XVIII IMEKO WORLD CONGRESS
Metrology for a Sustainable Development
September, 17 – 22, 2006, Rio de Janeiro, Brazil

MEASUREMENT – MODELING, MODELING – MEASUREMENT: A TRANSITIVE COUPLE OF REALITY AND ABSTRACTION IN EQUIPAGE OF COMPREHENSION AND PREDICTION FOR EXAMPLE OF BREATHING CONTROL

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Abstract: The paper presents the problems of modeling and measurements in the medical sciences in the context of a dynamical system theory. Modeling can be seen here not only by the optics of a concrete object – system of breathing control, but first of all by the features of the tools used during reality reconstruction, which directly transfer to measurement procedure. The article is an introduction to a given research area.

Keywords: modeling, measurement, comprehension and prediction.

1. INTRODUCTION

Thanks to observations, which we make everyday, just like thanks to more systematic, scientific observations we discover some regularities in the world. The principles of science are nothing more than the sentences (opinions) which express these regularities so precise, as it is possible. Thus, between the observation and the sentence occurs an essential interpenetration, on the ground of which, there is conditioned an understanding and a prediction of our surrounding reality.

For convenience, the scientific expressions, the same as the expressions of our everyday life, can be divided into three main groups: classificatory, comparative and quantitative, so in fact, into the categories direct systematizing the profiles of the conducted measurement experiments. Thus, the conclusions expressed in descriptive language (logic, mathematics) contain the same, three-gradual scheme of reality comprehension. The coupling of our observations and the expressed contents has to occur in clear-cut form, in order that final, practical dimension of measurement procedure would bring measurable, utilitarian advantages.

Science starts with a direct observation (measurement) of the isolated facts. Nothing more can be observed. Regularities are not observable directly, they are discovered just when comparing many observations. Such regularities are expressed by the sentences called the principles (laws). We need to introduce a distinction between the two kinds of principles: empirical and theoretical. The first, in obvious way, is a direct result of a measurement observation of an undertaken system. On the other hand, the theoretical, unobservable being, such as elementary particles or electromagnetic field, needs to be expressed by the theoretical laws. To that, we ought to include a structure of descriptive language with its abstractive form and the axioms. Closed in this way a cognition scheme admits evolution of each of the above-mentioned factors in any configuration, and a final benefit connected with its application is a fact, that the scientific laws finally give not only explanations of the observed facts but also the means to predict the new, still unobserved facts.

Complex bodily rhythms are ubiquitous in living organisms. These rhythms arise from stochastic, nonlinear biological mechanisms interacting with a fluctuating environment. Disease often leads to alterations from normal to pathological rhythm. Fundamental questions concerning the dynamics of these rhythmic processes abound. For example what is the origin of physiological rhythms? How the rhythms interact with each other and the external environment? Can we decode the fluctuations in physiological rhythms to better diagnose human disease? And can we develop better methods to control pathological rhythms? Mathematical and physical techniques combined with physiological and medical studies are addressing these questions and are transforming our understanding of the rhythms of life.

Very good example of functioning of the foregoing systematics is respiratory system, and more precise a mechanism of periodical generation of a respiratory signal. The paper shows the stages of getting knowledge on this object control, pointing, at the same time, at an important harmonization and a reciprocal progress within the limits of empirical and theoretical statements [1-3]. The virtue of the subject is located in still incomprehensible, so that research actual the problem of accurate association of the isolated facts and laws into a common, coherent theory which would explain the dangerous disorders of respiratory pattern. Applied by the authors strategy of a knowledge synthesis, by a moderately reductionistic modeling and the tools of nonlinear dynamics, in the next part of the presentation provides an example (in computer, simulation experiment) of possible activity direction, tending towards the practical systematization of a partial knowledge. Additionally, the clinical conditions suggest a need of knowledge on not only an actual state of the system but also a necessity of prediction of its future evolution, in what there is located efficacy of possible therapies, fixed to getting knowledge. Coupling the measurement with the theoretical basics of the tools of nonlinear dynamics gives hope on comprehension and usage of nature laws as well as further development of the methods of their analysis, satisfying the idea: measurement – modeling, modeling – measurement.

