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# Pulse oximetry: its invention, theory, and future

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## Introduction

The search for a noninvasive continuous monitoring method for $Sa_{O_2}$ (arterial blood oxygen saturation) started before the Second World War and was accelerated by military aviation needs, but no oximeter practical for use was obtained at that time. After the war, E.H. Wood succeeded in constructing the first quantitative monitor of $Sa_{O_2}$. This device was used in clinical physiological laboratories, but its use did not spread. The first oximeter in widespread use was the pulse oximeter. We can read this history in the work of J.W. Severinghaus [1]. I conceived the principle of pulse spectrophotometry in 1972. Our group made a pilot model of a pulse oximeter and publicly disclosed it in 1974 [2].

Nellcor's pulse oximeter was put on the market in 1983. It was excellent in construction and practical for use. Since then, the pulse oximeter has rapidly spread worldwide and has been adopted into standard anesthesia practice in many countries. This spread occurred without a general theory of pulse oximetry, but was based solely on the principle disclosed in 1974. This spread must therefore be attributed only to luck. However, with its spread to many areas and many situations, many problems have been noticed with the pulse oximeter. Among these problems, interference caused by external lights and electromagnetic fields has largely been overcome, but many other problems have been left unsolved. I have worked to develop the theory of pulse oximetry to establish a basis for improving pulse oximeter performance and for expanding application of the pulse spectrophotometry principle to other noninvasive measurements. Recently, the theory has been developed to a point where it has been proved effective for solving many problems. I will explain here this progress in theory development briefly. Although a complete explanation should involve strict mathematical proofs and detailed descriptions of experiments, including their methods and the interpretation of their results, I will omit these details here.

In the final section, I will sketch a vision of pulse oximetry in the near future, not as wishful thinking but as a realizable goal.

## Origin of pulse oximetry

In 1958, I graduated from Niigata University and was employed by Shimadzu Corporation at Kyoto. There, I became interested in patient monitoring. In 1969, I attended the summer school of physiology and measurement organized by H.A. Hoff and L.A. Geddes held at Baylor University, Houston, TX, USA. This was a very valuable experience for me. After that, I visited several institutions to see patient monitoring systems in the USA. Based on these experiences I came to have a belief that the final goal of patient monitoring must be the automatic control of patient treatment. Though the course to the final goal includes many difficult problems, real progress must be progress toward this goal. I also noticed that noninvasive continuous measurement must be the key technology to realize this goal.

Just after I was employed by Shimadzu Corporation, I read a report on an interview with Dr. Yoshio Ogino, founder of Nihon Kohden Corporation, in a newspaper. I was deeply impressed by his words: "A skilled physician can treat only a limited number of patients. But an excellent medical instrument can treat countless pa-

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tients in the world." And he enthusiastically expressed his dream and philosophy. I thought that the engineers working in his company must be happy. In 1971 I transferred to Nihon Kohden Corporation.

The first order made by our Research and Development division manager, Mr. S. Ouchi, was "Develop something unique." And he made me leader of a group of several members newly assigned to the division. In those days, research on automatic control of artificial ventilation was being carried out at Tokyo University in the Department of Anesthesiology by Professor H. Yamamura. I was very interested in this project and visited Professor Yamamura's group. Assistant Professor M. Kamiyama explained the system and told me that, "To make this system a practical product, a reliable continuous measurement of arterial $O_2$ ($Sa_{O_2}$) and $CO_2$ is indispensable." Stimulated by this visit, I started to examine noninvasive $Sa_{O_2}$ monitoring. The only non-invasive oximeta at that time was Wood's earpiece oximeter. I understood the shortcomings of this method, but I could not conceive of any better idea.

As a theme of our research group I decided to develop a high-accuracy noninvasive dye densitometer for cardiac output measurement. My new idea was to adopt the principle of Wood's earpiece oximeter to improve the accuracy of previous earpiece dye densitometers [3].

