

Comparative electrical impedance analysis of blood in normal and diabetes mellitus patients under fasting and postprandial conditions

Chomsin Sulistya Widodo^{1,*}, Farid Khoriyanto¹, Ekowati Retnaningtyas²

¹Department of Physics, Universitas Brawijaya, Malang 65145, Indonesia

²Department of Nursing, Politeknik Kesehatan Kemenkes Malang, Malang 65119, Indonesia

ABSTRACT

Type 2 diabetes mellitus (T2DM) alters blood biophysics, yet most bioelectrical impedance spectroscopy (BIS) studies examine only glucose and overlook hematological or morphological factors. This comparative study analyzed venous blood samples from normoglycemic individuals ($n = 5$) and type 2 diabetes mellitus (T2DM) patients ($n = 5$) under fasting and postprandial conditions. Assessments included glucose, hemoglobin, complete blood count, erythrocyte morphology, and wide-band BIS (100 Hz – 100 kHz). T2DM patients consistently showed higher impedance than controls, with partial reductions postprandially but clear intergroup separation. Morphological analysis revealed an increased number of abnormal erythrocytes, including schistocytes, teardrops, and elliptocytes, consistent with membrane remodeling and hemorheological disturbance. Wide-band BIS detected frequency-dependent signatures shaped by glucose, hemoglobin, membrane capacitance, and cytoplasmic resistance. By integrating biochemical, hematological, and morphological data, this study established a multidimensional electrohematological profile of diabetes. Including both fasting and postprandial states addressed a key gap in previous BIS work and emphasized the clinical relevance of postprandial variability. These findings highlight BIS as a promising, non-invasive adjunct for diabetes monitoring, with translational potential for hybrid diagnostic strategies, wearable sensors, and point-of-care technologies.

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* Corresponding Author

E-mail address: chomsin@ub.ac.id

1. INTRODUCTION

Diabetes mellitus (DM), particularly type 2, continues to pose a significant global health challenge, with its prevalence steadily increasing and contributing significantly to cardiovascular, renal, and neurological complications worldwide [1]. Accurate monitoring of glycemic status is essential for effective disease management and for preventing long-term adverse outcomes. However, current diagnostic and monitoring methods, such as finger prick glucose testing and venous blood sampling, are invasive, uncomfortable, and carry risks of pain or infection, making them unsuitable for frequent use. These limitations have driven growing interest in the development of non-invasive approaches to glucose monitoring that are both reliable and patient-friendly. In light of these limitations, researchers have turned to biophysical methods such as bioelectrical impedance spectroscopy (BIS) as potential alternatives for improving monitoring strategies in DM.

Among the emerging alternatives, BIS has gained attention as a promising tool. By assessing the electrical characteristics of blood and tissues, BIS provides physiologically meaningful insights into membrane capacitance, cytoplasmic conductivity, and ionic distribution. Several studies have reported associations between blood glucose levels and impedance spectra. For instance, Gong et al. introduced an equivalent bio impedance spectrum model that demonstrated strong intra- and inter-

individual correlations ($r = 0.89$ and $r = 0.87$, respectively) with glucose concentration [2]. Likewise, Pedro et al. (2020) developed a four-electrode BIS model that achieved high precision, with regression errors below 3.75% [3]. Nonetheless, most existing studies have primarily examined the direct relationship between glucose and impedance, without integrating broader hematological or morphological factors. This problem raises an important question: beyond glucose alone, how might hematological properties, particularly those altered in DM, shape the impedance spectrum and provide deeper diagnostic insights.

A growing body of evidence highlights that erythrocyte morphology and deformability are remarkably altered in DM. Chronic hyperglycemia induces biochemical and structural changes in the red blood cell membrane, resulting in reduced deformability, the formation of abnormal shapes such as teardrop or schistocyte forms, and increased cell aggregation [4, 5]. These changes disrupt hemorheology, raise blood viscosity, and impair microcirculatory flow. Importantly, Bourguignon et al. (2023) recently demonstrated that novel erythrocyte indices derived from Coulter-based impedance data could distinguish diabetic from non-diabetic individuals with remarkable sensitivity ($AUC \approx 0.95$) [6]. Yet, integrative investigations that combine impedance spectroscopy with biochemical markers (e.g., glucose, hemoglobin) and morphological parameters remain scarce, leaving a gap in the holistic characterization of blood in DM. Building on this, a further layer of complexity emerges when considering physiological variability, particularly the impact of dynamic states such as fasting versus postprandial conditions.

