COMPUTERS AND BIOMEDICAL RESEARCH **16**, 531–536 (1983)

Optimal Frequency Locations for Estimating Model Parameters in Studies on Respiratory Control

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Received March 4, 1983

Sinusoidal work rate inputs yield a dynamic ventilatory response which can be fitted to a mathematical model. The model structure leads to inferences about the underlying physiology of the respiratory control mechanism. A particular problem of interest in model parameter estimation concerns the location of the test frequencies. The effects of estimating the parameters of a relatively complex model developed by Fujihara *et al.* using arbitrary frequency locations from a study by Casaburi *et al.* versus using the frequencies derived from an optimization method presented in a recent paper by Engeman *et al.* were examined. The Fujihara model is indicated to be much more likely to be justified when optimal sinusoids are used to generate the data than when Casaburi's arbitrary frequencies are used. The implications are that more descriptive models of respiratory control may be developed with the aid of optimal frequency design for the input sinusoids.

INTRODUCTION

Studies on respiratory control frequently use mathematical models to characterize the ventilatory response to a dynamic input. Inferences about the physiological structure of the respiratory control mechanism are made by interpreting the model structure. A variety of recent studies in respiratory control have used sinusoidal inputs and frequency response methods to develop such mathematical models (*1–6*). In these studies, the frequency response was usually determined at six or seven discrete frequencies in the range of interest. These input frequencies have been arbitrarily located in past studies (e.g., equally spaced on a logarithmic scale), although a recent study (*1*) has expressed a need for specifically designed input frequencies.

0010-4809/83 $3.00

The descriptiveness of a parametric model in terms of the underlying physiology depends largely on the quality of the data. The signal degradation due to noise limits the usefulness of the data and, consequently, the descriptiveness of the resulting model by obscuring the response characteristics so that they are not apparent statistically. However, the degradation by the noise can be minimized by forcing the physiological system to behave in such a manner that the signal is enhanced in relation to the noise (*7*).

In the present paper we investigate the effect that optimizing the locations of frequencies for the input sinusoids has on estimating the parameters of a relatively complex model proposed by Fujihara *et al.* (*8*). These input frequencies are selected by using a recently presented optimal design method (*9*). For comparison we examine the arbitrary sinusoidal inputs and the resulting model presented by Casaburi *et al.* (*2*). Using each of these two sets of input sinusoids, we predict the effect that each would have on estimating the parameters of the Fujihara model.

Optimization Review

Recently, Engeman *et al.* (*9*) presented the derivation for a method whereby the locations of the input frequencies are optimized to enhance parameter estimation. The problem is formulated in the frequency domain where the input and output of the system are related by the following equation:

$$Z_y(\omega_i) = B(\omega_i)Z_x(\omega_i) + Z_n(\omega_i) \qquad [1]$$

where ω_i indicates the ith of k frequencies; $Z_y(\cdot)$, $Z_x(\cdot)$, and $Z_n(\cdot)$ are, respectively, the Fourier transforms of the output, input, and the corrupting observational noise process; $B(\cdot)$ represents a frequency response function that is nonlinear in the parameters (*9*). It is assumed that the noise process is stationary so that its Fourier transform is asymptotically uncorrelated at different frequencies (*10*). Using a Taylor series expansion (truncated at the first order), $B(\cdot)$ is linearized with respect to the parameters. This puts Eq. [1] into the statistical context of the general linear model. The optimal frequencies selected are those that minimize the generalized variance (*11*, *12*) for the parameter estimation error. The frequencies selected using the generalized variance as the design criterion are independent of the scaling of the model parameters.

Only the form of the frequency response function whose parameters are to be estimated and an initial guess at these parameters are needed to construct the design criterion (*9*). The selection of the optimal frequencies is accomplished by using a nonlinear minimization algorithm to minimize the generalized variance criterion. A logistic transformation (*9*, *13*) is used to prevent the computing from "blowing up" by restricting the frequencies to a range between steady state and a realistic upper bound.

In the present paper the input is an exercise work rate and the output is the ventilation response. The structure of the respiratory control mechanism is inferred from the estimated frequency response function.