In Wood's oximeter, the blood in the ear is expelled pneumatically before the measurement, and light transmitted through the blood is measured and the value is stored as a reference. Next, the blood is readmitted to the ear. After that, the optical density of the blood is calculated continuously against the reference value. Two light wavelengths, red and infrared, are used. The ratio of the optical densities at the two wavelengths is calculated and converted to $Sa_{O_2}$ by using an empirical calibration curve.

For our dye densitometry method, we adopted ICG (indocyanine-green) dye. The initial maneuver was the same as with Wood's oximeter. We used two wavelengths, 805 nm and 900 nm, to maximize dye sensitivity and to minimize $Sa_{O_2}$ sensitivity. The ratio of the two optical densities was calculated to obtain a dye curve. The dye curve was expected to correspond to dye concentrations in the blood. There was no theory of noninvasive measurement of the blood in tissue in those days. Wood's published human data graph [4] alone allowed us to anticipate our success.

I appointed Mr. K. Yamaguchi chief of this project. An experimental model was constructed. For animal experiments, secondhand monitors and instruments were brought into an old hut. Basic animal experimental methods and physiology were taught by a physician, one of our members. Just after starting the experiments, we noticed a pulsatile variation in the tissue optical density caused by arterial pulsation. This phenomenon made us anxious. The dye curve is an overlap of the first circulation and the lagged second circulation. To reject the second circulation, the early part of the decreasing portion of the dye curve must be extrapolated; therefore, the dye curve should be smooth. I investigated the effect of the pulsatile variation mathematically using the Lambert-Beer's law. Then I noticed that there was no problem, because calculating the ratio of two optical densities compensates the pulsation. This supposition was proved by later experiments.

At this point, I realized that both the pulsating and nonpulsating portions of the optical densities of the blood in tissue must have same information regarding blood color. Then I thought as follows:

(1) If the optical density of the pulsating portion is measured at two appropriate wavelengths and the ratio of the optical densities is obtained, the result must be equivalent to Wood's ratio.
(2) In this method, the arterial blood is selectively measured, and the venous blood does not affect the measurement. Therefore, the probe site is not restricted to the ear.
(3) In this method, the reference for optical density calculation is set for each pulse. Therefore, an accidental shift of probe location introduces a short artifact and quick return to normal measurements.

This was my conception of the pulse oximeter principle [5,6]. It was December 1972.

Dr. S. Nakajima of Hokkaido University became interested in this idea and encouraged our supervisor, Mr. Y. Sugiyama, to construct a prototype pulse oximeter. I assigned Mr. M. Kishi to be chief of this project. For this prototype, components of the dye densitometer were used. The light source was a small tungsten lamp. The transmitted light was divided into two beams, and each beam was received by a combination of an interference filter and a phototransistor. I used wavelengths of 630 nm and 900 nm. The wavelength of 630 nm was selected to maximize the hemoglobin extinction change caused by the oxygen saturation change, and the 900 nm wavelength was selected to avoid interference by the ICG dye. From the transmitted light intensity data, the pulsation amplitude AC and the total intensity DC were obtained, and the ratio, AC/DC, was calculated. This AC/DC ratio was obtained at both wavelengths, and their ratio, $\Phi$, was calculated. This is the so-called ratio of ratios. This $\Phi$ was supposed to correspond to $Sa_{O_2}$. The calculation and conversion were performed by simple analog circuits. In experiments, the probe was attached to the ear of an anesthetized dog, after the hair of the ear was picked off with tweezers. Then, the in-

spired $O_2$ concentration was changed, and the arterial blood was sampled. The $P_{O_2}$ and pH of the blood were measured with an Instrumentation Laboratory blood gas analyzer (IL 113-01, Lexington, MA, USA). The $Sa_{O_2}$ was calculated using a Severinghaus slide rule [7] and compared to simultaneous Φ. The phototransistors and the analog circuits were unstable and noisy, but we did not know a better way. One concern was whether the two divided light beams could be regarded as the same with respect to their wavelength components. But a clear result was not obtained.

