MEMS Laser Blood Flow Sensor with a built-in Contact Pressure Sensor

Renshi Sawada, Palmens Inc.

※This article is a literal translation of the Japanese manuscript into English

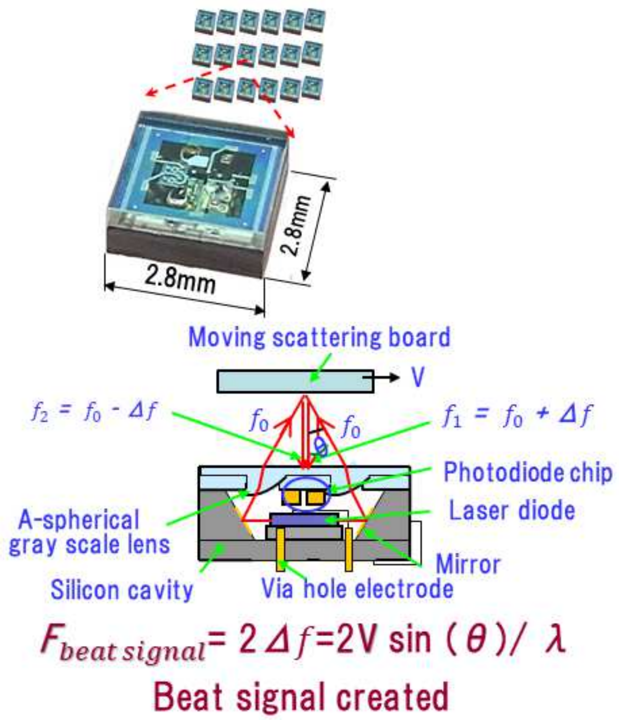
1. Introduction

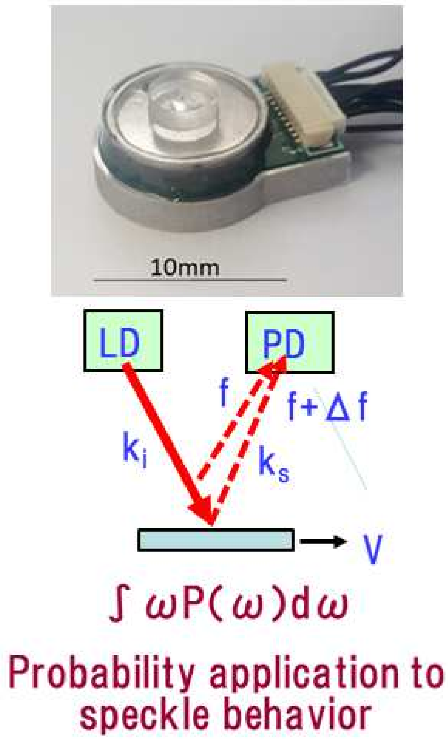
The LDF (Laser Doppler flowmetry) method, which is the basic principle of the laser Doppler blood flow meter, is a method that can non-invasively measure microcirculating blood flow by speckles of backscattered light from living tissue accompanying laser light irradiation in the early 1980s. Since then, it has been actively researched and is now commercialized under the general name of laser blood flow meter.

In 2002, the authors used MEMS (Micro-electro-mechanical systems) processing technology to abolish the blood flow meter that used the mainstream optical fiber probe, and mounted the sensor on the probe tip to drive the battery. A wearable portable laser blood flow meter that enables the entire system to be worn on the body was realized by designing the system part such as the signal processing unit and miniaturization. The realization of the wearable laser blood flow sensor enables stable peripheral blood flow measurement under dynamic environments such as during exercise and daily life, which was previously unthinkable, and microcirculation (peripheral blood vessels) from medical researchers. However, blood flow sensors have another major challenge. That is, blood flow is greatly affected by contact pressure and skin temperature. It will be describe in this article that a newly developed blood flow sensor integrated with a contact pressure and skin temperature sensor that can simultaneously measure the contact pressure and the skin temperature that greatly affects the blood flow.

2. Two types of Doppler sensors

Flowmeters based on the use of laser coherence fall into two categories: one is the speed using Doppler shift based on the interference of scattered reflected light from moving and stationary objects, etc. Total (Fig.1-a) [1]. The other is based on the application of mathematical probability of speckle pattern behavior resulting from interference of reflected scattered light (Fig. 1b) [2]. The velocity obtained in the former can measure a vector, that is, an absolute velocity and its direction. The latter is irrelevant to the direction of motion and it is difficult to obtain absolute speed without calibration.





(a) (b)

Fig. 1 Two types of MEMS Doppler sensors (velocity sensors) using micromachining technology developed so far. (a) Doppler shift based on the interference of scattered reflected light from moving and stationary objects Speedometer. (b)Velocity meter based on the application of mathematical probability of speckle pattern behavior resulting from interference of reflected scattered light

3. Research and development of micro encoder with optical system similar to blood flow sensor

In 1991, when the National Micromachine (MEMS) project was started in Japan, a monolithic laser microencoder was already realized (Fig. 1 (a)) [3-4].

The micro encoder measures the relative movement amount between the diffraction grating and the main body, and can measure the rotation angle of the small motor and the movement amount of the small linear stage with high accuracy. The micro-encoder can also be used as a Doppler sensor by using scattering objects instead of a diffraction grating of the scale, and it can be used as a Doppler sensor. By this method, the absolute velocity of the scattering object can be measured.

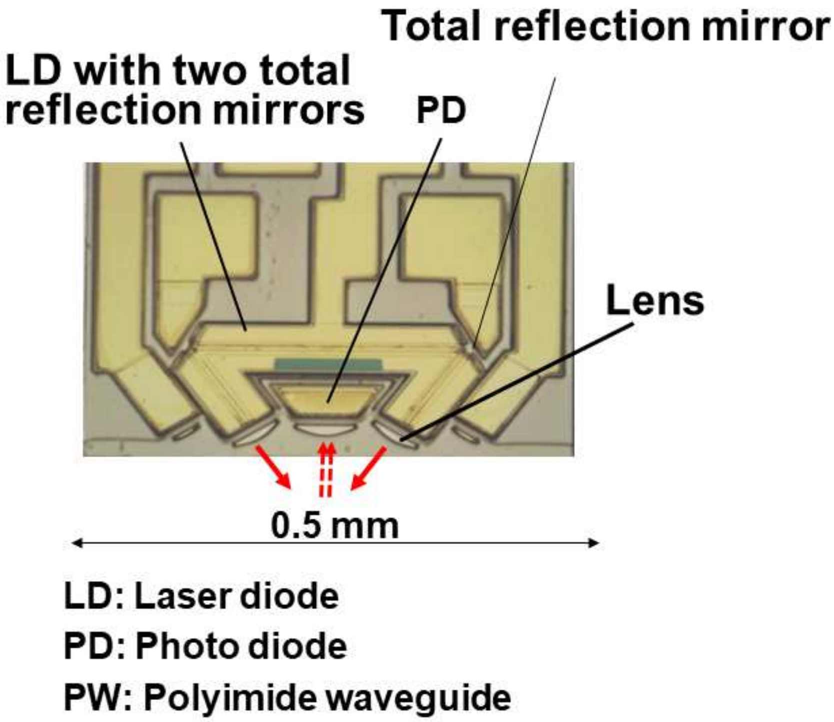


Fig. 2 Monolithically integrated Micro Encoder

Figure 2 shows the Doppler shift spectrum obtained by measuring the blood flow rate of a living body using this microencoder in comparison with the frequency spectrum of the output of a commercially available blood flow meter [5]. It has been confirmed that a pulsewave signal can be detected by this Doppler sensor.

