Development of a Quantitative Method for Assessment of Integrated Medicine

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Abstract

In this article, the mechanism of the response of the maximum correlation coefficient $\rho_{\max}$ between heart rate and blood pressure or pulse wave transmission time to acupuncture has been discussed with the concept of multivariable control system and holistic matching proposed here.

1. Introduction

Unlike Western medicine which almost always takes reductionism, integrated medicine takes holistic approaches to diseases, health and human existence. This stance has the possibility to solve or reduce many medical problems which Western medicine has not completely solved by itself and prevent the inflation of medical costs in the coming super-aging society.

In order to make people understand the importance of integrated medicine and direct the political leaders' attention and policy towards integrated medicine, it is important to assess its availability in a quantitative and objective fashion.

Such an assessment with a certain method based on reductionism is inconsistent with the stance of integrated medicine or Oriental medicine. However, the assessment is feasible and worth doing.

For example, there are many studies which have been trying to quantify the effects of acupuncture on the autonomic nervous system by means of cardiovascular parameters such as heart rate and blood pressure [1-8]. One of the simplest methods for analysis of acupuncture effects is to compare the difference in heart rate and blood pressure between their mean values before and after acupuncture. However, these parameters do not directly represent the activity of the autonomic nervous system and have too large individual difference and too low reproducibility to obtain quantitative and definitive results.

It has been reported that a physiological index $\rho_{\max}$ [9,11], which is defined as the maximum correlation coefficient between heart rate and blood pressure or pulse wave transmission time whose frequency components are limited to Mayer wave-related frequencies, is more sensitive to the response to acupuncture in comparison with methods using spectral analysis of heat rate [12].

In this article, the basic characteristic of the response of $\rho_{\max}$ to acupuncture is shown and an interpretation of its dynamic mechanism is presented on the basis of multivariable control engineering and the concept of "holistic matching" which is defined here as a situation ensuring consistency between a controller and a controlled object to optimize the whole system.

2. Effects of Acupuncture on Cardiovascular Parameters and Circulatory System Model

2.1. Effects of acupuncture on cardiovascular parameters

In many studies, cardiovascular parameters such as heart rate and blood pressure, which are easy to measure and noninvasive, have been used to understand the effects of acupuncture on the autonomic nervous system [1-8]. One of the simplest methods of analysis is to compare the difference in the parameters before and after acupuncture. In usual studies using rats or humans, it has been reported that heart rate and blood pressure tend to decrease during acupuncture. This phenomenon is modified by a drug or nerve resection which suppresses autonomic nervous activity. This fact means that acupuncture affects the autonomic nervous system [1,3].

As already described above, however, these parameters do not directly represent the activity of the autonomic nervous system and have too large individual difference and too low reproducibility to obtain quantitative and definitive results.

