Modern Methods for the Description of Complex Couplings in the Neurophysiology of Respiration

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Abstract—Breathing is a fundamental physiological process produced by movements generated and controlled by efferent signals from the nervous system. Improving our understanding of the mechanisms underlying breathing in humans is of particular interest. Another important practical issue is the design of noninvasive procedures for the diagnosis, prediction, and control of the respiratory system, which works as a subsystem embedded in the complex physiological environment of the human organism and its external environment. This paper provides a concise review of a selected set of modern techniques dedicated to the exploration of complex and varying systems and sets of time-series data. These methods are based on an 1D entropic tool (approximate and sample entropy, i.e., ApEn and SampEn, respectively), which is effective for assessing the regularity and complexity of information contained in data sets, as well as complex network theory, recurrence plot (RP) strategy, and the joint complex network-recurrence analysis mode. Exemplary results are given for real physiological data recorded in patients with symptoms of central sleep apnea syndrome. Although ApEn and SampEn are shown to be sensitive methods for the detection of pathological mechanisms affecting breathing patterns during sleep, qualitative and quantitative studies based on the RP strategy reveal even better efficiency for this task. In addition, the second mode of analysis enables multi-dimensional correlation of accessible data, which is important for studying the couplings between numerous physiological subsystems. Further work in this area is proposed to map the scheme of breathing physiology during sleep.

Index Terms—Biomedical monitoring, complex networks, computational complexity, sleep apnea.

I. INTRODUCTION

The respiratory system is embedded in a multi-input reality (Fig. 1), where mutual couplings and existing interactions constitute both short-term events (e.g., disruption of the profile of respiratory air-flow) and long-term tendencies, such as asthma [1]–[3]. The nervous system is responsible for the fundamental generation and control of breathing [4]–[8], thereby conditioning the quality of human life. At a macro-scale, the most visible manifestation of the coupling between the respiratory and nervous systems is the regulation of respiratory rhythm. Developmental (or organizational) processes in the infant respiratory system were monitored by Frey et al. in the context of breathing sighs [9]. Conversely, the commonly noted cough reflex, which is “centered” in the brainstem, can introduce a profound disorganization of the normal breathing pattern [5]. In humans, perturbations in this rhythm most commonly manifest as sleep-disordered breathing (SDB), which occurs during sleep apnea, congenital central hypoventilation syndrome, several degenerative syndromes, and sudden death syndrome [10].

Although a substantial and insightful literature describing the phenomenology of the neural control of breathing in human subjects is available, achieving an improved understanding of the mechanisms underlying this fundamental physiological process remains a particular interest. Some difficulties in achieving this objective have arisen from the limitations of conducting in vitro experiments in the mammalian nervous system. This has led to a situation in which the actions of the brain at the molecular, synaptic, cellular, and network levels are not easily accessible. Nevertheless, it is obvious that in humans, the nervous system functions as a complex sensory network and processor that governs the activity of underlying “blocks”. Until activity at the level of single neurons can be routinely and noninvasively measured in humans, other methods must serve as surrogates. One such alternative is modeling the action of single neurons [11] and incorporating...
them in an identifiable model, e.g., a tree-like ladder network structure [12]. This representation requires the application of an inverse conclusion proper for model-based predictive control [13], [14]. Another attempt is related to the exploitation of modern methods dedicated to the extraction of information from time series measured in an object (here of a physiological and complex nature). Because the number of elements and processed states in the coupled system from Fig. 1 is very large, inverse modeling can be ineffective, particularly because estimation of large numbers of parameters of an inverse analog is nontrivial. A distinctive class of algorithms devoted to complexity and variability analysis offers a measure of entropy [15]–[17]. Although this coefficient characterizes the mode of ordering in experimental data, it poorly relates to the networking properties of the system. One solution for this problem is the original Recurrence Plot (RP) tool and the associated Recurrence Quantification Analysis (RQA) [18], [19]. This combined tool has been extensively used to extract qualitative (RP) and quantitative (RQA) information from data recorded in complex objects; its application to characterize the coupling of subsystems in the neurophysiology of respiration is therefore justified.