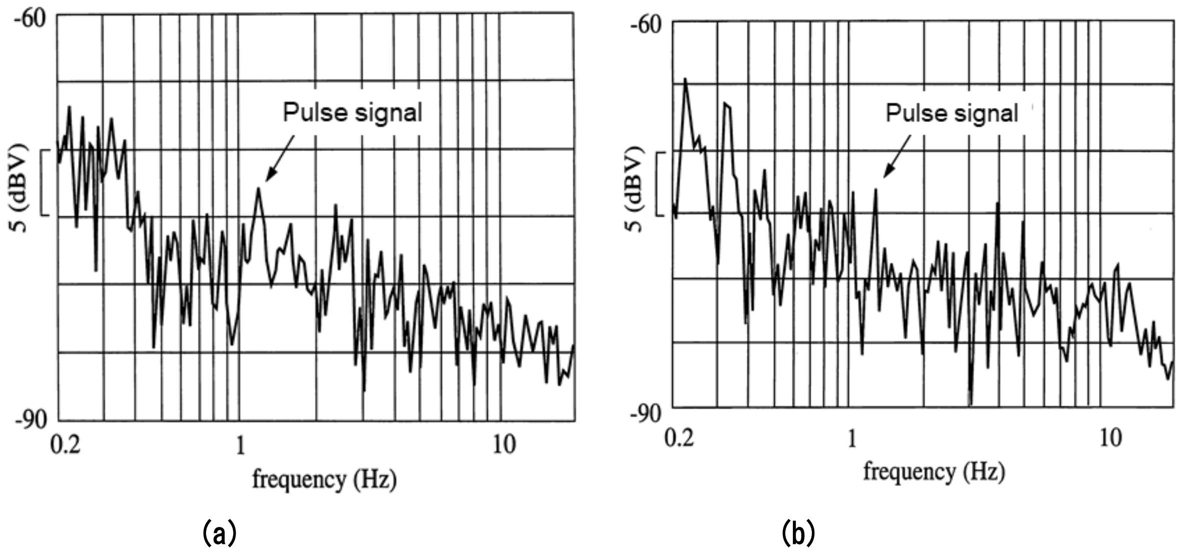


Fig. 3 Pulse signal detection by micro encoder (micro Doppler sensor) Frequency spectrum of commercial blood flow meter output (b) MEMS laser Doppler sensor output frequency

Even a Doppler sensor capable of measuring an absolute velocity has a velocity distribution in a blood vessel, and in measuring blood flow of a living body, blood flows through a complicated blood vessel. Therefore, the measurement of the absolute velocity itself is not necessarily useful. Rather, measurement of the blood flow with high reproducibility and high sensitivity is required rather than measurement of the absolute value.

4. Large fiber type blood flow meter and its MEMS blood flow sensor

In 1972, the first application of a laser blood flow meter was reported by C. Riva et al. [6]. In 1975, M.D.Stern demonstrated that blood flow and Doppler shift of scattered light obtained by emitting laser to the skin were related to blood flow [7].

Figure 4 shows the transition of research and development of the blood flow sensor. In 2001, when research on fabricating a blood flow sensor using MEMS technology, particularly its optical system, was started, the fiber type shown on the left side of FIG. 4 was the mainstream. Even today, the most widely used blood flow meters in medical practice use fibers guided by He-Ne laser light or semiconductor laser (LD), and scatter and reflect the laser light applied to the skin with fibers. It is a type that guides light and detects it with a photodiode (Fig. 5) [8-9]. Although the fiber type blood flow meter has a thin fiber tip at the measurement part, the optical system requires high-precision three-dimensional positioning and adjustment of individual parts, and the size of the entire device is as large as several tens of cm. It is hard to say that it is portable because it uses a 100V power supply. In addition, there is a problem that fiber vibrations and the like cause noise in optical signals [10].

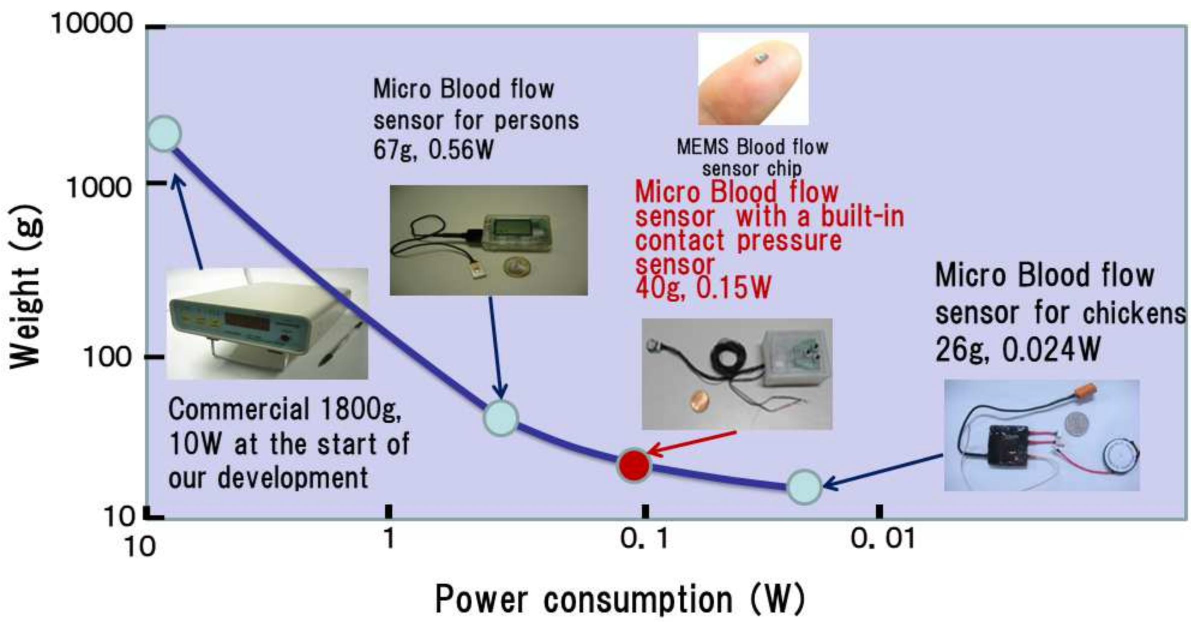
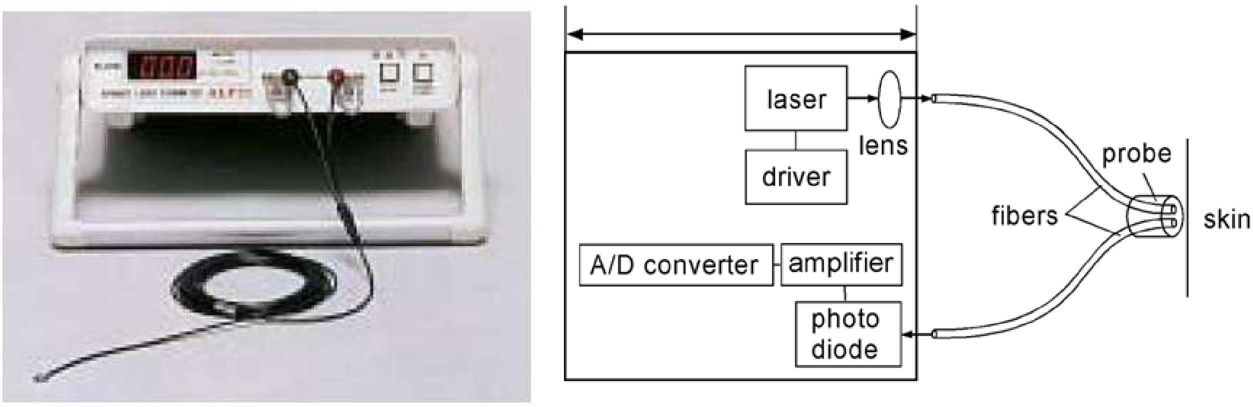


Fig. 4 Research and development trend of blood flow sensor

In the MEMS technology, the entire optical system is packaged using a laser chip or a photodiode chip without using an optical element packaged in Can or the like. In 2003, the optical system of the blood flow meter was announced using a MEMS technology to introduce a blood flow sensor composed of a VCSEL (Vertical Cavity Surface Emitting Laser) chip and a structure devised from a conventional PD [11]. The blood flow sensor shown on the right in Fig. 4 was developed for the detection of bird flu, and needs to be light to be mounted on chickens. The size of the electric circuit was reduced, and a coin-type battery was used. However, smaller batteries have lower electrical capacity, so we have devised power consumption one order of magnitude lower than that for humans [12]. As will be understood later, the blood flow sensor is effective for detecting bird flu because bird flu becomes so viscous that blood cannot be collected with a syringe.