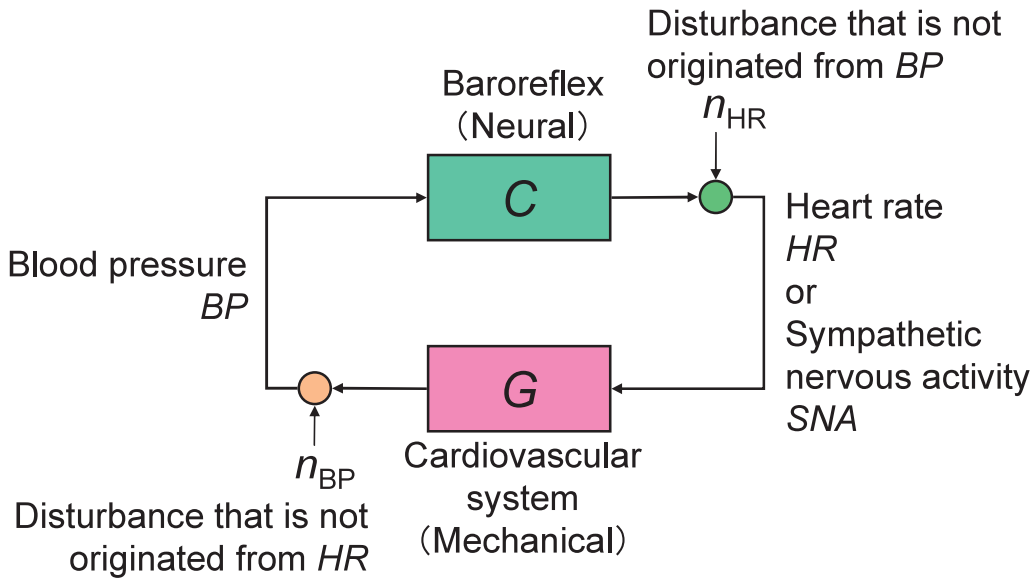

Fig. 1. Simplest model of the cardiovascular regulation system（single-input and single-output model）

On the other hand, engineering techniques have also been used to grasp the effects of acupuncture more objectively. Michikami, et al [8]. tried to apply the system identification of the dynamics of a closed loop-system which consists of the baroreflex system and the cardiovascular system of a rabbit as shown in Fig. 1. They showed that the operating point on the static characteristic from blood pressure to the sympathetic nervous activity was shifted by acupuncture to reduce the sympathetic nervous activity while the dynamic characteristic and linearity of each subsystem did not change with acupuncture.

2.2. The simplest model of circulatory system

From the viewpoint of system theory, one of the simplest models of the circulatory system can be depicted as shown in Fig. 1 [13,14], where G represents the mechanical dynamics of the cardiovascular system from heart rate HR to blood pressure BP, and C represents the baroreflex function of the cardiovascular center which regulate blood pressure measured by baroreceptors by manipulating HR. n_{HR} and n_{BP} are exogenous signals, and express a component which is not originated from BP and a component which is not originated from HR, respectively.

The result given by Michikami, et al. [9] indicates that G and C can be regarded as roughly linear systems. However, the animals were at rest under anesthesia, and thus, the result does not directly mean that the human cardiovascular system regulated by baroreflex when awaking is linear and stationary. For example, if an emotional reaction takes place, HR will vary irregularly and BP will be changed drastically by vascular motion [15]. In this case, it can be interpreted that disturbance components n_{HR} and n_{BP} will increase and the linearity of the closed-loop system will decrease.

On the contrary, the authors [9-12] positively utilize the linearity and nonstationarity to quantify the effects of emotional reaction and acupuncture by means of an index of $\rho_{\max}$.

3. Effects of Acupuncture on Linear Correlation of Circulatory System

3.1. Definition of $\rho_{\max}$

The index $\rho_{\max}$ [9-11] is calculated as the maximum value of the correlation coefficient (the correlation normalized by mean square values) between two biosignals (heart rate and blood pressure, or heart rate and pulse wave transmission time) whose frequency components are limited to Mayer wave-related frequencies by applying a band-pass filter with the pass-band of 0.08Hz-0.15Hz. The index $\rho_{\max}$ is roughly equal to the coherence function at the similar frequencies to the above ones.

The pulse wave transmission time (PTT) is defined as the length from the peak time of R-wave of ECG to the beginning time of pulse wave to rise. The PTT includes information on blood pressure because if blood pressure increases, blood vessels will be stiff and then the PTT will be reduced, and vice versa.

3.2. Experiment of acupuncture

As shown in Fig. 2, an acupunctural needle was pricked to the acupunctural point Tai Chong (Liver 3) shown in Fig. 3 of a male subject aged 50 in the supine position. The ECG signal was measured by the bipolar chest lead. Continuous blood pressure was measured at the index finger based on the volume-compensation method (Portapres; Finapres Co.). Photoplethysmogram was obtained at the middle finger with a photoelectric sensor (Nellcor; Envitec Co.). The measured signals were processed to calculate HR [min^{-1}], mean blood pressure BP [mmHg] and PTT [ms] as shown in Fig. 4.

