Uric acid detection by using contactless intensity modulation based displacement sensor

N N G M A Gan¹, N A M Taib*, M Abdullah², W M Mukhtar¹ and A R A Rashid¹

¹Faculty of Science and Technology, Universiti Sains Islam Malaysia
² Institute of Nano Optoelectronics Research and Technology, Universiti Sains Malaysia

athirahtaib@usim.edu.my

Abstract. A simple and contactless intensity modulated displacement sensor is proposed and demonstrated for sensing uric acid concentration. For a concentration change of uric acid from 0 ppm to 500 ppm, two peak voltages are obtained from the displacement curve corresponding to the highest reflectivity of each concentration. Those peak light intensities increase linearly with the concentration due to the increase of the refractive index of the uric acid solution. This implies that the higher concentration of uric acid tends to detect a stronger signal. The measured sensitivities are obtained at 0.0015 V/ppm and 0.0016 V/ppm for the first peak voltage and second peak voltage respectively. The result showed the percentage of similarity for the first peak to the second peak is almost 94% and the linearity more than 97% for both peak voltages is obtained suggested the consistency of the sensor system. The stability and simplicity of the contactless sensor offer a good and valuable opportunity for many applications especially in the hazardous chemical, pharmaceutical, process control and diagnostic sectors.

1. Introduction
Uric acid is a heterocyclic organic compound with C5H4N4O3 formula (7,9-dihydro-1H-purine-2,6,8(3H)-trione). It is the final oxidation product of purine metabolism as shown in Figure 1. The elevated uric acid level causes the deposition of monosodium urate crystals. As urate concentration increase in the blood, uric acid crystal formation increases. The normal reference interval of uric acid in human blood is 1.5 to 6.0 mg/dL in women and 2.5 to 7.0 mg/dL in men [1]. Meanwhile, Chauhan and Pundir cited the normal range of uric acid should fall in between 0.15-0.45 mmol/L for blood and 1.19-2.98 mmol/day in urine excretion [2].

![Figure 1. The final product of purine metabolism (uric acid)](image-url)
Overproduction of uric acid by the metabolism of purines has been proven to play emerging roles in human disease. The high uric acid content is regarded as a biomarker of gout that often linked with obesity, diabetes, muscle stiffness and heart diseases which can be diagnosed and treated based on the level of attack [3]. Similarly, uric acid may be potentially a sign for kidney disease [4] and there are some works have suggested that uric acid contributest to the development of cardiovascular disease [5] and respiratory disease [6]. In order to avoid those diseases from proliferating, the monitoring of uric acid level is pressing. Therefore, it is necessary to develop a simple and reliable method for the detection of uric acid level. Monitoring uric acid is important because it can be used as a powerful indicator for early sign of diseases.

There have been several kinds of research done on the detection of the uric acid level. UV-VIS spectrometer is the simplest high technology method capable of differentiating uric acid based on their respective absorbance [7]. Apart from that, the performance response of spectrophotometric by [8] is excellent and close to clinical method however required to deal with the sensitive enzymatic reaction which is expensive and prone to metabolite. In the electrochemical method, the modified electrode surface by nanomaterials such as reduced graphene oxide-zinc oxide nanorods composite [9] and gold nanoparticles [10] showed a very good result of low detection limit and large linear range capabilities for selective determination in uric acid. Another way to determine the uric acid level is by fabrication of fiber-coated sensitive medium [11–13]. These coating sensitive medium based fiber optic operate based on intensity modulation of guided light and evanescent wave concept. It is indeed undeniable that the incorporation of nanoparticles and nanomaterials will enhance the performance such as the sensitivity, limit of detection as well as the linear range, however, some of them are very costly, complicated and required a highly skilled to handle with during the modification and fabrication processes. Some part of the probes needs to be removed and immersed in the sample solution in other to obtain the output which tends to increase the chance of contamination and inconsistency area of removal parts.

In this paper, a simple, cost-effective and reliable contactless fiber-optic sensor based on displacement method is proposed and demonstrated for the detection of uric acid concentration. The sensor uses a bundled fiber of having a transmitting fiber and 16 receiving fibers as a probe and the probe is non-contact to the uric acid solution. The detection is based on contactless sensing of uric acid concentration using intensity modulation technique via displacement method that is the analysis of light reflectivity on the surface of uric acid solution.

