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Impedance Based Vitamin D Measurement Sensor and Algorithm for Human Wellness

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Abstract: While entering the modern society, medical technology has been able to cure almost all kinds of diseases. However, autoimmune diseases are increasing rapidly due to environment, food, and indoor life. In particular, vitamin D is lacking in about 90 % of Koreans. As a result of this, many middle-aged and older women are taking calcium, but most of them do not know their vitamin D levels. Based on this background, the goal of this paper is to develop a vitamin D measurement technique using a quantum analyzer that is capable of measuring various kinds of vitamins and minerals, and to prepare a plan to easily measure vitamin D by attaching it to a UVB device that is currently used in the hospital. The quantum analyzer was designed based on the impedance principle, and the impedance change according to vitamin D concentration was able to confirm a significant proportional relationship between vitamin D and impedance. In addition, the correlation between vitamin D and impedance was confirmed by in vitro experiment using lab mice, and the measurement error of the impedance meter for vitamin D concentration in the blood was confirmed to be about 12.7 %.

Keywords: Portable sensor, Data processing, Vitamin sensor, Impedance sensor.

1. Introduction

1.1. Vitamin D Status of the People

According to the Korea Centers for Disease Control and Prevention, when based on the 30 ng / ml in vitamin D level, 91.3 % of female and 95.0 % of males in Korean adults are vitamin D deficient. The average vitamin D level in urban women in Korea is 15 ng / ml, which is the highest vitamin D deficiency in the world. If the latitude is more than 35 degrees north, the shortage of vitamin D increases significantly in autumn and winter.

It is harmful to the human body when vitamin D is deficient, or excessive administration of vitamin D is done to the human body. Because Vitamin D is stored in the body fat due to its fat-soluble properties, toxic symptoms may occur. In addition, vitamin D, beyond safe quantities, can cause elevated uptake of calcium and phosphorus. It also can cause hypercalcemia, hyperphosphatemia and hypercalciuria due to increased bone resorption in the skeleton, In addition, some side effects such as gastrointestinal symptoms, neuromuscular symptoms, and thirst may occur.

Therefore, it is necessary to take the proper amount of vitamin D by auto synthesis.

However, in most cases, vitamin D levels in the body are unknown. Many women who are post-menopausal take in Ca to prevent their osteoporosis. But, they don't know the level of vitamin D, the mediator of Ca absorption.

The measurement of Vitamin D levels is optional in periodic test that is covered by National Health service, so people who want to know their own vitamin D levels have to pay the additional cost of the test. In addition to osteoporosis, vitamin D level related diseases are directly linked to immunity that is the underlying cause of modern chronic diseases such as cancer and allergic diseases, and the incidence of vitamin D related diseases continues to increase.

Therefore, it is essential to develop a vitamin D level diagnostic device that will help to absorb an adequate amount of vitamin D.

1.2. The Process of Ultraviolet B Making Vitamin D

The process that ultraviolet ray B makes vitamin D is as follows: 7-dihydrocholesterol, the cholesterol metabolite, is produced during digestion after eating food. Ultraviolet B then breaks the 7-dihydrocholesterol molecule ring in the skin and is synthesized as vitamin D3 (Cholecalciferol).

Liver Vitamin D3 goes to the liver through the blood stream, then converts to a 25-vitamin D by combining with enzyme (Half-life 3 weeks).

25-vitamin D, which circulates in the kidney blood, goes to the kidneys and turns into active vitamin D (Half-life 4 to 6 hours). Fig. 1 shows the example.

1.3. Existing Vitamin D Measurement Principle

Since Vitamin D is converted to a metabolite called 25 (OH) D in the body and is present in the blood, in the existing vitamin D measurement method, the concentration of 25 (OH) D is measured and is used as the concentration of vitamin D. The notation 25 (OH) D means that (OH) is bound to the 25^{th} carbon of vitamin D. For example, a blood level of 30 ng / mL means that 30 mg of vitamin D is contained in 1 mL(cc) of blood.

Therefore, in order to measure this, a visit to the hospital is necessary to conduct blood concentration test through blood sampling.

