Cardiovascular and Cardiorespiratory Interactions – From Physiological Mechanisms to Clinical Applications
Jessenius Faculty of Medicine, Comenius University (Martin, Slovakia), November 2–4, 2026
Project Visegrad Grant No. 22620137

Cardiovascular Network: Physiological Background, Data Sets and Future Perspectives

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joint work with Barbora Czippelová[2], Jana Čerňanová Krohová[2],
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This presentation outlines the complex interconnections in cardiovascular control network and possibilities to record its nodes behavior by non-invasive approach. Limitations of data interpretation and necessity to use causal bi-, tri- and multivariate data analysis approaches based on physiological background are stressed. Information on existing datasets recorded in our laboratory will be also provided.

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Analysis of Respiratory Heart Rate Variability Using Ordinal Patterns with Ties and Tolerance

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joint work with Grzegorz Graff[2,4], Maja Elstad[5], ...

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We propose a new approach based on the analysis of ordinal patterns to investigate respiratory heart rate variability (RespHRV), also known as respiratory sinus arrhythmia (RSA). We introduce ordinal patterns with ties and tolerance as a new method for symbolization of heart rate changes. By aligning heart rate data to the respiratory cycles, we analyze changes in heart rate at different phases of the respiratory cycle. The method uses RR interval time series derived from ECG signals, together with simultaneous respiratory recordings obtained with a respiratory belt. The method produces distributions of ordinal patterns that reflect the dynamics of heart rate variability throughout the respiratory cycle.

The approach will be illustrated using data from patients with obstructive sleep apnea (OSA) and healthy controls. Particular attention will be given to how introducing tolerance for small differences between RR intervals changes the observed pattern distributions and their physiological interpretation. The findings suggest that this approach may provide new insights into alterations in cardiorespiratory regulation associated with OSA.

[1] B. Graff, P. Pilarczyk, M. Elstad, K. Narkiewicz and G. Graff. Ordinal patterns with ties and tolerance provide a physiology-driven method to quantify cardiorespiratory interactions. *Biomedical Signal Processing and Control* **129** (2027), 111312. doi:10.1016/j.bspc.2026.111312

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Causal Discovery, Markov Chains, and the Degrees-of-Freedom Method

András Telcs[1],
joint work with Marcell Stippinger[1], Zsigmond Benkő[1], Dániel Fabó[2],
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We have time-series observations of two interacting systems. We investigate their separate and joint behavior. Taking into account their past states, can reveal their causal relationship.

The analysis can distinguish whether one system drives the other, the interaction is bidirectional, or whether their dependence is due to a common, possibly hidden, driver. In addition, investigation of their Markov properties can reveal whether one or both observed processes are subject to further separate hidden influences.

The lecture introduces causal discovery, Markov-chain analysis, and the degrees-of-freedom method as complementary tools for identifying these different causal structures from time-series data. [1, 2, 3]

[1] Stippinger, M., Bencze, A., Zlatniczki, Á., Somogyvári, Z. and Telcs, A., 2023. Causal discovery of stochastic dynamical systems: a Markov chain approach. *Mathematics*, *11*(4), p.852.

[2] Telcs, A., Kurbucz, M.T. and Jakovác, A., 2025. Unified causality analysis based on the degrees of freedom. *Physical Review E*, *112*(1), p.014204.

[3] Jakovác, A., Fabó, D., Erőss, L., Stippinger, M., Benkő, Z., Somogyvári, Z. and Telcs, A., 2026. Causality beyond the Reichenbach principle: the degrees-of-freedom method. *Scientific Reports*. doi:10.1063/5.0158923

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Data Analysis Methods Based on Dynamical Systems Theory: Unicorns, Dimensions and Higher-Order Hidden Drivers

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joint work with Zsigmond Benkő[1], Marcell Stippinger[1], David R. Rosenberg[3], Vaibhav A. Diwadkar[3], András Telcs[1,4]

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The presentation highlights several newly developed data-analysis methods based on dynamical systems theory. We show that attractor reconstruction based on Takens' theorem allows us not only to estimate the fractal dimension and Lyapunov exponents of a system, but also to identify a wide variety of events and interactions.

