CIRCULATORY SYSTEM ANALYSIS BY A STOCHASTIC METHOD USING AN ANALOGUE CORRELATOR*

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Introduction

Among the concomitant phenomena of the circulatory functions of vital importance, the periodic changes of variables like alterations in blood pressure and flow have been since long in front line of the scientific interest [1, 2]. Research activity directed on this line has been remarkably stimulated by the recent fast and wide-spread propagation of the cybernetics and the computer technique, as well as by the recognition that also biological systems — including the circulatory one — can be analysed succesfully by the methods of the control theory [3. 4, 5].

While studying periodic signals manifested in the circulatory system, only negligible attention has been devoted to the evaluation of the stochastic components. It is all the more surprising, because, due to the so called "disturbing effects" to what the organism is consistently subjected, also stochastic signals may be manifested on different circulatory variables. Apart from stochastic alterations in the physical characteristics of the environment, including climatic factors, manifestation of changes of endogenous origin must also be considered in this connection. Intestinal motility and bioelectrical activity of the brain are among the best known stochastic processes in a living organism, but many others, like the vasomotion, should also be included in this group. Stochastic signals may have a significance from more than one respect. Stochastic components manifested in different circulatory variables may be characteristic for the stress effect suffered by the circulatory system or even they may show the ability of the system to eliminate disturbances. It seems also plausible, that in regard to the multivariable system in question, application of stochastic test-signals may offer a more effective means for analysing different dynamic properties of a system, than employment of deterministic signals might do.

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In our present experiments stochastic methods and correlation technique were used for studying:

1. The characteristics of stochastic components manifested in circulatory parameters under basal condition;
   1.1. The weight of stochastic components manifested in spontaneous changes of mean arterial pressure and suprarenal blood flow,
   1.2. The relationship between stochastic changes of the mean arterial pressure and suprarenal flow analysing their cross-correlation functions,
   1.3. An approximated transfer function describing relationship between the two circulatory variables was determined;

2. Characteristics of pressure and flow responses obtained by applying stochastic test-signals in the form of nerve stimulation;
   2.1. Integrated pressure and flow responses obtained by stochastic nerve-stimulation were compared to the effects of a continuous type stimulation,
   2.2. Statistical properties of responses elicited by afferent and efferent nerve-stimulation,
   2.3. Approximated transfer function of the dynamic relationship developed between test-signals and circulatory variables was determined.

Methods

The experiments were performed on dogs. Chloralose anaesthesia and Flaxedyl immobilization was used. A schematic diagram of the measurements is presented in Fig. 1.

Electrical signals, analogue to the arterial pressure changes were supplied by the inductive pressure-transducer connected with the femoral artery. Its output signal — following amplification and averaging by a low pass filter (cross frequency =0.2 *c/s*) — was registered on a magnetic tape as well as on a polygraph.

Flow-analogue signals were obtained from the left suprarenal gland. A polyethylene tube was inserted into the lumbo-adrenal vein pushed forward up to the edge of the suprarenal gland. The adrenocaval vein was ligated simultaneously. The wound was closed surgically thereafter. Blood drops from the canule fell upon a membrane of a piezo-electrical transducer, mounted in a 10 cm distance below the canule edge. Blood was finally collected in a measuring cylinder. A monostable multivibrator was operated by the transducer impulses, the former gave an impulse of identical area in every instances when a drop of blood reached the membrane. The output signal of the multivibrator was led to a low pass filter (cross frequency = 0,2 c/s). As a result, a voltage, analogue to the drop-frequency was generated at the filter output. This was then taped, while impulses of the piezoelectrical transducer was registered on the polygraph.

