Multivariate closed-loop model for analysis of cardiovascular dynamics

I. Korhonen,
VTT Information Technology, Tampere, Finland

Abstract. **This paper introduces a closed-loop model for the analysis of interactions between heart rate and blood pressure variability, and respiration. The respiratory influence is modeled with an anti-causal structure to control the possible phase lead of heart rate to instantaneous lung volume. The closed-loop structure between heart rate and blood pressure allows the analysis of inter-relationships between the signals. Simulations and results on experimental data show the identifiability of the model and the robustness of the noise source contribution analysis over a wide range of model orders.**

Keywords: cardiovascular control, heart rate, blood pressure, respiration, closed-loop modeling, spectrum.

1. Introduction

The autonomous control of heart rate (HR) and blood pressure (BP) involves several feed-forward and feedback mechanisms. In addition, respiration affects HR and BP through neural and mechanical mechanisms. To analyze dynamic interactions between HR and BP variability, there is a need for closed-loop modeling methods, which can control the respiration-related influences.

Multivariate autoregressive (MAR) modeling of cardiovascular dynamics was proposed by Kalli et al [1], and further developed by us [2]. Baselli et al [3] presented a customized linear model which quantified the interactions between HR and BP together with respiration. In these approaches, the respiratory influence was assessed through linear prediction of HR and BP by present and past values of instantaneous lung volume (ILV). However, because of neural mechanisms, the onset of HR change is reported to preced the onset of ILV change [4]. This cannot be properly controlled by the causal methods presented [1,2,3].

Recently, Perrott and Cohen introduced an open loop modeling method, which could control the possible time lead of the ILV to HR [5]. However, their approach did not allow closed-loop analysis of HR and BP interactions.

This paper presents a closed-loop anti-causal multivariate model, which provides both control of respiratory influences and quantification of closed-loop relationships between HR and BP. The analysis of interactions is based on noise source contribution ratio (NSCR) analysis. Analysis with simulated and experimental data show that the model identification and NSCR estimates are robust over a wide range of model orders.

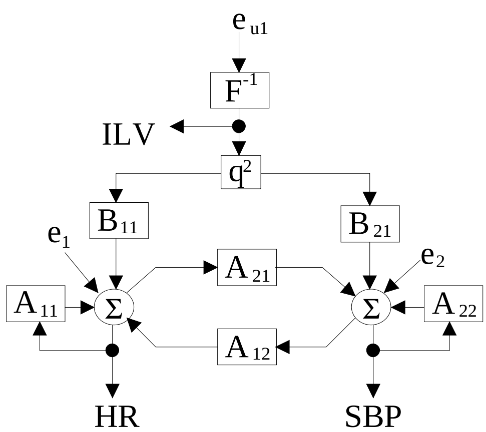


Fig. 1 Schematic presentation of the model.

2. Methods

2.1 The model

The model has a structure of a MAR model with an exogenous (X) AR input, or MARXAR model (Fig. 1) [6]. The closed-loop variables, HR and systolic BP (SBP), are modeled by a bi-variate MAR model with coefficients $\boldsymbol{A}$ [2]. The transfer function $\boldsymbol{A}_{12}$ describes SBP's effect on HR (baroreflex) while $\boldsymbol{A}_{21}$ depicts HR's influence on SBP (mainly mechanical effects). The zero-delay term of $\boldsymbol{A}_{21}$, $\boldsymbol{a}_{21}(0)$, presents fast, intra-beat mechanical effects of HR on SBP (Frank-Starling mechanism, runoff effect) [2,3]. $\boldsymbol{A}_{22}$ represents BP feedback mechanisms via control variables different from HR [3], while $\boldsymbol{A}_{11}$ model sinus-node modulations independent of SBP. White noise sources e_1 and e_2 represent unknown disturbances unique to HR and SBP, respectively. Respiratory influence enters HR (respiratory sinus arrhythmia) and SBP (mainly direct mechanical effects) as an exogenous input through the transfer functions $\boldsymbol{B}$. Central respiratory influence is modeled by ILV fed through a 2-sample negative delay [5]. This anti-causal structure allows control of possible phase lead of HR to ILV [4,5]. The ILV, in turn, is modeled as an AR process $\boldsymbol{F}$ with a noise source e_{u1}.