Another key limitation lies in the neglect of physiological variability. The majority of BIS studies have been performed under fasting or static conditions, overlooking postprandial states when glucose fluctuations are most pronounced. Since postprandial hyperglycemia plays a central role in driving oxidative stress and vascular damage, the lack of fasting–postprandial comparative impedance analyses represents a critical missed opportunity [7]. Addressing this gap requires an integrative approach that not only accounts for static blood properties but also captures how these parameters shift across different metabolic states.

This study aims to bridge these gaps by conducting a comparative impedance analysis of blood from normoglycemic and diabetic individuals under both fasting and postprandial conditions. Our approach integrates electrical impedance measurements with glucose levels, hemoglobin concentration, and erythrocyte morphology to construct a comprehensive electro-hematological profile. By examining blood properties across different physiological states, this work not only deepens understanding of the biophysical mechanisms underlying altered hemorheology in DM but also lays the groundwork for future development of non-invasive diagnostic and monitoring technologies in medical physics and biophysics. Beyond methodological advances, the integration of impedance, biochemical, and morphological data has the potential to enhance personalized medicine by providing more precise risk stratification and monitoring tools for diabetic patients. Furthermore, establishing reliable non-invasive diagnostic approaches could enable earlier detection of microvascular alterations and facilitate timely interventions, ultimately reducing the burden of diabetes-related complications on both patients and healthcare systems.

2. METHODS

This study employed a comparative experimental design involving two groups: five normoglycemic individuals and five patients with type 2 diabetes mellitus (T2DM). Researchers recruited participants from clinical settings and obtained informed consent before sample collection. Venous blood was drawn under two standardized conditions: fasting (after at least 8 hours of fasting) and postprandial (2 hours after meal consumption). Researchers collected blood samples in sterile vacutainer tubes and processed them immediately to minimize hemolysis. Each specimen was divided into aliquots for biochemical, hematological, morphological, and impedance analyses. Glucose levels were measured using both a glucometer and validated laboratory assays. Hemoglobin concentration and complete blood counts (erythrocytes, leukocytes, and platelets) were determined using an automated hematology analyzer. For morphological evaluation, peripheral smears were prepared, stained with Giemsa, and examined under light microscopy at $1000\times$ magnification to identify abnormal erythrocyte forms such as schistocytes, teardrops, elliptocytes, and bite cells.

Electrical impedance was measured with a bioelectrical impedance spectroscopy (BIS) system that consists of a signal generator, interdigitated electrodes (IDE), and acquisition software. A sinusoidal current of 10 μA was applied across a frequency range of 100 Hz to 100 kHz.

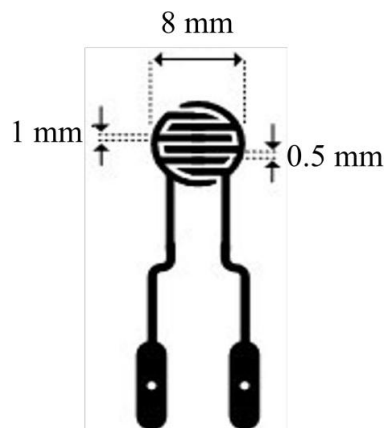


Figure 1. Design and electrode specification of IDE.

As shown in Figure 1, the IDE, fabricated on a glass substrate with seven pairs of gold electrodes (1 mm width, 0.5 mm inter-electrode gap, and 8 mm diameter), enhanced sensitivity to dielectric changes in the blood matrix. For each trial, 100 μL of whole blood was pipetted onto the IDE surface, and impedance spectra including resistance (R), reactance (X), and total impedance (Z)—were recorded. Each measurement was repeated five times to ensure reproducibility, and mean values were used for analysis.

Data analysis included plotting impedance spectra across frequencies, comparing outcomes between groups and metabolic states, and performing correlation and regression analyses to evaluate the relationships between impedance values, glucose concentration, and hemoglobin levels.