The main goal of this paper is to highlight the issue of mapping the properties of a complex physiological subsystem— in this case, the respiratory system, which is embedded in a multi-input environment, where the nervous system plays a dominant role in determining the course of the respiration process. Here, mapping relates to the methodological aspects of the measurements, i.e., assigning the appropriate classes of theoretical tools (descriptions) to a given object. For this purpose, selected entropy coefficients have been applied together with RP and RQA algorithms to sample data recorded in patients, thereby revealing episodes of sleep apnea. Comments on the usefulness of these forms of system descriptions to disentangle complex information from physiological data are provided in the discussion.

II. MODERN METHODS FOR COMPLEXITY CHARACTERIZATION

A. Entropy Measures

Entropy is a basic quantity with multiple field-specific interpretations. For instance, entropy has been associated with disorder, state-space volume, and a lack of information [20]. When dealing with information content, Shannon entropy is often considered the foundational and most natural interpretation [21]. This is a powerful tool for time series analysis; nevertheless, important information may also be codified in the temporal dynamics. This aspect is not usually taken into account, especially in theoretical constructions of entropy measures. However, progress in computer sciences and experimental data processing has triggered substantial work on variation in the fundamental conception of entropy measurement. The ability to work with relatively short sequences of time series is the main advantage of the new entropy constructions, e.g., approximate [22], [23] sample [17], [24], and permutation entropy [25], [26]. However, these measures assess the complexity and variability of data and systems for individual time series, and design work on the multidimensional mode has been initiated only recently [27]. The lack of a multi-dimensional analysis regimen determines the limits for entropy coefficients as measures of complexity and variability, particularly in physiological applications where numerous nonlinear, nonstationary and distributed (in space, time, or parameters) subsystems working in feedback architecture constitute complex and variable interrelations influencing the outward manifestations recorded with the appropriate sensors/sensor networks.

Approximate entropy and sample entropy were proposed as tools for evaluating finite and noisy time series. These methods examine the data set for similar epochs, such that more frequent and more similar epochs lead to lower values of ApEn or SampEn. Rigorous definitions and application details for these tools can be found in, e.g., [16], [17], [22]–[24]. Given N points, the family of statistics ApEn (m, r, N) is approximately equal to the negative average natural logarithm of the conditional probability that two sequences that are similar for m points remain similar, that is, within a tolerance r, at the next point. Thus, a low value of ApEn reflects a high degree of regularity [17]. To avoid the occurrence of ln(0) in the calculation, the ApEn algorithm counts each sequence as matching itself. This solution makes the approximate entropy the biased estimator.

Algorithm (see Fig. 2). Given N data points from a time series \( \{x(n)\} = x(1), x(2), \ldots, x(N) \), the ApEn is computed as follows:

1. Form \( m \)-vectors \( X_m(1), \ldots, X_m(N - m + 1) \), defined as \( X_m(i) = \{x(i), x(i+1), \ldots, x(i + m - 1)\} \), \( i = 1, 2, \ldots, N - m + 1 \). These vectors represent \( m \) consecutive x values, commencing with the \( i \)-th point.

![Fig. 2. Major steps in the approximate entropy (ApEn) calculation.](Image)
(2) Calculate the distance between $X_m(i)$ and \(X_m(j)\), as the absolute maximum difference between their scalar components
\[
d [X_m(i), X_m(j)] = \max_{k=0, \ldots, m-1} |(x(i+k) - x(j+k))| . \tag{1}
\]

(3) For a given $X_m(i)$, count the number of $j$ ($j \neq 1, 2, \ldots, N-m$) for $j \neq i$, such that $d[X_m(i), X_m(j)] = r$ is denoted as $N^m(i)$. Then, for $i = 1, 2, \ldots, N-m$
\[
C_m^r(i) = \frac{N^m(i)}{N-m+1}. \tag{2}
\]

The $C_m^r(i)$ values measure, within a tolerance $r$, the regularity (frequency) of patterns similar to a given window length $m$.

