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HYBRID MODELING OF BIOMEDICAL SYSTEMS AND MEASURING NONLINEAR CHARACTERISTICS OF BIOSIGNALS FOR IMPROVING QUALITY OF LIFE

The main purpose of this paper is to present some metrological aspects of the new concept of hybrid modeling (combined physical and *in silico*) of biological systems as well as possible applications of nonlinear (symbolic) biosignal analysis for improving quality of life through modeling and knowledge-based measurements in medicine.

Keywords: hybrid modeling, modeling errors, virtual instruments, nonlinear dynamics, biosignal analysis

1. INTRODUCTION

Modeling of circulatory system is important in biomedical engineering for testing and development of prosthetic devices and for planning of medical procedures as well as in education. Both numerical and physical models are used. Since different physical models have to be built for different applications such models are usually expensive while their accuracy and flexibility are rather poor. Numerical models are much cheaper, accurate and flexible, but their applicability is limited.

2. PURPOSE

To reduce costs and to shorten development time we have proposed so called *hybrid models* [1] - a combination of numerical and physical models. First, a numerical model is developed and then some of its parts are transformed into a physical model. To develop a hybrid model, any part of the numerical model can be replaced by a physical section (hydraulic, pneumatic, or electrical) and two interfaces (Fig. 1).

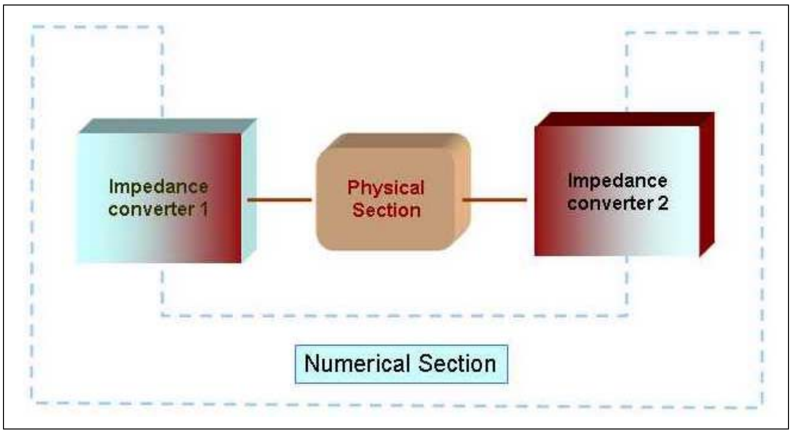


Fig. 1. The basic idea of hybrid model construction.

The advantages of such solution are evident: the physical model is minimized and reduced to the barest essentials of the specific application; the numerical model that can be easily replaced or modified is to reproduce the remaining parts of the whole circulatory system. If the electro-hydraulic analogy is applied the physical model can be either electrical or hydraulic. The critical issue, in both cases, is the interface. However, by using the lumped parameter method the exchange between the numerical and the physical sections can be limited to a single variable.

In our model the interface is based on an impedance converter. It may be realized by a pure analog RLC circuitry or by a personal computer resolving a set of equations describing analog circuitry (Fig. 2).

3. METHODS

3.1. Modeling and measurement using electro-hydraulic impedance transformation

To design such an interface we have chosen the method of a proportional electro-hydraulic impedance transformation (Fig. 2). Electrically controlled flow sources are needed to build up impedance converters. The key element of the design is the electrically (voltage) controlled flow source, delivering flow q proportional to the control voltage u_C independently of the pressure drop Δp

$$q \sim u_{C1}. \tag{1}$$

Combining the flow source and the voltage source we obtain

$$q = k_q i \quad \text{and} \quad u = k_u \Delta p \tag{2}$$

and as a result

$$Z_{in} = \Delta p/q = (1/(k_q k_u))(u/i) = 1/(k_q k_u) Z_e. \tag{3}$$

So, electrical impedance Z_e connected to the electric terminals is proportionally converted into hydraulic impedance Z_{in} obtained on the hydraulic side of the converter.

