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Recurrence based complex network analysis of cardiovascular variability data to predict pre-eclampsia

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Abstract—Pre-eclampsia in pregnancy is a serious disease with high risk of fetal and maternal morbidity. The usual positive predictive value is 20–30%. Including cardiovascular variability, it has been recently shown that this predictive power can be improved.

Here we propose a novel approach for analysing time series of systolic and diastolic blood pressure as well as heart rate variability measured in the 20th week of gestation in order to predict pre-eclampsia. For this aim, we identify the recurrence matrix (calculated from time series) with the adjacency matrix of a complex network and apply measures for the characterisation of complex networks to this recurrence matrix. We demonstrate the potential of the complex network measures for a further improvement of the positive predictive value of pre-eclampsia.

1. Introduction

Pre-eclampsia is a serious disorder in pregnancy and is related with a remarkable maternal and neonatal morbidity and mortality affecting 3–5% of pregnant woman. Characteristic symptoms are sudden hypertension (rise in blood pressure) and proteinuria, connected to life-threatening cramps for mother and fetus, under-supply of the fetus and its growth retardation. A typical treatment is early delivery, which can be problematic because of the prematurity of the fetus. Therefore, an early prediction is highly desirable as it would allow for earlier countermeasures to control this pregnancy-specific disorder. The standard diagnostic tool is a Doppler sonography with a positive predictive accuracy of 20–30%.

Recent studies have suggested to include heart rate, systolic and diastolic blood pressure in order to improve the positive predictive accuracy [9, 23]. Here we propose to apply a complex network based recurrence analysis of the available time series in order to predict the disorder.

Recurrence is a fundamental property of dynamical systems and has been studied in theory and real world applications by various methods. One of the more recent approaches is the recurrence plot [12]. A recurrence plot (RP) is the graphical representation of a binary symmetric square matrix which encodes the times when two states are in close proximity (i.e. neighbours in phase space). Based on such a recurrence matrix, a large and diverse amount of information on the dynamics of the system can be extracted and statistically quantified (using recurrence quantification analysis, dynamical invariants, etc.). Meanwhile this technique has been the subject of much interest from various disciplines [10] and has been successfully applied to a number of areas: the detection of dynamical transitions [21] and synchronisation [18], the study of cardiovascular health conditions [13], and economical dynamics [2, 8], or to monitor mechanical behaviour and damages in engineering [14, 19]. It is important to emphasise that recurrence plot based techniques are useful for the analysis of short and non-stationary data, which often presents a critical issue when studying real world data.

Besides, complex networks are powerful tools for the analysis of complex and, in particular, spatially extended systems [3, 20, 24]. 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 [24], food webs, transportation networks, power grids [1], or even in the global climate system [6]. The basis of complex network analysis is the adjacency matrix, representing the links between the nodes of the network. Like the recurrence matrix, the adjacency 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 exhibit a strong analogy: a recurrence matrix represents neighbours 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 resp. nodes). Therefore, we identify the adjacency matrix of a complex network with the recurrence matrix of a dynamical system [7, 11], allowing us to apply measures of complex network theory to a RP in order to quantify the RP's structure and the corresponding topology of the underlying phase space trajectory and to obtain additional information on the underlying process.

In the following, we will summarise the concept of the recurrence network analysis. Then we will apply this concept on a study of pre-eclampsia in order to improve its early preditcion.

2. Recurrence plots and complex networks

A recurrence plot (and, thus, the adjacency matrix) is a representation of recurrent states of a dynamical system in its m-dimensional phase space. It is a pair-wise test of all phase space vectors $\vec{x}_i$ ($i = 1, \ldots, N, \vec{x} \in \mathbb{R}^m$) among each other, whether or not they are close:

$$R_{i,j} = \Theta\Big(\varepsilon - \|\vec{x}_i - \vec{x}_j\|\Big) - \delta_{i,j}, \tag{1}$$

with $\Theta(\cdot)$ being the Heaviside function, $\delta_{i,j}$ the Kronecker delta, and ε a threshold for proximity [12]. The binary matrix $\mathbf{R}$ contains the value one for all close pairs $\|\vec{x}_i - \vec{x}_j\| < \varepsilon$. In terms of a complex network, each state vector in phase space represents one distinct node and closeness of two states (i.e., recurrence) represents a link.

A phase space trajectory can be reconstructed from a time series $\{u_i\}_{i=1}^N$ by time delay embedding [16]

$$\vec{x}_i = (u_i, u_{i+\tau}, \ldots, u_{i+\tau(m-1)}), \tag{2}$$

where m is the embedding dimension and τ is the delay.

Small-scale features in a RP can be observed in terms of diagonal and vertical lines. The presence of such lines reflects the dynamics of the system and is related to divergence (Lyapunov exponents) or intermittency [13, 17, 21]. Following a heuristic approach, a quantitative description of RPs based on these line structures was introduced and is known as recurrence quantification analysis (RQA) [10].