2. PURPOSE

The aim of the paper is the presentation of abilities to analyze the complex system by the theoretical tools of nonlinear dynamics, which assume moderate reductionism in the structure of reality perception.

3. METHODS

3.1. Model of the system

The object of the research is a subsystem of the respiratory system, which is responsible for generation and control of breathing pattern. The task is interesting in so far, as it hasn't comprehended effectively, so that, there is a chance to observe the new diagnostic indexes during the measurement experiment, apart from possibility of systematizing a knowledge on the tools and their applicability.

In the foregoing context, the authors are undertaking an attempt at tolerably simple, albeit global description of nonlinear dynamics in the medical system of respiratory assist. To this end, it was proposed intuitively division the system into the three parts: the central respiratory pattern generator (CRPG), the passive respiratory mechanics and the segment of mechanical support of ventilation (Fig. 1).

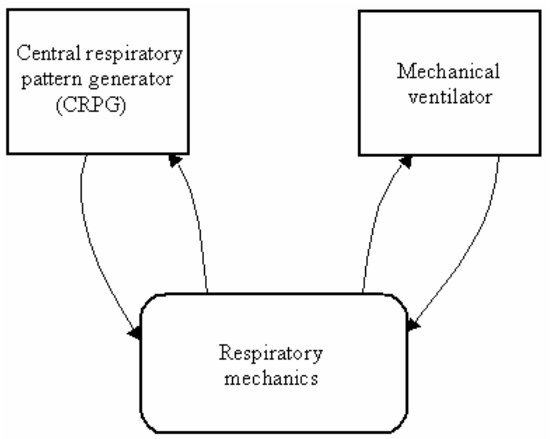


Fig. 1. Scheme of interaction between CRPG, respiratory mechanics and mechanical ventilator.

In a very general sense, breathing in humans relies on neural network located in the brainstem and on the mechanical respiratory system, both constituting the ventilatory system. The oscillatory activity of the central respiratory pattern generator induces the rhythmic contractions of the respiratory muscles which, in turn, periodically inflate the lungs. According to the earlier, generalized suggestions, there are the internal conditions which can regulate respiratory pattern by each of the structures, but the system as an integrity can also react on the inputs identified with the external conditions of its work, trying to adapt periodical cycles according to requirements and possibilities of nonlinear dynamical system, simultaneously. More than once, disturbance at one of the pointed levels lead to the problems with respiration which need an external interference into the respiratory process, consisting in an artificial support of ventilation. The disorder called sleep apnea syndrome (SAS) is especially dangerous for health and life and simultaneously difficult to study [4, 5].

To imitate the system generalized in Fig. 1, adapting a description proposed in [6-8] we prepared the mathematical model for each object using a set of differential equations.

3.2. Patients

The data of the respiratory volume (V_l) changes were collected both in healthy children and small patients revealed the symptoms of the respiratory mechanics disorders in the tissue region of the system (Fig. 2). The signals were then a basis to construction of their time series RRV (respiratory rate variability).