It was necessary to have some theoretical basis for the scattering optics. Dr. K. Shibata of the Tokyo Institute of Technology had been studying the in vivo measurement of pigments in plants for many years. I read his papers, and I met with him to ask him about the state-of-the-art in this field. According to Dr. Shibata, the way to increase the reliability of the measurement was to use a scattering plate. This method, is called the "opal glass method" [8]. We adopted this. However, a mathematical theory directly applicable to our system was not available.

We intended to make a presentation at a Japan Society of Medical Electronics and Biological Engineering (MEBE) meeting. In October 1973, I submitted an application with a short explanation of the pulse oximeter principle. The application was accepted, and in January 1974, I sent the abstract to the society [2]. We applied for a patent to the Japanese Patent Office on 29 March 1974. On 26 April, I made an oral presentation at the annual meeting of the MEBE meeting held at Osaka, Japan. The chairperson, Dr. T. Togawa, said, "I think this is a very interesting idea." But a negative opinion was also expressed by one of the audience. We did not apply for a patent to any foreign patent office, and in 1975 I left the research group at the annual personnel transferring. After that, I worked as a manager for 8 years and as a staff member for 2 years.

During my absence, from 1975 to 1985, pulse oximetry had made great progress:

(1) Minolta developed the OXIMET (1980), using two optical fibers and precision optics. They adopted a finger as the probe site, and proved that the pulse oximetry principle was accurate
(2) Nellcor developed the N-100 (1983), a convenient pulse oximeter that used high-performance light-emitting diodes (LEDs), a highly sensitive and accurate photodiode, and a microcomputer. Those excellent components were not available when we built the first pulse oximeter.

I thank deeply Minolta and Nellcor. Without them, the idea of pulse oximetry would have been buried.

In 1985, I decided to restart the study of pulse oximetry to obtain a Ph.D. degree. I asked Professor M. Saito of Tokyo University for his guidance. I started to construct an experimental model of a pulse oximeter with the support of new colleagues. A little later, our research group was ordered to develop a pulse oximeter of the Nellcor type. I visited Dr. K. Miyasaka of the National Children's Hospital and asked for his guidance. Later, we handed this work over to the product division and shifted to fundamental study on pulse oximetry.

On January 23, 1987, I met Dr. John W. Severinghaus, together with Dr. Y. Honda and Dr. Nakajima, at a Japanese hotel. Before this, Professor Honda of Chiba University had reported to Dr. Severinghaus that the inventor of the pulse oximeter was Takuo Aoyagi. Dr. Severinghaus asked me some questions and congratulated me on my work on pulse oximetry.

Dr. Miyasaka had the idea to develop a calibrator to standardize pulse oximeter testing. Already Minolta had developed a blood pulsator for experiments in pulse oximetry. Mr. A. Yamanishi of Minolta and I worked together to improve this system. A pulse oximeter probe was attached to the blood pulsator, but the $Sp_{O_2}$ (pulse oximetry oxygen saturation) was not consistent with the $S_{O_2}$ (oxygen saturation) of the blood in the pulsator despite all our trials. Therefore, the project was cancelled. A little later, Dr. Severinghaus gave me some pulse oximeter data concerning the effect of anemia on pulse oximetry measurements, which was published later [9]. From this data, I noticed that the tissue must have some effect. I tried to pulsate a double layer of blood and milk and obtained good consistency between the $Sp_{O_2}$ and $S_{O_2}$ [10]. I think the experimental results indicated two things: (1) in the body, the blood is surrounded by light-scattering tissue; therefore, the blood optical density must be measured with scattering light. (2) The effect of pulsation of tissue other than blood is included in the measured pulse. This experience was my important first step toward developing the theory of pulse spectrophotometry.

I studied the fundamentals of scattering optics using Shibata's book [11], and I decided to adopt Schuster's theory [12] as the basis for the theory of pulse oximetry. I applied Schuster's theory to blood and obtained theoretical formula of blood optical density and recognized good consistency between the theory and experimental data [13]. We built multiwave pulse photometers, and performed many experiments in parallel with experiments using a spectrophotometer (UV 3100, Shimadzu, Kyoto, Japan). In these experiments, the theoretical formulation was shown to be useful for improving pulse oximeter performance [14–16]. In 1993, I obtained the degree of Ph.D. in engineering at Tokyo University [17].