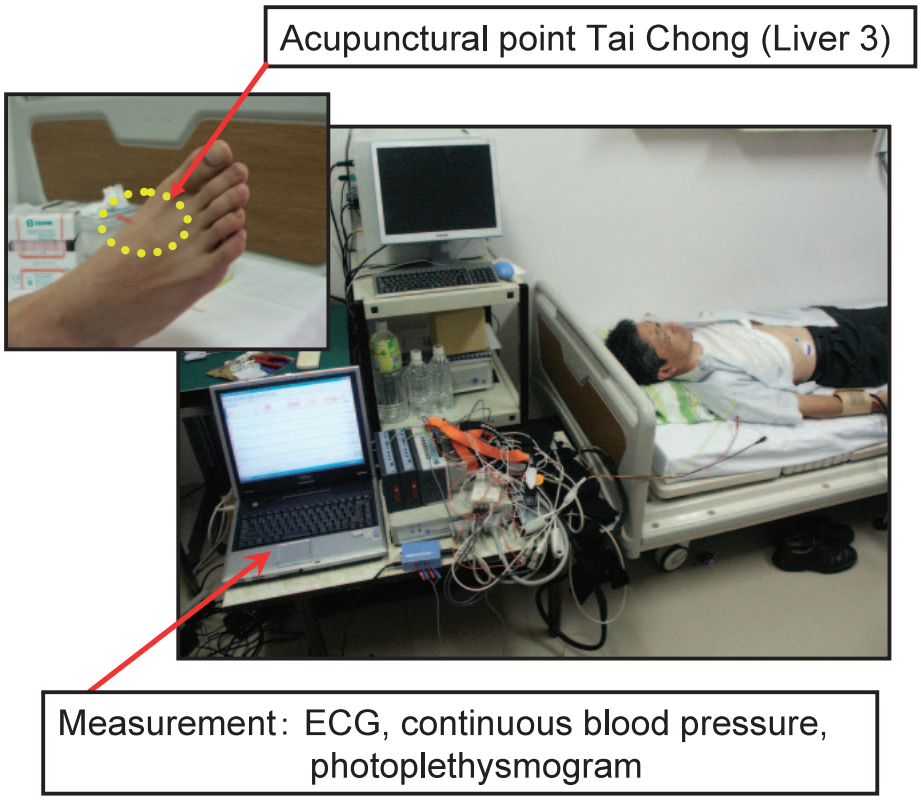

Fig. 2. Experimental setup

Fig. 3. Acupunctural point Tai Chong (Liver 3)

