensor [7]

Sensor	Range H (T)	Sensitivities (V/T)	Time Respon	Power Consumption	head size
GMR	10^{-12} - 10^{-2}	120	1 MHz	10 mw	10-100 μ m
Hall	10^{-6} - 10^2	0,65	1 MHz	10 mw	10-100 μ m
Squid	10^{-14} - 10^{-6}	Okt-14	1 MHz	10 mw	10-100 μ m
Fluxgate	10^{-12} - 10^{-2}	3.2	5 kHz	1 w	10-20mm

GMR for biosensor applications have been used by us along with the development of sensor technology and its application. At first GMR reported in the 1980s from the French research group headed by Albert Fert [8]. At the present time, GMR applications are being developed in several researchers: GMR sensor can be used to capture the antibody-labeled magnetic nanoparticles [9], real time monitoring of cell phagocytosis during the separation process [10], tumor detection with GMR biosensor microarray [11], measures the number of biomarkers through the magnetic nanoparticles bound to the sensor GMR-SV [12], measures the pulse of blood flow [13], GMR structure to determine bacteria [14], the GMR sensor to estimate the density of magnetic fluid in the tumor [15]. In this research, GMR sensor applications have been developed to measure the concentration of hemoglobin. The hemoglobin concentration measument used magnetization from strong magnetic field source.

The magnetization was the number of magnetic dipole moment of hemoglobin per unit volume, can be symbolized by M and can be written in equation

$$M = \sum \frac{m_{Hb}}{V} \quad (1)$$

Where M is the magnetization (A / m), m_{Hb} is the magnetic dipole moment of hemoglobin, (Am^2) and V is the volume (m^3). Magnetization can be influenced by hemoglobin flow rate. For diamagnetic and paramagnetic material the magnetic susceptibility χ relates magnetization of hemoglobin can be written:

$$M = \chi H \quad (2)$$

GMR sensor circuit was developed using wheatstone bridge. Four resistive elements were used to wheatstone bridge circuit shown in Figure 2 [16]. GMR sensor used AA002 series from product of NVE corporation [17].

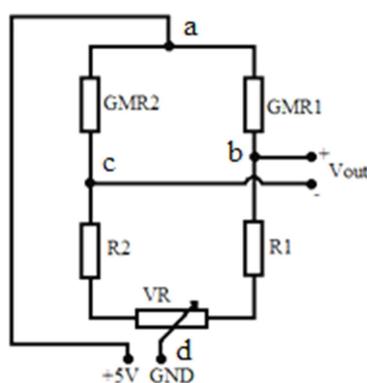


Figure 2. GMR Sensor Circuit

In Figure 2, GMR1 sensor was used to detect hemoglobin magnetic field, GMR2 sensor was used for noise compensator. Resistor R1 and R2 were fixed value, variable resistor VR was adjustable value. The variable resistor (VR) was used to adjust the balance of bridge circuit. Output voltage (V_{out}) was calculated from the potential difference V_b to V_c . If reference potential was the ground at the point d, the output voltage was expressed by the equation:

$$V_{out} = V_{bd} - V_{cd} \quad (3)$$

In balanced condition, potential at point b was equal point c. This condition determined the zero measurement and no environmental influences. When GMR sensor was induced by hemoglobin magnetic field, the potential at point b and c were not equal, so that resulting in a potential difference. Then, the potential difference was measured using a digital multimeter. Sensitivity of GMR sensor can be obtained from equation (1), (2) and (3):

$$S_{V,Hb} = \frac{V_{out\ GMR}}{n_{Hb}} \quad (4)$$

where $S_{V,Hb}$, $V_{out\ GMR}$, and n_{Hb} are the sensitivity of GMR sensor, the output Voltage of GMR sensor and the concentration of hemoglobin, respectively [18].

