Respiratory Parameter Estimation of Rats

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Abstract. A method was developed to estimate respiratory parameters of small laboratory animals. This method utilized a least squares estimation technique applied to a third order model of an animal respiring in a two chamber plethysmograph. The animal respiratory system was represented as generic second order model. This was followed by a first order filter representing the thermal effects of respiration of room temperature air. Data from four Sprague-Dawley rats measured in a two chamber plethysmograph were fitted to the model. Thorax flow and nares flow from each rat were measured three times. The rats were exposed to methacholine, and the flows were measured three more times. The model coefficients for each data set were then used to calculate the system poles. The location of the poles in the s-plane were then evaluated to show the respiratory response to methacholine could be detected.

Keywords: least squares, respiratory response, methacholine

1. Introduction. In the study of asthma and other respiratory disease, laboratory animals are often used to evaluate the effects of various aerosolized toxins on the respiratory system. This can be done by inhalation exposure of the animals to the various toxins and measurement of the respiratory response.

The purpose of this project was to develop a technique for estimation of rodent respiratory parameters indicative of a response to an inhaled toxin. The technique was to be noninvasive in nature and account for the thermal effects of respiration of room temperature air.

2. Methods. There are a number of lumped parameter, linear, second order models that can be used to describe the respiratory system [1,2]. For any given input and output, any of these models could be used to fit the data. A critical decision is to choose a model whose parameters have some meaningful, physical interpretation after having been fit to the data. This is often a difficult task due to the complexity of the airways in the lung and the simplicity of these models. Therefore, a simpler approach was taken. The animal respiratory system was represented using a generic second order model, followed by a first order filter representing the thermal effects of respiration of room temperature air [3]. This resulted in a third order filter whose coefficients were used to track the poles of the system before and after inhalation exposure. Each of four Sprague-Dawley rats were exposed to an aerosolized solution (15 mg/m^3) of methacholine (300 mg/mL) for approximately six minutes. Six seconds of data were recorded for each animal three times before exposure, and three times after exposure.

The flow produced by the thorax was considered the system input and the flow measured from the nares at room temperature was considered the output of the system. The system transfer function in the discrete domain was given by:

$$H(z) = \frac{b_0 + b_1 z^{-1} + b_2 z^{-2}}{1 + a_1 z^{-1} + a_2 z^{-2} + a_3 z^{-3}}$$

The filter coefficients were calculated using a batch least squares technique. The discrete domain roots of the system were then derived from the denominator coefficients. Next, these system poles were transformed to their equivalent in the s-domain. For each data set, this resulted in a complex conjugate pair of poles and another pole on the real axis. The pole on the real axis gave the inverse of the thermal time constant associated with the heating and cooling of respired air. The complex conjugate pairs respresented the poles of the generic second order respiratory model. Upon visual inspection, it was clear that the pre and post methacholine data separated based on the real part of these poles.

3. Results and Discussion. The average (± standard error) of the real parts of the system poles for the data before methacholine challenge was 335.25±28.32 rad/sec. After methacholine challenge, the average was found to be 242.67±16.65 rad/sec. The real parts of the model poles appeared to be a good indicator of respiratory response in rats. Of the four rats used in the methacholine challenge, one did not show a significant response. The results reflect this data, and an improvement would be the testing of a larger sample of rats along with another measure of airway reactivity for validation of response. This simple method of estimating respiratory parameters has promise as an indicator of change in airway function.

References.

1. Avanzolini G, Barbini P. A versatile identification method applied to analysis of respiratory mechanics. IEEE Trans Biomed Eng 1984; BME-31(7): 520-526.
2. Jackson AC, Watson JW. Oscillatory mechanics of the respiratory system in normal rats. Respiration Physiology 1982; 48:309-322.
3. Peslin R, Duvivier C, Vassiliou M, Gallina C. Thermal aritfacts in plethysmographic airway resistance measurements. J Appl Physiol 1995; 79(6):1958-1965.

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