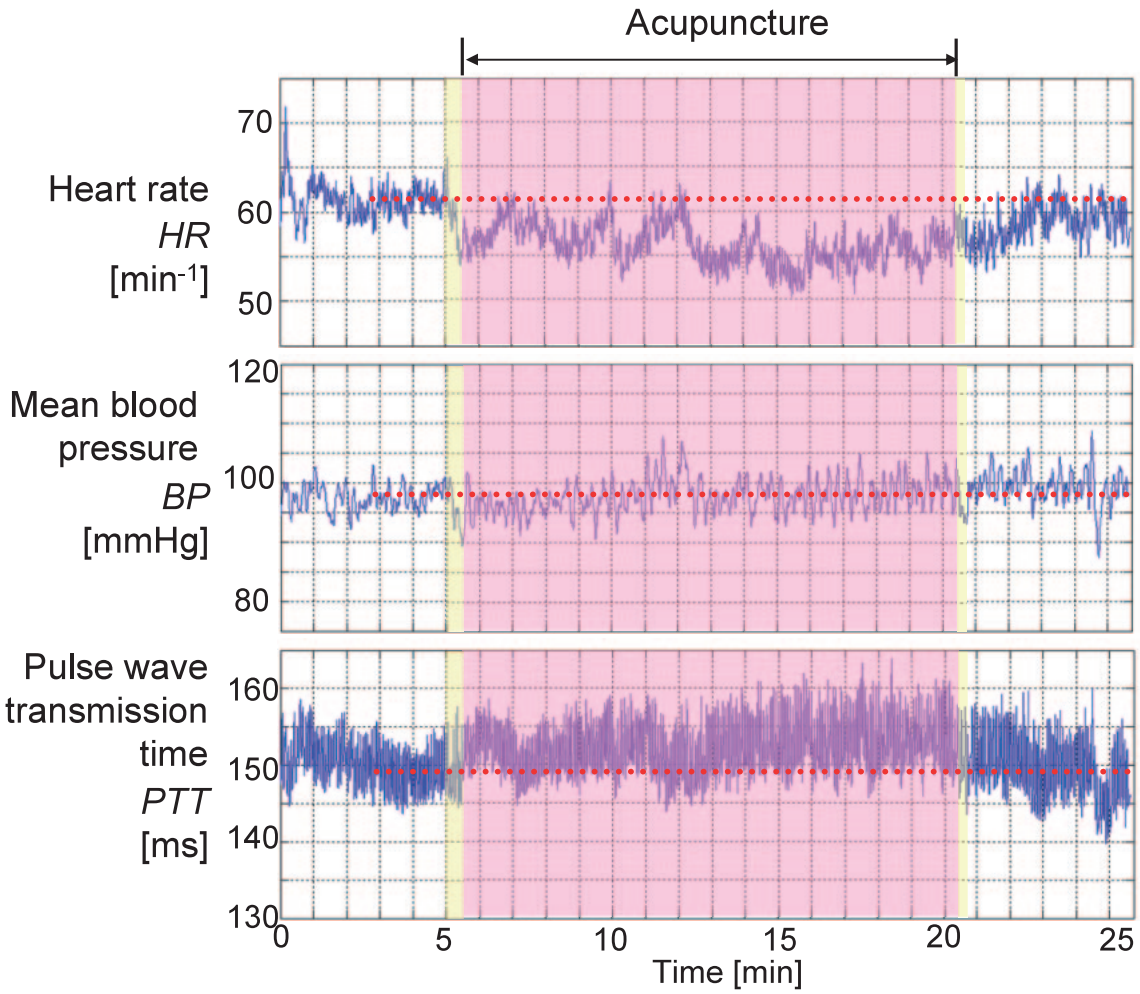

Fig. 4. Change in heart rate, mean pressure and pulse wave transmission time with time while acupuncture at Tai Chong (Liver 3) . The dotted red line represents the level averaged over 2 min before acupuncture.

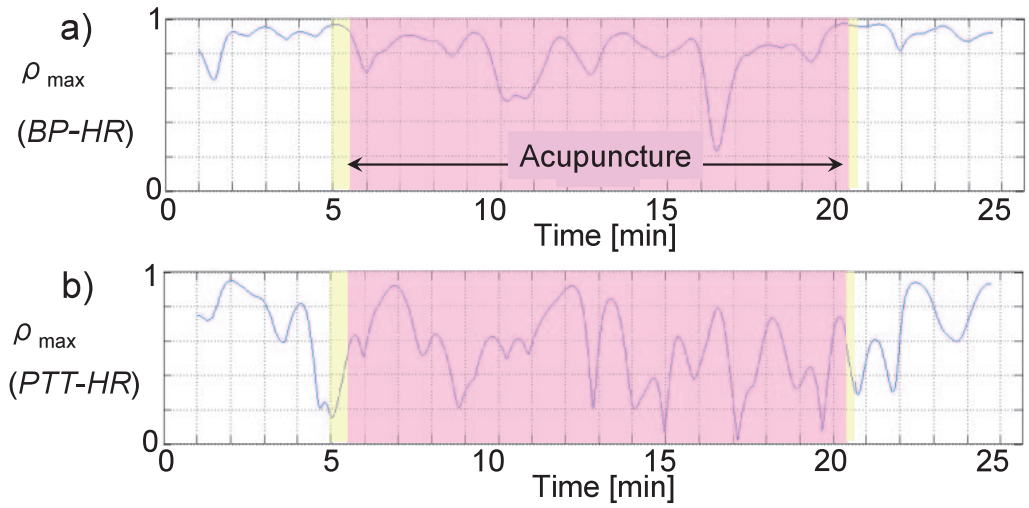

Fig. 5. Change in $\rho_{\max}$ with time [12]. a) correlation $\rho_{\max}(BR-HR)$ between BP and HR . b) $\rho_{\max}(PTT-HR)$ between PTT and HR .

