생체자극으로써의 PRTS 신호의 이용에 관한 연구

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Using Pseudo-Random Ternary Sequence as Physiological Stimulus

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Abstract

In this paper, pseudo-random ternary sequence (PRTS) was used to investigate the cardiovascular and respiratory responses to hypoxia and hypercapnia. The actual input for this study was the changes in inhaled oxygen and carbon dioxide concentrations. It is hard to randomly change the concentration within a given breath. Since PRTS has almost the same statistical properties as Gaussian white noise, plus it is physically realizable, PRTS is used for this study. Using PRTS and Volterra kernels by Gram-Schmidt orthogonalization procedure, the cardiovascular and respiratory responses to hypoxia and hypercapnia were analyzed.

Introduction

Oxygen and carbon dioxide tensions of blood are important chemical determinants of the ventilation level. To a large extent, these tensions are determined by the amount and distribution of oxygen and carbon dioxide stored in the body.[1] The greater the changes in the blood concentration of CO_2 (P_{CO2}) and the blood concentration of O_2 (P_{O2}), the greater the changes in the activity of the chemoreceptors, and the greater the increases in ventilation, and the more likely unstable breathing occurs. Using exercise, hypoxia, hypercapnia, and hypoxic-hypercapnia experiments that disturb the O_2 and CO_2 storage in the body, one can possibly characterize the respiratory control mechanism and corresponding mechanism of the cardiovascular system.[2][3][4]

The cardiovascular and respiratory responses to above experiment have been studied in the last three decades, and most of these studies have been performed by linear analysis using step, sinusoidal, or binary sequences as inputs.[2][3] These are not proper inputs for nonlinear analysis.

Most physical systems encountered in the real world are generally nonlinear. In particular, most physiological and biological systems are highly nonlinear. Thus the application of nonlinear system theory is necessary for such systems to obtain more advanced understanding and insight into the entire system under consideration.

An optimal input signal for the physiological system identification requires realizability, repeatability, robustness, and persistence.[5] Any input that satisfies the above conditions can be used for system identification. In fact, if a signal has suitable autocorrelation properties, then that signal can be used as a proper input signal for system identification. The ideal input for system identification is Gaussian white noise. But, in particular, for this study, it is difficult to use a Gaussian white noise signal. The actual input for this study was the changes in inhaled oxygen and carbon dioxide concentrations. It is hard to randomly change the concentration within a given breath. Since pseudo-random ternary sequence (PRTS) has almost the same statistical properties as Gaussian white noise, plus it is physically realizable, PRTS is used for this study.

Experiment

All subjects for the experiment were cats. The cats were anesthetized with ketamine (2.2 mg/kg) and chloralose (60.0 mg/kg). The objectives of this experiment were to measure blood pressure, heart rate, blood flow, minute ventilation, tidal volume, air flow and other ventilatory responses to changes in inhaled oxygen and carbon dioxide concentrations.

End-inspiratory oxygen concentration(F_iO_2) or end-inspiratory carbon dioxide concentration(F_iCO_2) was changed every breath as a pseudo-random ternary sequence. The sequence length was 242 breaths. A portion of the sequence was performed before data were recorded in order to allow the system to settle to a new operating point. F_iO_2 varied from 7% to 21% to 35% or 7%, 14%, 21%. F_iCO_2 varied from 0% to 5% to 10%.

The chemoreceptors respond to changes in P_{CO2}, pH, P_{O2}. These receptors are thought to have the major role in the dynamic response of the respiratory system. Thus the following 3 set of experiments was performed. Data were taken with intact nerves (INTACT), aortic depressor nerves severed (AD), and with complete sinoaortic denervation (SAD). Chemoresponsive carotid nerves have been reported to be responsive to a wide variety of chemical substances in the blood, e.g., oxygen, carbon dioxide, NaCl, acid, nicotine, and NaCN. The success of the SAD experiment was checked by stimulating the carotid sinus with NaCN.