(a) Commercial blood flow meter (b) Basic configuration diagram

Fig. 5 Fiber type blood flow meter

5. Measurement principle of blood flow meter

The laser beam emitted from the VCSEL chip diffuses concentrically. Part of the beam enters the skin and is backscattered inside the skin. In the backward scattered light, Doppler-shifted scattered light caused by moving fine particles such as red blood cells and scattered light without Doppler shift from stationary tissue interfere with the photodiode PD, and as a result, intensity modulation is detected. As shown by the following equation, the first moment $\langle\omega\rangle$ of the power spectrum P (ω) of the intensity-modulated photodiode output is statistically proportional to the flow rate Q.

$$<\omega>=\int \omega P(\omega)d\omega \propto Q \quad (1)$$

In the blood flow meter, a value obtained by multiplying a statistically derived average value $\langle\omega\rangle$ by a proportional constant is used as the blood flow Q.

Although the Doppler shift is a vector, it has directionality, but the flow rate calculated from the flow rate calculation equation (1) in the blood flow meter is a scalar and is independent of the sensor mounting direction. For example, even a flow meter capable of measuring an absolute value cannot measure the absolute value of blood flow of a living body having a blood vessel that has entered without calibration. If calibration is required at least in any case, it can be said that a blood flow sensor that calculates the blood flow by the formula (1) is preferable because it is stable and has high sensitivity.

Figure 6 illustrates the above-described calculation process. Another feature of the blood flow signal detection method is that the blood flow is calculated based on the spectral distribution of the photodiode PD output. This spectrum distribution includes not only a frequency spectrum related to the blood flow but also a frequency spectrum component due to a relative speed movement between the sensor and the living body. If the spectrum associated with body motion is known, by removing the components of the spectrum, a signal that is sufficient to detect the peak of the pulse wave can be obtained, so it is a pulse wave sensor that is not easily affected by body motion Is also promising [13].

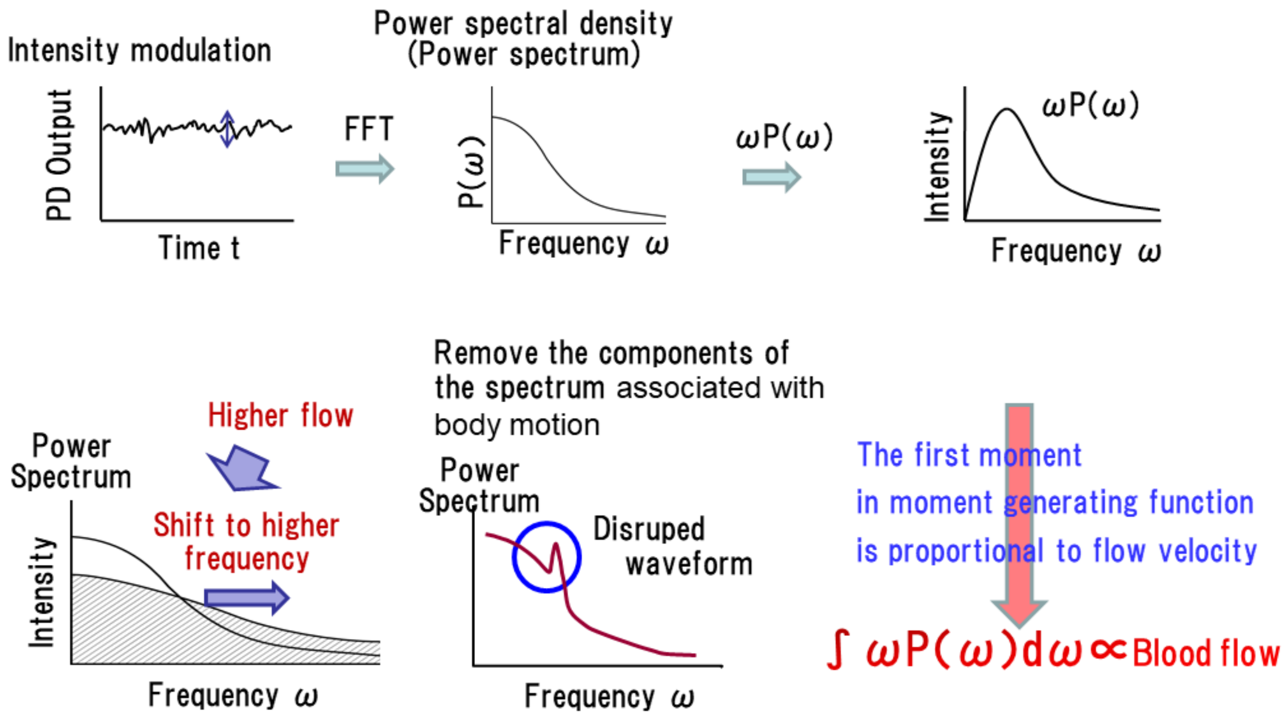


Fig.6 Arithmetic processing step for deriving blood flow

6. Integrated blood pressure sensor with contact pressure sensor

6.1 Effect of contact pressure on blood flow

In a conventional blood flow meter, since the force and contact area at the time of contact are not controlled, in some cases, the variation in measurement is larger than the change in blood flow due to the change in physiological state, and the change in the physiological state due to the change in blood flow. Changes are difficult to detect. The blood flow is measured by applying a probe to the site. Figure 7 shows the relationship between the contact pressure and the blood flow when the contact pressure is changed. Blood pressure and pulse wave amplitude greatly affected by contact pressure

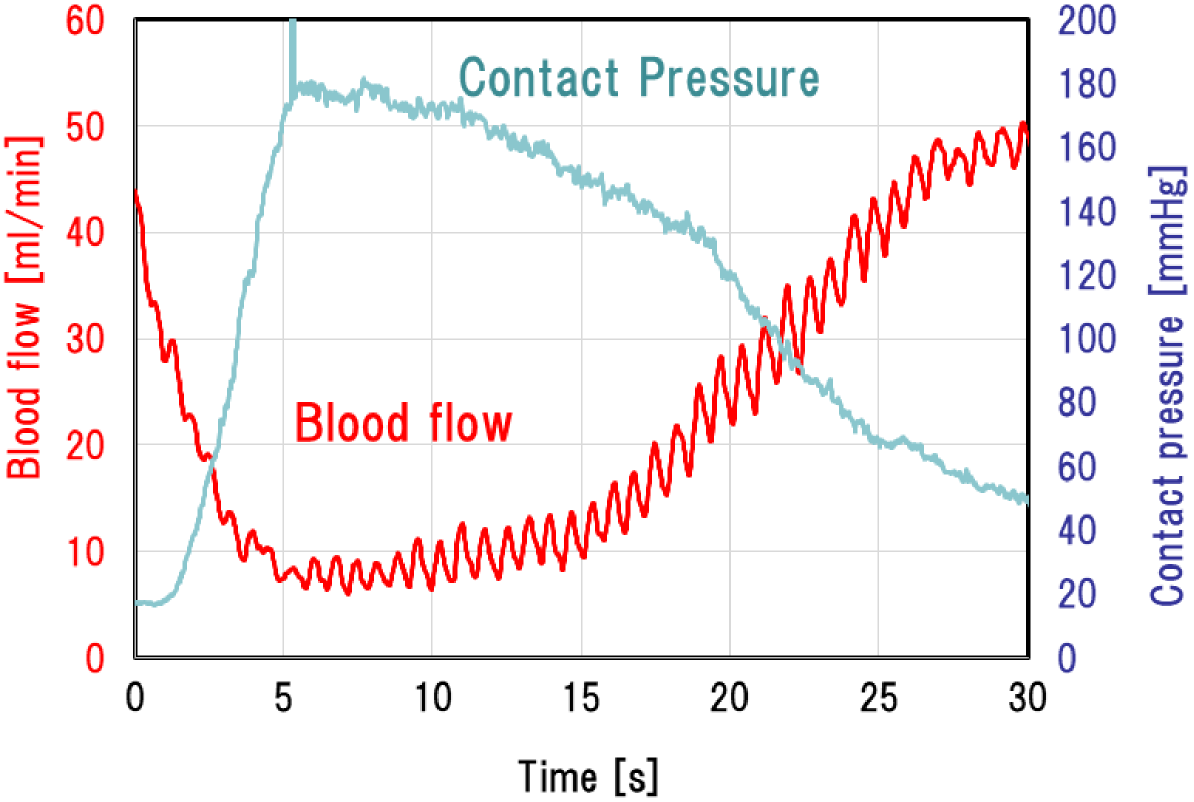
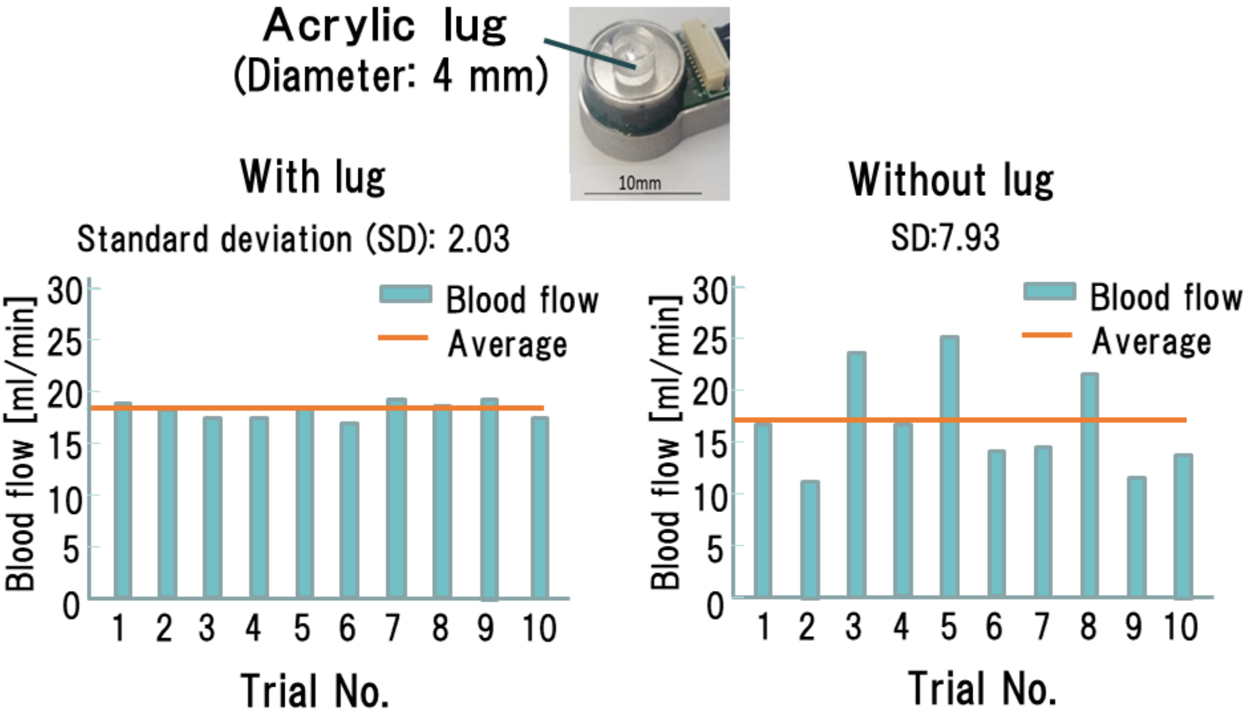