Figure 5 shows the change in $\rho_{\max}$ with time [12]. Figure 5a) was calculated as the correlation between BP and HR, which is denoted by $\rho_{\max}(BR-HR)$, and Fig.5b) was calculated as the correlation between PTT and HR, which is denoted by $\rho_{\max}(PTT-HR)$. $\rho_{\max}(BR-HR)$ was over 0.9 at rest before and after acupuncture. During acupuncture, however, it was reduced to around 0.8 and sometimes under 0.3. On the other hand, $\rho_{\max}(PTT-HR)$ was around 0.8 at rest before and after acupuncture but considerably reduced to around 0.5 during acupuncture.

The above result suggests that acupuncture decreases the linear correlation of the cardiovascular regulation system. The amount of change in $\rho_{\max}$ during acupuncture was larger than that of heart rate or blood pressure. In special, a sealed acupunctural needle with a 0.6 mm long tip significantly decreased $\rho_{\max}(PTT-HR)$ as shown in Fig. 6. The problem is that the above results is inconsistent with the result reported by Michikami, et al. [8] in which acupuncture changed the static characteristic of the cardiovascular regulation system but did not change its dynamics and linearity. The decrease in linear correlation can be explained by the increase in the disturbance components n_{BP} and n_{HR} shown in Fig. 1. However, the model of Fig. 1 cannot explain the reason why he disturbance components increase.

These problems may be solved by modeling the cardiovascular regulation system as a multivariable system.

4. Interpretation of the Effects of Acupuncture with a Multivariable Model of the Cardiovascular Regulation System

The model of Fig. 1 is based on the cardiovascular regulation system at rest. Once the system leaves the resting state, the accuracy of the model will become low. For example, if the posture changes, both blood pressure BP and cardiac output CO should be changed into the corresponding new values which are needed in the new situation. This idea can produce a two-input and two-output model with BP and CO as controlled variables and with heart rate HR and the vascular resistance R as manipulated variables as shown in Fig. 7.