Stochastic test-signals were elicited by stimulation of the efferent vagus —. and the afferent ischiadic — as well as brachial fibers. For the stimulation proper a paired platinum electrode was used. Continuous square-wave impulses of a biostimulator (during efferent stimulation: 6 V, 1 msec, 15 c/s; during afferent

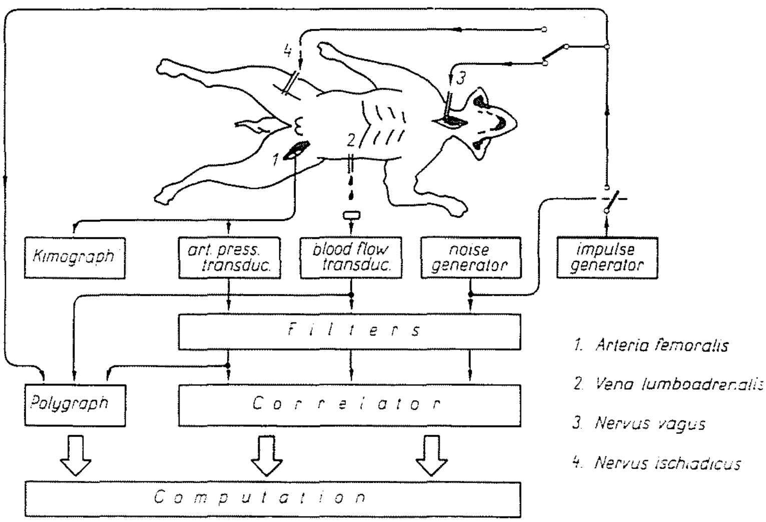

Fig. 1. Schematic representation of set used during the measurements

stimulation: 25 V, 2 msec, 15 c/s) were interrupted by a relay controlled by binar noise (band-width: $f_c = 0.2$ c/s) of a noise-generator. By this way the nerve stimulation occurred with impulse-trains of stochastically alternating duration registered on a polygraph. On other hand, electrical signal analogue to the duration of the individual impulse-trains was registered on a magnetic tape synchronously with the pressure and flow curves for the purpose of a subsequent correlation analysis.

A statistical analogue computer (ISAC — Noratom) was used to tape the signals and to perform the correlation analysis. Program elaborated for modelling both correlation and weight functions was fed into a universal Solartron analogue computer.

Some details of the methods have already been published [6, 7].

Conclusions

Data presented here were obtained from about 100 individual measurements performed on 14 dogs. Interpretation of the results was based upon analyses made on cca. 200—200 auto- and cross-correlograms as well as amplitude density spectra.

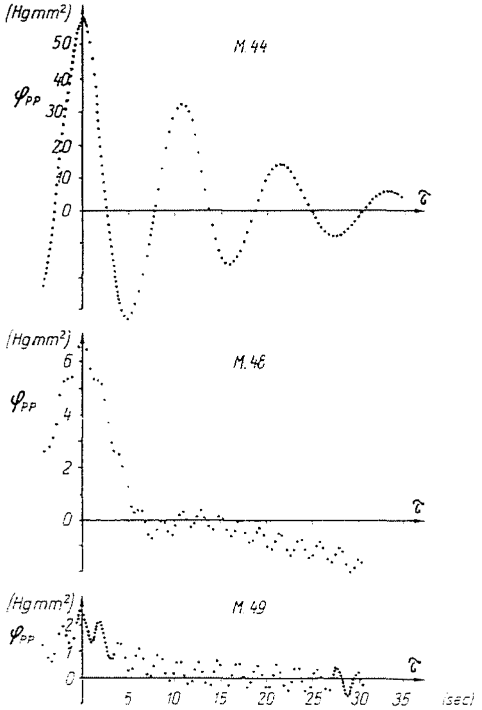

Fig. 2. Auto-correlograms (φ_{PP}) of changes in mean arterial pressure (P) obtained from the analysis of three measurements (M) performed on dog No 10. Period of registration: 10 min. M.44: control, M.48: 1,5 hour following transsection of nerve, M.49: 1 hour following hypophysectomy. Mean values of the arterial pressure: 130, 75 and 80 Hgmm, respectively

Discussion of the individual points follows the program already outlined in the introduction.