(4) Compute the natural logarithm of each $C_m^r(i)$, and compute the average of this expression over $i$:
\[
\phi^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} \ln C_m^r(i), \tag{3}
\]

where $\phi^m(r)$ represents the average frequency at which all the $m$-point patterns in the sequence remain close to each other.

(5) Increase the dimension to $m+1$. Repeat steps (1) to (4) and find $C_{m+1}^r(i)$ and $\phi^{m+1}(r)$.

(6) Theoretically, the ApEn is defined as
\[
\text{ApEn}(m, r) = \lim_{N \to \infty} \left[ \phi^m(r) - \phi^{m+1}(r) \right]. \tag{4}
\]

In practice, the number of data points $N$ is finite. Thus, this formula can be implemented by defining the statistic [22]:
\[
\text{ApEn}(m, r) = \phi^m(r) - \phi^{m+1}(r). \tag{5}
\]

To avoid a significant contribution of noise, in the ApEn calculation, one must choose a value of $r$ that is larger than most of the noise [22]. Experimental studies associate the optimal value of $r$ with the standard deviation (SD) of the analyzed time series ($r_{opt} \approx 10$–25% of SD) and propose the optimal number of matches of length $m = 2$ [22, 28].

SampEn statistics are free of the bias caused by self-matching. Furthermore, in contrast to ApEn ($m$, $r$, $N$), which calculates probabilities in a template-wise fashion, SampEn ($m$, $r$, $N$) calculates the negative logarithm of a probability associated with the time series as a whole [17]. Moreover, self-matches are not included while calculating the probability, and thus do not impact the value of SampEn.

Algorithm. Given $N$ data points from a time series \(\{x(n) = x(1), x(2), \ldots, x(N)\}\), SampEn can be defined as follows [17]:

1. Form vector sequences of size $m$, $X_m(1), \ldots, X_m(N-m+1)$, defined by $X_m(i) = \{x(i), x(i+1), \ldots, x(i+m-1)\}$, for $1 \leq i \leq N-m+1$. These vectors represent $m$ consecutive $x$ values, starting with the $i$th point.

2. Define the distance between vectors $X_m(i)$ and $X_m(j)$, as the absolute maximum difference between their scalar components:
\[
d [X_m(i), X_m(j)] = \max_{k=0, \ldots, m-1} |(x(i+k) - x(j+k))| . \tag{6}
\]

3. For a given $X_m(i)$, count the number of $j$ ($1 \leq j \leq N - m, j \neq i$), denoted as $B_i$, such that the distance between $X_m(i)$ and $X_m(j)$ is less than or equal to $r$. Then, for $1 \leq i \leq N-m$:
\[
B_i^m = \frac{1}{N-m+1} B_i. \tag{7}
\]

4. Define $B^m(r)$ as
\[
B^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} B_i^m(r). \tag{8}
\]

5. Increase the dimension to $m+1$ and calculate $A_i$ as the number of $X_{m+1}(i)$ within $r$ of $X_{m+1}(j)$, where $j$ ranges from 1 to $N-m$ ($j \neq i$). Then, $A_i^m(r)$ is defined as
\[
A_i^m(r) = \frac{1}{N-m+1} A_i. \tag{9}
\]

6. Set $A^m(r)$ as
\[
A^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} A_i^m(r). \tag{10}
\]

Therefore, $B^m(r)$ is the probability that two sequences will match for $m$ points, whereas $A^m(r)$ is the probability that two sequences will match for $m+1$ points. Finally, SampEn can be defined as
\[
\text{SampEn}(m, r, N) = -\ln \left[ \frac{A^m(r)}{B^m(r)} \right]. \tag{11}
\]

which is estimated by the statistic
\[
\text{SampEn}(m, r, N) = -\ln \left[ \frac{A^m(r)}{B^m(r)} \right]. \tag{12}
\]