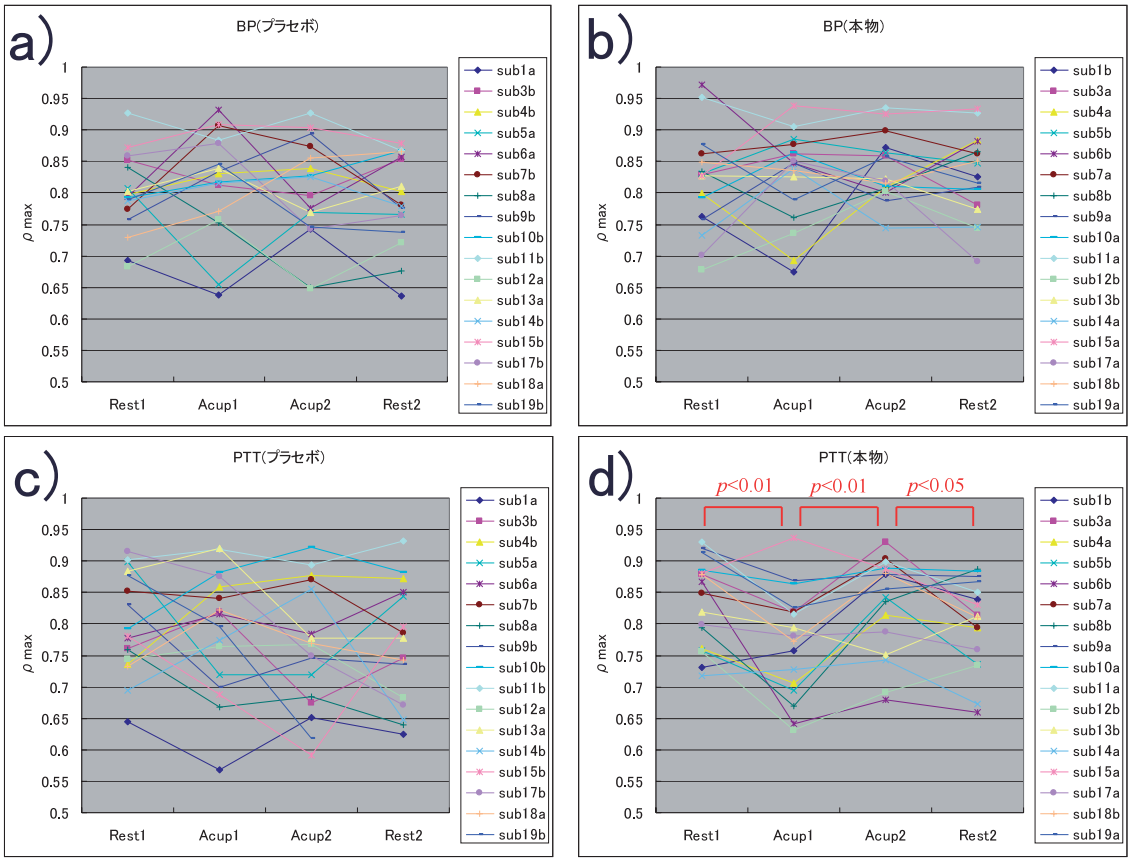

Fig. 6. $\rho_{\max}(BR-HR)$ and $\rho_{\max}(PTT-HR)$ for a sealed acupuncture and a placebo. a) $\rho_{\max}(BR-HR)$ in the placebo, b) $\rho_{\max}(BR-HR)$ in the sealed acupuncture, c) $\rho_{\max}(PTT-HR)$ in the placebo, d) $\rho_{\max}(PTT-HR)$ in the sealed acupuncture.

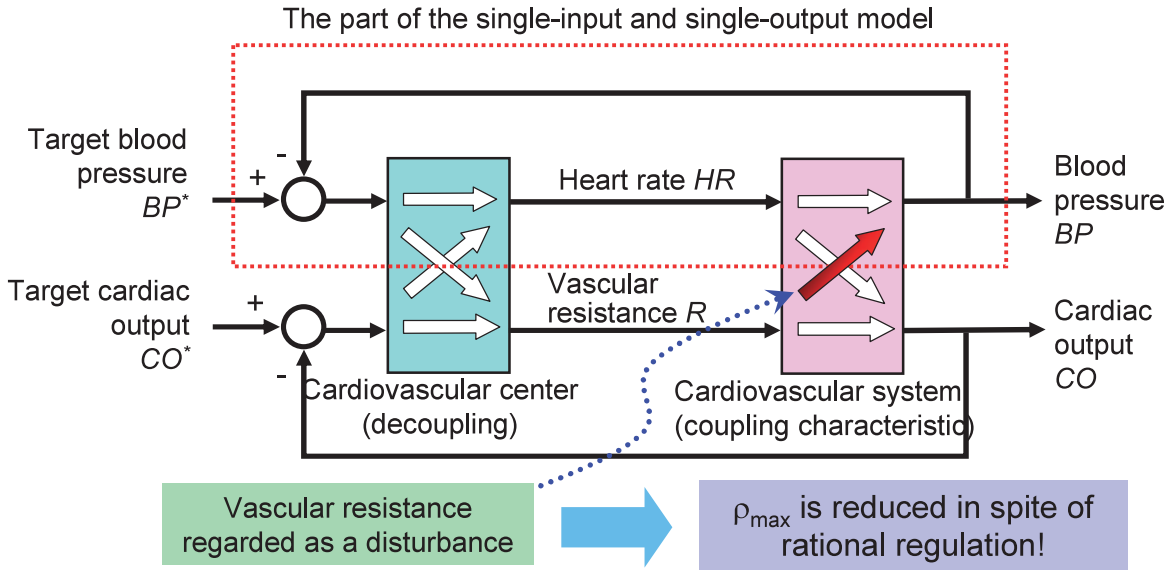

Fig. 7. two-input and two output model of the cardiovascular regulation model.