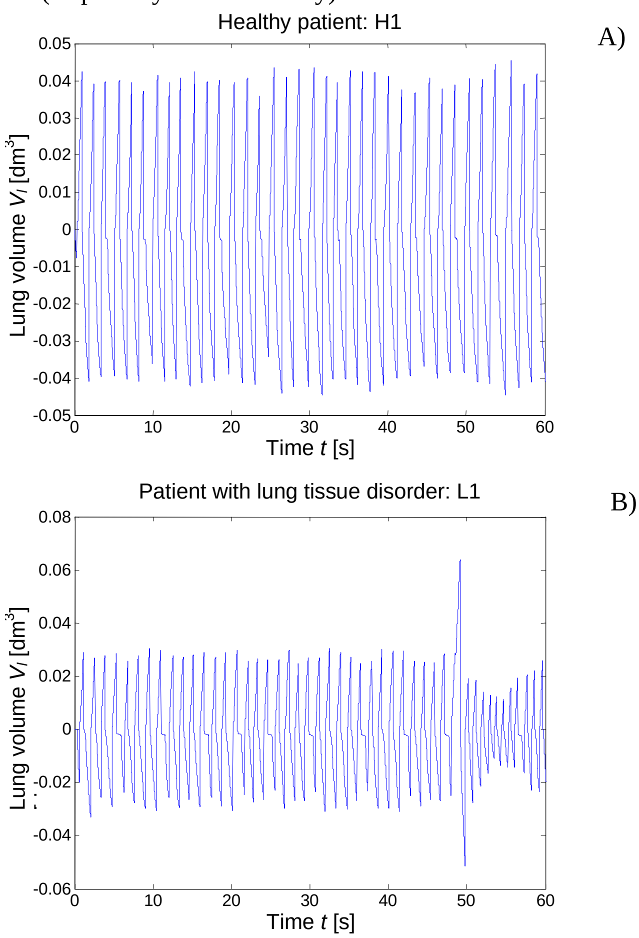


Fig. 2. Example of measured changes of lung volume in healthy child (A) and with the symptoms of respiratory mechanics disorders (B).

3.3. *Analysis of nonlinear dynamics*

In the paper, we limited ourselves to quantitative characterization for the system of the most popular measures used to evaluation of system nonlinear dynamics.

The first step was reconstruction of the phase space for the time series of the respiratory volume changes:

$$\mathbf{x}(t) = [x(t) \quad x(t+\tau) \quad \ldots \quad x(t+(D_e-1)\tau)] \tag{1}$$

where D_e is embedding dimension.

On its basis we can assess a measure of sensitivity of the system on the initial conditions, which is characteristic for the systems with the chaotic dynamics. In this case it is defined so-called maximal Lyapunov exponent λ_{max}, representing the rate of solution divergence:

$$\lambda_{\max} = \lim_{t\to\infty} \lim_{l\to\infty} \frac{1}{t} \ln\left(\frac{\|\mathbf{x}(t) - \mathbf{x}_l(t)\|}{l}\right), \tag{2}$$

where $l = \|\mathbf{x}(0) - \mathbf{x}_l(0)\|$.

The next quantity – capacity dimension D_C is determined from the minimal number $M(l)$ of regions (D-dimensional boxes) of length l that are needed to cover all the points of the attractor in the phase space:

$$D_C = \lim_{l\to 0} \frac{\ln M(l)}{\ln(1/l)}. \tag{3}$$

Equivalent approach consist in consideration D_C as a slope $\ln M(l)$ against $\ln(1/l)$ (when $l \to 0$) in the region in which this relationship is linear.

In the case of experimental data or dynamical systems with greater number of dimensions it is more precisely to calculate dimension other than capacity dimension; there is used a measure called correlation dimension D_G (5). We can calculate it by correlation integral $C(l)$ defined as:

$$C(l) = \lim_{N\to\infty}\left[\frac{1}{N^2}\sum_{i,j=1}^{N} H\left(l - \|\mathbf{x}_i - \mathbf{x}_j\|\right)\right], \tag{4}$$

where $\mathbf{x}_i$, $\mathbf{x}_j$ are the points at attractor, H – is Heaviside function and N is a number of points chosen randomly from the hole set of the data.

$$D_G = \lim_{l\to 0} \frac{\ln C(l)}{\ln l} \tag{5}$$

The correlation dimension can be interpreted as a slope of linear fitting $\log_{10} C(l)$ against $\log_{10} R$ [9].