1.3.1. Existing Vitamin D Measuring Devices

Existing vitamin D measuring devices –Vitastiq

The principle of "EAV (bio current measurement) Test" developed by Dr. Reinhard Voll from Germany in the 1940s, which is a test that measures the current of each meridian in the body to determine its health status, is applied to the products. The EVA (electro-acupuncture According to Voll) system considers the cell as a single ion battery and analyzes the characteristics of meridian reaction by external weak current stimulation.

If you touch the meridian with the pen-like vitastiq that corresponds to the elements you want to know, you can check the nutritional status of your body without a blood test.

Existing Vitamin D measuring device - How to use Cue Health Tracker ?

This device measures the amount of Vitamin D by collecting the samples of blood or body fluids with a product stick and placed in a cue box.

Existing Vitamin D measuring device - Smartphone devices that measure vitamin D levels

This is a smartphone device developed by researchers at Cornell University and measures the cholesterol and vitamin D levels. It looks similar to a credit card reader attached to a smartphone. This device attaches to a smartphone camera and measures the user's cholesterol and vitamin D levels in two minutes with a drop of blood. To use this device, the user drops a blood sample onto a test strip that is woven with chemicals designed to react in a particular way, then take picture of a test strip with the smartphone. This device processes blood samples that respond to test strips, determines the levels of cholesterol or vitamin D from the images, and displays the results on a smartphone display. This technology also works on saliva or sweat, and tells the users their cholesterol or vitamin D levels.

Although various vitamin D measuring devices are presently available, most of them have a problem that human blood or body fluids to be taken for the measurement of vitamin D. In addition, the sample sticks and strips for collecting blood or body fluids are usually for one-time use, so it is inconvenient to take care of them.

To complement these shortcomings, this paper developed vitamin D measurement technology using an application of impedance principle based quantum analyzer. It is convenient to use compared to existing measurement methods, since it measures only impedance without collecting body fluids or blood. It also has the advantage of reducing the inconvenience of users who want to measure vitamin D without using the sample sticks or strips.

2. Method

2.1. Development of Vitamin D Measuring Device

Development of vitamin D and calcium measuring device using quantum analyzer

We have developed a device that selectively displays signals that measure only vitamin D and calcium. We developed the display that can calibrates the measurement using vitamin D and calcium, and can displays them with numerical value. A quantum analyzer is a device that can measure various metabolic functions in the body.

Fig. 1. Example of using a quantum analyzer.

○ **Development of simulation board for analysis**

We designed and made a simulation board that can analyze and measure micro-current of human body by receiving signal from a sensor module.

It is designed to use external and internal power modes and LCD display is used as a display window (option). The User Controller is designed as a simple key shape for easy operation. In addition, it is made to be easily handled by making the board small as shown in Fig. 2.

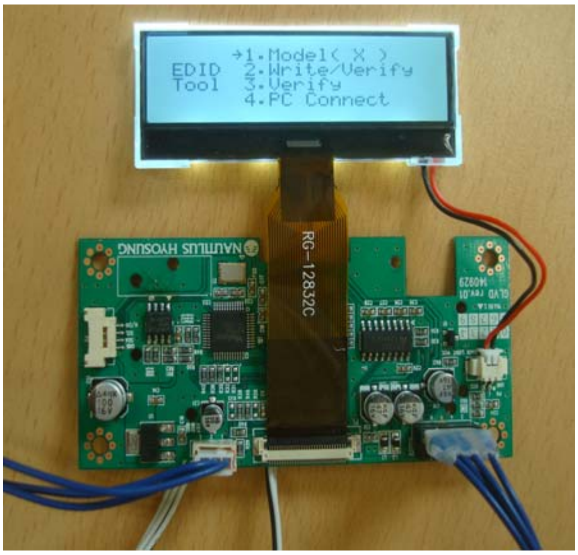

Fig. 2. Example of Simulation Board.

○ **Application Development**

The development of the device operating program for analysis and measurement of the output waveform from the sensor is to set the way of displaying measurement and to analyze the energy waveform of the sensor module.