Application and Discussion

First we present the modeling results and their physiological implications given in the Casaburi and Fujihara studies. Both models were derived to characterize data from subjects who exercised on a cycle ergometer with the ergometer pedaled at a constant rate. The predicted effect on estimating the parameters of the Fujihara model is examined when using optimally designed input sinusoids versus those used in the Casaburi study.

Casaburi *et al.* (*2*) studied the responses of five subjects to sinusoidal changes in work rate to derive a model of the form

$$G_2(s) = \frac{A}{1 + s\tau_1} \qquad [2]$$

where $G_2(s)$ is the transfer function between a work rate input and a ventilation response and "s" is the complex parameter in the Laplace transform, A is a gain term, and τ is a time constant. The subscript 2 refers to the number of parameters in the model. The resulting response has been interpreted as involving a humoral mechanism (*2*), that is, the ventilation response is postulated to be triggered by a blood borne element such as pH or CO_2 tension in the blood.

A contrasting model was developed by Fujihara *et al.* (*8*) from studying the responses of five subjects to impulse, step, and ramp work rate changes. The Laplace transform formulation indicates a complex, seven parameter model with two response modes:

$$G_7(s) = \frac{A\ e^{-s\mathrm{td}_1}}{1 + s\tau_1} + \frac{B\ e^{-s\mathrm{td}_2}}{(1 + s\tau_2)(1 + s\tau_3)}. \qquad [3]$$

The first term on the right-hand side of [3] is a fast-responding component of the model and the second term represents a slower response component (*8*). The parameters A and B indicate the relative contribution of the respective model components, whereas td_1 and td_2 indicate time delays to the two components, and τ_1, τ_2, and τ_3 determine the nature of the dynamic response. The fast component has traditionally been interpreted as a neuro-mechanism response, while the slow component is thought to be a humoral response. Thus, the Fujihara model (G_7) suggests a combination of neuro and humoral mechanisms, whereas the Casaburi model (G_2) suggests an exclusive humoral mechanism.

The average estimated parameter values (across subjects) for the models from the Casaburi and Fujihara studies are given in Table I. The frequency response plots for the Casaburi and Fujihara models using the parameter values in Table I are given in Fig. 1. In addition, Fig. 1 incorporates frequency response data in the high frequency range from the five Casaburi subjects. It is noteworthy that four out of the five Casaburi subjects indicate a high frequency response component similar to the Fujihara model. This component is apparently not strong enough to be distinguished from the background noise during the model fitting process.

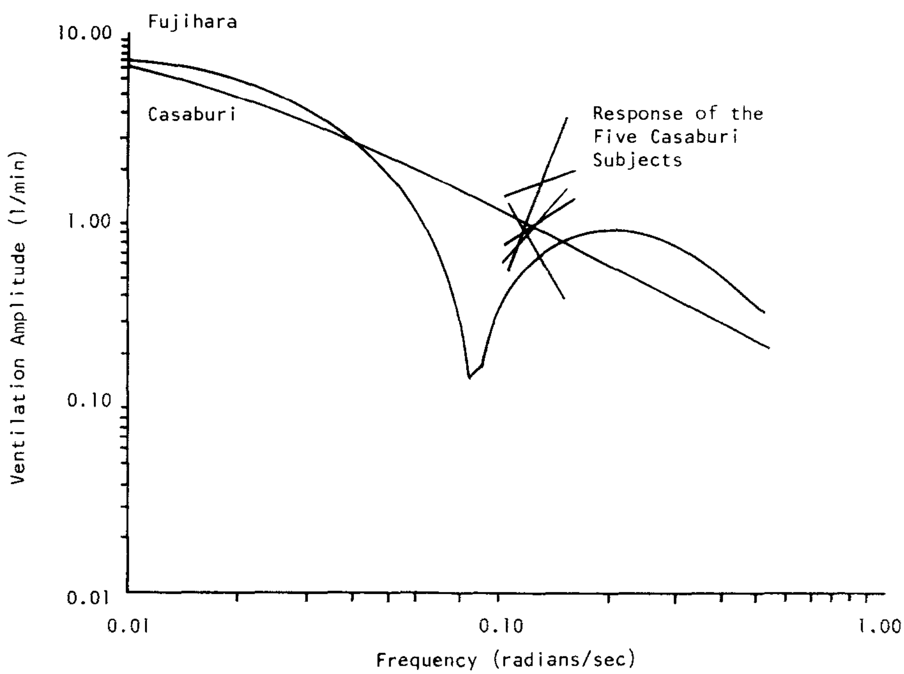

FIG. 1. Frequency responses for the Fujihara (G_7) and Casaburi (G_2) models. Also shown is the data for the five Casaburi subjects in the high frequency region.