Although $m$ and $r$ are critical for determining the outcome of SampEn, no guidelines for optimizing their values have been developed. In principle, the accuracy and confidence of the entropy estimate improves as the number of length $m$ matches increases. The number of matches can be increased by choosing small $m$ (short templates) and large $r$ (wide tolerance or filter width). However, penalties appear when too relaxed criteria are used [22]. For smaller $r$ values, poor conditional probability estimates are obtained, whereas for larger $r$ values, too much detailed system information is lost, and SampEn tends to 0 for all processes. To avoid a significant noise contribution to the SampEn calculation, one must choose a value of $r$ larger than most of the noise [22].

In our studies, the rules for setting $m$ and $r$ values were used in accordance with the instructions given for physiological signals by Pincus [29]–[31].

Both ApEn and SampEn were calculated via a short computer code written in Matlab (Mathworks, USA). Automation of work with physiological time series data was obtained with the function of a moving widow implemented in authorial software. The length of the window and its step were calibrated with synthetic (generated models of theoretical systems [32] and analogs of real object—PNEUMA model [33]) and real data.
The size of the matrix is \( N \times N \), where \( N \) is equal to the number of nodes. \( a_{ij} \) elements are equal to the number of connections between node \( i \) and \( j \). It is also possible to attribute direction to the edges (Fig. 3b). This allows the depiction of relationships in which one node influences another node (but not vice versa). Finally, a weight coefficient can be ascribed to a given link; this expresses the importance of the edge in the transmission of information to the other part(s) of the network (Fig. 3c).

An elementary property of a node is the degree, i.e., the number of connections with other nodes. Elements that are directly linked to each other are called neighbors. The degree \( k \) is expressed with the following equation:

\[
k_i = \sum_{j=1}^{N} a_{ij} = \sum_{j=1}^{N} a_{ji}.
\]

The number of edges in the network can be counted as follows:

\[
E = \sum_{i=1}^{N} k_i,
\]

and the mean degree of nodes as

\[
\langle k \rangle = \frac{2E}{N}.
\]

When moving from node \( i \) to node \( j \), one uses the edges that link consecutive nodes. A sequence of edges where all edges and nodes are different is called a path, and the number of such elements defines the length of the path. The distance \( d(i, j) \) can be calculated as the length of the shortest path from node \( i \) to node \( j \).

The distribution of node degrees \( S(k) \) can be interpreted as the probability that a randomly chosen node exhibits a degree equal to \( k \). Conceptual mapping of real objects with network-like structures is a type of reduction; thus, some information is lost in this projection. Nevertheless, it is possible to observe some new features of the analyzed system. The main advantage of this attempt is that it brings the various systems into the same notation, which makes the tools universal and lends objectivity to the conducted analyses and obtained results. Using the network taxonomy, Albert László Barabási discovered that an inherent property of various real networks is the power distribution of node degrees

\[
S(k) = \frac{C}{k^\alpha}.
\]

As opposed to the Gauss, Poisson or exponential distributions, the power law is free-scale. This means that operation on average values of nodal degree is incorrect and can lead to false conclusions. A large number of nodes with a small number of edges is a characteristic feature of free-scale networks; however, hubs with dense networking also occur. The existence of power law properties has also been stated in the context of characterizing respiratory complexity [9], [15]. In practice, it is worthwhile to write (16) in logarithmic coordinates (17), where the \( \alpha \) coefficient of linear dependence can be interpreted in the context of the degree of systemic complexity.

\[
\ln(S(k)) = -\alpha \ln(k) + \ln(C)
\]  \hspace{1cm} (17)