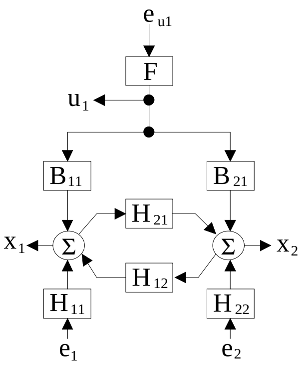
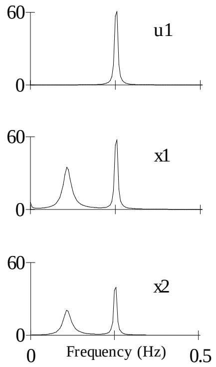
The model may be expressed as

$$HR(t) = -\sum_{i=1}^{M_A} \boldsymbol{a}_{11}(i) HR(t-i) - \sum_{i=1}^{M_A} \boldsymbol{a}_{12}(i) SBP(t-i) + \sum_{i=-2}^{M_B-2} \boldsymbol{b}_{11}(i) ILV(t-i) + e_1(t)\ , \tag{1}$$

$$SBP(t) = -\sum_{i=1}^{M_A} \boldsymbol{a}_{22}(i) SBP(t-i) - \sum_{i=0}^{M_A} \boldsymbol{a}_{21}(i) HR(t-i) + \sum_{i=-2}^{M_B-2} \boldsymbol{b}_{21}(i) ILV(t-i) + e_2(t)\ , \text{ and} \tag{2}$$

$$ILV(t) = -\sum_{i=1}^{M_F} \boldsymbol{f}(i) ILV(t-i) + e_{u1}\ , \tag{3}$$

Table 1. Simulations used to test the model identification procedure

Simulation system	Power spectral densities (arbitrary units)	Transfer functions #1	Simulations
		$B_{11}(z) = 1 + 0.1986z^{-1} - 0.0021z^{-2}$ $B_{21}(z) = z^{-1} + 0.1986z^{-2} - 0.0021z^{-3}$ $F(z) = \frac{0.3}{1 + 0.0016z^{-1} + 0.9541z^{-2}}$ $H_{11}(z) = \frac{0.3561 + 0.3561z^{-1}}{1 - 0.5252z^{-1}}$ $H_{22}(z) = \frac{0.2374 - 0.2374z^{-2}}{1 - 1.4687z^{-1} + 0.5252z^{-2}}$ $H_{12}(z) = \frac{-0.5z^{-1}}{1 - 1.2z^{-1} + 0.35z^{-2}}$ $H_{21}(z) = \frac{0.22068 - 0.22068z^{-2}}{1 - 1.5921z^{-1} + 0.6322z^{-2}}$	*Simulation #1* : Original transfer functions e_1, e_2, e_{u1} - white noises (σ^2=1) M = 40 N = 1500 *Simulation #2* : as #1, but e_2 - white noise (σ^2=2) *Simulation #3* : as #1, but $\lvert H_{12}\rvert_{\#3} = 0.6 * \lvert H_{12}\rvert_{\#1}$ M - number of data sets N - number of data points / set

where t is the sample time, $\boldsymbol{a}_{ij}$, $\boldsymbol{b}_{ij}$, and $\boldsymbol{f}$ are the model coefficients (Fig. 1), and M_A, M_B and M_F are the orders of the different parts of the model. By substituting $HR(t)=x_1(t)$, $SBP(t)=x_2(t)$ and $ILV(t)=u_1(t)$, we can write

$$\boldsymbol{A}(q)\boldsymbol{x}(t) = \boldsymbol{B}(q)u_1(t) + \boldsymbol{e}(t) \tag{4}$$

$$u_1(t) = \boldsymbol{F}^{-1}(q)e_{\boldsymbol{u}1}(t) \tag{5}$$

where $\boldsymbol{x}(t) = [x_1(t)\ x_2(t)]^T$, $\boldsymbol{e}(t) = [e_1(t)\ e_2(t)]^T$, and q is a delay operator justifying the notations

$$\begin{aligned}&\boldsymbol{A}(q) = \sum_{i=0}^{M_A} \boldsymbol{a}(i)q^{-i}; \boldsymbol{B}(q) = \sum_{i=0}^{M_B} \boldsymbol{b}(i)q^{-i};\\ &\boldsymbol{F}(q) = \sum_{i=0}^{M_F} \boldsymbol{f}(i)q^{-i}\end{aligned} \tag{6}$$