2. Methodology

The schematic diagram of the experimental setup for a contactless displacement sensor which is used to measure the uric acid concentration by using intensity modulation is shown in Figure 2. The setup consists of a light source, bundled fiber probe, automated displacement controller, silicon detector, oscilloscope and computer. A bundled fiber probe comprised of a transmitting fiber and 16 receiving fibers is connected to a 650 nm red laser diode source. The cross-sectional view for the bundle probe is also depicted in Figure 2. When the light from diode laser with output power of 9.3 mW is coupled into a transmitting fiber and illuminated the liquid surface which is meniscus due to surface tension effect, the light is reflected back assuming that the liquid surface is a virtual reflector [14], then the light signals are received by the receiving fibers which cascading them directly to the silicon detector. The silicon detector (DET100A2, Thorlabs) has an optical response of 320 nm to 1100 nm, making it compatible with a wide range of visible light for detection of light signals including 650 nm visible red laser used for optimum transmission. The working principle of the sensor is verified by the displacement as the main parameter. The position of the automated displacement controller is monitored by software provided by Cytron Technologies installed in a computer. The probe displacement is accomplished by attaching the displacement controller rigidly to a vibration free optical table. A precise displacement of 40 mm is taken for every sample by shifting the bundled probe away from liquid meniscus in a vertical axis. The range of the displacement is taken between 0 to 40 mm as a fingerprint of the sensor works effectively within this range.
The position of the fiber probe must be as close as possible to the liquid surface and located in the middle on the main axis of the liquid meniscus for this position is acting as a reference point of the probe shift. A single shot signal is captured by an oscilloscope (TDS1002B; 2 CH, 60 MHz, 1 Gs/s for data analysis and evaluation subsequently yielding an informative response graph which is important in sensor characterization. The uric acid concentration ranging from 0 ppm to 500 ppm is used as a sample and prepared by dissolving in distilled water. The different uric acid concentration has proven to have different refractive index [11].

![Diagram](image)

Figure 2. Schematic experimental setup of uric acid detection

3. Result and discussion

The relationship between concentration and refractive index of uric acid is plotted in Figure 3. The uric acid refractive index was found to be linearly increased from 1.3330 RIU to 1.3336 RIU with respect to its concentration. There is a high potential that different refractive index of uric acid in the solution influence the amount of light being reflected by the surface.

Figure 4 depicts the sensor fingerprint of output voltage against the displacement for different uric acid concentration. In general, all displacement curves have a similar trend; there are two maximum output voltages with a slightly broad distance between each curve. The positive front slope of the first peak curve rises up steeply and the negative back slope of the second peak drop gradually along with the displacement. The shape of displacement response occurs as a result of the meniscus formation of the liquid sample while the maximum voltages correspond to the difference in the refractive index value.

At small displacement, that means the sensor probe is nearly touched with the meniscus, there is a little overlapping between the core of receiving fiber and emitted a light cone of transmitting fiber leads to a quite low intensity has been detected by the photodiode. As the displacement increases, the intensity increases as the size of overlapping area becomes larger and eventually reaches the first maximum point when the core of the receiving fiber is totally immersed by the cone of the emitted light. The intensity reduces with further increase in displacement because of inverse square law. Interestingly, as the sensor probe approaches a distance of roughly around 9 mm, the displacement response comes to local minima.
The output voltage once again rises up attaining the second maximum point which is located at nearly 10 times of the first peak distance and decreases again following the inverse square law. That is, the power density of light from transmitting fiber now is weak and far enough from the meniscus and eventually, the output voltage drop as a result of less power is collected by the receiving fiber.

Figure 3. Refractive index and concentration relationship

Figure 4. Sensor fingerprint as a function of displacement
The peak voltage from each response curve of the uric acid solution is plotted against its respective concentration as shown in Figure 5. It can be observed that the peak voltage increases when the concentration increases for both peak voltages. The slope is used to determine the sensitivity of the sensor. In the figure, the sensor achieves approximately similar sensitivity up to 94% for both first and second peak voltage which are 0.0015 V/ppm and 0.0016 V/ppm respectively. This implies the consistency of the sensor able to detect the same output even the probe is displaced far away from the liquid surface. Moreover, the sensor exhibits good linearity of more than 97% with a low detection limit of 16.8 ppm and 15.8 ppm indicating that the sensor could work efficiently in detecting uric acid level in the human body and applicable to be a potential sensor for medical application concerning the issue of the uric acid-related diseases. The sensor performance of the uric acid detection is tabulated in Table 2.