EXPERIMENTAL SECTION

In the experiments hemoglobin concentration measurement based on magnetic sensor using equipment: digital multimeter, GMR sensor, permanent magnet, peristaltic pump, sample container and controller pump. Initially, various samples were prepared using 250 mL Package Red Cell (PRC) each bottle. The samples were labeled with PRC1-PRC8 code. (Figure 3) Samples were calibrated using Quick Check hemoglobin meter. Then, sample was placed into the sample container. Subsequently, the peristaltic pump generated hemoglobin flow in elastic tube. Next, hemoglobin was magnetized by external magnetic field 1.1T. Then, GMR sensor detected hemoglobin magnetic field for 8 samples (PRC1-PRC8) in various flow rate. The flow rate can be controlled using controller pump. The controller pump was adjusted for flow rate 0.29cm/s, 0.31cm/s, 0.33cm/s, 0.35cm/s and 0.37cm/s. Output voltage of

GMR sensor was measured using digital voltmeter. The Schematic of hemoglobin concentration measurement was shown in Figure 4.



Figure 3. Sample of Package Red Cell (PRC)

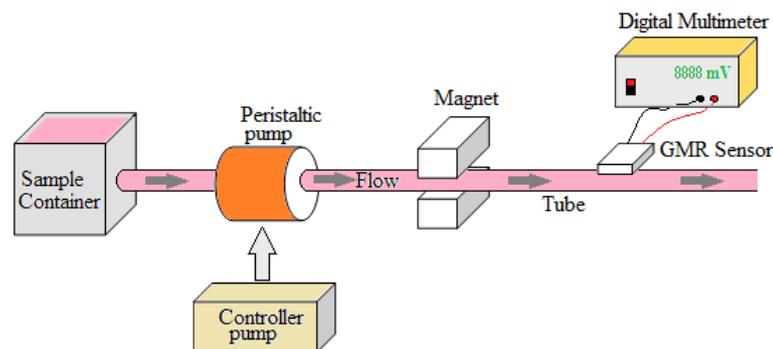


Figure 4. Schematic of hemoglobin concentration measurement

In Figure 3, when the hemoglobin flow past the magnet, the hemoglobin was influenced by an external magnetic field, so that change of the magnetic moment orientation. Hemoglobin had been magnetized by a strong magnetic field 1,1T. Then, the magnetic field of hemoglobin was detected by GMR sensor.

RESULTS AND DISCUSSION

Prototype tests of hemoglobin concentration measurement system have been done and have been analyzed based on linearity, sensitivity and zero drift correlate with flow rate and concentration. Figure 5 shows the results of the response tests of the GMR sensor versus hemoglobin concentrations at various flow rates.

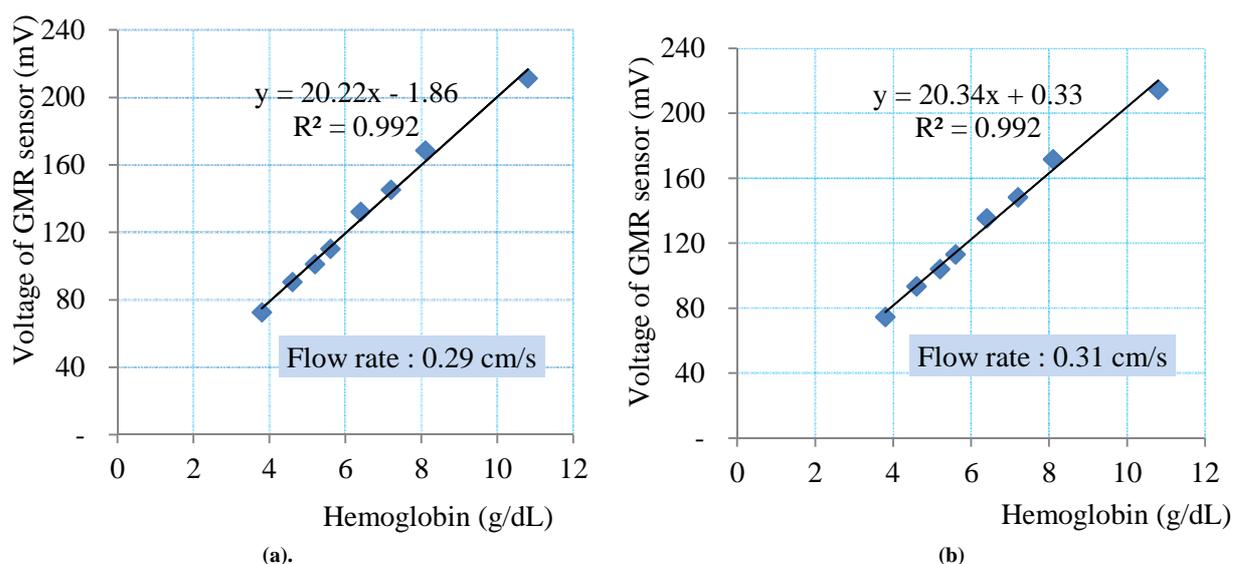


Figure 5. Voltage of GMR sensor versus hemoglobin concentration with (a) flow rate 0.29 cm/s and (b) flow rate 0.31 cm/s