2.2 Model identification

Equation (5) is a standard univariate AR model of a signal, but the model in (4) differs slightly from the MARX model utilized by the standard identification procedures [6,7,8] : 1. MAR structure contains zero-delay terms outside the diagonal of $\boldsymbol{A}(q)$ ($\boldsymbol{a}_{21}(0)\neq 0$); 2. input transfer function is anti-causal (i=-2..M_B-2). To enable the use of the standard model identification algorithms [7,8] a 5-step model identification procedure was designed:

1. Construct an anti-causal data matrix. The ILV signal is advanced to HR and SBP by 2 samples.
2. Use MATLAB-function `arx.m` in System Identification Toolbox [8] to identify $\boldsymbol{A}'(q)$, $\boldsymbol{B}'(q)$ and $\boldsymbol{e}'(t)$ according to (4). By default, $\boldsymbol{a}'(0)=\boldsymbol{I}$, the identity matrix with $\boldsymbol{a}'_{21}(0)=0$. The model orders M_A and M_B are pre-selected.
3. Utilize Cholesky decomposition method [2] to transfer the model to the form $\boldsymbol{a}_{21}(0)\neq 0$. First, compute the noise source covariance matrix Σ' for $\boldsymbol{e}'(t)$. Then utilize the Cholesky decomposition [2]: $\Sigma'=\boldsymbol{SDS}^*$, where $\boldsymbol{S}$ is a lower-triangular matrix with diagonal elements equal to one, $\boldsymbol{D}$ is a diagonal matrix with $\boldsymbol{d}_{ii}>0$, and * denotes matrix conjugate transpose. Use $\boldsymbol{S}$ to transfer to the equivalent model

$$\begin{aligned}&\boldsymbol{S}^{-1}\boldsymbol{A}'(q)\boldsymbol{x}(t) = \boldsymbol{S}^{-1}\boldsymbol{B}'(q)u_1(t) + \boldsymbol{S}^{-1}\boldsymbol{e}'(t) \Leftrightarrow\\ &\boldsymbol{A}(q)\boldsymbol{x}(t) = \boldsymbol{B}(q)u_1(t) + \boldsymbol{e}(t)\end{aligned} \tag{7}$$

   where $\boldsymbol{A}(q)$ and $\boldsymbol{B}(q)$ are the coefficients of the new model, with $\boldsymbol{a}_{21}(0)=\boldsymbol{s}_{21}$, and the noise source covariance matrix of the new noise sources $\boldsymbol{e}(t)$ is $\Sigma_D=\boldsymbol{D}$ [2].
4. Identify the univariate AR model for ILV according to (5) by using the least squares method.
5. Correct the phase advance of ILV by delaying the transfer function $\boldsymbol{A}(q)$, which becomes $q^{-2}\boldsymbol{A}(q)$.

2.3 The analysis of dynamic interactions

The analysis of the dynamic interactions between the variables may be carried out in frequency domain by analysis of NSCR:s [2,6]. If the noise sources $\boldsymbol{e}(t)$ are independent of the past input $u_1(t-i)$ in (4), the spectral matrix of $\boldsymbol{x}(t)$ may be written [6] :

$$\boldsymbol{S_x}(\omega) = \boldsymbol{A}^{-1}\boldsymbol{B}\boldsymbol{F}^{-1}\Sigma_{\boldsymbol{u}}\boldsymbol{F}^{-*}\boldsymbol{B}^*\boldsymbol{A}^{-*} + \boldsymbol{A}^{-1}\Sigma_{\boldsymbol{D}}\boldsymbol{A}^{-*} \tag{8}$$

where ω is the frequency, Σ_u is the variance of $e_{u1}(t)$ in (5); for clarity, $\boldsymbol{A}(e^{j\omega})$ is written $\boldsymbol{A}$, etc.. The partial spectra of $\boldsymbol{x}(t)$ arising from the input is hence

$$\boldsymbol{S}_{\boldsymbol{x}:\boldsymbol{u}1}(\omega) = \boldsymbol{A}^{-1}\boldsymbol{B}\boldsymbol{F}^{-1}\Sigma_{\boldsymbol{u}}\boldsymbol{F}^{-*}\boldsymbol{B}^*\boldsymbol{A}^{-*} \tag{9}$$

