Development of a surface plasmon resonance acetone sensor for noninvasive screening and monitoring of diabetes

F Usman 1,A, J O Dennis1 and F Meriaudeau2

1Department of Fundamental and Applied Sciences, Universiti Teknologi PETRONAS (UTP), Bandar Seri Iskandar, 31750 Tronoh, Perak, Malaysia
2Department of Electrical and Electronic Engineering, Universiti Teknologi PETRONAS (UTP), Bandar Seri Iskandar, 31750 Tronoh, Perak, Malaysia
3Department of Physics, Al-Qalam University Katsina, Nigeria

*Email: fahatu11@gmail.com

Abstract. Diabetes can cause many complications in the human body. The disease is commonly diagnosed using blood glucose test. A good correlation between blood glucose and exhale breathe acetone has opened a way for non-invasive diagnosis through the detection of the breath acetone from the exhale breathe. However, the conventional means of detecting exhale breathe acetone (e.g. GC-MS) are bulky, require technical knowhow, do not offer real time measurement and found only at advanced institutions that can afford the equipment. This work is aimed at developing a real time, sensitive and selective optical based Surface Plasmon Resonance (SPR) breath acetone biosensor for non-invasive monitoring and screening of diabetes. The motivation of this work arises from the promising advantages of optical based biosensors over other biosensors. Additionally, a novel doped polyaniline (PANI) conducting polymer would be the SPR metallic layer while Chitosan would be the selective sensing layer. Mathematical modeling and SPR simulation has been conducted. The result has shown that the replacement of conventional gold or silver SPR layer with doped Polyaniline (PANI) SPR layer provides better promising sensitivity at mid infrared wavelength range. Therefore, additional inclusion of chitosan layer on the proposed SPR based biosensor would give rise to a sensitive and selective breathe acetone biosensor for easy monitoring and screening of diabetes.

1. Introduction
Diabetes has been listed among the most common life threatening diseases affecting humanity globally. The number of persons suffering from diabetes (type-1 and -2) is increasing due to population growth, aging, urbanization, increasing occurrence of obesity and physical inactivity [1, 2]. In order to hinder its rapid occurrence, Proper means of diagnosis is fundamental to hindering the disease. Currently diabetes is diagnosed through blood glucose test. Unfortunately, the method requires trained personnel, consumes time, laboratory restricted usage, invasive procedures etc.[2, 3]. Exhale breathe acetone has been identified as a good biomarker for diabetes that can provide a non-invasive detection of diabetes [2, 4, 5]. It has been stated that Acetone concentration in the human body is generally very low (0.1 ppm - 0.8 ppm), while it might be high in the case of metabolism disorders, including diabetes mellitus (DM) (1.8 ppm – 5.0 ppm) [6].

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Since the recognition of exhale breath acetone as the diabetes biomarker, a lot of researches have been conducted in a move to its ease detection [7-14]. The conventional means of acetone detection includes gas chromatography – mass spectrometry (GC-MS), selected ion flow tube mass spectrometry (SIFT-MS), proton transfer reaction mass (PTR-MS), high performance liquid chromatography (HPLC), ion mobility spectrometry (IMS), plus laser techniques like tunable diode laser absorption spectroscopy (TDLAS) and cavity ring down spectroscopy (CRDS) etc. They are capable of detecting trace of acetone vapour with better sensitivity and selectivity relatively. However, these methods rely on sophisticated instrumentation, complicated sample collection methods, expensiveness and present only at advanced medical institutions that can afford [15].

Fortunately, the detection of exhale breath acetone via biosensors has been shown to feature many advantages over the conventional method. Easy and real time noninvasive detection is possible. In fact, it solves most of the problems associated with the other methods. Biosensors are generally devices that can respond to a physical stimulus (analyte) of biological interest and converts (transduce) the stimulus into a signal conveyed to another device (computer/detector) for interpretation [16-21]. Most of the exhale breathe acetone biosensors are fabricated using metal oxide semiconducting materials based on chemiresistive transduction method [4, 10, 11, 22-30]. However, metal oxide chemiresistive biosensors suffer from high operational temperature issue [15, 31, 32]. Contact resistance influence also results to unreliable selectivity[33]. Furthermore, the humidity influence is another issue of concern [23]. In addition, most of the fabrication processes were complicated; incorporating non-easy to find materials, difficult to process and synthesis materials and features poor biocompatibility.