A CPU with an A/D converter built-in is selected, and the standard value for sensor is selected as well. The program that supports C compiler, macro assembler, real-time OS, simulator, etc. was developed. In addition, the LCD display is configured to display the letters, numbers, etc. on the screen to show the operation status and debugging is possible without an external ROM / RAM.

2.2. Principle of Measurement Separation Signal and Quantitative Analysis of Vitamin D

Introduction of vitamin D measurement technique using the impedance measurement principle

The bioelectrical impedance measurement assumes that the living body is a homogenous tubular conductor, and it is used to calculate body water and body fat using a formula where capacity is proportional to the square of the height divided by the impedance. However, because in vivo impedance is not a homogeneous tubular conductor according to the assumption above, impedance and various variables may exist.

The bioelectrical impedance analysis (BIA) method has the advantage of being easy to use for patients regardless of age and gender by meeting the two conditions of precision and practicality of measurement, and it also has simplicity that does not require special techniques for measurement [5-7]. The bioelectrical impedance (BIA) is the method that utilizes the difference in electrical conductivity depending on the biological characteristics of the tissue and predicts the body composition. In this method, electrical conductivity is proportional to the amount of water and electrolytes, and decreases as the shape of the cells becomes closer to the circle, and is affected by moisture, muscle, and fat content.

2.3. Development of a Vitamin D Measurement Sensor Module

Development of an Impedance-based Quantum Analyzer Module

Many quantum analyzers are known to use the principle of impedance and analyze human body by measuring electrical in vivo. In this paper, we use an impedance meter to predict the concentration of vitamin D in vivo. When sending a minute alternating current signal to a living body, electricity flows along highly conductive water, and the impedance of body water, fat, muscle, etc. are different from each other depending on the water content. Fig. 3. shows the example of sensor.

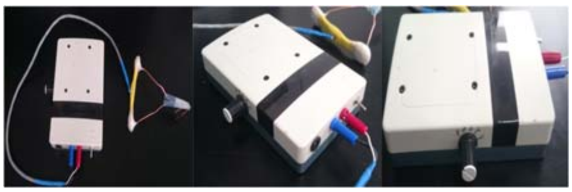

Fig. 3. Vitamin D measurement kit. Vitamin D measurement sensor module applying impedance measurement principle.

In this study, the impedance meter is developed in order to check the correlation between vitamin D and impedance. The impedance meter is consisted of two electrodes and a measuring instrument body and is designed to set the step according to the measurement intensity.

Impedance changes caused by vitamin D

In order to check the change in impedance due to vitamin D, we measured impedance using diluted solution of vitamin D concentration. As a result of confirming the impedance measurement value using vitamin D, we found that the impedance increased in a concentration-dependent manner. However, the difference in impedance according to the concentration of vitamin D was not found to be significant. This indicates that, in a practical application, there is not a large gap between the titration and the over or under-titration of vitamin D in vivo, thus indicating that there is difficulty getting an accurate measurement. Fig. 4. Shows the results.

Table 1. Impedance change according to vitamin D concentration (Unit: Ω, Concentration: ng/mL).

Vitamin D conc.	0	0.005	0.048	0.244	0.716	2.79	10.1	50.6	250
1	2.136	2.036	2.215	2.436	2.831	3.125	3.564	4.256	4.825
2	2.015	1.953	2.135	2.485	2.653	3.245	3.617	3.983	4.596
3	2.165	2.046	2.184	2.645	2.536	3.358	3.661	4.126	4.548
Average	2.105	2.012	2.178	2.522	2.673	3.243	3.614	4.122	4.656
SD	0,080	0.051	0.040	0.109	0.149	0.117	0.049	0.137	0.148

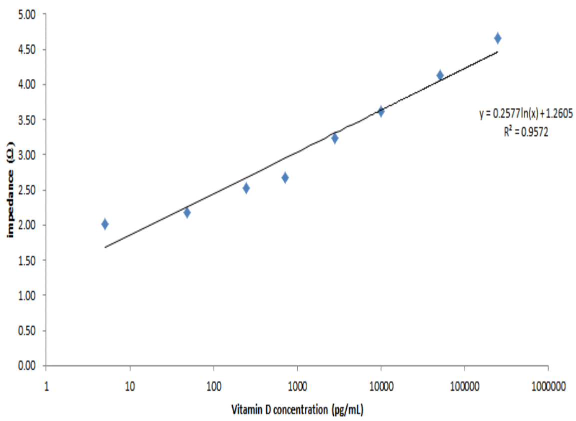

Fig. 4. Impedance change according to vitamin D concentration (unit: Ω, concentration: pg/mL).