and from the noise source $e_i(t)$

$$\boldsymbol{S_x}(\omega) = \boldsymbol{A}^{-1}\Sigma_{\boldsymbol{D}:\boldsymbol{i}}\boldsymbol{A}^{-*} \tag{10}$$

where the only non-zero element of $\Sigma_{D:i}$ is $\Sigma_{D:i}(i,i)=\Sigma_D(i,i)$. The NSCR from $x_j(t)$ to $x_i(t)$ is defined as [2] :

$$\Gamma_{ij}(\omega_1,\omega_2) = \left| \int_{\omega_1}^{\omega_2} \boldsymbol{S}_{ii:j}(\omega)d\omega \Big/ \int_{\omega_1}^{\omega_2} \boldsymbol{S}_{ii}(\omega)d\omega \right| \tag{11}$$

In case of mutually independent $\boldsymbol{e}(t)$ and $e_{u1}(t)$, $0\leq\Gamma_{ij}(\omega_1,\omega_2)\leq 1$ [2], and the NSCR states how much power of $x_i(t)$ is originating from $x_j(t)$ on a frequency range $\omega_1\leq\omega\leq\omega_2$.

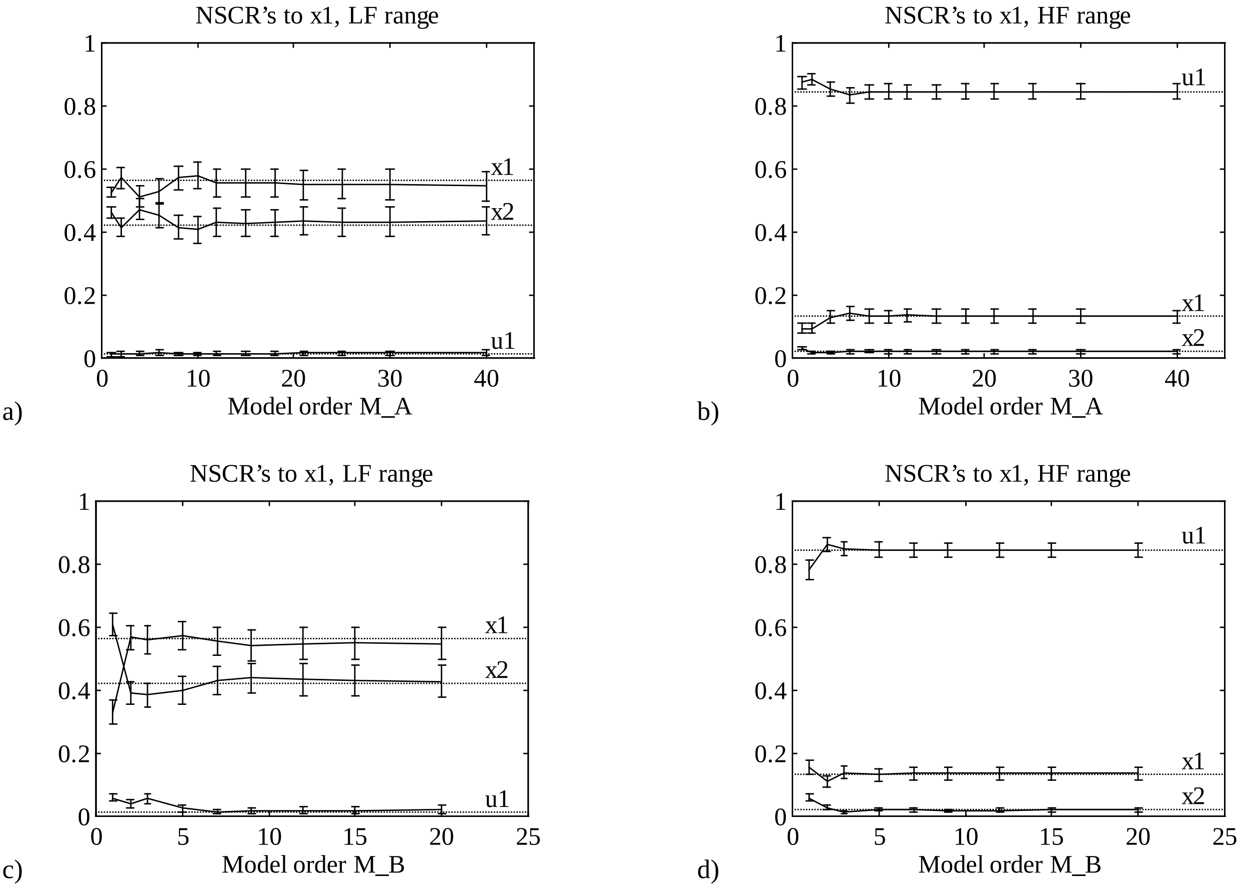


Fig. 2 The effect of the model order on the NSCR estimates on simulation data. The solid lines present the NSCR estimates from each variable according to the model identification (mean±SD) while the dashed lines show the theoretical NSCR values. Data from the simulation #1. In a) and b), M_B=7; c) and d) M_A=12.