Some of the advantages of optical biosensors over other types of biosensors are: greater sensitivity, electrical passiveness, freedom from electromagnetic interference, wide dynamic range, non-requirement of reference electrode, free from electrical hazards, high stability relatively, potential for higher-information content than electrical transducers, multiplexing capabilities etc[14, 24, 28, 34-38]. Surface Plasmon Resonance (SPR) based sensors has been identified to be a promising biosensor among optical biosensors [18, 19, 39]. It measures the amount of an analyte by exploiting the change in the refractive index at the interface of metal/heavily doped semiconductor-dielectric interface.

When a light source is incidented on a metal/heavily doped semiconductor-dielectric interface, after total internal reflection, a drop is observed on the reflected light at a particular angle called SPR angle. Presence of a biomolecule or any other material at the vicinity of the interface shifted the SPR angle. This shift is called dip. In order to achieve a cheapest, highly selective and sensitive breath acetone biosensor, this work is mainly aimed at developing an SPR based breath acetone sensor for diabetes’ monitoring and screening with doped Polyaniline (PANI) as the SPR layer and chitosan polymer as the highly selective active sensing layer. As part of the fabrication process, the initial result from the mathematical modeling and simulation is presented in this paper.

2. Mathematical modelling and simulation

2.1. Mathematical modelling

The mathematical modeling of the SPR based breathe acetone biosensor started with the modeling of the surrounding of the biosensor. Penetration depth through doped PANI layer ( \( \delta_{PANI} \) ) and dielectric ( \( \delta_d \) ) are the most important in this regard. The penetration depth in the dielectric gives idea on surrounding sensitivity, while the penetration depth into doped PANI gives idea of the thickness of the doped PANI film required for the coupling of light. The equations for the penetration depth through doped PANI and dielectric (air) are (equation (1) and (2), respectively):

\[
\delta_{PANI} = \frac{\lambda_0}{2\pi} \left[ \frac{\varepsilon_{PANI} + \varepsilon_d}{\varepsilon_{PANI}^2} \right]^{1/2}
\]

(1)

\[
\delta_d = \frac{\lambda_0}{2\pi} \left[ \frac{\varepsilon_{PANI} + \varepsilon_d}{\varepsilon_d^2} \right]^{1/2}
\]

(2)
Equations (3)-(7) were used for remaining part of the mathematical modeling. The values obtained by [40] and [41] at mid infrared wavelength range in table 1 were used throughout the modeling.

**Table 1.** Optical properties for the materials of the proposed PANI.

| S/N | Material   | Real dielectric constant | Imaginary dielectric constant | Refractive index |
|-----|------------|--------------------------|--------------------------------|------------------|
| 1   | Doped PANI | -30.62                   | 2                              | -5.5             |
| 2   | Chitosan   | 2.25                     | 0                              | 1.5              |
| 3   | Acetone    | 1.25                     | 0                              | 1.12             |
| 4   | Air        | 1.00                     | 0                              | 1.00             |
| 5   | Silica     | 2.1                      | 0                              | 1.45             |

\[ e_{\text{eff}} = \frac{1 + 2 f_{ch} \left( \frac{\varepsilon_{ch} - \varepsilon_{\text{PANI}}}{\varepsilon_{ch} + 2 \varepsilon_{\text{PANI}}} \right)}{1 - f_{ch} \left( \frac{\varepsilon_{ch} - \varepsilon_{\text{PANI}}}{\varepsilon_{ch} + 2 \varepsilon_{\text{PANI}}} \right)} \]  

\[ \theta_{\text{SPR}} = \sin^{-1} \left[ \frac{\varepsilon_{\text{PANI}} \varepsilon_d}{\sqrt{(\varepsilon_{\text{PANI}} \varepsilon_d + \varepsilon_p) \varepsilon_p}} \right] \]  

\[ \theta_{\text{SPRR}} = \sin^{-1} \left[ \frac{\varepsilon_{\text{eff}} \varepsilon_d}{\sqrt{(\varepsilon_{\text{eff}} + \varepsilon_d) \varepsilon_p}} \right] \]  