3.4. *Construction of the RRV time series*

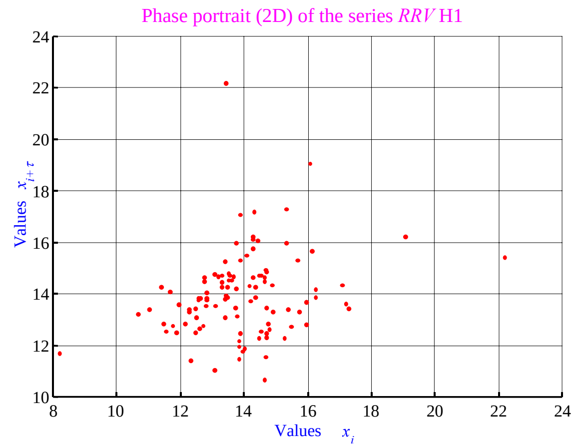
The recorded respiratory signal was processed in Matlab. First the linear trend was removed. Then the signal was filtered by a FIR passband filter with zero-phase shift. The cut-off frequencies were chosen as 0.05 and 1.0 Hz with the filter order equal to 100. Respiratory cycle values were determined by finding time instants in which the processed signal was changing its sign (from negative to positive). A vector of these succeeding values constitutes the respiratory rate variability (RRV) time series.

4. RESULTS

At the beginning, the model of control breathing was tested. It was simulated the conditions of healthy subject as well as the vagotomy was imitated. In the normal case, the vagus nerves are the anatomical support of afferent pathways bringing information on the state of the mechanical respiratory system back to the central respiratory pattern generator (CRPG). Vagotomy interrupts this loop and usually results in a specific change in ventilation: the respiratory rhythm decreases while tidal volume increases [7]. Reproducing described, experimental tendencies computer simulations of our analog confirmed its usefulness to the other trials, concentrated on evaluation of the properties connected with nonlinear dynamics of the system.

The example prints (Fig. 3 – Fig. 6) depict the selected results of the analysis.

A)



B)

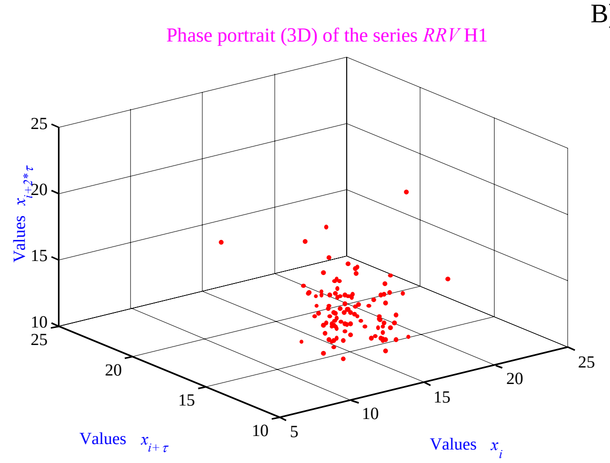


Fig. 3. The two- (A) and the three-dimensional (B) phase portrait of a chosen, measured *RRV*.