The tendency to assemble people with similar interests and separate teams with different views is an inherent property of social networks. This trend arises from the aspiration of individuals to acquire new knowledge and avoid conflicts. Analyzing such isolated groups that appear in the network can provide new information about the whole system. The clustering coefficient \( C_i \) has been introduced into network theory to quantify such phenomena [38]. In its basic form, \( C_i \) is the ratio of the number of edges between neighbors of the node to the number of all possible connections between them:

\[
C_i = \frac{2E_i}{k_i(k_i - 1)},
\]

and for the whole network:

\[
C = \langle C_i \rangle
\]  \hspace{1cm} (19)

An example of the \( C_i \) calculation in a simple network structure is presented in Fig. 4.

An important step in the multi-disciplinary research on time series analysis was establishing the methodology for transforming time series into complex networks. This active field is still growing [34], [39], with movement in two directions.
The resulting matrix $R$ exhibits the line of identity (LOI—the main diagonal) for $R_{i,i} = 1$. Using spatial distance as the recurrence criterion, the RP is symmetric. The presence of such lines reflects the dynamics of the system and is related to divergence or intermittency [19], [42]. Following a heuristic approach, a quantitative description of RPs based on these line structures was introduced and is now known as RQA [19], [43]. Whole spectra of indexes defined to quantify system complexity with RP and RQA, together with the physical interpretation of these measures, were reported in a review by Marwan et al. in [18]. For example, the recurrence rate (or percent recurrent rate) (RR) is a measure of the density of recurrence points in the RP; the determinism (or predictability) of the system (DET) describes the ratio of recurrence points that form diagonal structures (of at least length $l_{\text{min}}$) to all recurrence points; the maximal diagonal line length ($L_{\text{max}}$) provides information about the longest diagonal line found in the RP; and entropy (ENTR) refers to the Shannon definition, which enables finding a diagonal line of exactly length $l$ in the RP (this parameter thus reflects the complexity of the RP with respect to diagonal lines). The index of trend (TREND) is a linear regression coefficient calculated over the recurrence point density RR of the diagonals parallel to the LOI, and the ratio (RATIO) expresses the ratio between DET and RR. Laminarity (LAM), analogous to the definition of determinism, quantifies the ratio between the recurrence points forming vertical structures and the entire set of recurrence points, and trapping time (TT) gives the average length of the vertical structures. An attractive feature of the RP and RQA methodology is that these tools are suitable for working with short and nonstationary data composed of deterministic (including chaotic) and random components. The following indexes, defined by the vertical and horizontal structures of the RP, are sensitive to the existence and intensity of various classes of processes observed in real complex systems.

Although the conception of the RP was initially established for individual time series, it rapidly became clear that it is possible to identify the presence of relationships between the dynamics of two or more time series. A cross RP (CRP) is a graph that shows all of those times at which a state in one dynamic system occurs simultaneously in a second dynamic system. In other words, the CRP reveals all the times when
the phase space trajectory of the first system visits roughly the same area in the phase space as the phase space trajectory of the second system. The data length of the two systems can differ, leading to a nonsquare CRP matrix. A joint RP (JRP) is a graph of all those times at which a recurrence in one dynamic system occurs simultaneously with a recurrence in a second dynamic system. JRP can be computed from more than two systems, although this case, the data length of the considered systems has to be the same [44]. Both CRPs and JRPs are suitable to investigate synchronization and interrelations between subsystems.

Local and global properties (statistical measures) of complex networks are helpful to understand complex interrelations and information flow between different components in extended systems, such as social, computer or neural networks [45]. As noted earlier, the basis of complex network analysis is the adjacency matrix, which, similar to the recurrence matrix, is also square, binary, and symmetric (in the case of an unweighted and undirected network). In fact, the recurrence matrix and the adjacency matrix are strongly analogous: a recurrence matrix represents neighbors in phase space, and an adjacency matrix represents links in a network; both matrices embody a pair-wise test of all components (phase space vectors respond nodes) [19]. Therefore, analogies in the statistical analysis of these matrices are possible. This conclusion has enabled the further development of qualitative description of RPs (classical, joint and cross), i.e., defining new measures with which to treat complex network taxonomy.