2.4 The analysis of the model

Simulations. The behavior of the model and NSCR estimates were studied with simulations (Table 1). The simulation system and its parameters were designed to reproduce the main spectral features present in ILV, HR and SBP signals. The simulation system transfer functions $\boldsymbol{H}_{ij}$ were designed to have different structure (zero-pole) than the corresponding MARXAR model transfer functions (all-zeros / all-poles).

Experimental data. BP, ILV and ECG were recorded at 200 Hz sampling frequency from a healthy male subject in supine and standing positions. BP and ECG signals were transformed into beat-to-beat series of instantaneous SBP and HR, respectively. As in [2], the series were resampled at 1 Hz and detrended. Nine-minute stationary periods during each posture were extracted for the analysis.

The modeling was carried out with model orders M_A and M_B varying between 1 and 40 to study the effect of the model order on the NSCR estimates. M_F was set to 5 (simulation data) or 10 (experimental data). Whiteness and mutual independence of the $\boldsymbol{e}(t)$ [2] as well as the independence of $\boldsymbol{e}(t)$ and past inputs $u_1(t-i)$ [7] were tested. NSCR:s were computed on two frequency ranges : low frequency (LF; 0.05-015 Hz) and high frequency (HF; 0.15-0.35 Hz), corresponding to vasomotor and respiratory bands, respectively.

3. Results

The model was identifiable in all the cases studied. The prediction error was decreasing with increasing model order. The noise sources $\boldsymbol{e}(t)$ were white, mutually independent and independent with the past inputs when the model order was sufficiently high.

Simulation results. The NSCR estimates were found to be robust over a wide range of model orders. When a sufficient model order was reached, further increase of the order did not significantly affect the NSCR estimates or their standard deviations (Fig. 2). The sufficient order was M_A=12 and M_B=7. The NSCR estimates converged to the true values when the model order was sufficient (Fig. 2)

Slight modifications of the simulation system parameters were clearly visible on the NSCR estimates (Fig. 3). An increase in the noise source $e_2(t)$ power increased all the NSCR:s from this variable, but especially on the LF range. A decrease in the $\boldsymbol{A}_{12}$ gain, in turn, decreased the NSCR from $x_2(t)$ to $x_1(t)$ on the LF range but did not alter the NSCR to the opposite direction.

Results with the experimental data. The model could explain 93-99% of the HR and SBP variability. As with the simulation data, the NSCR estimates computed from the experimental data converged to certain values when the sufficient model order was reached, and further increments

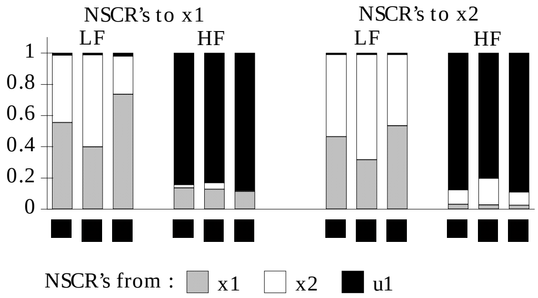


Fig. 3 Mean NSCR estimates from the different simulations (#1, #2, #3).