\[ \theta_{\text{SPRRA}} = \sin^{-1} \left[ \frac{\varepsilon_{\text{eff}} \varepsilon_{Ac}}{\sqrt{(\varepsilon_{\text{eff}} + \varepsilon_{Ac}) \varepsilon_p}} \right] \]  

\[ \theta_{\text{shift}} = (\theta_{\text{SPRRA}}) - (\theta_{\text{SPR}}) \]

where, \( \varepsilon_{\text{PANI}} \) is the real part of the dielectric constant of doped PANI, \( \varepsilon_d \) is the relative permittivity of the dielectric (air), \( \lambda_0 \) is the free space wavelength, \( \varepsilon_p \) is the dielectric constant of the material of the prism, \( e_{\text{eff}} \) is the effective dielectric constant of the doped PANI/chitosan bilayer, \( e_{ch} \) is the dielectric constant of chitosan, \( f_{ch} \) is the fractional thickness of chitosan, \( \theta_{\text{SPR}} \) is the SPR angle, \( \theta_{\text{SPRR}} \) is the SPR Angle (doped PANI/chitosan bilayer), \( \theta_{\text{SPRRA}} \) is the SPR Angle (bilayer plus Acetone), \( \theta_{\text{shift}} \) is the SPR shift (which is correlated with the concentration of breathe acetone) and \( \varepsilon_{Ac} \) is the dielectric constant of the analyte (Acetone).

2.2. SPR simulation

The simulation has been carried out using WinSpall SPR simulation software built based on Fresnel equations. Mid infrared wavelength (3000nm) and hemispherical prism options were also selected for the simulation in the case of the doped PANI. However, visible wavelength was used in simulating SPR curves for gold and silver that were aimed for comparison purpose.

3. Result and discussion

3.1. Theoretical calculations

Theoretically, the SPR phenomenon is expected to occur at 43° (table 2). This indicates wide detection range capability. The penetration depth also shows the need for increasing the thickness of doped PANI layer. Also, the penetration depth through the dielectric (2.68 \( \mu \)m) shows how sensitive the sensor could be. A very huge SPR shift is observed (6.41°) after slightly changing the refractive index.
of the dielectric medium by exposing the biosensor to breathe acetone. This indicates promising high sensitivity of the proposed biosensor.

Table 2. Result of theoretical modeling of SPR breathe acetone biosensor.

| Parameter | Value  |
|-----------|--------|
| $\delta_{PANI}$ | 88 nm |
| $d$ | 2.68 µm |
| $\theta_{SPR}$ | 42.77° |
| $\theta_{SPRB}$ | 42.84° |
| $\theta_{SPRBA}$ | 49.25° |
| $\theta_{shift}$ | 6.41° |

3.2. WinSpall simulation

The simulated result in figure 1(a) confirms the good sensitivity of this SPR based biosensors to slight change in the refractive index of breathe acetone. Similar to the modeling result, it shows an SPR shift with acceptable deviation (8°). Also, the expected better sensitivity of this SPR based biosensor over conventional gold and silver based SPR based biosensors is highlighted in figure 1 (b). Its SPR curve using is sharper than Gold and silver ones. The sharpness generally indicates greatness in terms of sensitivity and accuracy.

Figure 1. (a) SPR simulation of $\theta_{SPRB}$, $\theta_{SPRBA}$ and $\theta_{shift}$ (b) Comparison of SPR angle between doped PANI, gold and silver layers.

4. Conclusion

The mathematical modeling and the SPR simulation of the doped PANI layer produces almost similar results. The shifts in SPR angle were 6.41° and 8° for the modelling and the simulation respectively. Slight change in dielectric constant of 0.1 order has shown to be detectable by the biosensor. Also, the doped PANI/Chitosan SPR curve was sharper than that of both the conventional gold and silver. Therefore, our proposed biosensor is expected to provide a reliable non-invasive monitoring and screening of diabetes.