Based on the construction of recurrence (R) and adjacency (A) matrices, a large and diverse amount of information on the complexity and dynamics of the system can be extracted from time series. An undirected and unweighted network is represented by the binary adjacency matrix A, where a connection between nodes i and j is marked as $A_{i,j} = 1$. Excluding self-loops, we obtain A from the RP by removing the identity matrix:

$$A_{i,j} = R_{i,j} - \delta_{i,j},$$

(22)

where $\delta_{i,j}$ is the Kronecker delta. Henceforth, it is justified to interpret the recurrence matrix in the context of the adjacency matrix. Local and global properties of the network are statistically described by complex network measures based on the adjacency matrix $A_{i,j}$, analogous to Section II.B. Here, only selected coefficients—equivalents to those described above, which can be defined for complex networks—are presented, but thorough considerations on qualitative and quantitative transitions between RPs and complex network approaches can be found in, e.g., [34], [38].

The degree of centrality

$$k_v = \sum_{i=1}^{N} A_{v,i}$$

(23)

gives the number of neighbors of node $v$. A complex network may also be globally described by its link density, clustering coefficient, and average path length. While the normalized averaged degree centrality, called link density

$$\rho = \frac{1}{N(N-1)} \sum_{j=1}^{N} A_{i,j}$$

(24)

corresponds to the global recurrence rate, the latter two measures allow for the quantification of novel aspects of recurrence matrices. The clustering coefficient

$$C = \sum_{v} C_v / N$$

(25)

gives the probability that two neighbors (i.e., recurrences) of any state are also neighbors [45]. It is obtained as the average of the local clustering coefficient

$$C_v = \frac{\sum_{i,j=1}^{N} A_{v,i} A_{i,j} A_{j,v}}{k_v(k_v - 1)}.$$  

(26)

The average length of the shortest paths between all pairs of nodes is given by the average path length

$$L = \frac{1}{N(N-1)} \sum_{i,j=1}^{N} d_{i,j},$$

(27)

where the length of the shortest path $d_{i,j}$ is defined as the minimum number of links that have to be crossed to travel from node i to node j [19], [46].

In summary, it is possible to join the RP strategy with the theory of complex network analysis and to measure the complexity and variability of complex physiological systems and data using the methodology depicted in Fig. 5.

### III. EXPERIMENTAL PROTOCOL

Two central objectives have emerged from the research into designing noninvasive devices for the automatic detection and
characterization of pathological events during sleep: proposal of new algorithms and optimization of existing procedures for assessing the complexity of systems/data and for collecting new information about physiological systems, which can, via feedback, provide batch knowledge for future algorithms and improved diagnostics. These ideas were implemented in the experimental protocol used in the studies reported herein (Fig. 6).

Software procedures written in Matlab (Mathworks, USA) were tested and calibrated with the use of synthetic signals generated in a mathematical model of a generalized complex system [32] and also in a modified physical-mathematical PNEUMA model of the cardio-respiratory system [33].

Physiological signals were collected with an Elmiko polysomnograph (Elmiko, Poland) in the sleep laboratory of the Chair and Clinic of Otolaryngology, Medical University of Warsaw. Comparable groups of healthy people and patients with episodes of central, obstructive or mixed apnea were selected for investigation. All subjects were males, with an average age of 61 ± 7 years.

Polysomnography uses numerous sensors for monitoring the evolution of physiological states during sleep. Nasal airflow (NF), chest wall (CM) and abdomen (AM) movement, oxygen saturation ($\text{SaO}_2$), and electromyography (EMG) signals are the most popular parameters used by physicians for establishing and diagnosing sleep disorders.
Fig. 11. (a) Recurrence plots calculated for chest wall movements measured in a healthy man and (b) a patient with symptoms of central sleep apnea.