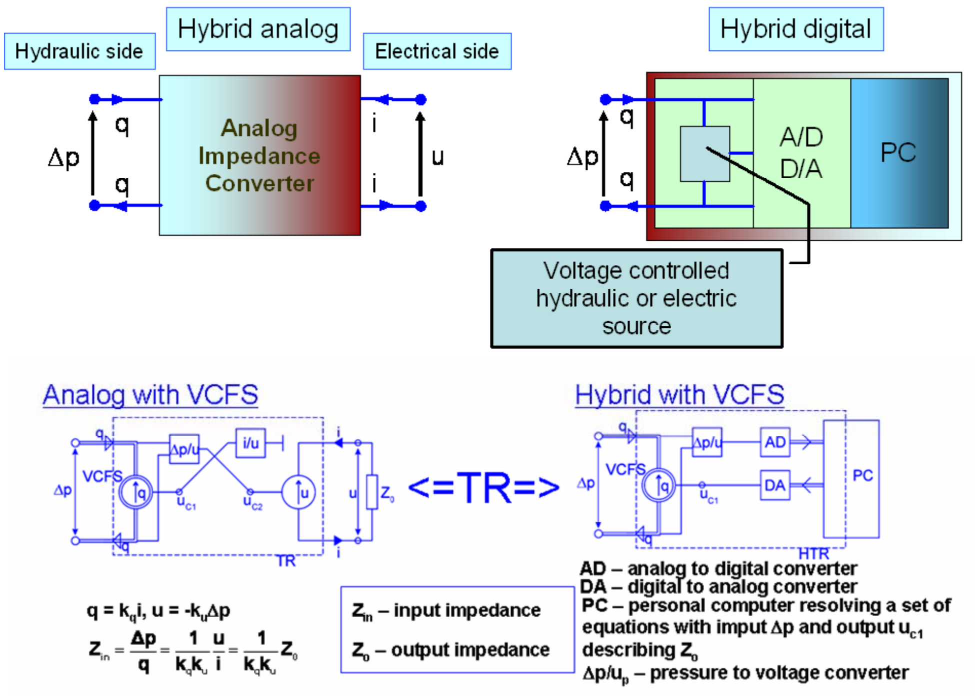


Fig. 2. Transformer - impedance electro-fluidic proportional converter.

3.2. Accuracy of the impedance transformation

Static and dynamic errors of impedance transformation are closely connected with accuracy of the voltage controlled flow source, VCFS (Fig. 2), which in our design is represented by a hydraulic measuring gear pump (made by IBIB PAN), driven by the MAXON DC-motor and controller. Static and dynamic characteristics of this VCFS are shown in Fig. 3. They are fairly linear and pressure independent as it should be in the case of a nearly ideal flow source. The cut-off frequency exceeds 500Hz that is sufficient to reproduce hydrodynamic phenomena of blood circulation.

The total relative error ε_T (including nonlinearity, hysteresis and temperature errors) of the transformation depends on the applied converter. In the case of the pure analog "transformer" shown in Fig. 2 we have

$$\varepsilon_T = \varepsilon_g + \varepsilon_e , \tag{4}$$

where

ε_q – total relative error of VSFS,

ε_e – total relative error of the electronic circuitry of voltage controlled voltage source VCVS.

As found experimentally, ε_q never exceeds ±1% and is mainly related to temperature variations in the lab (15ºC ÷ 35ºC). On the other hand, the total error of an analog VCFS is by one order smaller and may be neglected.

In the case of the hybrid digital "transformer" (Fig. 2b) one obtains

$$\varepsilon_T = \varepsilon_g + \varepsilon_d = \varepsilon_q + \varepsilon_{ad} + \varepsilon_{da} , \tag{5}$$