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References
[1] S. Wild, G. Roglic, A. Green, R. Sicree, and H. King, "Global prevalence of diabetes: estimates for the year 2000 and projections for 2030 Diabetes Care 27: pp 1047-53," 2004
[2] M. Righettoni and A. Tricoli, "Toward portable breath acetone analysis for diabetes detection," Journal of breath research, vol. 5, p. 037109, 2011
[3] P. Songthung and K. Sripanidkulchai, "Improving type 2 diabetes mellitus risk prediction using classification," 13th Int. Joint Conf. on Computer Science and Software Engineering (JCSSE), 2016, pp 1-6
[4] B. Bhowmik, V. Manjuladevi, R. Gupta, and P. Bhattacharyya, "Highly selective low-temperature acetone sensor based on hierarchical 3-D TiO2 nanoflowers," IEEE Sensors Journal, vol. 16, pp 3488-95, 2016
[5] S. Das, A. Bag, R. Kumar, and D. Biswas, "Fast Response (7.6 s) Acetone Sensing by InGaN/GaN on Si (111) at 373 K," IEEE Electron Device Letters, vol. 38, pp 383-86, 2017
[6] A. Rydosz, K. Wincza, and S. Gruszczynski, "Microsystem in LTCC technology for the detection of acetone in healthy and diabetes breath," in ANDESCON, 2016 IEEE, 2016, pp 1-4
[7] A. Nooke, "Gas Detection by Means of Surface Plasmon Resonance Enhanced Ellipsometry," Dissertation, Berlin, Technische Universität Berlin, 2012
[8] B. Lakard, S. Carquigny, O. Segut, T. Patois, and S. Lakard, "Gas sensors based on electrodeposited polymers," Metals, vol. 5, pp 1371-86, 2015
[9] S. Karthikeyan, H. M. Pandya, M. Sharma, and K. Gopal, "Gas sensors-a review," J. Environ. Nanotechnol, vol. 4, pp 01-14, 2015
[10] Z. Jiang, R. Zhao, B. Sun, G. Nie, H. Ji, J. Lei, et al., "Highly sensitive acetone sensor based on Eu-doped SnO2 electrospun nanofibers," Ceramics International, vol. 42, pp 15881-888, 2016
[11] T. Hyodo, T. Kaino, T. Ueda, K. Izawa, and Y. Shimizu, "Acetone-Sensing Properties of WO3-Based Gas Sensors Operated in Dynamic Temperature Modulation Mode—Effects of Loading of Noble Metal and/or NiO onto WO3—," Sensors and Materials, vol. 28, pp 1179-89, 2016
[12] G. W. Hunter, R. A. Dweik, D. B. Makel, C. C. Grigsby, R. S. Mayes, and C. E. Davis, "Portable Breath Monitoring: A New Frontier in Personalized Health Care," The Electrochemical Society Interface, vol. 25, pp 63-67, 2016
[13] K. Toda, R. Furuie, and S. Hayami, "Recent progress in applications of graphene oxide for gas sensing: A review," Analytica chimica acta, vol. 878, pp 43-53, 2015
[14] J. Lou, Y. Wang, and L. Tong, "Microfiber optical sensors: A review," Sensors, vol. 14, pp 5823-44, 2014
[15] Q. Zhang and D. Wang, "Room temperature acetone sensor based on nanostructured K 2 W 7 O 22," in SENSORS, 2016 IEEE, 2016, pp 1-3
[16] A. Biacore, "Biacore sensor surface handbook," GE Healthcare Bio-Sciences AB: Uppsala, Sweden, 2003
[17] G. Healthcare, "Biacore assay handbook," Bio-Sciences AB, Uppsala, Sweden, 2012
[18] L. Kapinos, R. Schoch, and R. Y. Lim, "Surface Plasmon Resonance (SPR)."
[19] M. Lesňák, F. Staněk, I. Hlavatý, J. Pištor, and J. Procházka, "SPR Method and Its Utilisation for Low Alcohols Concentrations Determination," Journal of Modern Physics, vol. 6, p 363, 2015
[20] V. Perumal and U. Hashim, "Advances in biosensors: Principle, architecture and applications," Journal of Applied Biomedicine, vol. 12, pp 1-15, 2014
[21] A. P. Turner, "Biosensors: sense and sensibility," Chemical Society Reviews, vol. 42, pp 3184-96, 2013