For example, slowly changing states, as occurring during laminar phases (intermittency), result in vertical line structures in the RP. Therefore, the distribution $P(v)$ of vertical line lengths v can be used to quantify laminar phases occurring in a system. A useful RQA measure for quantifying such laminar phases is the fraction of recurrence points forming vertical structures of minimal length $v_{\min}$,

$$LAM = \frac{\sum_{v=v_{\min}}^{N} v\,P(v)}{\sum_{v=1}^{N} v\,P(v)}, \tag{3}$$

which is called laminarity [12].

Following the idea of complex networks, the RP can also be heuristically quantified by complex network measures, that are well studied in literature [3, 7]. A complex network is invariant under permutation of the node order. Consequently, network measures will not directly reflect the dynamical properties of the system studied with RPs, but topological properties of the attractor.

For example, the averaged clustering coefficient $C = \sum_v C_v/N$ gives the probability that two neighbours (i.e. recurrences) of any state are also neighbours [24]. It is obtained as the average of the local clustering coefficient

$$C_v = \frac{\sum_{i,j=1}^{N} R_{v,i}R_{i,j}R_{j,v}}{k_v(k_v - 1)}, \tag{4}$$

with $k_v = \sum_{v,j=1}^{N} R_{v,j}$ the number of neighbours of the state at time v. C_v characterises localised higher-order spatial correlations along the phase space trajectory. Specifically, high values of C_v often coincide with dynamically invariant objects, such as periodic or unstable periodic orbits or, more generally, invariant manifolds [7], and low values correspond to higher variability or less regularity of the phase space trajectory.

We illustrate the potential of the discussed measures by an analysis of the logistic map

$$x_{i+1} = a\,x_i\,(1 - x_i)\,. \tag{5}$$

In the analysed range of a, various dynamical regimes and transitions between them occur (Fig. 1A), e. g., accumulation points, periodic and chaotic states, band merging points, period doublings, inner and outer crises [4, 15, 22], and can be identified with RQA [13]. The RQA measure LAM reveals intermittent dynamics (laminar regimes) by sudden increase of its values (Fig. 1B). The clustering coefficient indicates periodic dynamics by high values up to value one (Fig. 1C, D). As the system's dynamics behaves rather regular also during intermittency, the laminar regimes are clearly revealed by C_v as lines in the bifurcation diagram – coinciding with supertrack functions (Fig. 1D).

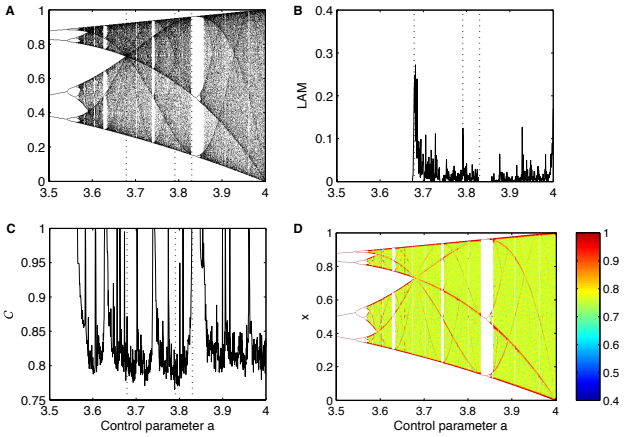

Figure 1: (A) Bifurcation diagram of the logistic map ($N = 10,000$). (B) Maxima in LAM reveal laminar regimes (band merging point, intersection points of supertrack functions). (C) Averaged clustering coefficient C and (D) local clustering coefficient are indicating periodic and intermittent regimes. For calculation of the RP the time series have not been embedded; the recurrence threshold was $\varepsilon = 0.05\sigma$.

3. Data

We analyse data of beat-to-beat values $H(t)$ (30 min, resting conditions, approx. 1800 values) and diastolic $D(t)$ and systolic $S(t)$ blood pressure measured in the 20th week of gestation. These data series were measured on 96 pregnant woman, 24 of them have finally suffered on pre-eclampsia. The data have not been pre-processed.

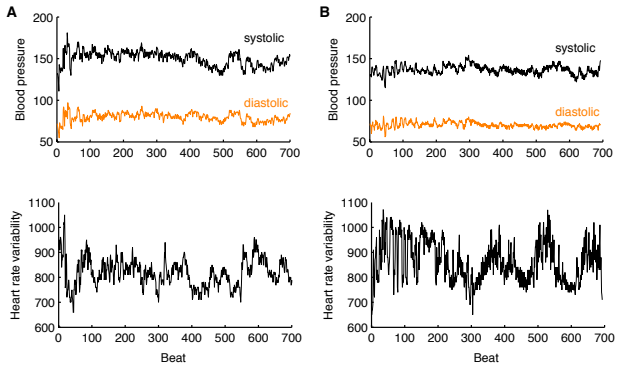

Figure 2: Exemplary data series of blood pressure and heart rate variability for (A) pre-eclampsia and (B) control group.