## Theory of pulse oximetry

*Basis of optical absorption measurement*

The basis of optical absorption measurement is Lambert-Beer's law:

$$A \equiv \log(Lin/Lout) = ECD,$$

where "≡" indicates a definition, "=" indicates a theoretical relationship, Lin and Lout are incident and transmitted light intensities, respectively, C and D are the concentration and thickness of the optical absorber, respectively, and E is a proportionality constant called the "extinction coefficient," which is intrinsic to the absorber and wavelength. This law assumes that the object is uniform and nonscattering. A is called the "optical density." This definition of A is used for both scatterers and nonscatterers. We can make a rough prediction about scatterers using Lambert-Beer's law.

*Principle of Wood's earpiece oximeter*

The measuring process with Wood's oximeter is as follows:

1. Attach a probe to an ear.
2. Pneumatically expel the blood from the ear.
3. For two wavelengths of light, $\lambda_1$ and $\lambda_2$, measure the transmitted light, $L_{o1}$ and $L_{o2}$, respectively, and store the measured values as reference values.
4. Readmit the blood to the ear and measure the transmitted light $L_1$ and $L_2$ continuously.

When Lambert-Beer's law is applied:

$$A_1 \equiv \log(L_{o1}/L_1) = E_{h1}HbD \quad \text{and}$$
$$A_2 \equiv \log(L_{o2}/L_2) = E_{h2}HbD,$$

where D is effective thickness of the blood in the ear and Hb is hemoglobin concentration.

$$E_{h1} = SE_{o1} + (1 - S)E_{r1} \quad \text{and}$$
$$E_{h2} = SE_{o2} + (1 - S)E_{r2},$$

where S is oxygen saturation, Eo and Er are the extinction coefficients of the oxyhemoglobin and deoxyhemoglobin, respectively.

$$\psi \equiv A_1/A_2 = E_{h1}/E_{h2}$$
$$= [SE_{o1} + (1 - S)E_{r1}]/[SE_{o2} + (1 - S)E_{r2}],$$

where $\psi$ corresponds to S. The ear consumes little oxygen. Moreover an increase in the blood flow in the ear with heat or chemical irritants was assumed. Therefore, $\psi$ is supposed to correspond to $Sa_{O_2}$.

This principle was first proposed by J.R. Squire [1]. Wood reported good correlation between $\psi$ and $Sa_{O_2}$ for many human data [4]. Therefore, he can be regarded as having developed the first quantitative noninvasive measurement of $Sa_{O_2}$. However, the following problems remained:

Problem 1. If the probe location accidentally shifts, the obtained $Sa_{O_2}$ value becomes unreliable. Therefore, this method is not suitable for long-term monitoring.
Problem 2. The probe site is limited to the ear.
Problem 3. The mathematical relationship between measured $\psi$ and $Sa_{O_2}$ is unknown.

Later, R. Shaw discovered another principle [1], which used eight wavelengths and eliminated the necessity of expelling the blood. $Sa_{O_2}$ was mathematically calculated, but the constants in the equation were statistically determined. Therefore, Shaw's method solved Problem 1, but Problems 2 and 3 remained.

*Principle of pulse oximetry*

Arterial blood in tissue pulsates by $\Delta Db$.

This causes transmitted light pulsation as follows:

$$L_1 = L_{o1} + \Delta L_1, \quad L_2 = L_{o2} + \Delta L_2.$$

Therefore, the optical densities of the pulsating portion of the arterial blood are, if Lambert-Beer's law is applied,

$$\Delta A_1 \equiv \log[(L_{o1} + \Delta L_1)/L_{o1}] = E_{h1}Hb\Delta Db \quad \text{and}$$
$$\Delta A_2 \equiv \log[(L_{o2} + \Delta L_2)/L_{o2}] = E_{h2}Hb\Delta Db.$$