[22] M. Esmaeili, G. Kiani, F. Shahriari Nogorani, and S. Boroomand, "Acetone sensing properties of hierarchical WO3 core-shell microspheres in comparison with commercial nanoparticles,"
[23] A. Fioravanti, S. Morandi, and M. Carotta, "Chemoresistive gas sensors for sub-ppm acetone detection," Procedia Engineering, vol. 168, pp 485-88, 2016
[24] J. Fraden, Handbook of modern sensors vol. 3: Springer, 2010
[25] I. Fratoddi, I. Venditti, C. Cametti, and M. V. Russo, "Chemiresistive polyaniline-based gas sensors: A mini review," Sensors and Actuators B: Chemical, vol. 220, pp 534-48, 2015
[26] V. Galstyan, E. Comini, I. Kholmanov, A. Ponzoni, V. Sberveglieri, N. Poli, et al., "A composite structure based on reduced graphene oxide and metal oxide nanomaterials for chemical sensors," Beilstein Journal of Nanotechnology, vol. 7, pp 1421-27, 2016
[27] H. Jamalabadi and N. Alizadeh, "Enhanced Low-Temperature Response of PPy-WO3 Hybrid Nanocomposite Based Gas Sensor Deposited by Electropinning Method For Selective and Sensitive Acetone Detection," IEEE Sensors Journal, vol. 17, pp 2322-28, 2017
[28] J. L. Santos and F. Farahi, Handbook of optical sensors: Crc Press, 2014
[29] Y. G. Song, Y.-S. Shim, S. Kim, S. D. Han, H. G. Moon, M. S. Noh, et al., "Downsizing gas sensors based on semiconducting metal oxide: Effects of electrodes on gas sensing properties," Sensors and Actuators B: Chemical, vol. 248, pp 949-56, 2017
[30] Y. Wang, F. Liu, Q. Yang, Y. Gao, P. Sun, T. Zhang, et al., "Mesoporous ZnFe2O4 prepared through hard template and its acetone sensing properties," Materials Letters, vol. 183, pp 378-81, 2016
[31] A. Simo, K. Kaviyarasu, B. Mwikikunga, M. Mokwena, and M. Maaza, "Room temperature volatile organic compound gas sensor based on vanadium oxide 1-dimension nanoparticles," Ceramics International, vol. 43, pp 1347-53, 2017
[32] R.-C. Wang, S.-N. Lin, and J.-y. Liu, "Li/Na-doped CuO nanowires and nanobelts: Enhanced electrical properties and gas detection at room temperature," Journal of Alloys and Compounds, vol. 696, pp 79-85, 2017
[33] H. Bai and G. Shi, "Gas sensors based on conducting polymers," Sensors, vol. 7, pp 267-307, 2007
[34] G. Gauglitz, "Direct optical sensors: principles and selected applications," Analytical and bioanalytical chemistry, vol. 381, pp 141-55, 2005
[35] V. V. Tuchin, Handbook of optical sensing of glucose in biological fluids and tissues: CRC press, 2008
[36] X. Chen, C. K. Wong, C. A. Yuan, and G. Zhang, "Nanowire-based gas sensors," Sensors and Actuators B: Chemical, vol. 177, pp 178-95, 2013
[37] R. Tabassum, S. K. Mishra, and B. D. Gupta, "Surface plasmon resonance-based fiber optic hydrogen sulphide gas sensor utilizing Cu-ZnO thin films," Physical Chemistry Chemical Physics, vol. 15, pp 11868-84, 2013
[38] D. Ahuja and D. Parande, "Optical sensors and their applications," Journal of Scientific Research and Reviews, vol. 1, pp 060-068, 2012
[39] J. Homola, I. Koudela, and S. S. Yee, "Surface plasmon resonance sensors based on diffraction gratings and prism couplers: sensitivity comparison," Sensors and Actuators B: Chemical, vol. 54, pp 16-24, 1999
[40] K. Lee, S. Cho, S. H. Park, A. Heeger, L. Chan-Woo, and S.-H. Lee, "Metallic transport in polyamiline," Nature, vol. 441, p 65, 2006
[41] M. N. Polianskiy, "Refractive index database," https://refractiveindex.info. Accessed on 2017-10-03