Fig. 7 Changes in blood flow ridge signal (blood flow and pulse wave shape) when contact pressure is changed.

It is understood that it is done. The force applied at the time of contact is not always the same, and since the living body is soft and not flat, the contact area changes depending on the contact pressure. This makes it difficult to measure blood flow reproducibly with a conventional blood flow meter.

When measuring the blood flow with the blood flow sensor probe applied to the measurement site of the living body, even if the blood flow changes due to a change in the physiological state, the change in the blood flow is not due to the change in the contact pressure. It is important to clarify. FIG. 8 shows the results of measuring the blood flow 10 times and the average value of the measured values with and without the protrusion at the contact portion. It can be seen that the reproducibility of the measurement is greatly improved by the projections that make the standard deviation (SD) of the measured value the contact area constant [14].



(a) (b)

Fig. 8 Results of blood flow measurement repeated 10 times when the contact part has (a) transparent projections and (b) no transparent projections

6.2 Measurement of contact pressure using measurement principle of laser displacement sensor

It is important to fabricate a contact pressure sensor without increasing the size of the measuring device. When contact pressure occurs between the protrusion and the skin, the PPT sheet flexes down. Part of the light emitted from the VCSEL chip is reflected by a micromirror attached to the back of the PPT sheet, and detected by a contact pressure measuring photodiode (PD) [15]. The output of the photodiode changes according to the displacement of the micromirror. As shown in the right diagram of FIG. 9, in a region where the relationship between the displacement and the output of the contact pressure monitoring photodiode PD is proportional, the contact pressure and the displacement also show a proportional relationship in the region indicated by the measuring range.

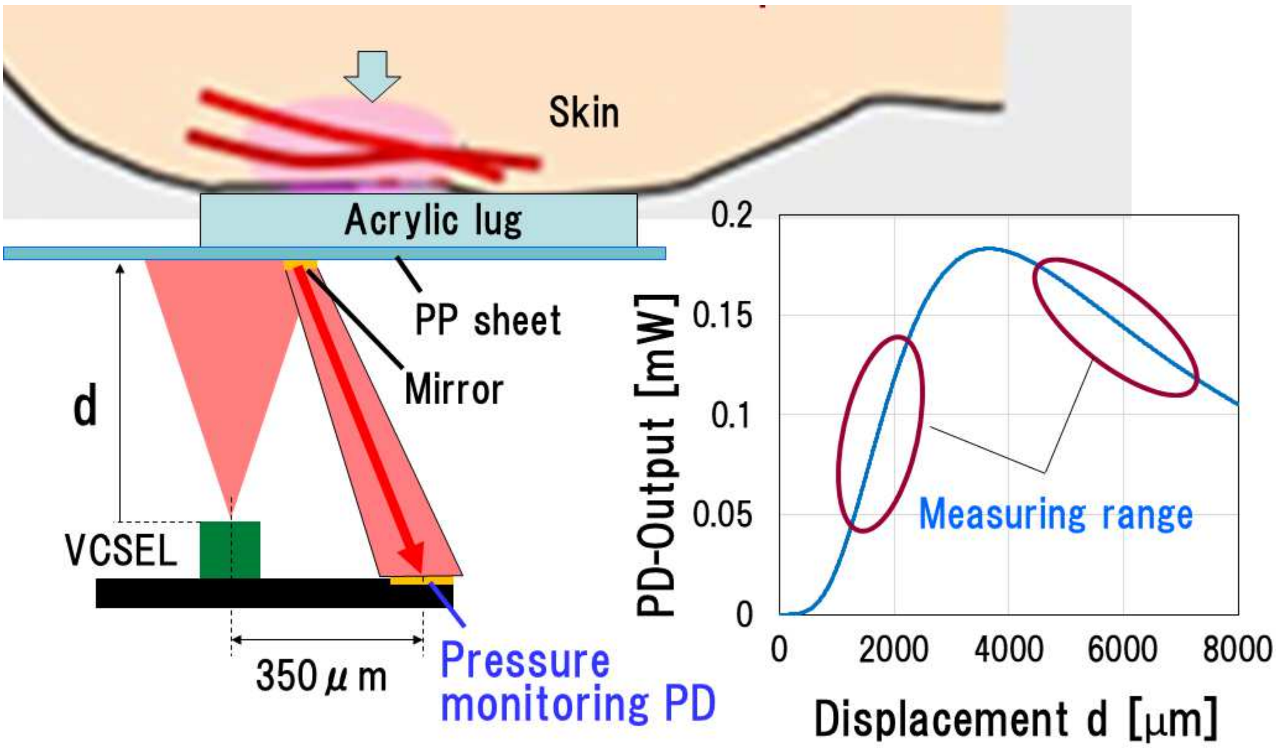
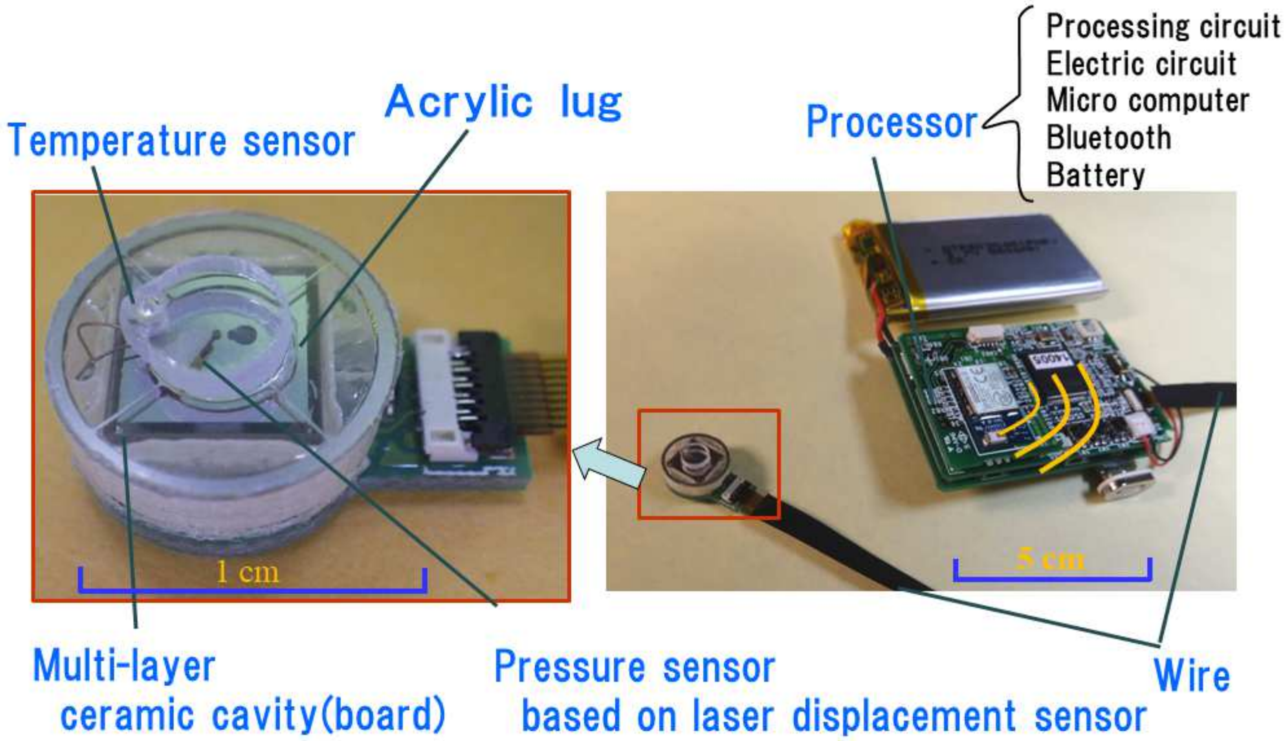


