International Journal of Ethics in Engineering & Management Education
Website: www.ijeee.in (ISSN: 2348-4748, Volume 1, Issue 4, April 2014)

MEASUREMENT OF BLOOD COAGULATION TIME

Rutu.S.Prabhu [1], Profkalpana.V [2]
[1] M.Tech in Biomedical Electronics & Industrial Instrumentation
E-mail:rutu.prabhu99@gmail.com
[2]Professor and HOD department of IT, PDACEG
E-mail:hodit@pdaengg.com

Abstract: **Blood coagulation is an extremely complicated and dynamic physiological process. Monitoring of blood coagulation is essential to predict the risk of_hemorrhage and thrombosis during cardiac surgical procedures. In this, a high throughput microfluidic chip has been developed for the investigation of the blood coagulation process under temperature and hematocrit variations. The electrical impedance measurement for the definition of blood coagulation process provides a fast and easy measurement technique. The microfluidic chip was shown to be a sensitive and promising device for monitoring blood coagulation process even in a variety of conditions.**

Keywords: ***Bloodcoagulation*****, microfluidic chip,hemorrhage, thrombosis.**

1. INTRODUCTION

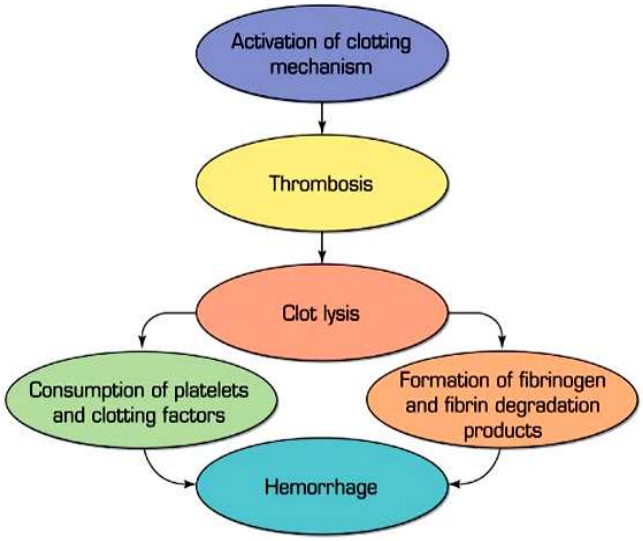
Blood coagulation is a complex, dynamic physiological process by which clots are formed to end bleeding at an injured site.

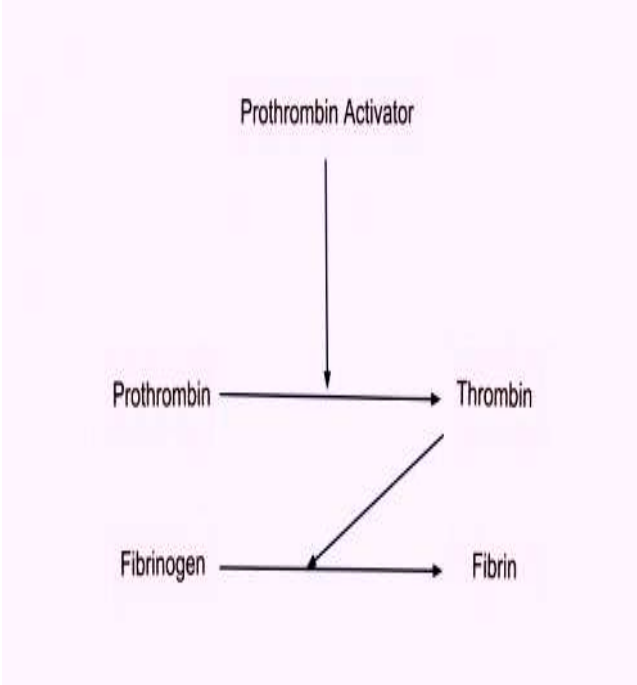
During heart-bypass surgery, blood is diverted out of the body to a heart-lung machine, which maintains heart- and lung function.The machine is operated by a *per fusionist*, whose role includes monitoring appropriate parameters to ensure that the patient is

effectively treated with an anticoagulant to avoid blood clots. Forthis purpose, heparin, an anticoagulant drug, is administered during surgery—followed by a rapid reversal afterwards to prevent excessive bleeding.