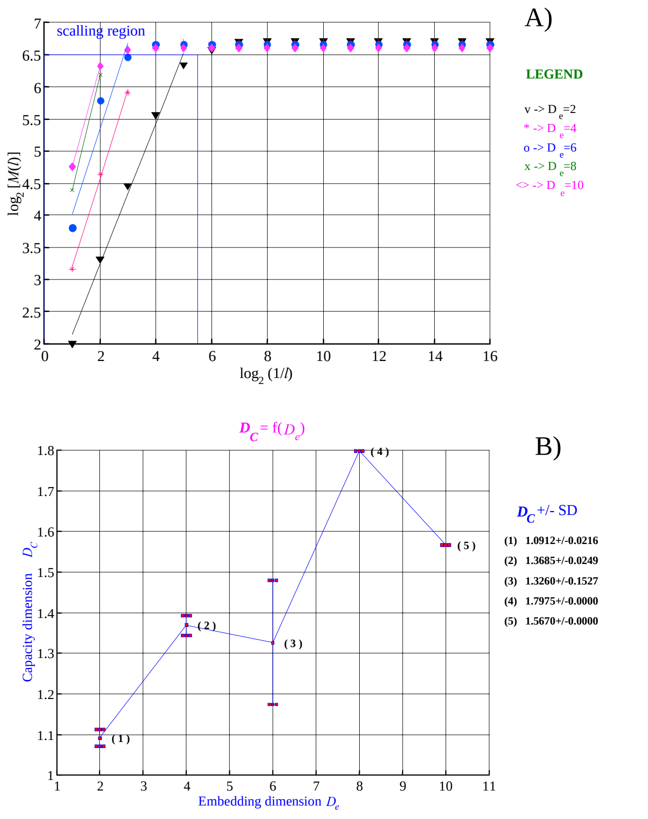


Fig. 4. Example of D_C estimation on the basis of dependence between $\log_2 M(l)$ and $\log_2(1/l)$ (A) and the capacity dimension D_C against the embedding dimension D_e (B).

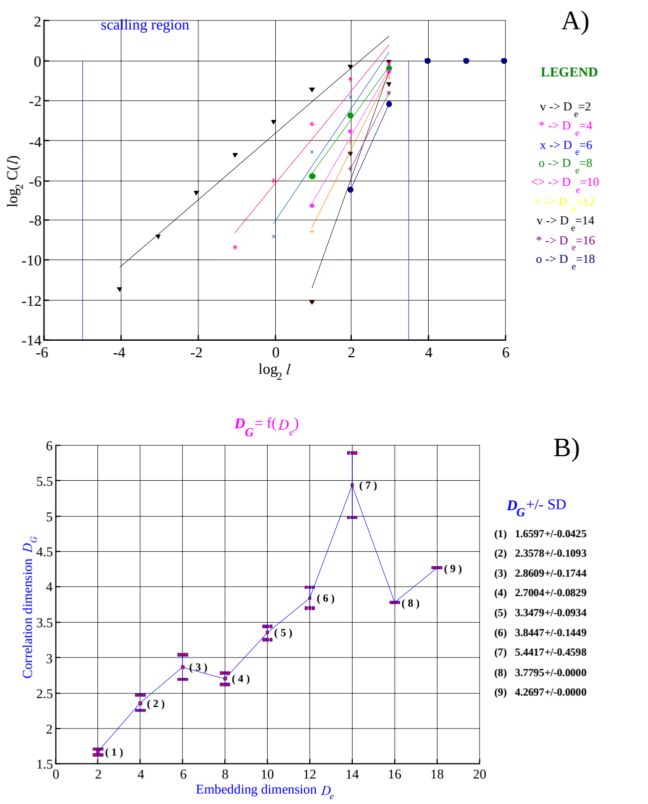


Fig. 5. Example plot of $\log_2 C(l)$ against $\log_2 l$ (A) and dependence of the estimated correlation dimension D_G on the embedding dimension D_e (B).

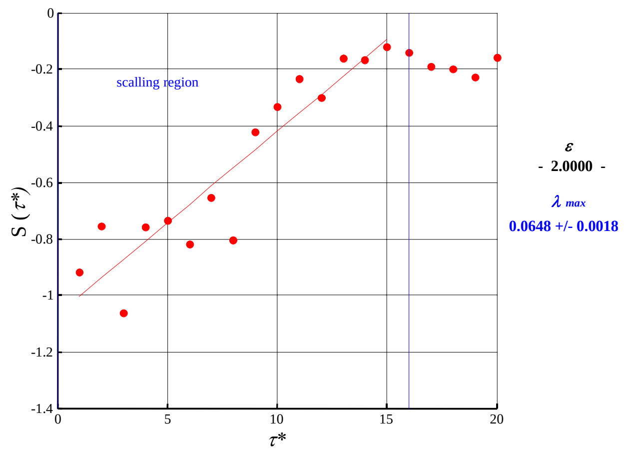


Fig. 6. Example of maximal Lyapunov exponent calculation.