1.1. The autocorrelation functions describing the spontaneous fluctuation of the mean arterial pressure and the suprarenal flow indicated that beside the well known periodic components, stochastic ones also participated in the evolution of the signals (Figs 2 and 3). Variance read at $\tau = 0$ was generally 2—50 Hgmm^2 in case of pressure, and it was 0.04—0.3 ml^2/min^2 in case of flow. It should be mentioned, however, that the value of the stochastic component changed individually and it was considerably influenced by many such interferences — like hypophysectomy or bleeding — which are known to change the systemic properties of the organism (Figs 2, 3 and 4).

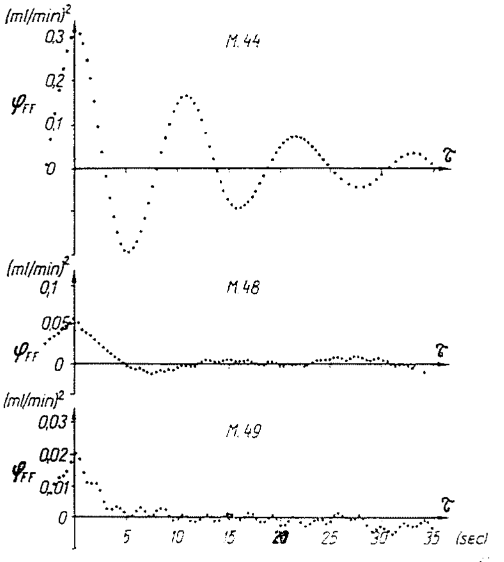

Fig. 3. Auto-correlograms (φ_{FF}) of changes in suprarenal flow (F). Mean values of flow M44: 3,9, M.48: 3,8 and M.49: 4,2 ml/min.

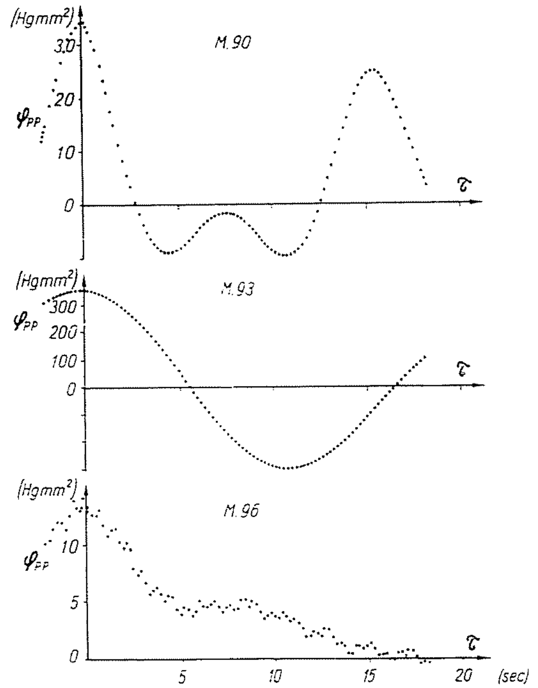

Fig. 4. Auto-correlograms (φ_{PP}) of changes in mean arterial pressure computed from data of three mesurements performed on dog No 14. Period of registration M.90, M.93: 5 min, M.96: 15 min. M.90: control, M.93: 20 min after bleeding, M.96: 10 min after retransfusion accomplished at the end of a 3 hours hypotensive period. Mean arterial pressures 150, 85 and 100 Hgmm, respectively

1.2. Analysis of the cross-correlograms shows a causal relationship between stochastic component of the pressure and flow signals (Fig. 5).

