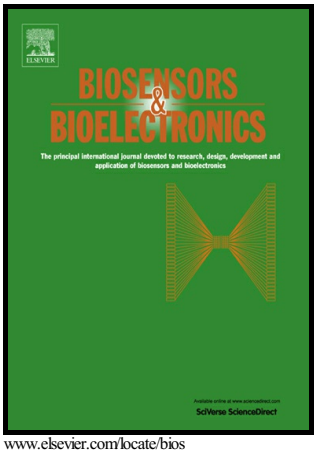

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Linear Relationship between Cytoplasm Resistance and Hemoglobin in Red Blood Cell Hemolysis by Electrical Impedance Spectroscopy & Eight-parameter Equivalent Circuit

A. Kiet Tran[a], Achyut Sapkota[b, *], Jianming Wen[c], Jianping Li[c, a], Masahiro Takei[a]

a. Graduate School of Mechanical Engineering, Division of Artificial System Science, Chiba University, 1-33 Yayoi, Inage, Chiba 263-8522 Japan

b. Department of Information and Computer Engineering, National Institute of Technology, Kisarazu College, 2-11-1 Kiyomidai-Higashi, Kisarazu, Chiba 292-0041 Japan

c. Institute of Precision Machinery, Zhejiang Normal University, China

* Corresponding author. *E-mail address:* sapkota@ieee.org (A. Sapkota).

Abstract

We have developed a non-invasive rapid and real-time red blood cell (RBC) hemolysis detection method which is a more accurate for point of care testing of hemolysis in various medical settings. An eight-parameter equivalent circuit is employed to quantify the release of hemoglobin (H_b) and the cytoplasm from RBC into the blood plasma. RBC hemolysis is induced by adding different volume fractions of distilled water into the blood. The cytoplasm released following RBC hemolysis is estimated from the experimental values. A strong relationship between RBC hemolysis and change in the electrical characteristics of blood has been demonstrated. The cytoplasm resistance (R_c) shows a linear relationship with the H_b. This relationship between R_c and H_b is described by the equation $R_c = 0.2203H_b + 2.4775$, with a correlation coefficient of 0.9905.

Keywords: hemolysis, electrical impedance spectroscopy, cytoplasm, red blood cells.

1. Introduction

RBC hemolysis is characterized by the release of H_b with the cytoplasm from RBC into the blood plasma (Jacob et al., 1965). RBC hemolysis occurs during blood collection, transportation, processing, handling and storage within the transfusion apparatus (Sowemimo-Coker, 2002). In a blood sampling process, RBC hemolysis is the most frequent source of error which is responsible for over 40-70% of blood sample rejection (Carraro and Plebani, 2007). In addition to that, recollection of blood samples from the patients cause extra suffering, delayed treatment, and unnecessary extra financial burden to the health care systems. Processing delays also escalate the RBC hemolysis occurring in the sample during the period between recollection and analysis. In order to minimize the blood sample rejection, real-time detection of RBC hemolysis is necessary so that an intervention measure is put in place (Crookston et al., 2000; Linden et al., 2000).

Generally, RBC hemolysis is detected by measuring the concentration of H_b in blood serum or plasma by traditional visual inspection (Janatpour et al., 2004) , hemolysis index (*HI*) (Lippi et al., 2009), or by microfluidic (Son et al., 2014). In the traditional visual inspection method, the blood serum or plasma which is light pink indicates slight RBC hemolysis, whereas deep red coloration represents gross RBC hemolysis. However, the traditional visual inspection method is unreproducible, inaccurate and lacks standardization. Hawkins reported errors in over-reporting RBC hemolysis in this case of traditional visual inspection method leading to rejection of blood that is still viable for transfusion (Hawkins, 2002). The use of *HI* method of RBC hemolysis detection is based on the absorbance of light at different wavelengths. However, the *HI* method requires the usage of different diluents such as distilled water, saline and other buffers in the procedures. Oosterhuis reported that variation of diluents induces spurious turbidity while the samples are mixed with the reagent which directly affects the effectiveness of the *HI* method (Oosterhuis et al., 2009). Microfluidic method require calculation of the concentration of the blood plasma (Son et al., 2014). In this context, electrical methods based on multi-frequency measurement of impedance (i.e. electrical impedance spectroscopy, EIS) is a potentially better alternative to the previous methodologies because it is a non-invasive method and therefore no diluents are required during the procedures, which guarantees reproducibility (Wang et al., 2017). EIS has been widely used to study various biophysical and biochemical properties of blood. For example, in one of our earlier studies, it has been found that there is a linear change in the electrical properties of blood sample with respect to the change in the size and RBC concentration of the thrombus (Fuse et al., 2015). Similarly, we successfully studied the quantitative measurement of the agreeability of RBC (Li et al., 2018) and blood flow rates (Li et al., 2018) by using electrical methods.

Electrically, blood can be represented in terms of a typical equivalent circuit (McAdams and Jossinet, 1995), where R_p is the plasma resistance, C_m presents the cell membrane capacitance and R_i presents the interior resistance of the RBC. Most of the existing studies on EIS measurement of blood are centered on this simple understating of equivalent circuit. However, this conventional blood equivalent circuit is not sufficient in representing RBC hemolysis because blood with hemolyzed RBC contain