We construct the phase space vectors $\vec{x}(t)$ not by embedding but using all three measurements $\vec{x} = (H, S, D)^T$. In the next step we calculate the RP from this phase space trajectory by using a constant recurrence threshold of 0.8.

4. Results

The RPs of the pre-eclampsia and the control group do not visually differ much (Fig. 3). A complex network representation based on a force directed placement algorithm [5] already shows some slight differences, nevertheless difficult to reliably explain just by visual inspection (Fig. 4).

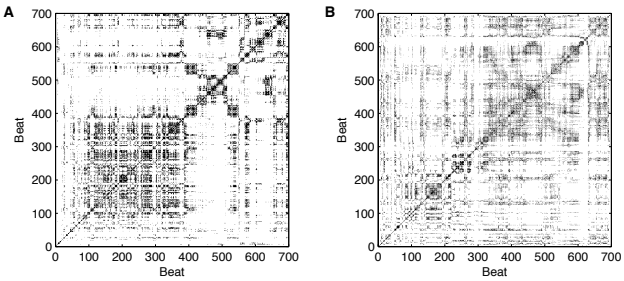

Figure 3: Exemplary recurrence plots for (A) pre-eclampsia and (B) control group.

The calculation of RQA and complex networks measures allows a quantitative characterisation of the recurrence structure of the cardiovascular data of the pre-eclampsia and control group (Tab. 1). We apply a Mann-Whitney U test for testing whether the medians of the distributions of the calculated measures of pre-eclampsia and control group differ. Considering the measurements of heart rate variability, systolic, or diastolic blood pressure alone, the medians are not able to distinguish between the two groups. The RQA measure *LAM*, which has been found to be a good candidate for the detection of cardiovascular disorders [13], is also not able to distinguish between the two groups (we have also tested other RQA parameters: only the recurrence rate *RR* performed slightly better than *LAM*). In

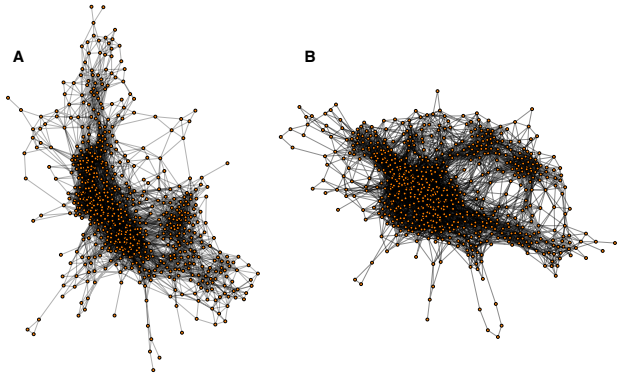

Figure 4: Exemplary complex networks representation for (A) pre-eclampsia and (B) control group (based on RPs shown in Fig. 3).

Table 1: Median (standard deviation) of the cardiovascular measurements and the recurrence based measures for pre-eclampsia and control group as well as their corresponding p-value.

	Pre-eclampsia	Control	p
H (ms)	734.5 (±110.8)	760.5 (±111.7)	n.s.
S (mmHg)	123.0 (±15.4)	123.5 (±20.0)	n.s.
D (mmHg)	75.5 (±10.4)	66.6 (±13.9)	n.s.
LAM	0.80 (±0.10)	0.83 (±0.08)	n.s.
C_v	0.60 (±0.03)	0.62 (±0.04)	0.0015

contrast, the clustering coefficient C_v is able to discriminate the two groups of pre-eclampsia and control with good confidence. The positive predictive accuracy is 60% and the negative accuracy value is 80%. Thus, using the complex network approach we could improve the early prediction of pre-eclampsia from currently 20–30% to now 60%. For pre-eclampsia, C_v is slightly lower than for the control group, suggesting a less regular cardiovascular oscillating regime related to the disorder. However, these are very first and preliminary results and are still subject of thorough research.

5. Conclusions

We have linked the recurrence matrix with the adjacency matrix of a complex network. This allows us to calculate complex network measures of a time series. As most of the complex network measures have no direct counterpart in recurrence quantification analysis, they give additional insights into the recurrence structure of dynamical systems. In general, this method allows to distinguish between different dynamical regimes and also to detect corresponding dynamical transitions.

By applying this novel approach to the cardiovascular data of pregnant woman, we have been able to early predict the serious disorder of pre-eclampsia with a positive predictive value of 60% (standard method: 20–30%).

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