1.3. One of the advantages of stochastic system-analysis method lies in the fact, that seemingly accidental, so called "noise signals" — to what every kind of control systems is subjected — may be used for analytical pur-

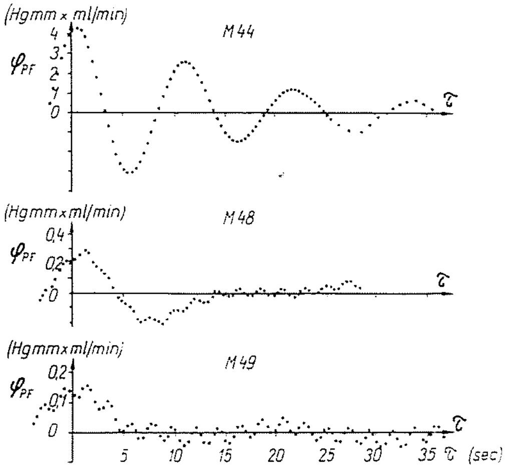

Fig. 5. Cross-correlograms (φ_{PF}) of pressure and flow signals obtained from the analysis of measurements M.44, M.48 and M.49

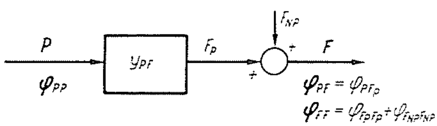

Fig. 6. Block diagram of relationship between pressure and flow

poses without applying test-signals. Accordingly, dynamic relationship existing between pressure and flow may be also determined by considering the spontaneous pressure waves (P) as input signal and the pressure-correlated flow component (F_P) as output signal of the section under test of the circulatory system (Fig. 6). F_{PN} is not correlated to the pressure and corresponds to those flow components which are invariant regarding the pressure. The relationship between the cross-correlation function of the input and output signal of the system as well as its weight function can be described by a convolution type integral [8]:

$$\varphi_{PF}(\tau) = \int_0^\tau y_{PF}(t)\, \varphi_{PP}(\tau - t)\, dt \tag{1}$$

where φ_{PP} is the auto-correlation function of the pressure.

If the input signal — in relation to the output one — were to be regarded as a white noise the φ_{PF} would be equal to y_{PF}. This condition, however, failed to be fulfilled in cases of spontaneous pressure and flow waves as it turns out from the band-width of spectra of the signals (Fig. 7). Consequently, the convolution type integral (1) should be solved for y_{PF}.

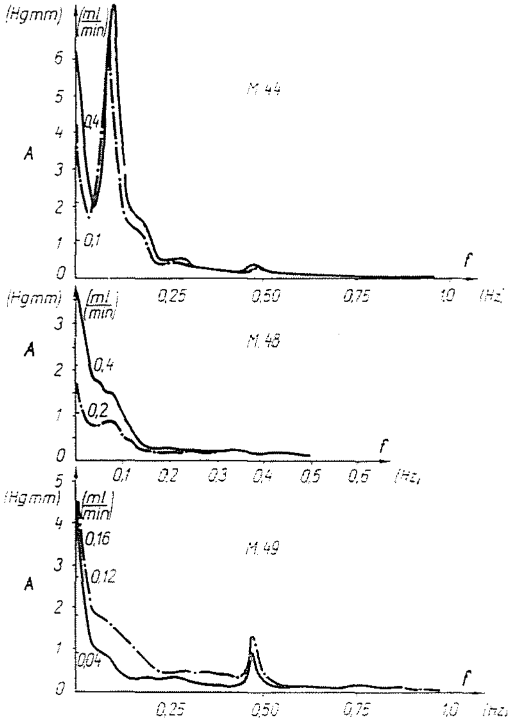

Fig. 7. Amplitude density spectra of pressure (continuous line) and flow (dotted line) registered in measurements M.44, M.48 and M.49

Deconvolution was performed by means of a universal analogue computer by approximating the system dynamics with a dominant pair of poles. The system was supposed linear and the process stationary from the aspect of fluctuations, in the mean pressure and flow. Auto-correlation function of the blood pressure were approximated by the weight function $q_P(t)$ of a block described by a transfer function expressed in the form of a ratio of polynomials of the second degree:

$$Q_P(s) = \mathcal{L}\{q_P(t)\} = \frac{A_P\left(1 + \dfrac{T_P}{2\zeta_P}s\right)}{1 + 2\zeta_P T_P s + T_P^2 s^2} \tag{2}$$