These can be approximated as follows:

$$\Delta A_1 \fallingdotseq \Delta L_1/L_{o1} = E_{h1}Hb\Delta Db,$$
$$\Delta A_2 \fallingdotseq \Delta L_2/L_{o2} = E_{h2}Hb\Delta Db$$

$$\Phi \equiv \Delta A_1/\Delta A_2 = E_{h1}/E_{h2}$$
$$= [SE_{o1} + (1 - S)E_{r1}]/[SE_{o2} + (1 - S)E_{r2}]$$

$\Phi$ is equivalent to Wood's $\psi$. By this principle, a reference value is set for each pulse. Therefore, a probe location shift causes only a temporary artifact and allows a quick return to reliable measurement. The discovery of this principle solved Problems 1 and 2 [2]. Problem 3 was solved by the following theory of pulse oximetry.

*Basic theories of optical scattering*

There are two basic theories of optical scattering: Rayleigh-Mie's theory [18,19] and Schuster's theory [12]. Rayleigh-Mie's theory describes the optical attenuation of a parallel light beam passing through scattering particles. The scattering depends on the wavelength of the light and is affected by the size and shape of the scattering particles. This type of scattering is very complex, and a pseudocolor appears. In contrast, Schuster's theory desribes, for instance, the optical attenuation at the surface of the sun caused by the

surrounding gas. In this case, the radiated light is equivalent to the scattered light. Therefore, if there is no absorption, the wavelength dependence is not there. In this case, the phenomenon is very simple.

*Pulse oximetry and Schuster's theory*

I adopted Schuster's theory as the theoretical basis for pulse oximetry. Though the model of Schuster appears to be very different from pulse oximetry, its applicability can be understood as follows:

1. At the surface of the sun, the light source radiating the gas is wide enough. Therefore the transmitted light at any point is an assembly of rays coming from all parts of the surface.
2. In the pulse oximeter, if the light source is assumed to be point light source, and if the transmitting light receiving area is wide enough, the receiving light is an assembly of all of the transmitted light.

These two patterns of rays in the objects are thus the same (but opposite in their direction). Therefore, Schuster's theory can be applied to the pulse oximeter. The actual light-receiving area of the pulse oximeter is limited, but this is not a problem. Later, I will explain why.

An actual pulse oximeter does not completely fit either basic theory. But Schuster's model is a very good simulation of the pulse oximeter. Analysis using Schuster's theory gives us very practical insights as to how to improve the pulse oximeter. The discrepancies between Schuster's assumptions and the actual pulse oximeter cause some errors. Therefore, the theory of pulse oximetry must include the following two aspects:

1. Analysis of pulse oximetry based on Schuster's theory
2. Improvements of pulse oximeter optics to satisfy Schuster's assumptions

*Analysis of pulse oximetry*

The arterial blood thickness change, $\Delta Db$, causes the blood optical density to change by $\Delta Ab$.

When Schuster's theory is applied to blood:

$$\Delta Ab = \sqrt{Eh\left(Eh + F\right)}Hb\Delta Db \quad \text{and}$$
$$Eh = SaEo + \left(1 - Sa\right)Er,$$

where F is a scattering coefficient, which is constant for a wide range of Hb values. Experimentally, this relationship has been proved. When the receiving area is limited, the following relationship is obtained experimentally:

$$\Delta Ab = \sqrt{Eh\left(Eh + F\right)}Hb\Delta Db + Zb\Delta Db,$$

where Zb is a wavelength-independent constant.

During arterial pulsation, the thickness of tissue other than blood also changes by $\Delta Dt$.