To explore the effect of sinusoidal frequency location for minimizing parameter estimation error, we determine the seven optimal frequencies that minimize the first order generalized variance for the Fujihara model. For comparability with Casaburi's input format and since it is traditional in respiratory control studies (e.g., (*1*, *2*, *6*)), we consider only an equal power allocation among the seven input sinusoids. The optimal frequencies selected by the design procedure as well as Casaburi's frequencies are presented in Table II. Note that the set of optimal frequencies includes a long period analogous to the steady state in Casaburi's frequencies, and includes higher frequencies not present in the

TABLE I

ESTIMATED PARAMETER VALUES FOR THE CASABURI MODEL AND THE FUJIHARA MODEL[a]

	A	B	td_1 (sec)	td_2 (sec)	τ_1 (sec)	τ_2 (sec)	τ_3 (sec)
Casaburi	7.74				85.2		
Fujihara	1.24	6.50	3.20	18.8	7.4	43.0	16.0

[a] The steady state response of all models is set to 7.74 ($A + B = 7.74$), the average for the Casaburi subjects.

TABLE II

OPTIMAL FREQUENCIES FOR THE FUJIHARA MODEL[a]

Optimal period (sec)	Casaburi periods (sec)
1386	(Steady state)
335	600
176	360
77	240
42	120
19	60
8	42

[a] Frequencies are tabulated by period in seconds.

Casaburi input spectrum (the upper frequency bound was assigned a period of 8 sec because it was believed that this is approximately the highest frequency that the body could resolve).

The predicted coefficients of variation for the parameter estimates for the Fujihara model are indicated in Table III when the optimal and Casaburi sinusoids are used on input. The model was set to yield the steady state gain equivalent to the average of the five Casaburi subjects. The work rate sinusoidal inputs had an amplitude equivalent to the average work rate amplitude of the five Casaburi subjects. Since the residual noise variance is not known, it was assumed to be equal to 1.0 for purposes of comparison. The predicted coefficients of variation (Table III) resulting from the optimally designed input sinusoids are smaller (generally substantially smaller) than those resulting from the Casaburi sinusoids. This implies that a much larger work rate amplitude on input would be necessary with the Casaburi sinusoids than with the optimal sinusoids to justify the Fujihara model. However, the input signal must be below the anaerobic threshold for the system to be considered linear (*14*). Hence, it appears unlikely that the Fujihara model would be justified from data gathered by using the Casaburi input sinusoids.

TABLE III

COEFFICIENT OF VARIATION FOR THE MODEL PARAMETER ESTIMATES[a]

	A	B	td_1	td_2	τ_1	τ_2	τ_3
Optimal	1.03	0.23	1.48	0.92	2.41	0.77	1.80
Casaburi	9.43	1.78	19.0	6.80	29.6	0.84	3.86

[a] For purposes of comparison, the noise variance was assumed equal to one.

Conclusions

The inability of the Casaburi study to justify a more descriptive (complex) model may be caused in part by the arbitrary placement of the work rate sinusoidal frequencies used to generate the data. The results presented above indicate that parameter estimation can be enhanced by optimally located sinusoidal test signals. Further improvement may be gained by simultaneously optimizing the sinusoidal amplitudes in addition to the frequency locations (*9*). Enhanced parameter estimation implies that more complex models can be identified which, as applied to a model of respiratory control during exercise, suggests that more of the underlying physiology may be described. Thus, the application of the optimal design procedure to modeling efforts on respiratory control during exercise may assist in resolving the underlying structure of the respiratory control mechanism (*15*).

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