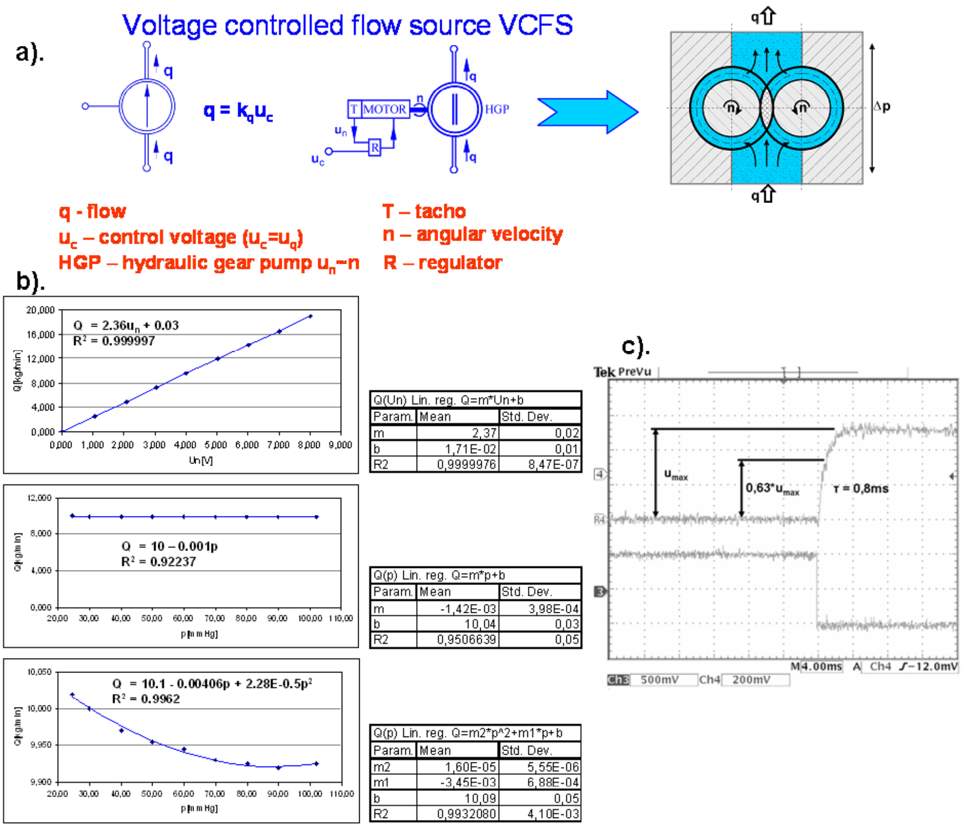
where

ε_q – total relative error of VSFS (as in the analog case),

ε_d – resultant quantization error of AD and DA conversions.

In our experiment we use a National Instrument LabView Real Time platform with 16 bit AD and DA converters, which assures a conversion error less then 0.1% that is also negligible.

So, the modeling error introduced by impedance transformation is smaller than 1%. It does not mean that the whole hybrid model is so accurate. The actual errors are mostly related to mathematical description of the living system under consideration. Even if mean errors of the applied mathematical model exceed 10%, the accuracy of the presented standard numerical model (Fig. 4) is often considered as being “good”. The errors of impedance transformations are usually very small in comparison with the mathematical model errors.



Q(Un) Lin. reg. Q=m*Un+b		
Param.	Mean	Std. Dev.
m	2,37	0,02
b	1,71E-02	0,01
R2	0,9999976	8,47E-07

Q(p) Lin. reg. Q=m*p+b		
Param.	Mean	Std. Dev.
m	-1,42E-03	3,98E-04
b	10,04	0,03
R2	0,9506639	0,05

Q(p) Lin. reg. Q=m2*p^2+m1*p+b		
Param.	Mean	Std. Dev.
m2	1,60E-05	5,55E-06
m1	-3,45E-03	6,88E-04
b	10,09	0,05
R2	0,9932080	4,10E-03

Fig. 3. Electrically controlled flow source VCFS: a) Symbolic and physical realization of VCFS; b) Statical characteristics for the given pump and statistics for the family of six pumps (R^2 – correlation factor; m, m1, m2, b – regression coefficients 0); c) Dynamical step response of the VCFS (τ – time constant, τ = 0.8ms).

VCFS may be treated as a flow standard and no additional flow-meters are required in the hybrid model - it is enough to measure pressure to describe mechanical parameters of the model.

VCFS may easily be redesigned to obtain the Voltage Controlled Pressure Source, VCPS, if needed. Then the pressure drop Δp should be measured, replacing the angular velocity voltage signal u_n in the feedback loop presented in Fig 3. The tacho output u_n is still available as a signal proportional to the delivered flow q.

It is important to point out that in all existing “classical” physical models of the human circulatory system flow measurements are supposed to be rather accurate (1%) in a relatively wide frequency range (3dB cut off frequency of about 30Hz) whereas in reality flow fields are very unstable and there is no place for long connecting tubes to stabilize flow profiles.

In our approach this problem does not exist because VCFS delivers a well-known flow, so additional flow measurements are not necessary at all.