Fig. 12. RQA indexes calculated for nasal airflow data measured in a healthy man.

Each recording included at least 7 hours of sleep sampled at 128 Hz. The data were first described by physician who indicated the appearance of breathing events during sleep. A medical statement and interpretation of the results were also given by this medical specialist. The collected physiological data were then used to explore the use of entropy measures and RP strategy. Both raw experimental data and time series of the inter-breath interval (IBI), formed according to the algorithmic scheme given in [47], were investigated. Entropy algorithms (AppEn and SampEn), the procedures for RP calculation and RQA, with reference to complex network theory, were first calibrated in the “Modern algorithms” block and then applied as “Optimized modern algorithms” (Fig. 6).

IV. RESULTS AND DISCUSSION

Studies of breathing control during respiration require multi-thread analyses, including tests realized under spontaneous and breathing conditions. The goal at present is to show the potential of selected modern tools for differentiating the processes underlying pathological behavior and to reveal facts about a system consisting of numerous interacting subsystems. The results presented herein are exemplary and should not be perceived as a quantitative discrimination test and/or medical material fully documenting neuro-respiratory interactions during sleep.

First, approximate and sample entropies were calculated for the raw nasal airflow data (Fig. 7), and chest wall movement data were transformed into the appropriate IBI time series (Fig. 8), i.e., IBI_CM. Both measures are sensitive to changes in the ordering of experimental data recorded in a particular patient who revealed the symptoms of central sleep apnea. Appropriate critical events were observed at ∼63 min, ∼68 min and ∼163 min. The simplest medical classification can be performed with the rules given in Fig. 9. Figs. 7 and 8 reveal that more regular data are represented by lower values of the test indexes, i.e., ApEn and SampEn. One problem with using these measures is determining the optimal values for
function variables—\( m \), \( r \), window length \( w_L \) and the time step of window movement \( S_w \). This problem manifests as unstable changes in the test parameters as the time window moves along the experimental data.

Comparative studies in the range of the RP were conducted for a healthy man and a patient with symptoms of central sleep apnea (the same individuals who were considered in Figs. 7 and 8). A qualitative assessment of the graphical representation of the nasal flow (NF) and chest wall movement (CM) data revealed an important textural difference (Figs. 10 and 11). The healthy man exhibited a more homogenous texture, whereas some level of pixel clustering was observed during apneic episodes. Quantitative investigations supported with the RQA measures showed for exemplary NF data (see Figs. 12 and 13) that critical events can be easily decoded from respiratory time series. The concentration of recurrence points (value of RR index) and length of diagonal lines (value of \( L \) coefficient) were especially sensitive to pathological disruptions in data trends.

Coefficients calculated using the recurrence matrix \( R \) and derived from complex network theory reveal significant potential to distinguish critical events in respiratory data recorded during sleep. Link density (Figs. 14 and 15) was lower \( (\rho \approx 10^{-3}) \) in zones where the respiratory data show regular and cyclic behavior, whereas episodes of central sleep apnea disturbed this regularity and increased the local value of \( \rho \) (Fig. 15). The clustering coefficient \( (C_\upsilon) \) was lower when the time series data were regular over some horizon of time (Fig. 16), but increases in its value can herald unexpected changes in data trends (Fig. 17). Moreover, during critical moments of central apnea, the value of the \( C_\upsilon \) index rapidly dropped to zero, which was not the case in healthy subjects.