Method

Volterra [6] showed that for a nonlinear time-invariant system with memory, the relationship between the input signal x(t) and the output signal y(t) can be expressed as the following infinite series:

$$y(t) = k_0 + \int_{-\infty}^{\infty} k_1(\tau_1)\, x(t-\tau_1)\, d\tau_1 + \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} k_2(\tau_1, \tau_2) x(t-\tau_1) x(t-\tau_2)\, d\tau_1\, d\tau_2 + \ldots$$

in which $k_r(\tau_1, \tau_2, \ldots, \tau_r)$ is the r*th*-order Volterra kernel. The kernels of the Volterra series completely describe the response of the system. Consequently mathematical identification of a system is equivalent to calculation of the kernels.

In this study, the input signal was 242 sequences of pseudo-random ternary sequence. If the input was pseudo-random signals based on m-sequences, the first and second-order Volterra kernels can be exactly calculated.[7][8] By using the Gram-Schmidt orthogonalization procedure, Korenberg et al. [9][10] have proposed the computation method of the kernels. Since the results by orthogonalization reduce the kernel estimation error and noise susceptibility, PRTS and Volterra kernels by orthogonalization procedure was used in this study.

Results and Discussion

Fig. 1 (a) is the true 242 PRTS (i.e., -a, 0, +a) and Fig. 1 (b) is the modified PRTS based on inspiratory duration. The actual input of this experiment is the changes in inhaled oxygen and carbon dioxide concentrations, i.e., the duration of input is actually the inspiratory duration of breathing of cat. Thus the sampling time is not a constant. Instead of using (-a, 0, +a), (-a ± Δa, ± Δa, a ± Δa) can be used to compensate for the different sampling time, where Δa can be calculated from the average value of inspiratory duration and each inspiratory duration time.

Another desirable characteristic of the PRTS in this application is that it is inverse-repeat (anti-symmetric), so that its odd-order autocorrelation functions are identically zero. Thus the calculation of the second-order Volterra kernels becomes relatively simple. The inverse-repeat property of PRTS gives that the total responses can be divided into even- and odd-order responses. Using this property, the nonlinearity of the given system can be examined.

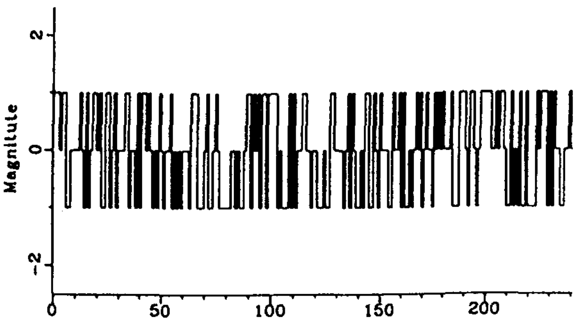

Fig. 1 (a) Original 242 Pseudo-Random Ternary Sequence. The inverse-repeat property of PRTS states that the second half of PRTS is the first half of PRTS multiplied by -1.

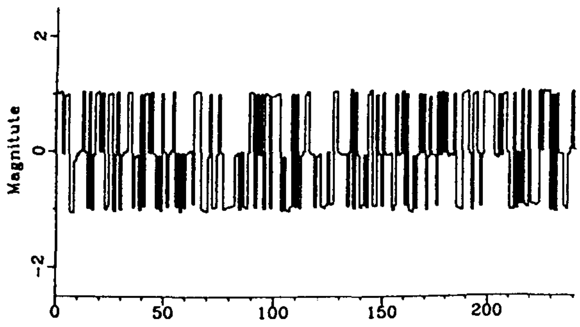

Fig. 1 (b) Modified PRTS Based on Inspiratory Duration. In order to compensate for the different sampling time which depends on the inspiratory duration of cat's breathing, this modified PRTS was used for kernel calculation.