3. In Vitro Experiment

3.1. Estimation of Vitamin D by Impedance Measurement Using Animal Model

The mouse used in the experiment

- It is C57BL. C57BL/6 or C57Black66 (C57 black 6) is an inbred mouse strain for research, and the model is mainly used for the cause and analysis of human genetic diseases. It is the most commonly used mouse strain because it is a similar-genotype mouse, easily reproduced, and sturdy.

○ Impedance measurement in animal model

- Impedance is measured using a C57BL/6 mouse (male, 8 weeks old). Impedance was supplemented by connecting a copper wire to the electrode to enable measurements on the back of the mouse. The measurements were performed three times for each individual. No conditions specific to vitamin D were administered, and impedance was measured in a normal mouse.

- After measuring the impedance, the blood of the mouse was collected and the amount of vitamin D in the blood was measured. Fig. 5 and Fig. 6 shows the experimental procedures and results.

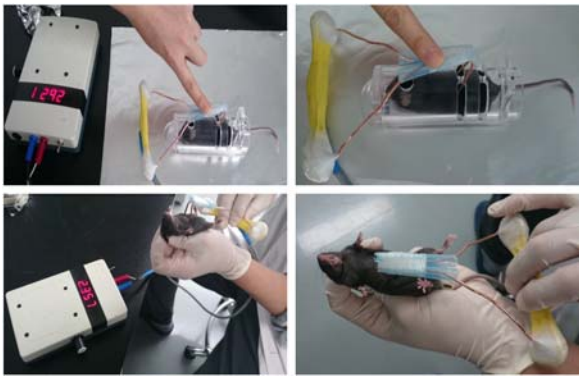

Fig. 5. Measurement of Mouse Impedance Using Impedance Measuring device.

Table 2. Impedance in mouse skin.

Impedance (Ω)	Mouse					
	1	2	3	4	5	6
1	2.518	2.431	2.24	2.313	2.46	2.382
2	2.501	2.357	2.255	2.328	2.445	2.387
3	2.524	2.372	2.229	2.269	2.343	2.401
4	2.513	2.328	2.269	2.284	2.328	2.387
5	2.521	2.313	2.255	2.269	2.372	2.416
Average	2.5154	2.3602	2.2496	2.2926	2.3896	2.3946
SD	0.009017	0.045899	0.015421	0.026726	0.059794	0.013903

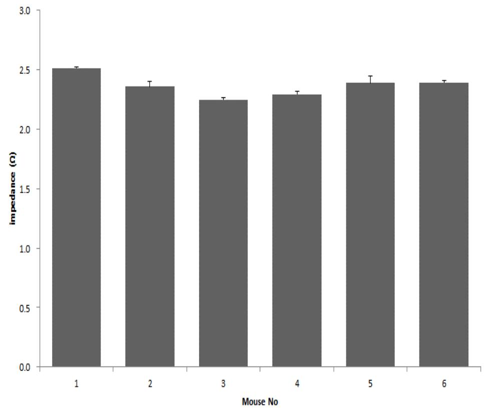

Fig. 6. Impedance measurement on mouse skin.

3.2. ELISA Analysis According to the Vitamin D Concentration

Vitamin D measurement using the kit

The amount of vitamin D was measured using the Vitamin D measurement kit (Enzo, ADI-900-215), 25(OH) Vitamin D ELISA kit. Fig. 7 shows the results

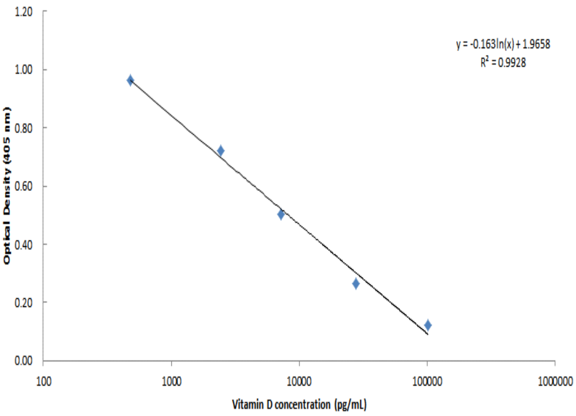

Fig. 7. Vitamin D standard measurement using vitamin D assay kit.