In this model, the reason why n_{BP} and n_{HR} increase in the transient state can be explained that the variation of BP is caused by the change in R without regarding to the change in HR and the variation of HR is caused by a top down command from a higher center. In other words, the shift from the resting state into a new state requires the change in the set point (the target) of BP, and then both R and HR will transiently change to realize the new operating point. This fact will bring the change in BP without regard to the change in HR and the change in HR without regard to the change in BP. This action means that the correlation between BP and HR is reduced.

The single-input and single-output model of Fig. 1 corresponds to the part surrounded by the broken line in the two-input and two-output model. In this part, the operation of R is regarded as the disturbance n_{BP} yielding the change in BP which is not related to the change in HR and this action decreases the correlation between BP and HR.

In fact, however, the operation of R should be regarded as a rational action to regulate BP caused by the cardiovascular center through the sympathetic nervous activity in the same way as the operation of HR.

To represent the linear correlation of the multivariable system, not only the linear correlation of $HR \rightarrow BP$ but also the linear correlation of $R \rightarrow BP$ should be summed up, that is to say, the multivariate coherence function, which is defined as the sum of the two values of the linear correlation, should be used. In this situation, even if the linear correlation of $HR \rightarrow BP$ becomes low, the multivariate coherence function will keep a high value as long as the linear correlation of $R \rightarrow BP$ is high. This means that the cardiovascular center would maintain a rational blood regulation.

While the calculation of $\rho_{\max}$ between HR and BP is done in the narrow band of Mayer wave-related frequencies around 0.1 Hz, the responses of BP and CO to the change in the set point must have a much wider frequency band. Therefore, the calculation of the correlation in the transient state should be done in a much wider frequency band while the Mayer wave-related band [16].

Consequently, it can be noted that the decrease in $\rho_{\max}(BP-HR)$ and $\rho_{\max}(PTT-HR)$ caused by acupuncture does not always mean the decrease in linearity of the whole cardiovascular regulation system if the two-input and two-output model is introduced.

On the other hand, the comparison between Figs.7a) and b) suggests that $\rho_{\max}(PTT-HR)$ using pulse wave transmission time PTT is more sensitive than $\rho_{\max}(BP-HR)$ using blood pressure BP. This reason has been explained in the literature [12].

5. Holistic Matching

As mentioned above, the change in the linear correlation of the cardiovascular regulation system caused by acupuncture can be explained by regarding it as a multivariable control system. However, the reason why heart rate and blood pressure decrease is still unknown. It seems that this reaction is related to a kind of defense response to traumatic stimulation such as acupuncture to suppress bleeding, reduce metabolism or modulate pain. This phenomenon may be associated with the holistic optimization as mentioned in the following.