V. CONCLUSION

Monitoring respiratory physiology is a nontrivial task. In practice, this procedure is realized with the significant participation of physicians. The state-of-the-art methodology of this field is conditioned by our incomplete knowledge of respiratory control and the lack of a fully automatic, noninvasive and reliable technical solution to follow and classify pathological events of respiration, especially sleep breathing disorders. Decoding the rules of breathing control will be an important step for designing methods suitable for the detection, prediction and management of respiratory processes. Attaining all of these goals will become possible if the complexity in the structure and behavior of the respiratory subsystem can be mapped together with its many interactions with other subsystems regulating the function of the human organism.

A good example of breathing neuro-control is central sleep apnea syndrome, where the absence of respiratory movements occurs as a consequence of compromised regulation of the central respiratory drive. The diagnosis and differentiation of SDB is usually performed under so-called polysomnography in expensively equipped sleep medicine centers. Therefore, cheaper alternatives are of great clinical interest.

A review of modern theoretical methods suitable to solve the issue of diagnosis and prediction of pathological events in breathing patterns was provided in the first part of this paper. A characteristic feature of this systematization is perceiving...
the respiratory subsystem, embedded in a larger environment, as a complex object exhibiting varying and complex behavior. As a result, issues related to the neurophysiology of respiration should be studied in conjunction with other subsystems and not as isolated objects/processes. One attractive way to describe complex systems is the complex network approach. The efficiency of systems analysis in this context can be increased by using analogies between accessible tools used to monitor the complexity and variability of data and systems. A good example of such a tool is the RP combined with RQA. Exemplary results given in the present paper provisionally but unambiguously show the usefulness of an RP strategy in the qualitative differentiation and quantitative description of neuro-respiratory pathologies during sleep. Moreover, this approach enables working in multi-dimensional space, where signals of different natures and/or measured in other subsystems can be related to each other. This attempt can be perceived as a type of data fusion. In this way, this paper also reveals a possible direction for mapping the complex coupling characteristic of the neurophysiology of respiration.

Another value of this technique is the methodological consistency expressed in Fig. 6. All tools were calibrated in the first stage using synthetic signals recorded in a modified PNEUMA model, and then the data processing algorithms were applied to real data. The lack of this practice at the level of designing and standardizing new tools for physiological data analysis was highlighted as an important problem for making reliable conclusions about the diagnosed system [48].

A general task for researchers is to design a noninvasive diagnostic procedure that can effectively discriminate between various factors affecting the inherent respiratory rhythm. The next steps will be the prediction of future respiratory states and finally controlling breathing actions. The focus of this paper was primarily the original depiction of neurophysiological conditioning of breathing during sleep, using both synthetic (PNEUMA model) and experimental data. This strategy revealed the important potential of RP and the complex network approach for the automatic detection and classification of SDB. Inserted into a device, these algorithms might facilitate on-line monitoring of the respiration of patients in the ICU or a home environment. Another advantage derives from the hypothesis resulting from Figs. 14–17. When there are no clear apneic episodes, link density (ρ) is low (Fig. 14; also see some zones of Fig. 15), whereas the inflow of any parasitic factors increases the number of links and is reflected by increasing values of ρ (Fig. 15). A physical interpretation in the context of network theory is that such inflow increases the number of interconnections to other nodes, which represent concrete items (rather of parasitic characters) of the considered system. At the same time, the cluster coefficient (C), which—according to the complex network theory—in its basic form is the ratio of the number of edges between the neighbors of the node to the number of all possible connections between them, increases just before and just after the critical event but falls quickly to zero during apneic episodes (see Fig. 17). This pattern can be physically interpreted as follows. External inflow increases the number of edges just before apnea (new connections with harmful items are set prior to apnea). The parasitic action then “damages” the (“good”) links, and the number of interconnections falls to zero, resulting in apnea.

Next, the central nervous system sends various triggering signals to arouse the system, and the number of edges (C) increases. When the central respiratory generator switches on, it tends to stabilize its function; thus, the nonused links are abandoned, expressed as decreasing values of C. This hypothesis will be verified in future studies involving a wide range of pathological cases of sleep-disordered respiration and on a greater number of subjects.

REFERENCES