Twenty different variables are measured or calculated as a result of applying a 242 breath PRTS. However the select set of variables will be presented. Fig. 2 shows typical measured stimuli and responses. Fig. 2 (a) is the actual input of the oxygen experiments, i.e., change in end-inspiratory oxygen concentration. Fig. 2 (b) is the corresponding average inspiratory blood pressure response.

Using Gram-Schmidt orthogonalization procedure, the typical calculated responses of hypoxia and hypercapnia stimuli are given in Fig. 3. Hypoxic SAD response shows a hypo-additive effect, i.e., response decreases about 1 mmHg and continues much longer than in the INTACT and AD cases. But hypercapnic SAD response still shows a hyper-additive effect, i.e., response reaches about 0.8 mmHg and continues about 100 sec. By cutting more nerves, the peak value reduces and appears later but the effect of hypercapnia continues longer.

Conclusion

In this study, pseudo-random ternary sequence was used to investigate the cardiovascular and respiratory responses to hypoxia and hypercapnia. This signal has some desirable properties in this particular study.

1. Using relatively short duration of experiment, i.e., 242 sequences and combining with Gram-Schmidt orthogonalization procedure, the calculation of Volterra kernels becomes relatively simple and exact.
2. The inverse-repeat property of PRTS gives that the total responses can be divided into even- and odd-order responses. Using this property, the nonlinearity of the given system can be examined.
3. As step, sinusoidal, and binary sequences are used for the linear system analysis, PRTS can be applicable to the nonlinear system since most biological and physiological system can be regarded as highly nonlinear.

References

1. N.S. Cherniack, G.S. Longobardo, F.P. Palermo, and M. Heymann, "Dynamics of oxygen stores changes following an alteration in ventilation," J. Appl. Physiol., Vol. 24, No. 6, pp. 809-816, 1968.
2. F.M. Bennett, P. Reischl, F.S. Grodins, S.M. Yamashiro, W.E. Fordyce, "Dynamics of ventilatory response to exercise in humans," J. Appl. Physiol., Vol. 51(1), pp. 194-203, 1981.
3. Pseudo-random testing of ventilatory response to inspired carbon dioxide in man," J. Appl. Physiol. Vol. 49(6), pp. 1000-1009, 1980.
4. G.S. Longobardo, N.S. Cherniack, K.P. Strohl, J.M. Fouke, "Respiratory control and mechanics," Handbook of Bioengineering, McGraw-Hill Book Comp., pp. 25.1-25.35, 1987.
5. P.Z. Marmarelis, V.Z. Marmarelis, Analysis of Physiological Systems - The White Noise Approach, Plenum Press, New York, 1978.
6. V. Volterra, Theory of Functionals and of Integral and Integro-Differential Equations, Dover Publications, New York, 1959.
7. H.A. Barker, S.N. Obidegwu,. "Combined cross-correlation method for the measurement of the 2nd-order Volterra kernels," Proc. IEE, Vol. 120, No. 1, pp. 114-118, 1973.
8. H.A. Barker, R.W. Davy, "Measurement of the second-order Volterra kernels using pseudo-random ternary signals," Int. J. Control, Vol. 27, No. 2, pp. 277-291, 1978.
9. M.J. Korenberg, S.A. Billings, Y.P. Liu, P.J. McIlroy, "Orthogonal parameter estimation algorithm for nonlinear stochastic systems," Int. J. Control, Vol. 48, No. 1, pp. 193-210, 1988.
10. M.J. Korenberg, "A robust orthogonal algorithm for system identification and time-series analysis," Biol. Cybern. Vol. 60, pp. 267-276, 1989.