First, we introduce a novel anomaly-detection method for identifying unique events, which we call unicorns, in continuous time series. Dynamical systems theory provides a framework for defining the uniqueness of a state even in real-valued time series. We demonstrate the method on various datasets, ranging from ECG signals and gravitational waves to stock market indices.

Second, we introduce the principle of Dimensional Causality (DC) and a method that can identify directed causal interactions and distinguish them from bidirectional connections and interactions mediated by hidden common drivers. We show that hidden common drivers form a rich hierarchy in multivariate time series and introduce a method for uncovering this hidden structure.

Finally, we demonstrate that it is possible not only to detect the existence of a hidden common driver but also to reconstruct its time series, up to topological equivalence.

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Applications of Impedance Cardiography (ICG) Signals in Analysis of Cardiovascular System Diagnosis and Description

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The analysis of cardiovascular system response to various physiological stimuli as for example active orthostatic maneuver, head-up tilt test, handgrip or dynamic exercise may provide some supplementary diagnostic data on autonomic control activity and might help to predict the occurrence of some critical events, e.g. orthostatic syncope. Heart rhythm/rate variability (HRV) has been intensively studied in supine and other body positions in humans. However, only limited study results were published describing rhythms, fluctuations and generally dynamics of hemodynamic parameters, especially monitored during transient phase of physiological tests. Usually, the data are collected from small groups of subjects eg. healthy or with atrial fibrillation.

We plan to present several applications of Impedance Cardiography (ICG) analysis and directions for future research, while highlighting some limitations and precautions of the method.

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Bridging Global and Local Causal Discovery in Physiology: From Observational Networks to Dynamic Cardiorespiratory Interactions

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Identifying causal relationships in human physiology and sports medicine is crucial for understanding complex systemic interactions and improving diagnostic strategies and designing personalized training patterns.

Traditional global causal discovery methods, such as the Greedy Fast Causal Inference (GFCI) algorithm, provide robust frameworks for mapping static variable dependencies in observational data [1]. For instance, applying data-driven GFCI modeling to physiological and physical assessments of youth soccer players, then knowledge-adjusted, successfully generated a directed acyclic graph (DAG) identifying non-dominant leg performance, or symmetry between strength achievable by dominant and non-dominant legs in general, as a potentially modifiable determinant linked to aerobic capacity, and proposing the prospective interventional study to assess the relationship [1].

However, while such "top-down" global models are effective for macroscopic physiological profiling, they average out dependencies over entire recording sessions or datasets [2]. This aggregation obscures the transient, short-term fluctuations inherent to non-stationary biological signals, limiting their applicability in dynamic cardiovascular assessment, where interactions are rarely static; the strength and directionality of couplings fluctuate continuously under the influence of the autonomic nervous system as well as changes in measurement conditions. To address

the limitations of static structural assumptions, we introduced *tempord*, an open-source Python framework designed to estimate local temporal orders and causal vectors (CV) directly from non-stationary time series [2]. Employing a "bottom-up" analytical strategy, *tempord* evaluates the short-term stability, directionality, and strength of links between signals within narrow sliding windows [2].

We demonstrated the capabilities of the *tempord* algorithm by evaluating cardiorespiratory coupling (CRC) dynamics. By analyzing continuous tidal volume and tachogram (RR intervals) data, the framework was able to parameterize local temporal stability and detect minor step changes during autonomic nervous system state transitions, such as the shift from spontaneous breathing to music-induced relaxation [2].

Ultimately, this transition from global observational networks to dynamic signal-level analysis allows for a deeper understanding of the transient mechanisms governing cardiovascular networks, supporting earlier diagnosis and risk stratification of cardiovascular diseases.