The pulsation of tissue optical density, $\Delta At$, is as follows:

$$\Delta At = Zt\Delta Dt,$$

where Zt is a wavelength-independent constant. Therefore, total optical pulsation $\Delta A$ is

$$\Delta A = \sqrt{Eh\left(Eh + F\right)}Hb\Delta Db + \Delta As,$$

where $\Delta As \equiv Zb\Delta Db + Zt\Delta Dt$

Thus,

$$\Phi = \Delta A1/\Delta A2$$
$$= \left[\sqrt{Eh1\left(Eh1 + F\right)} + Ex1\right]\Big/\left[\sqrt{Eh2\left(Eh2 + F\right)} + Ex2\right],$$
$$Exi \equiv \Delta Asi/\left(Hb\Delta Db\right).$$

The condition of the blood affects the scattering coefficient F, but F has only a minor effect on $\Phi$. The term Exi depends on pulse amplitude $\Delta Db$ and hemoglobin concentration Hb; therefore, it is an unknown variable. Exi actually has a little wavelength dependency, but it can be regarded as a single variable because it can be assumed to be as follows:

$$Exi = AiEx2 + Bi.$$

Today, all pulse oximeters use two wavelengths. If the number of wavelengths is increased, we can obtain important insights into pulse oximetry. For example, if three wavelengths, $\lambda 1$, $\lambda 2$, and $\lambda 3$, are used, then

$$\Phi_{12} \equiv \Delta A1/\Delta A2 \quad \text{and} \quad \Phi_{32} \equiv \Delta A3/\Delta A2.$$

If the probe is attached to a finger, and if the hand is lowered, pulse amplitude decreases, and Exi increases. If a graph of $\Phi 12$ (in x-axis) and $\Phi 32$ (in y-axis) is supposed, increase of Exi draws a trajectory of slanting lines on the graph. Therefore, this line can be regarded as the equi-$Sa_{O_2}$ line. Therefore, Exi is a major source of error in a two-wavelength $Sp_{O_2}$ system. A three-wavelength system and simultaneous equations eliminate the effect of Exi and increase the accuracy of the pulse oximeter [14–16].

*Improvements of pulse oximeter optics*

In a pulse oximeter, a ray radiating the tissue is gradually scattered as it penetrates the tissue. This type of scattering is the subject of Rayleigh-Mie theory. There-

fore, the scattering depends on the wavelength, and the light path at each wavelength is different. This phenomenon is also a source of error in $S_{pO_2}$, and the nonuniformity of the tissue increases the error. This error can be reduced by attaching a thin scattering plate on the incident-side tissue [20]. If another scattering plate is placed on the other side, $\Delta Ab/\Delta At$ increases. From a total signal-to-noise point of view, this technique is effective only when the light intensities of LEDs are high enough.

## Future of pulse oximetry

The death of a patient ultimately results from a lack of delivery of $O_2$ to the brain or the heart, no matter what the original sickness. Therefore, monitoring and treatment of $O_2$ supply is a struggle against time, which is the reason that pulse oximeters are used. This purpose is the most important point to be considered when considering the future of the pulse oximeter. The major aspects to be considered are (1) accuracy, especially for optimum alarm level setting; (2) a quick response time; (3) the low-pulse problem, and (4) the motion-artifact problem. The theory of pulse oximetry allows us to imagine many ideas for solving these problems. Some examples are as follows.

### *Improvement of accuracy*

The major error factor Exi is eliminated by the three-wavelength system. Another factor, the effect of wavelength dependency on the light path, is reduced by an incident scattering plate. Simultaneous use of these two techniques improves accuracy and permits many probe sites to be used, including a reflectance probe that could be applied, for instance, to the forehead.

### *Motion-artifact elimination*

Motion artifacts result from tissue movement, venous blood movement, and probably optics movement. The effect of tissue movement and optics movement are wavelength-independent and can be eliminated by using a three-wavelength system. The effect of venous blood movement can be shown as follows:

$$\Delta Ab = \sqrt{Ea(Ea + F)}Hb\Delta Da + \sqrt{Ev(Ev + F)}Hb\Delta Dv$$

Where "a" and "v" indicate arterial blood and venous blood, respectively.

$$\Phi_{12} \equiv \Delta A1/\Delta A2 = \frac{\sqrt{Ea1(Ea1 + F)} + \sqrt{Ev1(Ev1 + F)}V + Ex1}{\sqrt{Ea2(Ea2 + F)} + \sqrt{Ev2(Ev2 + F)}V + Ex2}$$

where

$$V = \Delta Dv/\Delta Da$$

There are four variables: Sa, Sv, V, Ex2. Therefore, to eliminate the effect of venous blood movement, the a five-wavelength system is necessary. The usual motion-artifact elimination method has been statistical and causes both late response and a flattening of the $S_{pO_2}$ trend. The new technique based on the theoretical equation is a deterministic method that eliminates the shortcomings of the statistical method [21].