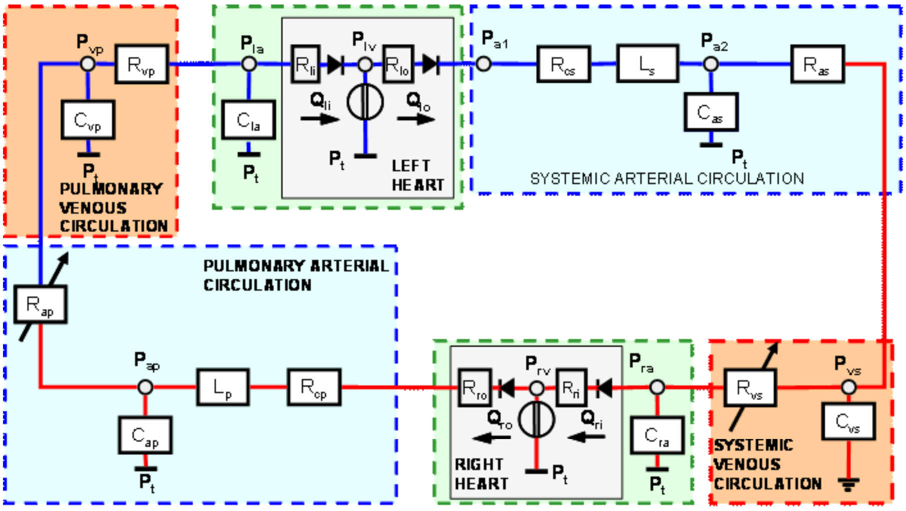


Fig. 4. Standard numerical model of blood circulation.

Practical examples

Let us consider the "standard" circulatory numerical model shown in Fig. 4, represented by a connection of physical lumped electrical elements with those in the numerical part of the model.

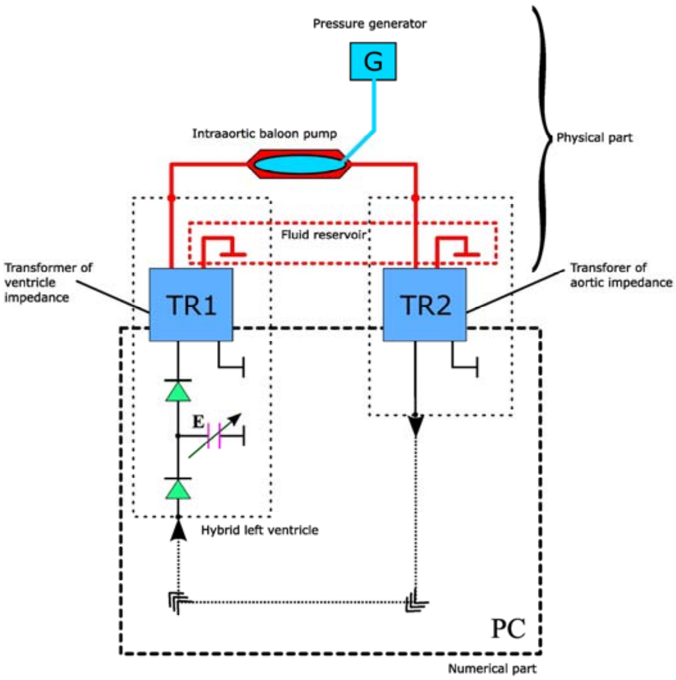


Fig. 5. Hybrid model of circulatory system prepared for experiments with the intra-aortic Baloon Pump.

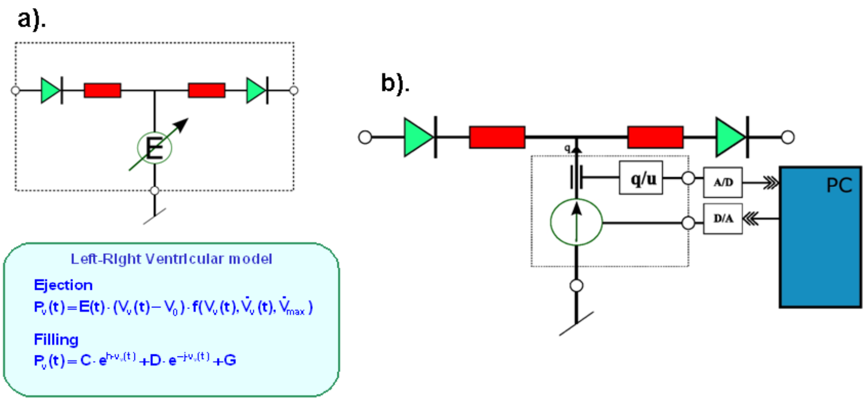


Fig. 6. Time variable elastance model of the left ventricle: a) general concept (description in the text); b) actual design with hybrid impedance transformer.