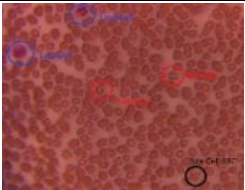
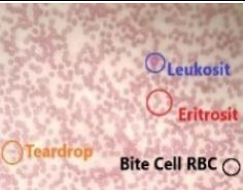
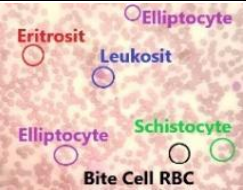
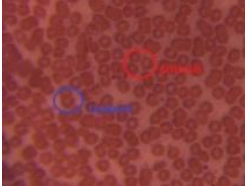
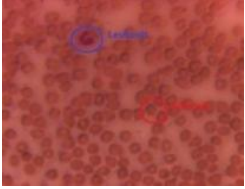
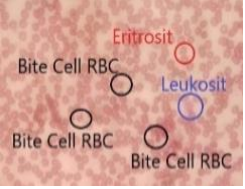
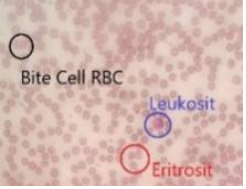
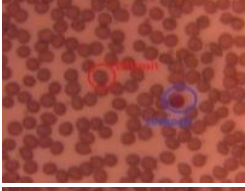
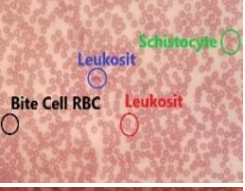
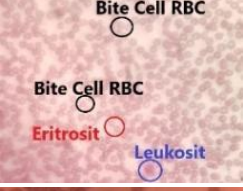
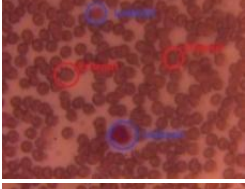
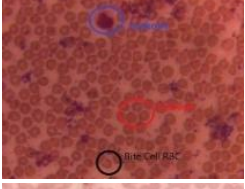
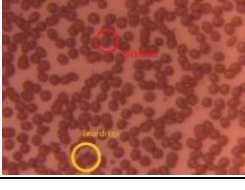
3. RESULTS AND DISCUSSION

This study demonstrates that whole-blood electrical impedance exhibits systematic differences between normoglycemic individuals and patients with type 2 diabetes mellitus (T2DM) across the 100 Hz 100 kHz range, and that these alterations are further influenced by metabolic state (fasting versus postprandial). The observed pattern showed elevated impedance values in T2DM, with partial reduction following meals; however, the persistent separation between groups reflects the biophysical expectation that hyperglycemia, ionic imbalance, and remodeling of red blood cell membranes jointly contribute to the increased resistive and capacitive properties of blood. These findings expand the evidence supporting bioelectrical impedance spectroscopy (BIS) as a minimally or non-invasive tool for assessing glycemic status and hematologic health in diabetes [8, 9].

As shown in Table 1, Morphological analyses reinforced these results, revealing higher frequencies of schistocytes, teardrops, and elliptocytes in T2DM patients. Such alterations align with recent clinical evidence demonstrating reduced red blood cell deformability (RBCD) in diabetes and its role in the development of microvascular complications. For example, a 2024 NIH cohort study using ektacytometry highlighted significant group-level differences in RBCD and identified diabetes related membrane changes as early contributors to vascular dysfunction [10].

Complementary evidence from microdevice research further supports the electrical–mechanical interplay in diabetic erythrocytes; a 2024 Lab on a Chip study applied dielectrophoresis to assess RBC deformability for diagnostic purposes, illustrating how changes in cellular permittivity and viscoelasticity critical determinants of β -dispersion in BIS are measurable in diabetes [11]. Similarly, Coulter-based impedance analyses have yielded novel RBC-derived metrics capable of distinguishing diabetic from normoglycemic individuals, supporting the integrative approach adopted here, which combines hematological, morphological, and impedance data [6].

Table 1. Morphological analyses reinforced these results.

Subject	Normal		DM	
	Fasting	Postprandial	Fasting	Postprandial
1				
2				
3				
4				
5				

The linkage between impedance and glucose dynamics was also evident in the fasting–postprandial comparison, where impedance consistently decreased after meals yet remained higher in T2DM relative to controls. This trend is consistent with controlled experimental models and previous BIS studies that related conductivity to glucose concentration and ionic redistribution. A 2024 “BGP model” employing a four-electrode system, grounded in Geselowitz theory, demonstrated a sigmoidal conductivity response with minimal regression error, echoing the frequency-dependent patterns observed in our study [8]. Classical effective medium frameworks, which differentiate between membrane and cytoplasmic contributions, further explain how changes in red cell capacitance and intracellular conductivity underlie the impedance signatures detected across dispersive regimes [9].

From a clinical standpoint, postprandial glycemia (PPG) is now recognized as a critical target in diabetes care, with inter-individual variability in postprandial glucose responses (PPGRs) even under standardized meals. This variability highlights the importance of multimodal biomarkers, such as BIS, which are sensitive to metabolic state transitions. Recent research emphasizes the importance of 1 – 2 hour postprandial windows for accurate assessment, which aligns closely with our sampling strategy [12].