### *Low-pulse problem*

There are two approaches: one is to attach the probe at the best site. For this purpose, it is necessary to permit many probe sites. Another is to add some tremor to the measuring site to cause an artifact. If there is blood flow, then the $S_{aO_2}$ can be extracted from the artifact by using a five-wavelength system.

### *Sensitivity to $Sa_{O_2}$ change*

To detect a change in $S_{aO_2}$ quickly, many techniques are required. For instance, the probe should attach where the effective distance from the heart is short. The deterministic method for motion-artifact elimination would also detect change quickly. Finally, $S_{pO_2}$ calculation by, for instance, 0.1% steps should be used.

### *Elimination of the venous blood effect*

The five-wavelength method eliminates the effect of venous pulsation, caused for instance, by tricuspid insufficiency or by neighboring arteries.

### *Measurement of $Sv_{O_2}$ (venous blood oxygen saturation)*

$S_{vO_2}$ might be measured by the five-wavelength method, but the meaning of the result is not clear.

### *Calibrator for pulse oximeters*

The two-wavelength pulse oximeter has a major error source. Therefore, it is difficult for a calibrator to replace testing with human volunteers. For multiwavelength pulse oximeters, a calibrator containing blood in a scatterer will be required [10]. Such a calibrator will give us the $\Phi$-$S_{pO_2}$ relationship until $S_{aO_2} = 0\%$. The most difficult problems from the point of view of designing a calibrator would be the wavelength dependency of the light path and the nonuniformity of the tissue.

*Pulse dye densitometry*

Pulse spectrophotometry provides long-term continuous dye dilution measurement [22]. Therefore, not only the cardiac output but also the circulating blood volume and the hepatic clearance can be measured. For good accuracy at least four wavelengths are necessary. The circulation of the probe site must not be regionally regulated. A multiwavelength probe can be used for the dye dilution method and for oximetry simultaneously, if probe motion is avoided. Therefore, the dye dilution method might become a convenient bedside technique. One problem is that ICG (indocyanine-green) causes shock, though very rarely. ICG has been used because it has high extinction at 805 nm, where $Sa_{O_2}$ does not interfere. But in a multiwavelength system, this characteristic of ICG is not important. More appropriate dyes are needed for frequent measurement and for various other purposes.

*Application to non-pulse photometry*

This theory of pulse photometry could probably be modified for non-pulse photometry. Non-pulse photometry would be useful, for instance, for the measurement of substances in the blood in small quantities. The weakest point of pulse spectrophotometry is that the signal is small.

## About creativity

The process by which the concept of pulse oximetry was obtained is a typical example of the genesis of a creative idea as follows:

1. Conceive the ultimate goal.
2. Notice actual barriers to achieving the ultimate goal.
3. Do what others have not done, and see what others have not seen.
4. With some luck, a concept to solve the problem may result.

The concept of pulse oximetry was at first unbelievable. To calculate $Sp_{O_2}$ theoretically was at first unbelievable. To eliminate the motion artifact deterministically was at first unbelievable. The phenomena of light scattering were at first too complicated to believe understandable. I experienced many times to obtain 1% inspiration after 99% perspiration, just like Edison said.

## Conclusion

In April 2002, the award of Japanese Society of Anesthesiologists was given to me as a contributor to anesthetic practice. But I desire the theory of pulse spectrophotometry to be effectively used to improve actual medical practice. This theory would be the first of quantitative noninvasive blood measurement. I look forward to new efforts by engineers to apply this theory:

(1) to realize a new de facto standard of pulse oximetry, and
(2) to realize some additional long-desired noninvasive measurements in clinical fields.

Those technical results will lead us to new findings in physiology and pathophysiology and show us new horizon of patient monitoring and treatment.

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