Vitamin D measurement in mouse blood

- After confirming the skin measurement value, the blood of the mouse was collected and the plasma was separated. The collected blood was kept in a refrigerated state, and after about 1 hour, the blood was centrifuged at 2000 rpm for 10 minutes. Then, the plasma of the upper layer was separated and used for vitamin D analysis.

Relationship between Impedance and Blood Vitamin D

Through in vitro experiments, we confirmed the correlation between mouse impedance analysis value and vitamin D measurement. Fig. 8 and 9 shows the results.

Experimental results show that the relationship between impedance and blood vitamin is proportional to a certain proportion. However, further study is needed to apply animal experimental measurements directly to humans in significance. From the result of this research, it is difficult to determine the exact amount of vitamin D with the vitamin D measurement method using impedance. However, if the range of vitamin D to impedance is set, it is possible to judge whether the vitamin level is deficient, normal or excessive. However, when applied to a human, it is necessary to reset the data of the relevant experiment. Impedance basically measures the electrical resistance, and measurement of the impedance using the living human body is influenced by various factors. Especially, the effect on the fat seems to be great, and it is thought that it will affect not only the measurement of the Vitamin D but also various kinds of bio-phenomena measurements using the impedance. Measurement of vitamin D using impedance seems to be correlated and more detailed study is needed.

Table 3. Measurement of vitamin D in mouse blood using ELISA kit.

Optical Density	Mouse					
	1	2	3	4	5	6
1	0.264	0.223	0.284	0.249	0.246	0.238
2	0.245	0.264	0.296	0.258	0.244	0.238
3	0.251	0.236	0.248	0.236	0.234	0.253
4	0.213	0.269	0.234	0.275	0.258	0.237
5	0.212	0.246	0.246	0.261	0.237	0.241
O. D. Average	0.237	0.2476	0.2616	0.2558	0.2438	0.2414
O. D. SD	0.023399	0.019165	0.02681	0.014481	0.009338	0.006656
Vitamin D Conc. (pg/mL)	28166.99	25312.6	22131.18	23376.68	26286.91	26929.7
SD (pg/mL)	2780.892	1959.281	2268.145	1323.371	1006.849	742.4994

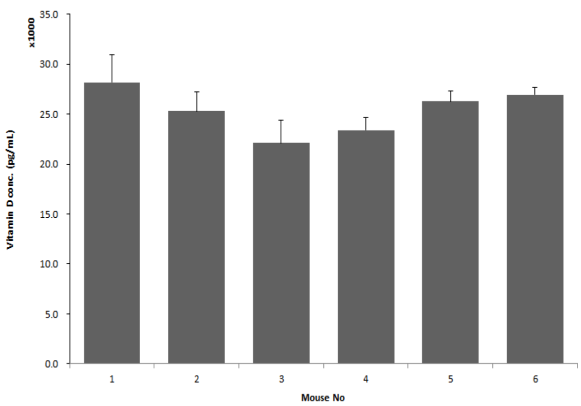

Fig. 8. Blood concentration of vitamin D by mouse.

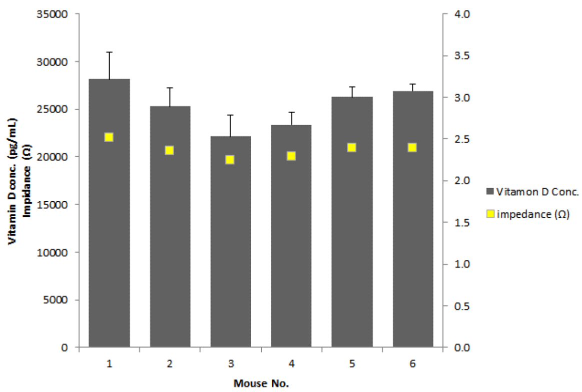

Fig. 9. Comparison of mouse impedance value and vitamin D value in the blood.