Fig. 9 Application of laser displacement sensor to contact pressure measurement of blood flow sensor

6.3 Probe for blood flow sensor integrated with contact pressure sensor

Figure 10 shows photographs of the MEMS blood flow sensor before mounting the contact pressure measuring component (FIG. 10-a) and the MEMS blood flow sensor after mounting the contact pressure sensor and the skin temperature sensor (FIG. 10-b). The optical system and the first-stage amplifier are mounted inside a 6.2 mm square, 2.3 mm thick cavity ceramic substrate, which is sealed with glass. An FPC (Flexible printed cable) is connected to the processing circuit on the microconnector, and a blood flow signal, a contact pressure signal, and a skin temperature signal are transmitted to the personal computer from the arithmetic processing circuit by Bluetooth wireless transmission. It is expected that the IOT (Internet of Things) will replace this arithmetic processing circuit with arithmetic in the cloud. A micro blood flow sensor without a contact pressure measurement can be used as a conventional MEMS blood flow sensor without mounting a contact pressure measurement component.



(a) (b)

Fig. 10 Contact pressure integrated blood flow sensor

(a) Enlarged photo of probe (built-in optical system and first-stage amplifier) of blood flow sensor integrated with contact pressure sensor (b) Blood flow sensor

6.4 Measurement example

6.4.1. Simultaneous measurement example

Figures 11, 12 and 13 show examples of simultaneous measurement.

Figure 11 shows a graph of the online measurement results of the blood flow signal, the contact pressure signal, and the skin temperature signal. The feature is that the contact pressure, skin temperature, and blood flow at the contact portion, that is, the measurement site, can be measured simultaneously.

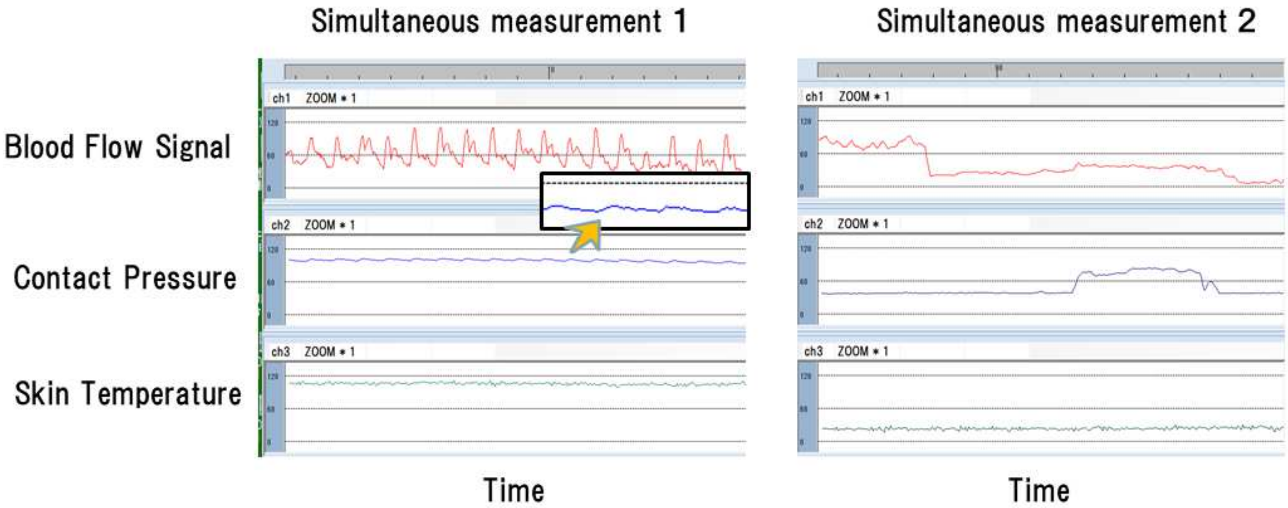


Fig. 11 Simultaneously measured data using Bluetooth is sent to a personal computer and displayed as a graph.

Figure 12 shows a measurement result when a finger that has been bitten is placed on the blood flow sensor. It can be seen that, with the contact pressure hardly changing, the skin temperature is delayed by several tens of seconds and increases with the blood flow.

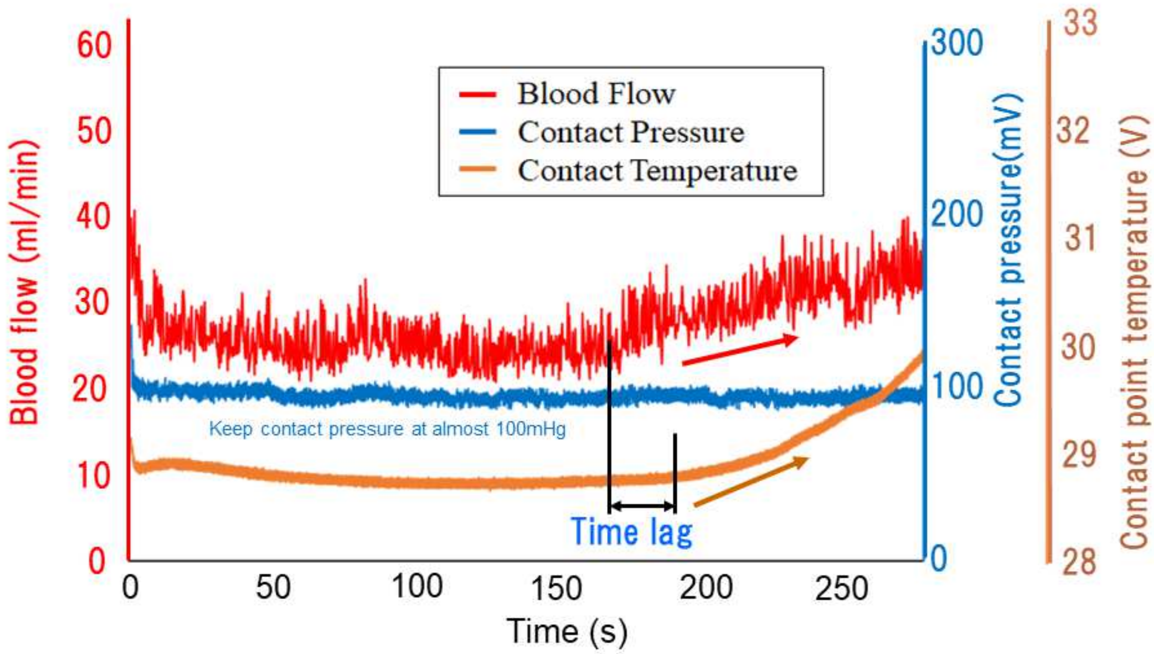


Fig.12 Simultaneous measurement of blood flow measurement and contact pressure and skin temperature of a biting finger

(2) The blood flow decreases as the contact pressure increases, the pulse wave amplitude increases at a contact pressure of 100 mHg, and as the contact pressure increases, the blood flow decreases, and

the blood flow decreases to a minimum at a maximum contact pressure of 200 mmHg. Observable.