![Figure 5. Peak voltage (V) as a function of concentration (ppm)](image)

Table 1. Sensor performance of uric acid detection

| Parameter                | Peak Voltage (V) |
|--------------------------|------------------|
|                          | First Peak Voltage | Second Peak Voltage |
| Sensitivity (V/ppm)      | 0.0015            | 0.0016              |
| Measurement range (ppm) | 0 - 500           |                     |
| Linearity (%)            | > 97              | > 98                |
| Resolution (ppm)         | 16.8              | 15.8                |
4. Conclusion
An uric acid sensor has been introduced using an intensity modulation technique as a device to detect uric acid concentration. The sensor operates based on the contactless displacement sensor. In the experiment, the probe is non-contact with the liquid surface but must be as close as possible in order to attain uniform displacement pattern. Two peak voltages extracted from the displacement curves show excellent characteristics in determining the concentration of uric acid in the range of 0 ppm to 500 ppm. The peak voltages are proportional to the concentration due to the difference in the refractive index value. The sensitivities obtained are 0.0015 V/ppm and 0.0016 V/ppm respectively with slope linearity of more than 97% and detection limit of 16.8 ppm and 15.8 ppm which are differed in slightest value suggesting that the sensor is capable of producing output voltage consistently. This finding has great potential and useful for many applications especially in a diagnostic sector such as for liquid parameter calibration like surface tension, which has becoming a new interest in the medical area due to surface tension in human fluids are discovered varying with pathological disorders.

References
[1] Maiuolo J, Oppedisano F, Gratteri S, Muscoli C, and Mollace V 2016 Regulation of uric acid metabolism and excretion. Int. J. Cardiol, 213, 8–14.
[2] Chauhan N and Pundir C S 2011 An amperometric uric acid biosensor based on multiwalled carbon nanotube-gold nanoparticle composite. Anal. Biochem, 414(2), 97–103.
[3] Tausche A K, Jansen T L, Schröder H E, Bornstein S R, Aringer M, and Müller-Ladnay U 2009 Gout--current diagnosis and treatment. Dtsch. Ärzteblatt Int, 106(34–35), 549–555.
[4] Giordano C, Karasik O, King-Morris K, and Asmar A 2015 Uric acid as a marker of kidney disease: Review of the current literature. Dis. Markers, 2015.
[5] Borghi C 2015 The role of uric acid in the development of cardiovascular disease. Curr. Med. Res. Opin, 31(S2), 1–2.
[6] Horsfall L J, Nazareth I, and Petersen I. 2014 Serum uric acid and the risk of respiratory disease: A population-based cohort study. Thorax, 69(11), 1021–1026.
[7] Norazmi N, Abdul Rasad Z R, Mohamad M, and Manap H 2017 Uric acid detection using UV-VIS spectrometer. IOP Conf. Ser. Mater. Sci. Eng. 257(012031), 1-6.
[8] Hamzah H H 2013 Spectrophotometric determination of uric acid in urine based-enzymatic method uricase with 4-Aminodiphenylamine diazonium sulfate (Varamine Blue RT Salt),” J. Anal. Bioanal. Tech. S7, 1-6.
[9] Fu L, Zheng Y, Wang A, Cai W, Deng B, and Zhang Z 2016 An electrochemical sensor based on reduced graphene oxide and ZnO nanorods-modified glassy electrode for uric acid detection. Arab. J. Sci. Eng, 41(1), 135–141.
[10] Shi Y, Wang J, Li S, Yan B, Xu H, Zhang K and Du Y 2017 The enhanced photo-electrochemical detection of uric acid on Au nanoparticles modified glassy carbon electrode. Nanoscale Research Letter, 12(455), 1–6.
[11] Batumalay M, Harun S W, Ahmad F, Nor R M, Zulkepely N R and Ahmad H 2014 Tapered plastic optical fiber coated with graphene for uric acid detection. IEEE Sens. J, 14(5), 1704–1709.
[12] Batumalay M, Harith Z, Rafaei H A, Ahmad F, Khasanah M, Harun S W, Nor R M and Ahmad H 2014 Tapered plastic optical fiber coated with ZnO nanostructures for the measurement of uric acid concentrations and changes in relative humidity. Sensors Actuators, A Phys, 210(2014), 190–196.
[13] Batumalay M, Ahmad F, Lokman A, Jasim A A, Harun S W, and Ahmad H 2014 Tapered plastic optical fiber coated with single wall carbon nanotubes polyethylene oxide composite for measurement of uric acid concentration. Sens. Rev., 34(1), 75–79.
[14] Krishnan G, Bidin N, Abdullah M, Ahmad M F S, Bakar M A A, and Yasin M 2016 Liquid refractometer based mirrorless fiber optic displacement sensor. Sensors Actuators, A Phys., 247(2016), 227–233.