The block diagram of deconvolution is shown in Fig. 8. Parameters of the weight function were selected by trial in such a way that cross-correlation function $\varphi_{PF}(\tau)$ be satisfactorily approximated by the output signal $\varphi_{PF}(t)$. Pressure-flow dynamics were described by the Laplace-transform of the weight function, that is by the transfer function $Y_{PF}(s)$:

$$Y_{PF}(s) = \mathscr{L}\{y_{PF}(t)\} = \frac{A_{PF}}{1 + 2\zeta_{PF} T_{PF}\, s + T_{PF}^2\, s^2} \tag{3}$$

Constants of function (3) calculated from results obtained during measurement M.44 already mentioned, disclosed the following values:

transfer coefficient	A_{PF}	$= 0.16$	ml/min/Hgmm
time constant	T_{PF}	$= 1.8$	sec
damping ratio	ζ_{PF}	$= 0.6.$	

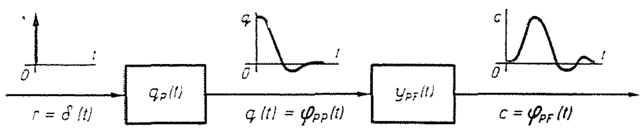

Fig. 8. Block diagram for analogue computer programming cross-correlation and weight functions describing pressure-flow relationship

Quality of approximation of the weight function y_{PF} depends on the accuracy of computer representation of the correlation functions. As it is seen in Fig. 9, the approximation proved to be satisfactory in this case.

After the approximated transfer function $Y_{PF}(s)$ had been determined, auto-correlation function $\varphi_{F_pF_p}(t)$ was also established by means of a computer model. Block diagram of the computation is shown in Fig. 10. The transfer function

$$Q_{PF}(s) = \mathscr{L}\{q_{PF}(t)\} = \frac{A_{PF}^2}{2} \cdot \frac{\left(1 + \frac{T_{PF}}{2\zeta_{PF}}\, s\right)}{1 + 2\zeta_{PF} T_{PF}\, s + T_{PF}^2\, s^2} \tag{4}$$

which possessed left side poles only was obtained by decomposition into partial fractions as follows:

$$Y_{PF}(s) \cdot Y_{PF}(-s) = Q_{PF}(s) + Q_{PF}(-s) \qquad (5$$

2.1. It has been established that deviation from the mean level of pressure and the suprarenal flow were elicited also by stochastic stimulation when stimulus parameters were selected as indicated. Stimulus-correlated pressure

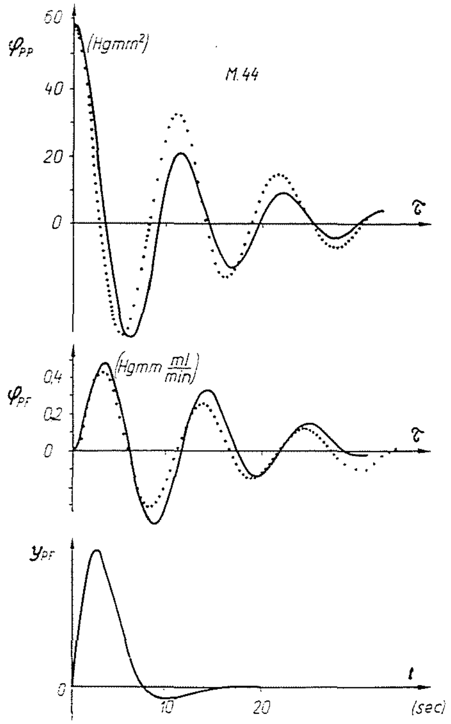

Fig. 9. Correlograms φ_{PP} and φ_{PF} (dotted line) obtained from measurement M.44 as well as their computed versions (continuous line) together with the weight function y_{PF}