The measurement error of the impedance meter to the concentration of vitamin D in the blood is the sum of the mouse measurement impedance error (2.5 %) and the maximum value of the vitamin D measurement error (10.2 %) in the blood, and there was an error of about 12.7 %. The correlation between the Impedance measured in the mouse and the impedance in the blood was verified. The formula for measuring vitamin D in the blood using impedance was Y = 23624X-30550 (Y: predictive value of vitamin D in blood (pg/mL), X: impedance value), and predicted vitamin D in the blood with this formula. Fig. 10. Shows the results.

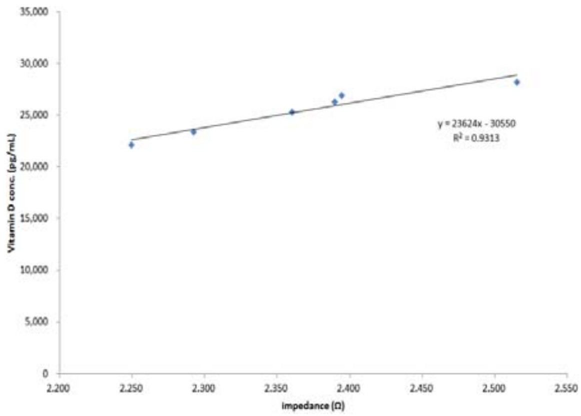

Fig. 10. Correlation check between Impedance and vitamin D.

3.3. Test Result

We made the Impedance-based vitamin D analyzer, one of the principles of the quantum analyzer, and performed in vitro experiments. In this experiment, the impedance analysis by vitamin D concentration verified change in amount of the impedance depending on the concentration. The similarity of the impedance measurement and the pattern in the mouse skin was also verified as a result of measuring the amount of vitamin D in the mouse blood of mice using an ELISA-based vitamin D kit.

Impedance-based vitamin D measurements were patterned depending on the concentration in the blood, but there was a difference in accuracy. Measurement of vitamin D using impedance has been difficult to get precise quantification due to the variation of values depending on various environmental factors (such as Body composition, fat, protein ratio, etc.). However, it seems that patterns of the concentration are similar, so it is possible to predict the deficiency, normal, and excess levels of vitamin D.

The measurement error of the impedance meter for the vitamin D concentration of vitamin D in the blood was confirmed to be about 12.7 %. (Measurement error = maximum value of mouse measurement impedance error + maximum value of vitamin D measurement error in blood). The predicted value of vitamin D in blood using impedance measured in mouse was predicted by the formula Y = 23624X-30550 (Y: predicted value of vitamin D in blood (pg/mL), X: impedance value).

4. Conclusions

To reduce the incidence rate of vitamin D related diseases, we have developed a vitamin D diagnostic device that will help to absorb adequate amounts of vitamin D. We also developed vitamin D measurement techniques using the impedance principle based quantum analyzer by complementing the disadvantages of existing vitamin D measuring devices.

To measure the amount of vitamin D in the body, we developed a vitamin D measuring device using a quantum analyzer, a simulation board for analysis, and an application, and introduced a vitamin D measuring method using the impedance measurement principle.

We also developed a vitamin D measurement sensor module and an impedance-based quantum analyzer module and measured the impedance changes caused by vitamin. Through this process, we could confirm a significant correlation between the vitamin D concentration and the impedance.

After verifying the correlation between the vitamin concentration and the impedance, an in vitro experiment using an animal model was conducted. In this experiment, the amount of change in impedance depending on the vitamin D concentration was confirmed. The result of measuring the amount of vitamin D in the blood of the mouse using an ELISA-based vitamin D kit verified the similarity of patterns. However, additional research is needed to apply animal test measurements directly to humans in significance.

The measurement error of the impedance meter for the vitamin D concentration of vitamin D in the blood was confirmed to be about 12.7 %. (Measurement error = maximum value of mouse measurement impedance error + maximum value of vitamin D measurement error in blood). The predicted value of vitamin D in blood using impedance measured in mouse was predicted by the formula Y = 23624X-30550 (Y: predicted value of vitamin D in blood (pg / mL), X: impedance value).