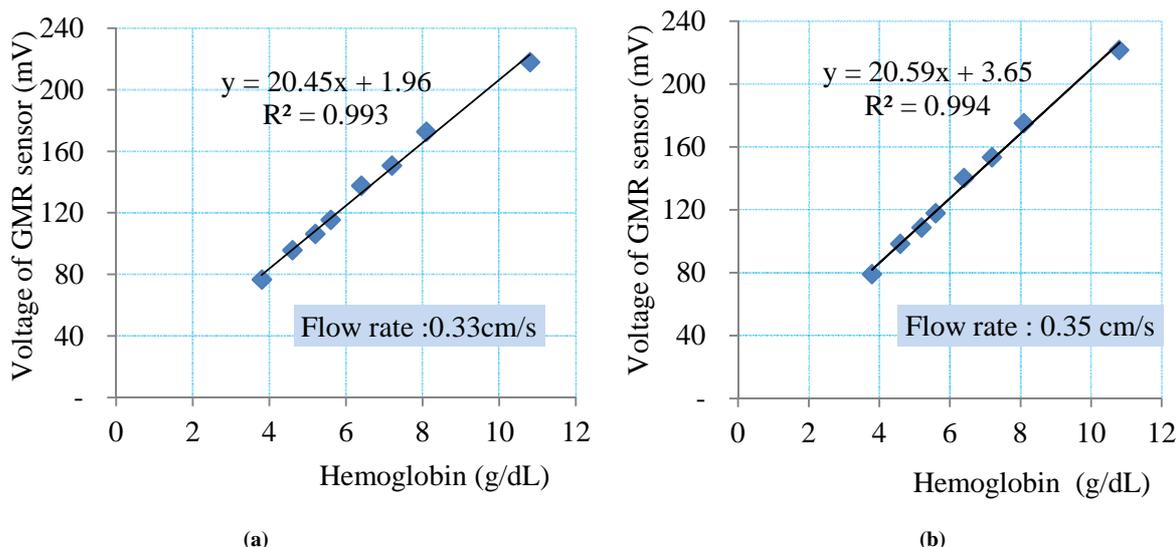


Figure 6. Voltage of GMR sensor versus hemoglobin concentration with (a) flow rate 0.33 cm/s and (b) flow rate 0.35 cm/s

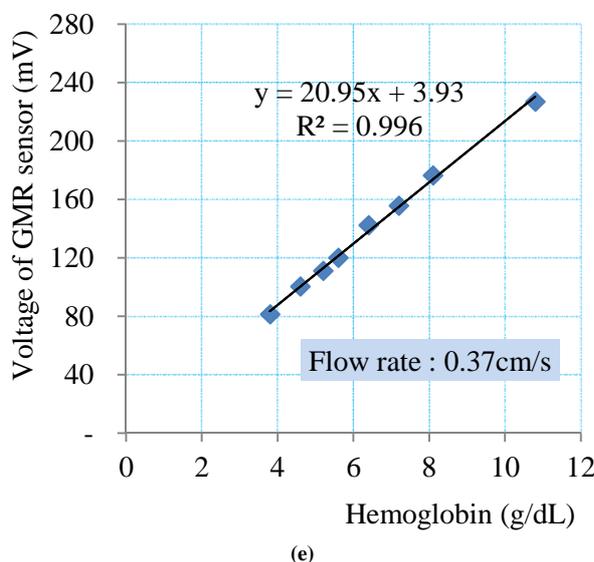


Figure 7. Voltage of GMR sensor versus hemoglobin concentration with flow rate 0.37cm/s