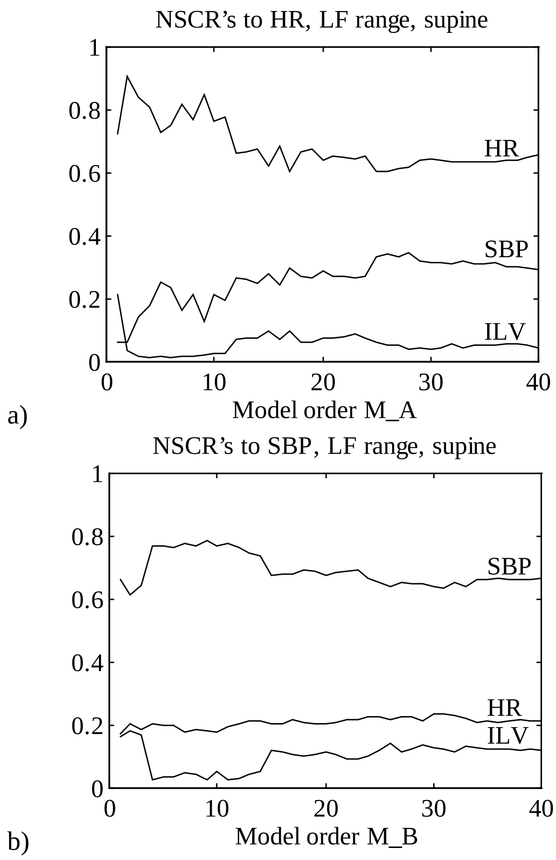


Fig. 4 The effect of the model order on the NSCR estimates on the experimental data. The lines present the NSCR estimates from each variable as a function of the model order. In a) M_B=20 and b) M_A=25.

did not affect the estimates (Fig 4.). The sufficient model order was found to be M_A=25 and M_B=20 in both the supine and standing positions. The NSCR analysis showed the domination of the ILV on the HF range, while on the LF range HR and SBP had remarkable interactions (data not shown).

4. Discussion

This study shows that the MARXAR model presented is identifiable with the method described. The model is capable of describing the dynamics of the linear simulation system, transfer function structure of which differed from that of the model. With the simulation system, the sufficient order was significantly higher than the system order. With the experimental data the sufficient model order was found to be higher than the orders used in the previous studies [1,3,5]. This is due to the principle according to which a linear non-optimal model is capable of describing any linear system if the model order and data length are sufficient [6,7].

The analysis of the system interactions was carried out by the NSCR analysis which appeared to be robust over a wide range of model orders. This is a nice property since the selection of the model order is not an easy task [2,5,6,7]. With the NSCR analysis a slight overestimation of the model order does not cause error on the results whereas an underestimation may do so.

The NSCR:s provide a spectral decomposition analysis which should be combined with the spectral analysis. The simulations show how the changes in system parameters are reflected on the NSCR:s (Fig 3.). A change in the noise source power, corresponding e.g. to vasomotor activation, increases all the NSCR:s from this variable. The decrease in the transfer function gain, corresponding e.g. a decrease in the baroreflex sensitivity, leads to a decrease in the NSCR to one direction only. Hence, the NSCR analysis provides robust specification of the system interactions.

References

1. Kalli S, Turjanmaa V, Suoranta R, Uusitalo A. Assesment of blood pressure and heart rate variability using multivariate autoregressive modelling. Biomed Meas Inf Contr 1988; 2:46-56.
2. Korhonen I, Takalo R, Turjanmaa V. Multivariate autoregressive model with immediate transfer paths for assessment of interactions between cardiopulmonary variability signals. Med Biol Eng Comp 1996; 34:1-8.
3. Baselli G, Cerutti S, Civardi S, Malliani A, Pagani M. Cardiovascular variability signals: towards the identification of a closed-loop model of the neural mechanisms. IEEE Trans Biomed Eng 1988; 35:1033-46.
4. Saul JP, Berger RD, Chen MH, Cohen RJ. Transfer function analysis of autonomic regulation II. Respiratory sinus arrhythmia. Am J Physiol 1989; 256:H153-61.
5. Perrott MH, Cohen RJ. An efficient approach to ARMA modeling of biological systems with multiple inputs and delays. IEEE Trans Biomed Eng 1996; 43:1-14.
6. Korhonen I, Mainardi L, Loula P, Garrault G, Baselli G, Bianchi A. Linear multivariate models for physiological signal analysis : theory. Comp Meth Progr Biomed. In press.
7. Ljung L. *System Identification. Theory for the User.* Englewood Cliffs, NJ,USA: Prentice-Hall 1987.
8. Ljung L. *System Identification Toolbox for use with MATLAB.* South Natic, MA, USA: The Mathworks; 1988.

Address of the author:
Ilkka Korhonen
VTT Information Technology
PO BOX 1203, FIN-02044 VTT, Finland
tel. +358-0-456 6575, fax +358-0-456 7028
E-mail: Ilkka.Korhonen@vtt.fi