This study showed that the measurement method of vitamin D using impedance has a difficulty to determine precise amount of vitamin D. However, we think that it is possible to judge the vitamin deficiency-normal-excessiveness when the range of vitamin D to impedance is set.

When we use the vitamin D measurement device using the impedance-based quantitative analyzer developed in this research, it is possible to check the amount of vitamin D in an individual's body, so that it can help to absorb an appropriate amount of vitamin D by blocking vitamin D deficiency and excess. In particular, it can help female osteoporosis patients after their menopause to control the absorption of vitamin D which acts as a mediator of calcium absorption, and is expected to provide new information on disease prevention and treatment technologies. It is expected that the impedance-based quantum analyzer principle will be used to analyze various body components in the future.

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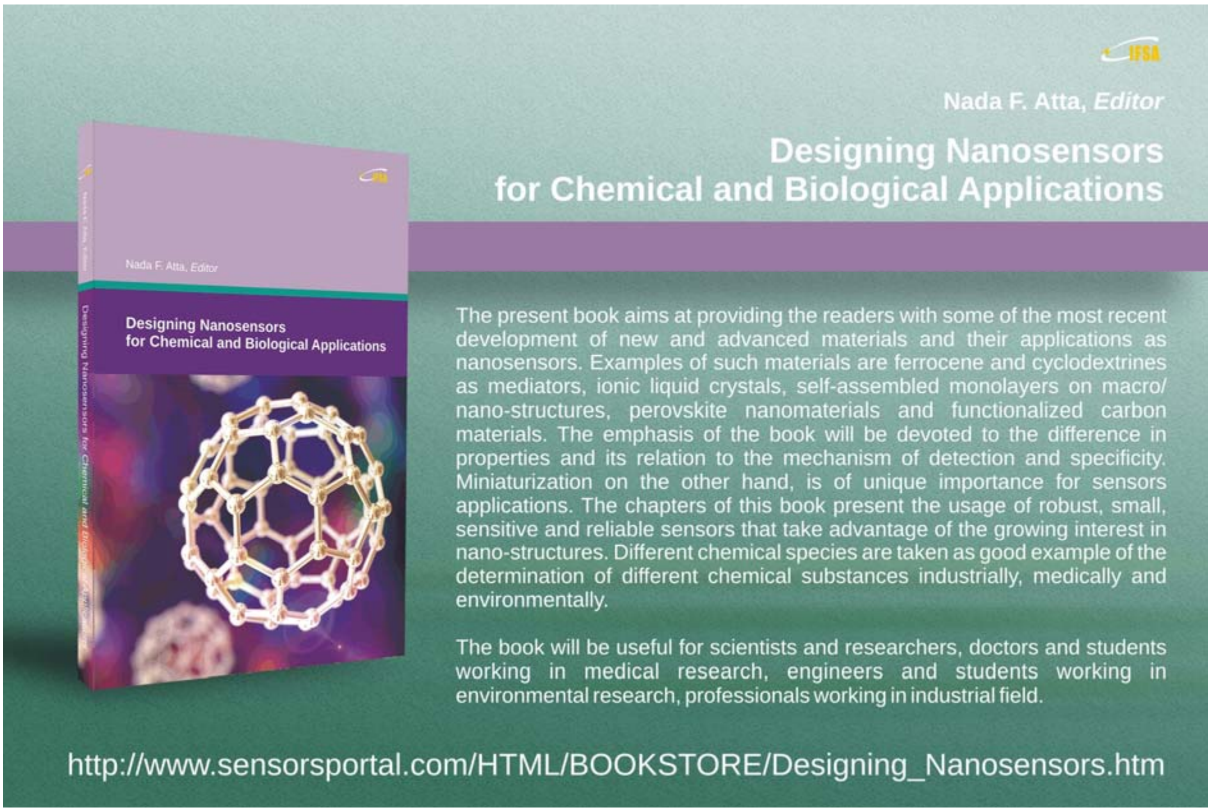

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