In the context of emerging non-invasive glucose monitoring, BIS should be considered alongside optical (NIR, Raman), microwave, and ultrasound approaches. Systematic reviews increasingly suggest that hybrid strategies combining multiple modalities yield greater robustness than any single technique. Within this landscape, BIS holds unique value because it simultaneously captures biochemical (glucose), hematological (hemoglobin), and biophysical (RBC membrane) determinants of blood impedance [13-15]. The major strength of this study lies in its integrative design. Combining biochemical, hematological, and bioelectrical assessments within the same cohort

provides a multidimensional perspective on diabetes-related blood alterations that surpasses the scope of single-marker analyses. Wide-band impedance measurements (100 Hz – 100 kHz) situate the data within established dispersion models, facilitating mechanistic interpretation through effective-medium and circuit-based frameworks. Moreover, the inclusion of both fasting and postprandial states enhances clinical relevance by reflecting guideline-recommended evaluation windows and real-world challenges of PPGR variability.

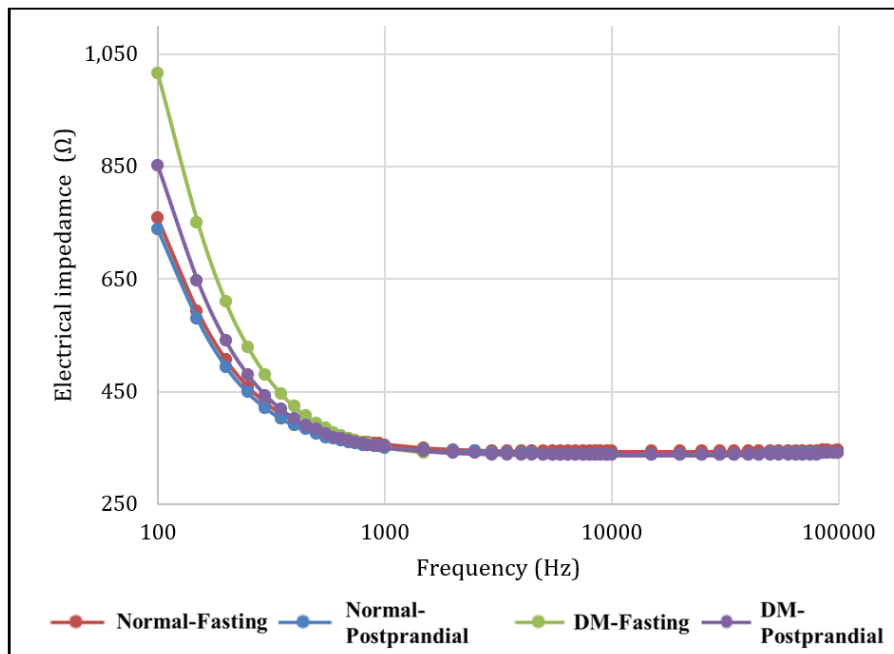


Figure 2. Normal and diabetes mellitus patients under fasting and postprandial conditions.

Nevertheless, certain limitations should be acknowledged. The modest sample size ($n = 10$) restricts statistical power and precludes detailed subgroup analyses, such as by medication class or diabetes duration. Furthermore, the absence of HbA1c, continuous glucose monitoring (CGM), and standardized meal tests limits external validity and the capacity to compare across short- and long-term glycemic indices. Future research should therefore expand cohort sizes to enable multivariable modeling and the integration of machine learning with impedance, hematology, and CGM data; evaluate reproducibility across different electrode geometries and thermal conditions; and benchmark BIS against other non-invasive modalities to assess its incremental value within hybrid monitoring frameworks.

4. CONCLUSION

This study demonstrates that the electrical impedance properties of blood are significantly altered in individuals with type 2 diabetes mellitus compared with normoglycemic controls, and that these alterations are influenced by metabolic states such as fasting and postprandial conditions. By integrating biochemical, hematological, and biophysical parameters — namely, glucose concentration, hemoglobin levels, and erythrocyte morphology —our work establishes a comprehensive electro-hematological profile that reflects the multifaceted impact of diabetes on blood biophysics. The use of wide band impedance analysis (100 Hz – 100 kHz) further provides mechanistic insights into the interplay between glucose, membrane capacitance, and cytoplasmic resistance in shaping impedance spectra. Notably, the inclusion of both fasting and postprandial assessments enhances the clinical relevance of these findings, given the established role of postprandial hyperglycemia in the development of vascular complications. Collectively, these results highlight the promise of bioelectrical impedance spectroscopy as a supportive, non invasive, or minimally invasive tool for diabetes monitoring, with potential applications in wearable and point-of-care technologies within the fields of medical physics and biophysics.

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