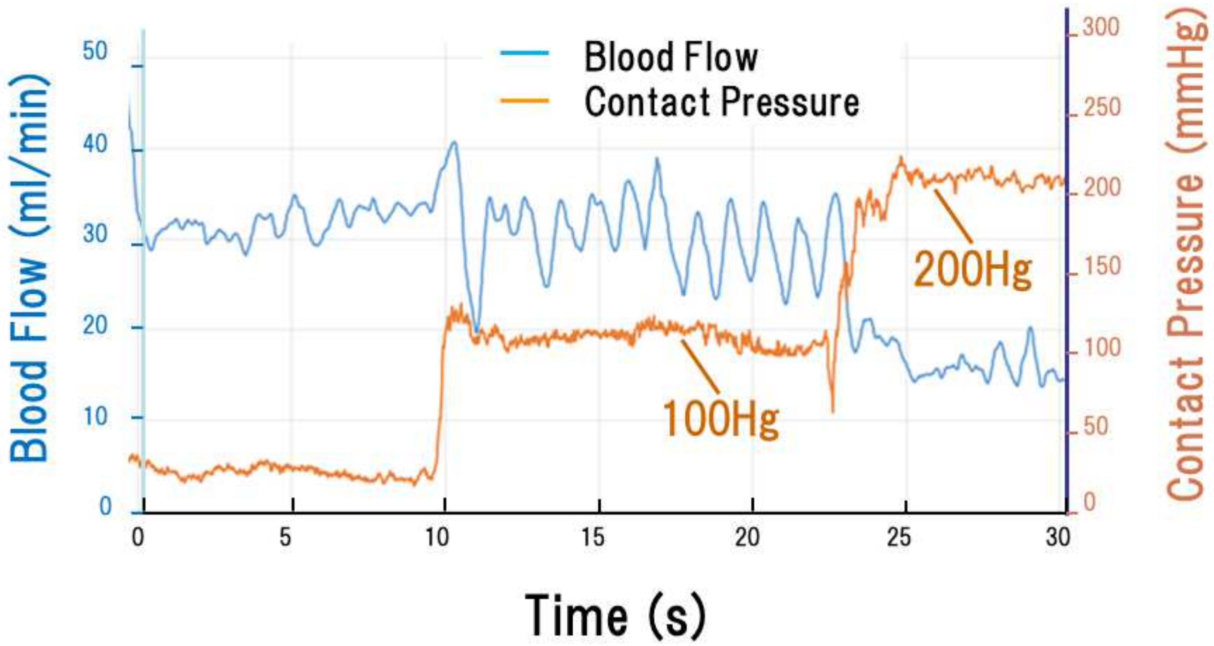


Fig. 13 Simultaneous measurement with finger blood flow when changing contact pressure

6.4.2. Other application examples

Until now, using the micro laser blood flow sensor [16] we have developed, we have been using jogging [17], detecting scleroderma [18], detecting dehydration [19], drinking alcohol [20], We report blood flow measurements performed during stress loading [21] and avian influenza infection [22].

(1) Example of blood flow measurement during jogging

Figure 14 shows a blood flow measurement result when the blood flow sensor probe is attached to the ear during the blood flow sensor probe jogging. At the time of warming-up, in the case of jogging that is severe for the living body, the blood flow is rising at a stretch. In the case of athletes, it is interesting to see if blood flow rises to this extent. The application is considered effective for sports medicine and the like. In addition, the blood flow decreases immediately after the warm-up for any jogging speed. This is thought to be due to the fact that blood flows to muscles such as feet due to jogging, so that the blood flow in the ears drops momentarily.

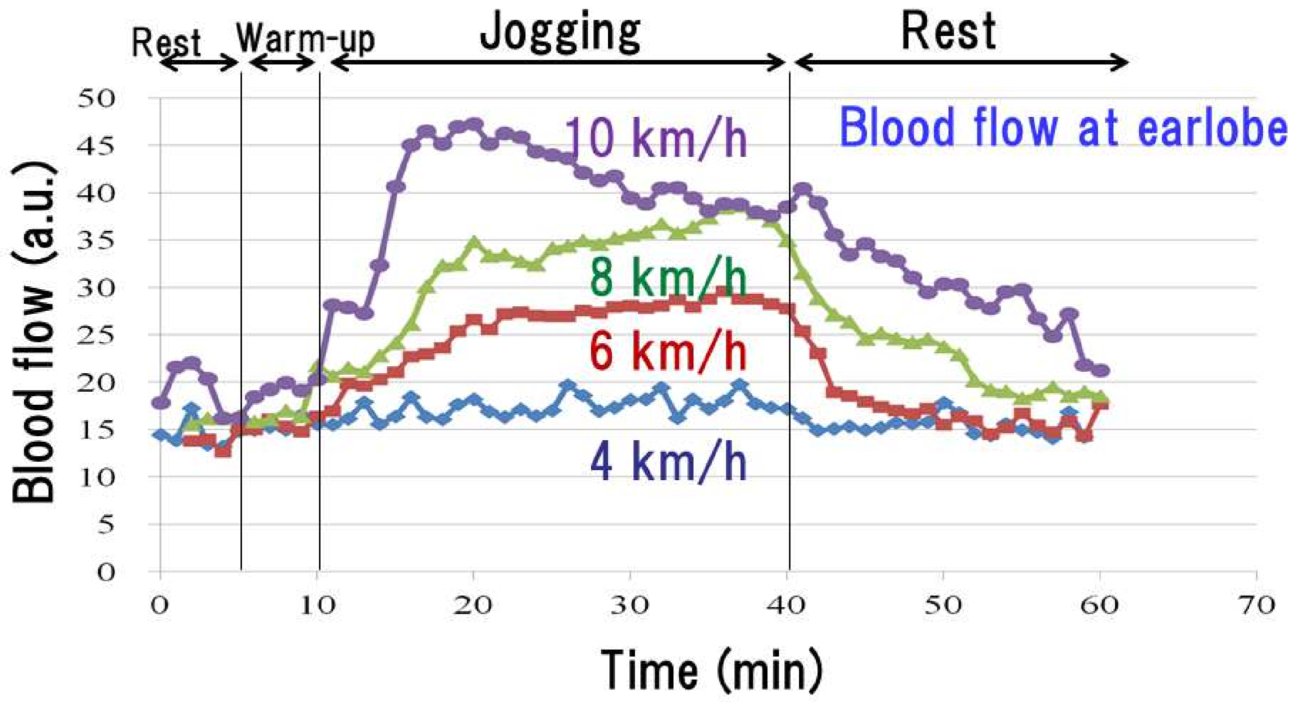


Fig. 14 Blood flow measurement during Jogging

(2) Detection of dehydration

By performing an upper limb elevation test in which a sensor probe is attached to a finger and a hand is raised, it is possible to detect Raynaud (scleroderma) and dehydration. FIG. 15 shows the results of the upper limb elevation test before and after dehydration. When the hand is raised, the measurement site is higher than the heart serving as a pump, so that the heart is burdened by potential energy, and the blood flow decreases. However, it gradually begins to rise due to the function of the living body that is gradually returning to its original state. The slope of the rise differs greatly before and after dehydration. Further, it is characteristic that the pulse wave height becomes smaller when dehydrated.