5. DISCUSSION AND CONCLUSIONS

The present report isn't a pure attempt of rigorous, systematic solution of the one, concrete problem concerning modeling and, in consequence, measurement in medicine. However, at its basics there is desire to pay attention to the essence of the methodological proceedings during the process of surrounding reality comprehension. Modeling can be seen here not only by the optics of a concrete object, but first of all by the features of the tools used during reality reconstruction, which directly transfer to measurement protocol.

The investigation of the origin and dynamics of the rhythmic processes – once the sole province of physicians and experimental physiologists – is coming under increasingly close examination by mathematicians and physicist. Mathematical analyses of physiological rhythms show that nonlinear equations are necessary to describe physiological systems [10-11]. In contrast to the linear equations of traditional mathematical physics (for example, Maxwell's equations, the heat equation, the wave equation or Schrödinger's equation), nonlinear equations rarely admit an anlytical solution. Numerical simulations are one essential feature of quantitative studies of physiological systems. A complementary approach is to analyse qualitative aspects of simplified mathematical models of physiological systems. This involves a mathematical analysis of those features of physiological systems that will be preserved by classes of models that are sufficiently close to the real system.

The technical aspect of the work can be associated with a simple attempt of application of the nonlinear dynamics theory in the case of the respiratory system. The reported results were generated both by computer simulations and during experiment with physiological system.

We estimated the basic measures, typical for the questions of nonlinear dynamics. They gave us the evidences of existence of chaotic properties in the respiratory signal, probably due to chaotic dynamics of the central pattern generator. It is difficult to link the presented results to any reported observations in this area, because of their poor resources. Nevertheless, the found trends and regularities can be the introductory indicators during more fundamental research, especially in the question of sleep apnea syndrome. Very helpful can be here exploitation of the other signals, e.g. oxygen saturation, etc. The other profit of our investigations is the statement, that in the future we need to use longer sequences of RRV time series to our analysis, to avoid the ambiguities during estimations of the defined measures.

Biological signals, thus respiratory ones, in addition to being nonlinear, also exhibit important features connected to non-stationarity, noise and high dimensionality [12-14]. Consequently, there are cases in which low dimensional chaos analysis becomes unable explain the investigated phenomena. Wavelets, surrogate testing and other so-called nonlinear methods result strongly inadequate since they are still based on linear systems theory and require stationarity. The contributions of Eckmann and Ruelle were extremely clear to this regard [15]. As reported Bruce [16], a record of respiratory activity may include breath-to-breath variability of several types: random uncorrelated, random correlated, periodic, and nonlinear deterministic. Under such circumstances, very perspective can be applying the more sophisticated tools of nonlinear dynamics in the future, for example the recurrence quantification analysis with its recurrent plots [17] characterizing the signal in more topological way.

These initial studies indicate the rich dynamics of the respiratory signal, and in the future we need to look for differences between normal individuals and patients. The issue of whether or not the dynamics reflect chaos is much less interesting than elucidating the underlying mechanisms controlling the dynamics. These mechanisms are a reflection of structural and interaction complexity, hence it seems unlikely that the information can be ‘decoded’ simply by observing spontaneous behaviour.

The future efforts should be devoted to develop better diagnostic and prognostic methods by analysis of dynamics of physiological rhythms. Very important issue is also the fact, that the empirical methods used to develop and test medical devices have not included a detailed mathematical analysis of interactions of the physiological rhythm with the device, what in the case of the respiratory system can be invaluable significant [18].

ACKNOWLEDGMENTS

The article published with the support of the Foundation for Polish Science.

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