For experiments with left ventricle supporting systems (e.g. intra-aortic balloon pump) we replace the numerical model of the left ventricle by the equivalent physical part as shown in Fig. 5. The obtained hybrid model of the circulatory system has two physical terminals available to connect the physical supporting unit. On the other hand, the left ventricle may be itself an object of experiments. First of all, its mathematical model must be tested. In Figure 6 the mathematical model of the left ventricle, represented by the so called time-variable elastance, is shown.

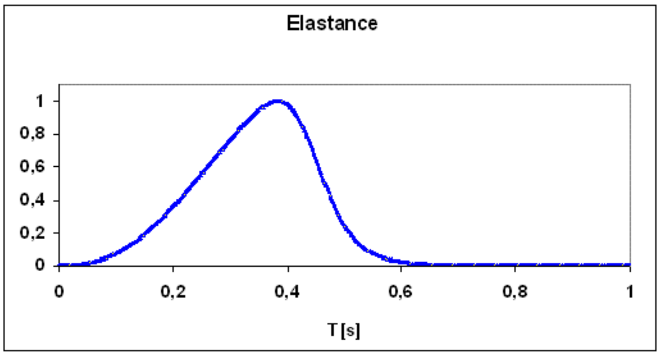


Fig. 7. Typical normalized shape of the time-variable elastance.

Elastance, considered as the reciprocal of capacitance, is presented as a function of time (Fig. 6a) of a typical normalized shape (Fig. 7); this function is a part of the computer program of the hybrid impedance converter.

In the systolic (ejection) phase the heart function is described by the equation proposed by Suga and Sagawa [5] (cf. Fig. 6a) where:

- $P_v(t)$ – ventricular pressure,
- $E(t)$ – time variable elastance,
- $V_v(t)$ – current ventricle volume,
- V_0 – rest volume,
- $dV/dt = q$ – blood flow,
- $f(V_v(t), d\,V_v(t)/dt, (d\,V_v(t)/dt)_{max})$ – correction factor taking into account the ejection rate and the ejection volume.

In the diastolic (filling) phase the variable elastance is described by a sum of exponentials [1] (cf. Fig. 6a) where:

- C, D, G, h, j – experimentally found constants.

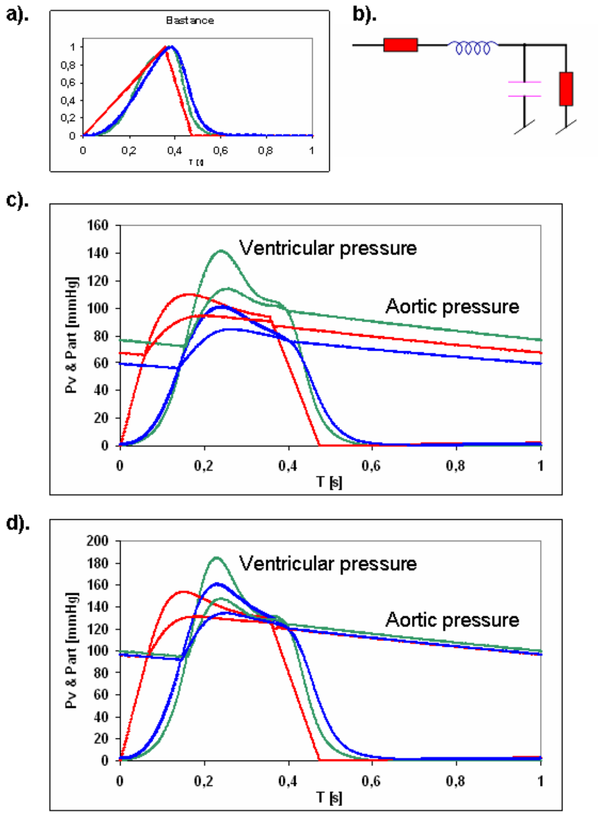


Fig. 8. Ventricular and aortic pressure changes for different elastance functions: a) Elastance profiles; b) Applied model of the aorta; c) Pressure changes for different elastance profiles – open loop case; d) Pressure changes for different elastance profiles – closed loop case.