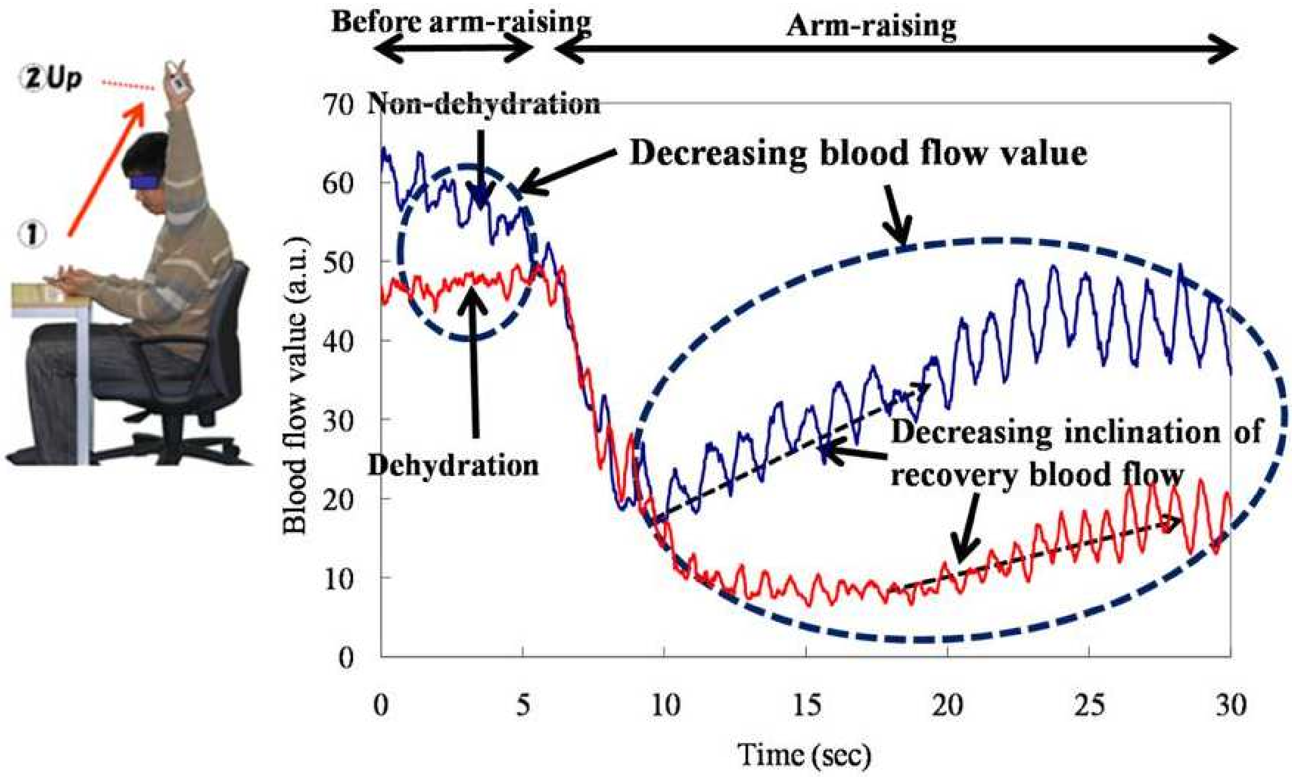


Fig. 15 Detection of dehydration

3) Stress detection by using as a pulse wave sensor resistant to body movement

Figure 16 shows the result of application to stress evaluation based on the time distance between pulse wave peaks instead of RRI of an electrocardiogram. It has been recognized that the time distance between Rs corresponding to the peak of the electrocardiographic waveform, that is, the degree of variation in RRI indicates the degree of stress. A pulse wave sensor is used as an alternative to an electrocardiograph because an electrocardiographic signal is easily disturbed by a body motion. Since the pulse wave is also detected by the blood flow sensor, the time distance between the pulse wave peaks instead of the RRI can be similarly obtained. By removing the spectrum region based on the body movement from the spectrum distribution used for calculating the power spectrum by the blood flow sensor, the influence of the body movement can be significantly reduced. Since a blood flow signal cannot be obtained but a peak of a pulse wave can be obtained, it is also useful to use it as a pulse wave sensor that is strong against body movement [23].

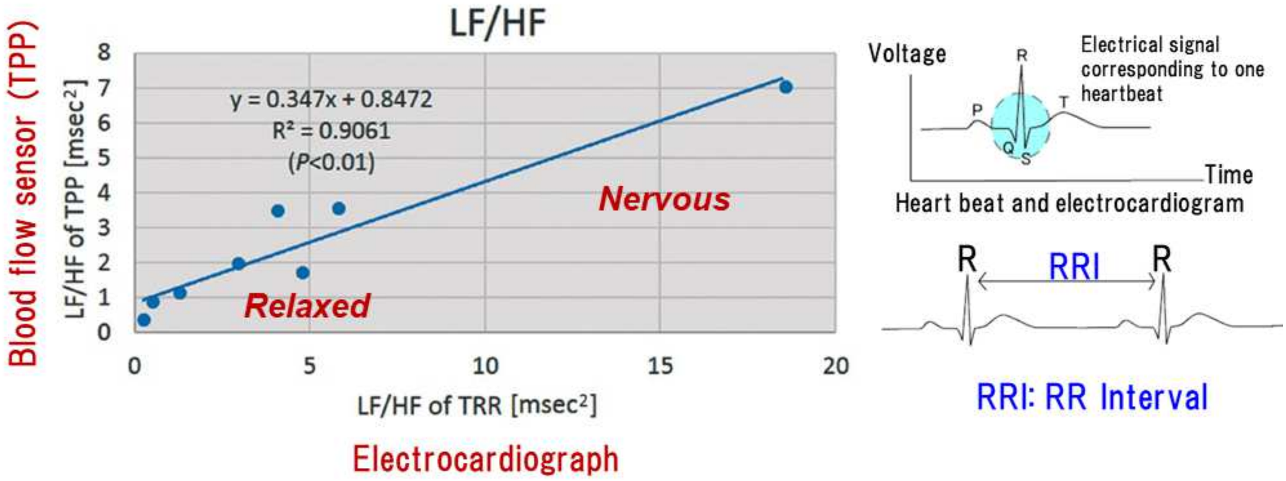


FIG. 16 Correlation with the time distance between the peaks of the pulse wave signal instead of the electrocardiogram signal distance (RR distance) of the electrocardiograph. Correlation between blood flow signal (TPP) and electrocardiogram (ECG)

Low frequency region of RR Interval. LF: 0.04-0.15 Hz, High frequency region of RR distance HF: 0.15-0.40 Hz

(4) Application to oriental medicine

Figure 17 shows a signal of a blood flow sensor attached to a finger when a point of a foot is touched. As soon as you touch the point, you can see that the blood flow is reacting. It can be understood from this result that nerves and blood flow are deeply related.

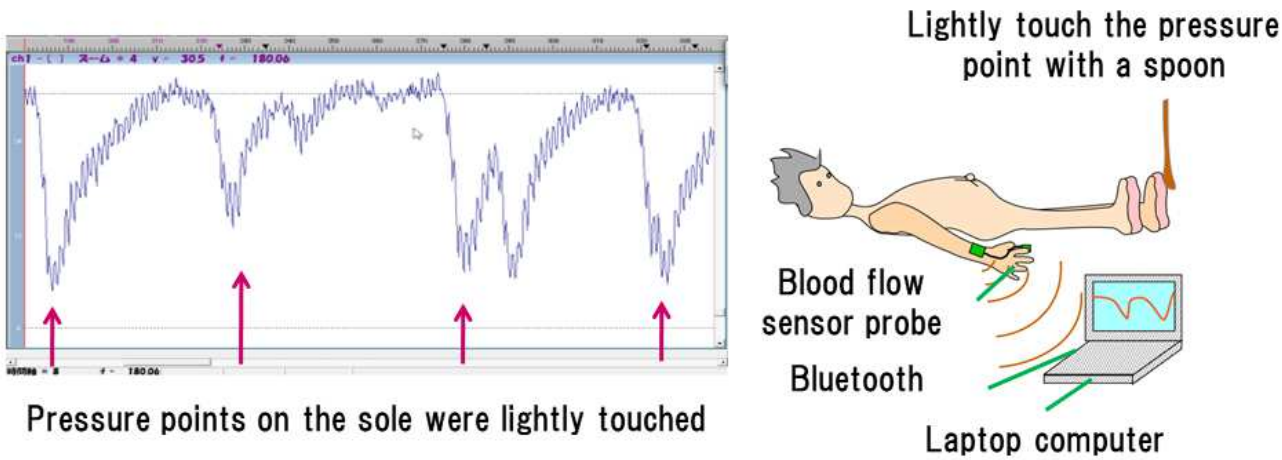


Fig. 17 Application to Oriental Medicine

6.5 Measurement of blood flow per heartbeat

In the experiments so far, in order to remove the influence of the contact pressure, the blood flow rate was measured by attaching a blood flow rate sensor probe to a site such as a finger using Ryoumen tape. Figure 18 shows the changes in physiological status before, during and after exercise [24]. It is worth noting that, after exercise, the heart rate has decreased, but the blood flow per heart rate has increased or leveled off. In the past blood flow sensors, the reproducibility of the measurement was poor, in other words, the variation in the measurement was larger than the change in the physiological state, so that it was difficult to recognize a significant change in the physiological state. The presence of highly reproducible blood flow, which also takes into account the effects of contact pressure, has made it possible to remarkably observe changes in blood flow per heartbeat, which cannot be measured with an electrocardiograph or pulse wave monitor.