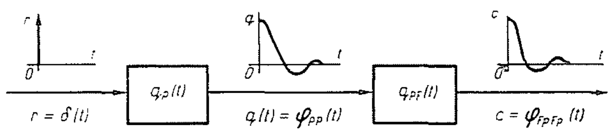

Fig. 10. Block diagram for computer programming auto-correlation function of the flow component F_P

and flow signals were manifested on this altered level thereupon. Stimulation of the vagus nerve resulted generally in a decrease while that of the ischiadic and brachial nerves in an increase of the appropriate levels. All the changes were the most expressed at the onset of stimulation; a nearly stationary stabilization of the circulatory parameters was regularly preceded by a few minutes transient response. It was conspicuous that amplitudes of pressure transients elicited by stochastic stimulation were considerably larger than those observed during continuous stimulation if performed with otherwise identical parameters. This is all the more remarkable because in case of a stochastic stimulation a mere 50% of the impulses produced by the biostimulator reached the nerves due to established 1 : 1 signal to pause ratio of the binar noise. As it is indicated in our measurement No 15/15—18 a 3 minutes continuous stimulation of the brachial nerve resulted in a 63% increase of pressure, on the other hand a 84% increase was elicited while stimulated stochastically. Data presented were collected from comparisons made on integrated values of the pressure signals.

2.2. Based upon the amplitude density spectra of the mean arterial pressure and suprarenal flow a significant increase of stochastic components — with a simultaneous decrease in that of the periodic ones — were demonstrated during stimulation compared to the basal state (Fig. 11). Stimulus spectrum was followed by the signal spectra. The diminution in the amplitude of the periodic components could be convincingly demonstrated also by analysing the auto-correlation functions of the signals (Figs 15 and 16). The variance of the pressure signal was elevated substantially during stimulation compared to the basal state. Values of variance amounted to 10—25 Hgmm² with afferent stimulation; the higher values belonged to the brachial-stimulation while the lower values to the ichiadic one. On the other hand, value of variance reached 14—75 Hgmm² with efferent stimulation. At the same time value of variance in relation to changes in suprarenal flow remained essentially unaltered and amounted to 0.04—0.2 ml²/min².

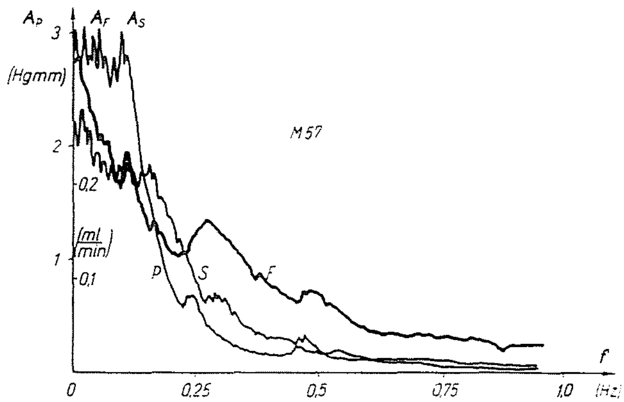

Fig. 11. Amplitude density spectra of the pressure (A_P), the flow (A_F) and the stimulus (A_S) obtained from measurement M.57 in case of vagus stimulation

The signals carried more useful information pro unit time during stimulation than they did in basal state. As a result, the necessary observation period could be reduced by cca. 50%. Stimulation itself had no irreversible effect upon the physiological parameters and the original state had been re-established almost immediately after the stimulation was terminated.

2.3. Auto-correlation function of the stimulus $\varphi_{SS}(\tau)$ as well as cross-correlation functions of stimulus versus pressure $\varphi_{SP}(\tau)$ and stimulus versus flow $\varphi_{SF}(\tau)$ have been equally established. Operation of the system was investigated according to the block diagram presented in Fig. 12. Neither the P_N nor F_{NS} components are correlated to the stimulus and they correspond to those components of pressure and flow which are essentially invariant regarding the stimulus.