Pressure changes obtained for the different elastance profiles are presented in Fig. 8a for the same mathematical model of aorta - standard Windkessel (Fig. 8b). In Fig. 8c we show the case of an “open loop circuit” when the standard model from Fig. 4 is “cut” before the left atrium (connected to constant pressure of 7 mmHg) and after the peripheral resistance (connected to the virtual mass). The evident difference of pressures may be observed. In Figure 8d we show the same set of variable elastances but for the case of a closed loop. It is interesting that the pressure changes reproducing aortic pressures practically coincide, thanks to the feedbacking action i.e. the human circulatory system compensates the variability of the elastance profile.

In Figure 9 the case of a constant elastance profile for different mathematical models of the aorta is presented. The open-loop circuit is applied and the aorta is represented by four different models (Fig. 10).

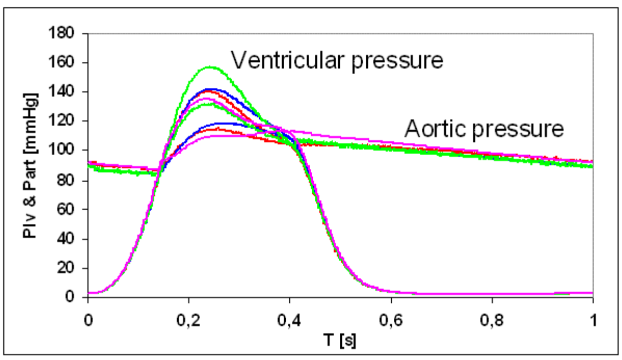


Fig. 9. Pressures changes for different aortic models.

The resultant capacity C is always the same ($C_1 + C_2 + C_3 = C$). It can be observed that aortic pressures practically coincide. The ventricular pressures differ more because of the influence of inertance L.

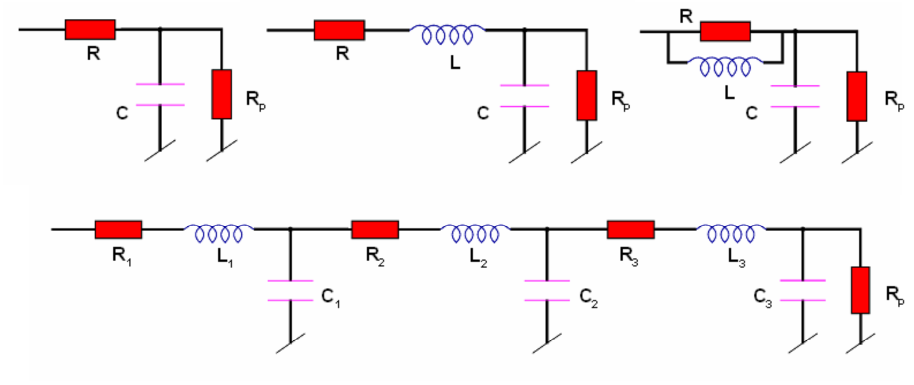


Fig. 10. Different models of the aorta.

These application examples give good evidence of high flexibility of the presented hybrid modeling approach. Practical limitations are connected rather with limited knowledge about physiological phenomena than with technical aspects of modeling. In particular it is very easy to take into account strongly nonlinear properties of living systems as it is in the case of the heart elastance function.

Similarly, by changing chaotically the time scale of the heart elastance function we can introduce a given heart rate variability function to simulate the behaviour of natural systems e.g. for symbolic or fractal analysis of the pressure and flow signals. It mimics the situation when the ECG signal shows a considerable time variable component. Works on this topic are in progress in the Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences in Warsaw.

3.3. Modeling of nonlinearities

Thanks to the proportional impedance transformation any nonlinearity existing in the blood circulation system (e.g. heart elastance, aorta elastance) may be "transformed" to hydraulic terminals. This is a consequence of the fact that this type of transformation does not influence the topology of the original electrical (numerical) circuit i.e. electrical resistances, inductances, capacitances, voltage and current sources are transformed into equivalent hydraulic resistances, inertances, pressures, flows, while preserving the topology of the system. All time constants remain unchanged as transformation invariants.