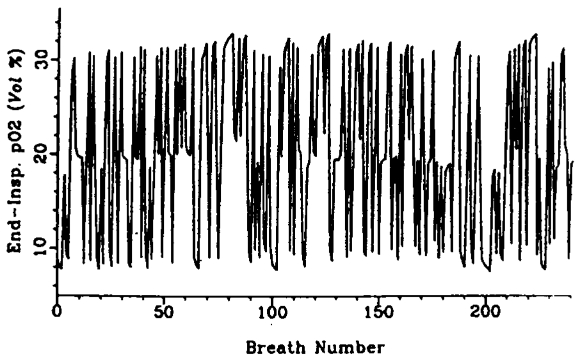

Fig. 2 (a) Actual Stimulus of Oxygen Experiment. A PDP 11/73 microcomputer was used on-line to generate the breath-by-breath sequence of inhaled gas mixture and collect the data. F_iO_2 or F_iCO_2 was changed every breath as a pseudo-random ternary sequence.

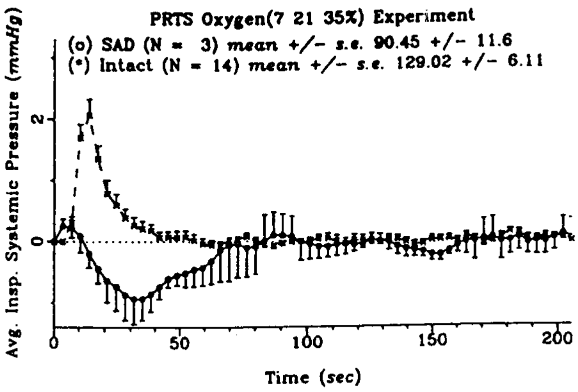

Fig. 3 (a) INTACT vs SAD Response to Oxygen Stimulus. By completely removing sinoaortic nerves, the average systemic blood pressure response to hypoxia decreases and the effect of hypoxia continues much longer. This demonstrates that the central chemoreceptors does not respond the changes in blood concentration of oxygen.

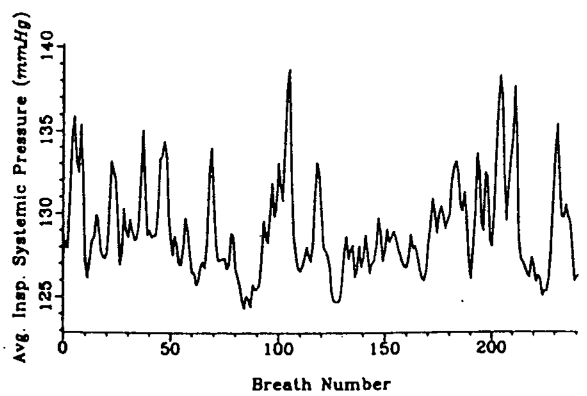

Fig. 2 (b) Corresponding Measured Average Inspiratory Systemic Blood Pressure. This shows the typical blood pressure response to the hypoxic stimulus. Results were stored in microcomputer for later off-line analysis. A MT-9500 multi-task 8 channel chart recorder (Astrom-Med Inc.) was also used to record the results.

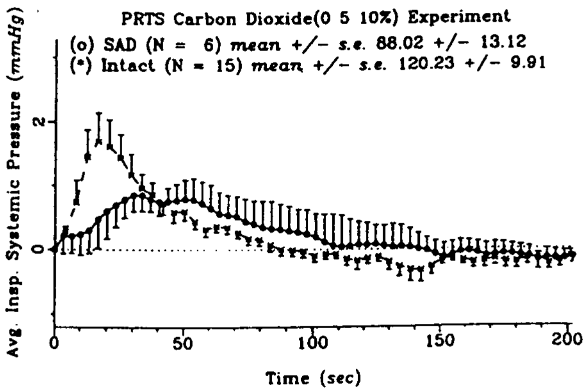

Fig. 3 (b) INTACT vs SAD Response to Carbon Dioxide Stimulus. By completely removing sinoaortic nerves, the average systemic blood pressure to hypercapnia still shows hyper-additive effect. This explains the role of central chemoreceptors to hypercapnic stimuli.