Correlation functions were modelled by means of an analogue computer using the method and approximation as it has been described in 1.3. Weight

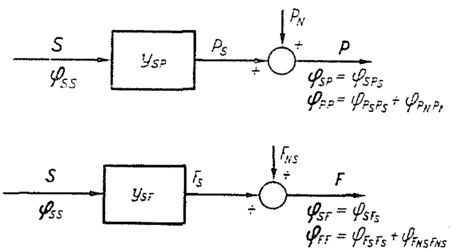

Fig. 12. Block diagram of the relationship existing between stimulus and pressure, and between stimulus and flow

functions y_{SP} and y_{SF} as well as transfer functions Y_{SP} and Y_{SF} have been also established as follows:

$$Y_{SP}(s) = \mathscr{L}\{y_{SP}(t)\} = \frac{A_{SP}}{1 + 2\zeta_{SP} T_{SP} s + T_{SP}^2 s^2} \tag{6}$$

$$Y_{SF}(s) = \mathscr{L}\{y_{SF}(t)\} = \frac{A_{SF}}{1 + 2\zeta_{SF} T_{SF} s + T_{SF}^2 s^2} \tag{7}$$

Transfer function Y_{PF} has been determined also during stimulation by using Eqs (1)—(3) and according to the block diagrams presented in Figs 6 and 8.

The constants of transfer functions changed individually and were dependent on different factors effecting the organism as well as on location and type of the stimulus applied. Details of this aspect are not discussed in this paper, but the ranges of the different parameters are presented in the following table:

Index	A	T	ζ
SP	3.5 —15	1.8—2.7	0.15—0.7
SF	0.2 —0.85	1.7—2.9	0.15—0.7
PF	0.05—0.8	1.8—3	0.4 —0.8

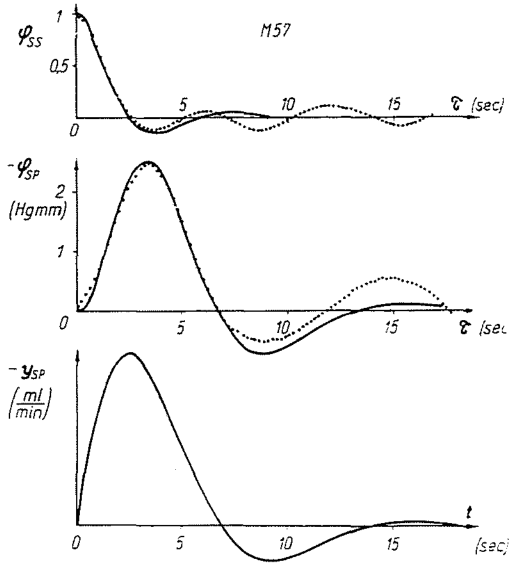

Fig. 13. Auto-correlation function of the stimulus φ_{SS}, cross-correlation φ_{SP} and weight function y_{SP} of stimulus versus pressure obtained from the measurement M.57 in case of vagus stimulation

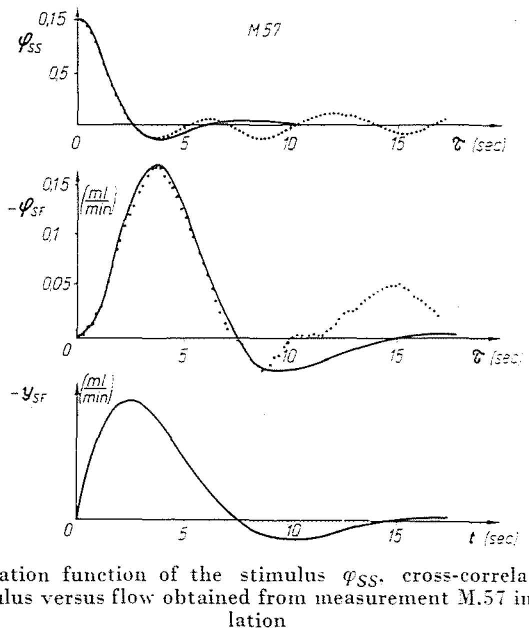

Fig. 14. Auto-correlation function of the stimulus φ_{SS}, cross-correlation φ_{SF} and weight function y_{SF} of stimulus versus flow obtained from measurement M.57 in case of vagus stimulation