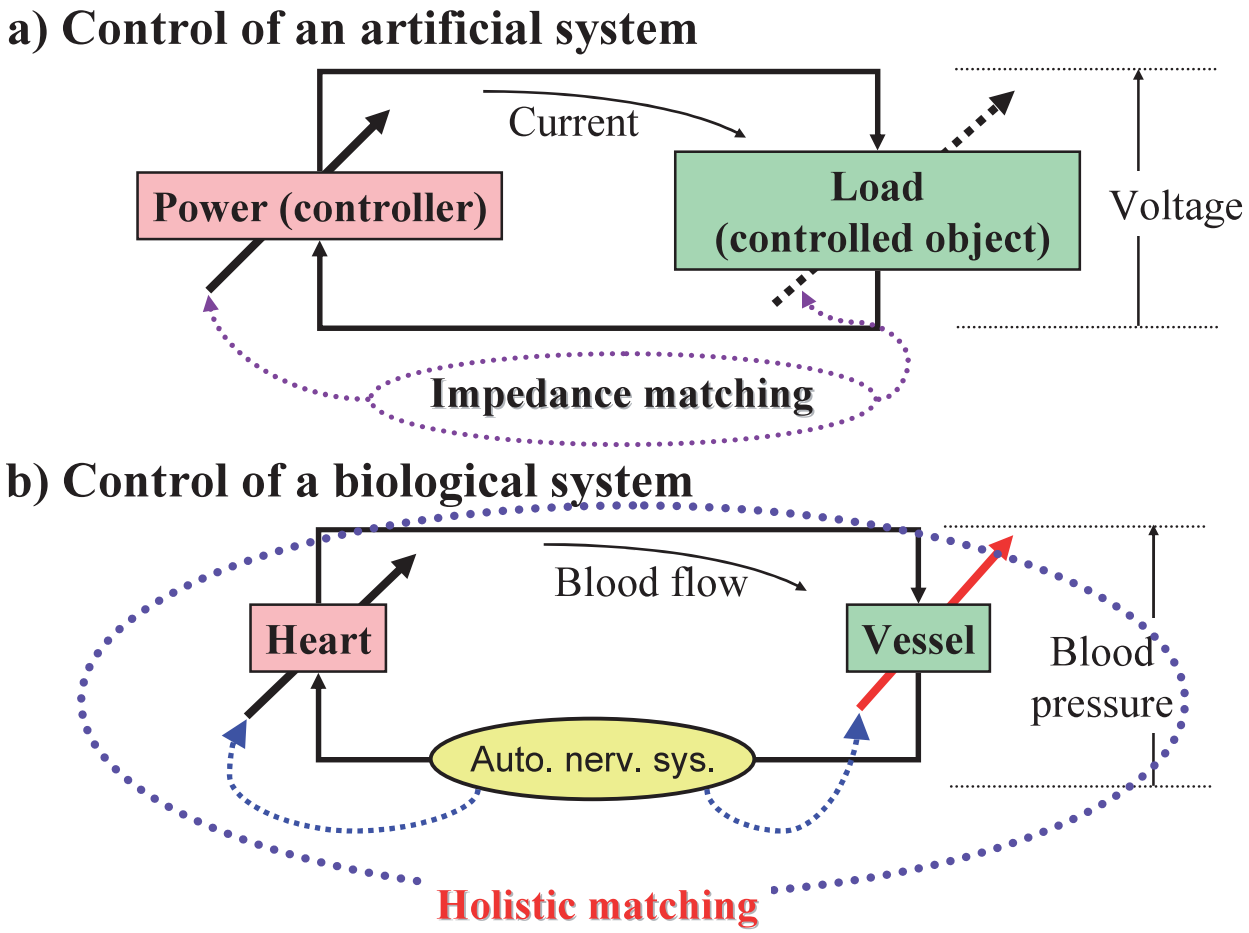

Fig. 8. Control methods of an artificial system and a biological system

Consider an electrical circuit shown in Fig. 8 as an example of control of an artificial system. In this case, it is well known that "impedance matching", in which the inner impedance of the power source is set to be equal to that of the load, should be applied to send energy from the source to the load most effectively. Usually, such adjustment is executed previously in the design phase or the characteristic of the source (or the controller) is changed to match the characteristic of the load (or the controlled object).

On the other hand, the different aspect is seen in the case of the control of a biological system such as the cardiovascular control system shown in Fig. 8b). In the system, not only the maximum elastance deciding the cardiac contractility corresponding to the power source (or the controller) is changed but also vascular resistance and compliance corresponding to the load (or the controlled object) is varied actively to regulate cardiac out and blood pressure [17].

This phenomenon implies that both the controller and the controlled object are collaborating with each other to optimize the multivariable system. This can be interpreted as a kind of holon which is a system (or phenomenon) that is a whole in itself as well as a part of a larger system [17]. The authors call this concept "holistic matching," comparing to impedance matching used in artificial systems.

Although acupuncture is a kind of stimulation to peripheral organs, its effect transmits to not only the cardiovascular regulation system and the autonomic nervous system but also the whole body. In such a manner, it can be interpreted that acupuncture is a therapy which can evoke the holistic matching artificially.

6. Conclusion

In this article, the mechanism of the response of the maximum correlation coefficient $\rho_{\max}$ between heart rate and blood pressure or pulse wave transmission time to acupuncture was discussed with the concept of multivariable control system and holistic matching that was proposed here.

If a more precise model can be attained by regarding the cardiovascular regulation system governed by the autonomic nervous system as a multivariable system on the basis of noninvasive cardiovascular parameters, the effects of acupuncture on humans will be dealt with in a more quantitative and objective fashion.

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