1 To maintain the delicate balance between clotting and bleeding, the clotting time of the patient is monitored every 30 to 60 minutes during surgery and several times after surgery, until a normal clotting time is restored.

2 Currently, blood samples taken from a patient's intravenous line are tested at bedside, with measured clotting-time values used to adjust the anticoagulation therapy.



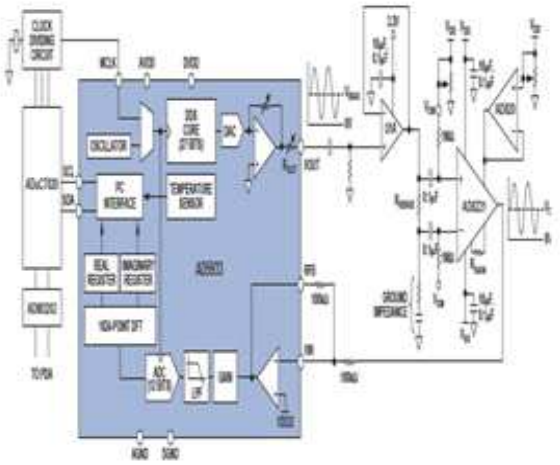


International Journal of Ethics in Engineering & Management Education
Website: www.ijeee.in (ISSN: 2348-4748, Volume 1, Issue 4, April 2014)

2. ELECTRICAL MEASUREMENT OF BLOOD COAGULATION

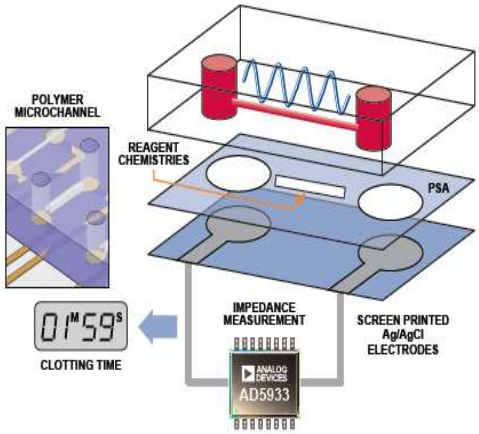
Blood coagulation in the body is modulated by a number of cellular and other active components. The *coagulation cascade* describes the components of blood and how they are involved in the process of clot formation. As the cascade becomes activated, the blood progresses from a nonclotting to a clotting state, causing changes in both molecular charge states and effective charge mobility. The final steps of the cascade involve two components, *thrombin* and *fibrinogen*. Thrombin acts by cutting the fibrinogen, forming fibrin filaments—which spontaneously aggregate. The endpoint of clotting time has been defined as the time at which a fibrin clot is formed.

By monitoring the global impedance of a clotting blood sample, the changes in conductivity associated with clot formation are measured. To evaluate instrument performance, the clotting time
determined from the data was correlated to a "gold standard" clinical measurement of clotting time.



3. THE BLOOD-COAGULATION MEASUREMENT SYSTEM

The interface between the blood-sample delivery and the measurement instrumentation is critical. In this case, a specific microfluidic channel into which the blood sample was delivered was designed to connect to the AD5933 instrumentation circuit
(Figure). The microfluidic device consists of three layers. The bottom layer comprises two screen printed electrodes, which were connected to the input/output port pins of the AD5933 circuit. The top micromolded polymer channel consists of two reservoirs connected via a microchannel. The chemical reagents that modulate the clotting reaction can be contained either within this microchannel or on the central bonding layer. The top- and bottom
channels are bonded using a pressure-sensitive adhesive (PSA). The blood sample applied to one reservoir filled the microchannel.
This was contacted by the screen-printed electrodes, which were in turn interfaced to the AD5933 circuit



. A schematic illustration of the
impedance measurement system with the polymer microchannel that contains the blood sample to be measured is showm. It allows the sample to interact with the specific reagents that modulate the clotting event, and creates the interface between the sample and the AD5933 instrumentation.