3.4. Modeling and measuring of Heart Rate Variability

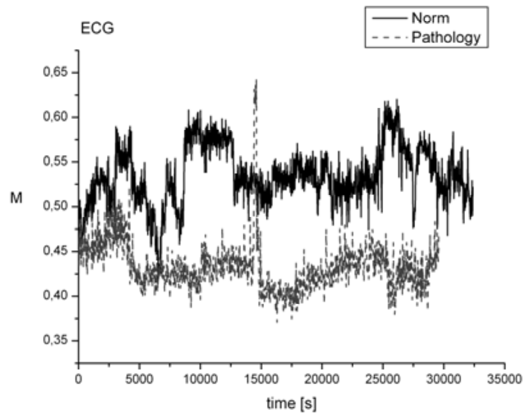
The presented hybrid model may be used to test new measurement and control methods. The human heart is an autonomic biological oscillator whose frequency is influenced by a number of biofeedback mechanisms. If Heart Rate (HR) is extracted as a result of analysis of pressure and flow changes in the hydraulic section then Heart Rate Variability (HRV) may easily be introduced into the numerical section of the hybrid model.

Nonlinear methods of contemporary physics are much more appropriate for modeling and analysis of living systems and of biosignals they generate than linear methods traditionally used in medicine (like FFT or wavelets) since living systems are highly nonlinear and operate far from thermodynamic equilibrium. It is often forgotten that in principle linear methods apply to periodic stationary signals while signals generated by living systems (biosignals) are ***'3N'*** - **N**on-stationary, **N**on-linear, **N**oisy. Nonlinear methods that assess signal's *complexity*, like calculation of fractal dimension, may be used for biosignal analysis no matter if the signal itself is chaotic, deterministic, or stochastic, also when it is nonstationary and noisy.

The problem with fractal dimension is that the same notion is used to denote many, often very different quantities [2]. In the time domain fractal dimension provides the correct adjustments for very short-lasting events. There exist methods introduced in Nonlinear Dynamics that measure the complexity of the signal in the time domain, like Higuchi's Fractal Dimension, *HFD* , that enables to detect dynamical patterns hidden in seemingly random time series representing biosignals. Complexity of a biosignal should be regarded, at least partially, as a measure of regulatory processes of the physio-anatomical system that generated the analyzed signal.

Whereas in 'classical' methods one has always tried to work with linear parts of systems' characteristics, the introduction of PCs enables to take advantage of nonlinear methods that are much more appropriate for biomedical applications [3]. It used to be a paradigm in medicine that constancy is best for human health. New developments in Physics, such as Nonlinear Dynamics and Deterministic Chaos Theory, when applied to analysis of biosignals have shown that just the opposite is most probably true - *it is healthy to be chaotic*. For example, analysis of heart rate demonstrated that heart rate variability (HRV) drastically diminishes shortly before the patient's death.

We have also recently demonstrated that for ECG signals a newly introduced nonlinear characteristic of a signal - its *monotony, M*, corresponding to what is also called redundancy and measures the extent of signal's diversity, is generally lower in pathological cases than in healthy subjects [4], and so measuring *M* might be applied for screening of persons with sleep pathologies.



Fig, 11. Monotony of sleep-ECG signal calculated for healthy subject and insomniacs.

To the PC on Fig. 2 one may add another external loop that measures blood pressure of the patient and passes the signal to a PC. The PC calculates HR and HRV and extracts the necessary information by calculating lumped parameters in real time, such as *HFD* or *M.* Then calculated parameters are compared with knowledge-based values of these parameters for a healthy person and the signal passed to the physical sections is controlled in such a way that the output pressure changes in time in an appropriate way.

A similar device may be used for modeling of the respiratory system. If the outer loop is equipped with a monitor that enables the observation of the calculated *M* or *HFD* and/or other characteristics of the patient's own physiological state, such a device may be used for *biofeedback*.

4. RESULTS

To apply new hybrid models and measuring methods we have constructed in our Lab impedance electro-fluidic proportional converters. In particular, we developed a Voltage Controlled Flow Source (VCFS) - a special gear pump that shows excellent characteristics.

The general method presented above may be applied to build any part of the hybrid physical-numerical model of the circulatory or pulmonary system. The final shape of the model depends on the application. For example, we investigated the application of an intra-aortic balloon pump.

5. CONCLUSIONS

The presented method reveals opportunities not earlier available, like modeling and measuring complex blood flow dynamics while simultaneously taking into account heart rate variability. This will enable better understanding of physiology and pathology of human cardiovascular system and so it will also contribute towards better quality of life through better health-care.

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