Based on the linearity, the curves in Figure 5 obtained highly linear with a correlation coefficient of tests 1-5 were 0.992, 0.992, 0.993, 0.994 and 0.995 respectively. Figure 5, 6 and 7 shown curves of the voltage of GMR sensor versus the concentration of hemoglobin. From curves have been obtained the linear equations. The linear equations are

$$V_{out-1} = 20.22 n_{Hb1} - 1.86 \text{ on the flow rate } 0,29\text{cm/s}, \quad (5)$$

$$V_{out-2} = 20.34 n_{Hb2} + 0.33 \text{ on the flow rate } 0,31\text{cm/s}, \quad (6)$$

$$V_{out-3} = 20.45 n_{Hb3} + 1.96 \text{ on the flow rate } 0,33\text{cm/s}, \quad (7)$$

$$V_{out-4} = 20.59 n_{Hb4} + 3.65 \text{ on the flow rate } 0,35\text{cm/s} \text{ and} \quad (8)$$

$$V_{out-5} = 20.95 n_{Hb5} + 3.93 \text{ on the flow rate } 0,37\text{cm/s}. \quad (9)$$

Figure 5, 6 and 7 obtains the impact of hemoglobin concentration to voltage of GMR sensor. A strong correlation between the voltage of GMR sensor and the concentration of hemoglobin was revealed. From this figure, it is confirmed that the voltage of GMR sensor increased with increase of hemoglobin concentration.

Equation (5)-(9) can be used to obtain sensitivity, zero drift and correlation coefficient (R^2).

Table 2 shows list of sensitivity, zero drift and correlation coefficient (R^2) on various flow rate.

Based on Table 2, the sensitivity of GMR sensor were $20.22 \frac{mV}{g/dL}$, $20.34 \frac{mV}{g/dL}$, $20.45 \frac{mV}{g/dL}$, $20.59 \frac{mV}{g/dL}$ and $20.95 \frac{mV}{g/dL}$ for the flow rate 0.29 cm/s, 0.31 cm/s, 0.33 cm/s, 0.35 cm/s and 0.37 cm/s respectively.

Table 2 shown, increasing the flow rate, rising the volume of hemoglobin. Increasing the volume of hemoglobin, rising magnetic susceptibility and increasing magnetization according to the equation (2). Increasing the magnetization, rising the sensitivity of GMR sensor. Finally, the sensitivity of GMR sensor increased with increase of flow rate. The zero drift of GMR sensor were 1.86 mV, 0.33 mV, 1.96 mV, 3.65 mV and 3.93 for the flow rate 0.29 cm/s, 0.31 cm/s, 0.33 cm/s, 0.35 cm/s and 0.37 cm/s respectively. Increasing the flow rate, rising the unbalance of the bridge circuit and increasing the zero drift of GMR sensor.

Table 2. List of sensitivity, zero drift and correlation coefficient (R^2) on various flow rate

No	Flow rate (cm/s)	Sensitivity ($\frac{mV}{g/dL}$)	Zero Drift (mV)	R^2
1	0.29	20.22	-1.86	0.992
2	0.31	20.34	0.33	0.992
3	0.33	20.45	1.96	0.993
4	0.35	20.59	3.65	0.994
5	0.37	20.95	3.93	0.995

CONCLUSION

From above data, we conclude that experimental system can be used for hemoglobin level measurement based on magnetic sensor. Respons of the voltage of GMR sensor versus the concentration of hemoglobin have been obtained the linear equations. A strong correlation between the voltage of GMR sensor and the concentration of hemoglobin was revealed. The sensitivity of GMR sensor were $20.22 \frac{mV}{g/dL}$, $20.34 \frac{mV}{g/dL}$, $20.45 \frac{mV}{g/dL}$, $20.59 \frac{mV}{g/dL}$ and $20.95 \frac{mV}{g/dL}$ for the flow rate 0.29 cm/s, 0.31 cm/s, 0.33 cm/s, 0.35 cm/s and 0.37 cm/s respectively. The sensitivity of GMR sensor increased with increase of flow rate and concentration of hemoglobin. The zero drift of GMR sensor were 1.86 mV, 0.33 mV, 1.96 mV, 3.65 mV and 3.93 for the flow rate 0.29 cm/s, 0.31 cm/s, 0.33 cm/s, 0.35 cm/s and 0.37 cm/s respectively. Increasing the flow rate, rising the unbalance of the bridge circuit and increasing the zero drift of GMR sensor.

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