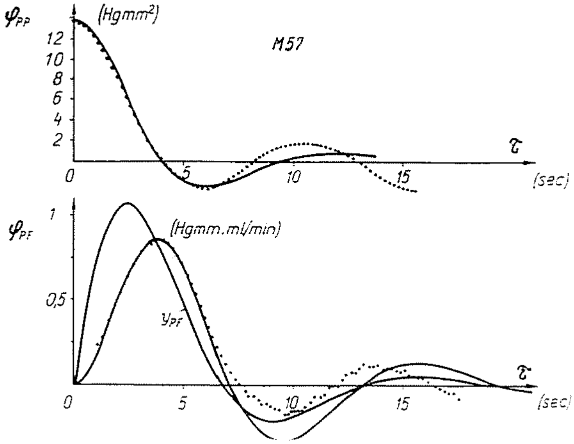

Fig. 15. Auto-correlation function of the pressure φ_{PP} and cross-correlation φ_{PF} and weight function y_{PF} of pressure versus flow obtained from measurement M.57 in case of vagus stimulation

Correlation functions and resultant weight functions are shown in Figs 13—15, as they were computed (dotted line) and modelled (continuous line) from data obtained during measurement M.57 in case of vagus stimulation. Fig. 16 depicts the flow-related auto-correlation functions φ_{FF}, $\varphi_{F_pF_p}$ and $\varphi_{F_sF_s}$ modelled according to the measurement M.57.

These indicate auto-correlation functions of the measured flow signal that of the flow components elicited by pressure and stimulus, respectively

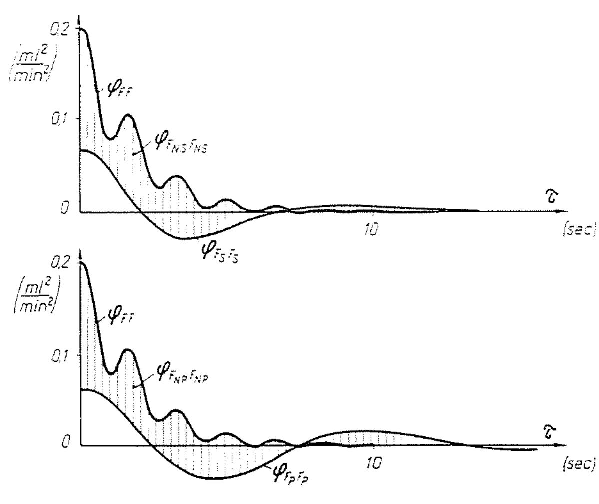

Fig. 16. Components of the auto-correlation function of the flow φ_{FF} demonstrated according to the Figs 6 and 12. Data were obtained from measurement M.57 in case of vagus stimulation

(see Figs 6 and 8). Calculation was based upon Eqs (2), (4) and (5) as well as upon the method outlined in Fig. 10. As it is seen in Fig. 16, both flow components F_S and F_P, elicited by stimulus and pressure, respectively, possess wider spectra than do components F_{NS} and F_{NP} which contain other effects.

Summary

Changes in mean arterial pressure and suprarenal blood flow, manifested under basal condition or elicited by stimuli applied upon both afferent and efferent nerves in the form of a binar noise, have been studied on anaesthetized dogs. Based upon analysis of the auto- and cross-correlograms of the signals, the approximated transfer functions of a section under test of the circulatory system have been determined on an analogue model. Properties of "useful" and "noise" components of the signals have been estimated. Stochastic methods were found to be very efficient also in studies concerned with investigation of signals and dynamic properties of the circulatory system.

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