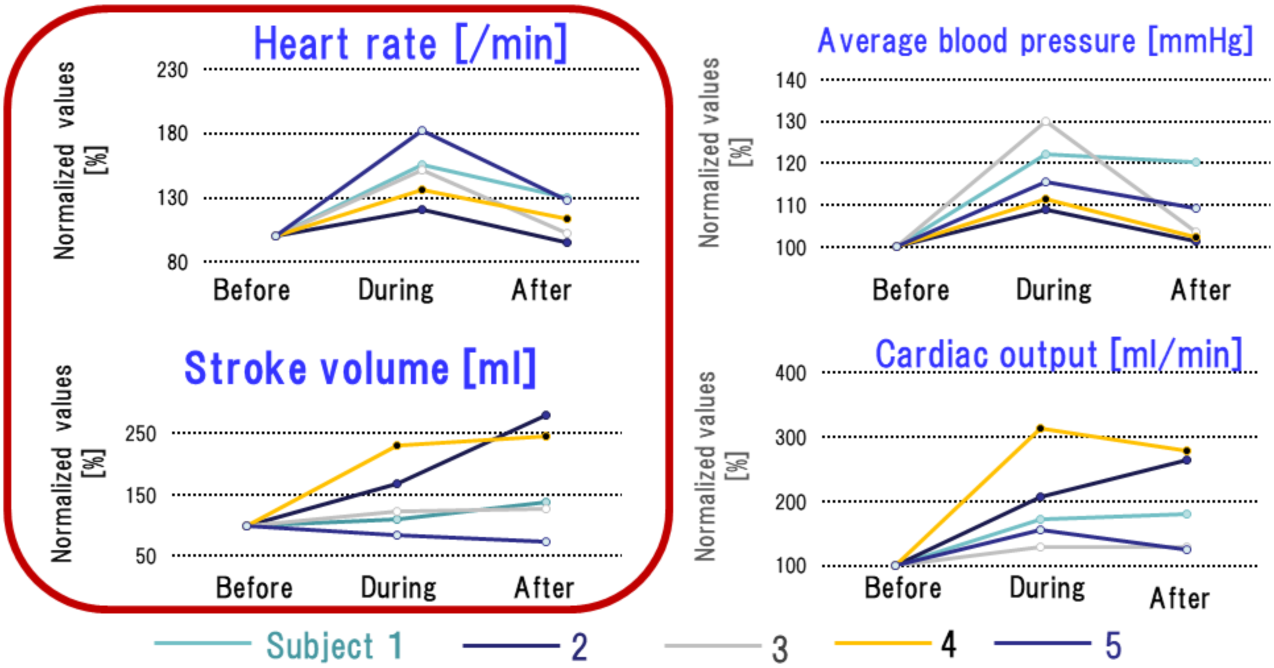


Fig. 18 Measurement of blood flow per heartbeat before, during, and after examination.

6.6 For example where blood flow is key

Table 1 shows the expected uses of the blood flow sensor in medical fields.

Table 1 Examples of possible cases where blood flow is key

Internal medicine	Examination of peripheral circulatory blood flow, peripheral circulatory disturbance of diabetic patients, autonomic nervous disorder, fingertip blood flow measurement thanks to Raynaud's disease, nerve function test, gastric mucosal blood flow measurement during endoscopy, fire extinguisher blood flow in animal experiments

Anesthesiology	Quantification of effect at pain clinic, early detection of intraoperative shock
Intensive care department	Emergency department Blood flow measurement during burns, peripheral circulation monitor
Gastrointestinal surgery	Gastrointestinal organ blood flow measurement (clinical and experimental), blood flow confirmation during organ transplantation
Neurosurgery	Brain tissue blood flow measurement (clinical and experimental)
Respiratory department	Blood flow measurement of bronchial mucosa
Vascular Surgery	Measurement for the diagnosis of Burger's disease (obstructive thromboangiitis), etc. (measurement of systolic blood pressure of the finger using a combination of cuff and mercury column), skin blood flow measurement for obstructive arterial disease, ASO (obstructive atherosclerosis)) Measurement for diagnosis
Plastic Surgery Dermatology	Flap blood flow measurement, blood flow monitoring in skin transplantation, quantification of allergic PCA reaction, measurement of skin (face) blood flow status
Orthopedic surgery	Spinal cord, nerve blood flow measurement, adhesive finger blood flow measurement
Urology	Testis blood flow measurement, blood flow erectile dysfunction (VED) diagnosis, human blood flow measurement during kidney transplantation
Pediatrics	Peripheral blood flow monitor at NICU, measurement of neonatal cerebral blood flow in animal experiments
Obstetrics and gynecology	Uterine cancer blood flow measurement, breast cancer blood flow measurement
Otolaryngology	Cochlea, nasal mucosa, flap blood flow measurement
Radiology Department	Tissue blood flow measurement during radiation therapy
Hypertension treatment department	Measurement of tissue blood flow during hypertension treatment
Oriental Medicine	Quantification of effects during acupuncture and moxibustion treatment

Dental and oral surgery	Gingival, pulp blood flow measurement, oral mucosal blood flow measurement
Pharmacology	Determination of drug effects (vasodilation, contraction, etc.)
Physiology	Autonomic nervous function and peripheral blood flow measurement, influence of stress on autonomic nervous system
Hygien	e Measurement of fingertip blood flow in white wax disease, Raynaud's disease, etc.
Forensic medicine	Examination of tissue blood flow during forensic suffocation
Department of Physical Education	Exercise rearranging research (measurement of blood flow during exercise, measurement of blood flow change before and after exercise)
Department of Home	Economics Clothing and Skin Blood Flow
Pharmaceutical companies	Evaluate the effects of drugs (vasodilators, blood flow constrictors, blood flow increasing substances, etc.)
Maintenance of daily health	Measurement of blood circulation and blood dryness, relaxation and sleep (drowsiness)
Others	Research on environmental physiology (comfort) and measurement of bedsores at R & D companies (automobiles, electricity, textiles, cosmetics, construction industry, etc.)

7. Conclusion

This paper mainly described a blood pressure sensor integrated with a contact pressure sensor and a skin temperature sensor that includes an optical system manufactured using MEMS technology. The features are listed below.

- Ultra-compact and portable
- Highly reproducible blood flow measurement. Evaluation by measuring blood flow per heartbeat is also possible.
- Even when used as a pulse wave sensor, it is less susceptible to vibration than conventional pulse wave sensors

The following are assumed as applications.

- Detection of dehydration, detection of stress, evaluation of exercise effect
- Sports medicine
- Daily health management by checking blood circulation
- Foot care for diabetics

Presence of highly reproducible blood flow that takes into account the effects of contact pressure enables measurement of changes in blood flow per heartbeat that cannot be measured with an electrocardiograph or pulse wave monitor, and is also used for scientific verification of sports and other activities I'm sure you can.
In order to make the most effective use of the blood flow sensor with a built-in contact pressure sensor, it is more important to attach (fix) it to a living body to stabilize the contact pressure. Conversely, there are reports that the contact pressure is controlled and changed, and the blood pressure and the like can be measured based on the change in the pulse wave signal amplitude.
It is thought that if the arithmetic processing by the cloud can be realized, not only a minute but also a great low cost can be realized.

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