4. BLOOD SAMPLE HANDLING

Fresh whole blood was mixed with 15% acid citrate dextrose (ACD) ant icoagulation solution at the slaughterhouse in order to prevent coagulation during transportation. Then, the blood was passed through a sponge to filter out impurities, such as hair and fatty tissue, and discarded whenever coagulation is observed. The whole blood was subsequently centrifuged at 3,200 rpm for 12 min to separate the blood into the composition of packed erythrocytes and the plasma. The red blood cells were then rinsed twice by a buffered saline solution. Then, the erythrocytes and the plasma were stored at 4°C before the experiments. Blood sample in storage was discarded if the experiments were not started within 1 week.

5. MEASUREMENT OF THE BLOOD SAMPLE UNDER TEMPERATURE AND HEMATOCRIT VARIATIONS

The red blood cells aggregation is a normal, reversible, physiological process occurring in whole blood. It is the kinetics of rouleaux formation depending on the various parameters, such as temperature and hematocrit. The aggregation may increase blood viscosity, increase flow resistance, form sludge blood in vessels, increase the interaction of leukocytes with the endothelium, and promote blood coagulation. As the coagulation mechanism is induced, thrombin acts as an enzyme to convert fibrinogen into fibrin

fibers that enmesh blood cell and plasma. The blood then becomes a solid gel and a clot forms that comprises a meshwork of fibrin fibers running in all directions that entrap erythrocytes and plasma. The coagulation of blood is an extremely complicated and dynamic process and this work is to investigate the blood coagulation process based on the electrical impedance change of the blood.

Prior to each measurement, the erythrocytes and the plasma were taken out from the storage and placed at room temperature for 30 min. Then, the whole blood sample was mixed by the erythrocytes and the plasma at a certain volume ratio. The ratio is represented by hematocrit. Blood coagulation is induced by adding 0.5 M $CaCl_2$ solution into the blood sample in the volume ratio of 1:10. Hence, 10 µl blood sample was loaded to the well on the microfluidic chip by manual pipetting. The chip was placed in a temperature controlled incubator and investigation of the blood coagulation process was started. Electrical impedance of the blood including magnitude and phase angle was measured across the electrodes. Potential of 0.1 V was applied and the impedance was measured from 100 Hz to 10 kHz. The impedance of blood was recorded continuously with a step of 20 sec until the finish of blood coagulation.

5. CONCLUSION

The AD5933 single-chip impedance analyzer has been successfully applied to the measurement of blood-impedance changes during coagulation. It offers flexibility, power, and size advantages to
the end user over the existing commercially available solutions. Combining integrated-circuit technologies of this sort with new technologies in other media, such as microfluidics and sample handling, provides a powerful platform for future medical device
research and development.

REFERENCES

[1]. Murano G, Bick RL (2000) Basic concepts of hemostasis and thrombosis, CRC Press.
[2]. Langdell R, Wagner R, Brinkhous K (1953) Effect of antihemophilic factor on one-stage clotting tests; a presumptive test for hemophilia and a simple one-stage antihemophilic factor assay procedure. J. Lab. Clin. Med. 41(4): 637–647. doi: 10.1016/b978-012448510-5.50174-6
[3]. White GC (2003) The partial thromboplastin time: defining an era in coagulation. J. Thrombosis Haemostasis 1: 2267–2270. doi: 10.1046/j.1538-7836.2003.00459.x
[4]. Carpenter GP, Neel TG, Parker JR (1994) Overview of a novel point of care instrument system for measuring whole blood prothrombin time. Proc. Soc. Photo Opt. Instrum. Eng. 2136: 205–213. doi: 10.1143/jjap.45.7191
[5]. Huang CC, Wang SH (2006) Characterization of blood properties from coagulating blood of different hematocrits using ultrasonic backscatter and attenuation. Jap. J. App. Phys. 45: 7191–1796. doi: 10.1143/jjap.45.7191
[6]. Puckett LG, Barrett G, Kouzoudis D, Grimes C, Bachas LG (2003) Monitoring blood coagulation with magnetoelastic sensors. Biosens. Bioelectron. 18: 675–681.