Acknowledgements
This research was funded by the National Science Centre, Poland, grant number 2025/57/B/NZ4/01470.

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[2] M. Młyńczak, M. Rosoł, K. Korzeniewski, J. S. Gąsior. Evaluating Temporal Orders for Local Non-Stationary Biological Signals Analysis: A Python Framework and Simulation Study. *bioRxiv* (2026), preprint. doi:10.64898/2026.07.26.740785

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Respiratory Instability in Heart Failure and Hypertension: A Cross-Species Mathematical Model and Direct Observation of Intermittency in Anaesthetized SHR Rats

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Introduction. Respiratory instability is a common problem in congestive heart failure (CHF), as well as in primary hypertension (HT). Although certain attempts to mathematical modelling have been made [1], still a substantial effort is required, as both of these therapeutic targets represent a huge population. For V4 countries it reaches 2 million CHF patients, and at least 17 million of HT patients. We are still missing good methods that would provide an early diagnosis of HT and early symptoms of decompensation in already diagnosed patients. A common handler for both these conditions is, quite surprisingly, the respiratory rhythm. The CHF patients are known to develop respiratory disorders such as Cheyne–Stokes respiration (CSR). Observations of instabilities in the HT patients are less frequent, however an increased chemoreflex sensitivity is reported as an important adverse biomarker [2]. A better understanding of the mechanisms underlying respiratory rhythm instability may contribute to the development of improved monitoring techniques and a more precise assessment of breathing

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pattern alterations accompanying the progression of primary hypertension in humans.

In this translational work we have started from an animal model: spontaneously hypertensive rats (SHR), that constitute a well-established model of primary hypertension, to obtain experimental data. Numerous pathophysiological alterations associated with the development of hypertension and its complications have been described in this strain. However, disturbances of respiratory rhythm are rarely investigated in this context.

Aim. To assess the occurrence of Cheyne–Stokes-like breathing in SHR rats and to propose a cross-species mathematical model describing this phenomenon, that can be applied to human subjects.

Methods. Male and female SHR and Wistar-Kyoto (WKY) rats were studied at the ages of 1, 3, 6, 12, and 16 months. Following anaesthesia with ketamine, animals were connected to a pressure sensor (Pressure Pad/Respiration Transducer; Biopac Systems, Inc.; Interlab), which recorded respiratory activity both during anaesthesia and after recovery. Inspiratory peaks were subsequently identified and visualized using carpet plot analysis [3], enabling the evaluation of signal dynamics and periodicity, as well as Argand diagrams.

Results. A long-short type respiratory rhythm instability was observed exclusively in the SHR group and only under anaesthesia.

An example recording is shown, where each horizontal strip corresponds to a segment of respiratory activity encoded by color. The underlying time series is displayed beneath each carpet plot. In the WKY group, occasional sighs are visible as horizontal lines. In contrast, SHR rats exhibited increased variability of the respiratory cycle, and from 3 months of age onward a short-long sequence became apparent, likely resulting from loss of stability through a bifurcation mechanism. Intermittency was also observed, characterized by irregular switching between stable breathing and the short-long oscillatory pattern.

The proposed cross-species mathematical model of CO_2 balance, based on [1], identifies increased chemoreceptor sensitivity (typical to HT) and prolonged circulation time (typical to CHF) as the principal causes of respiratory instability. These factors generate a delay between sensor and effector, thereby destabilizing the feedback control loop. Anaesthesia prolongs reflex-loop latency, unmasking the instability substrate. A similar mechanism may operate during sleep in humans, for example in heart failure or at high altitude. Rebreathing into a bag was found to regularize the respiratory rhythm, consistent with the predictions of the mathematical model.The model may be applied to both rats and humans, as the general mechanisms are common to all mammals, and intra-species differences may be introduced by suitable parametrization.

Conclusions. Respiratory instability was observed in anaesthetized SHR rats, and the data obtained were used to calibrate a cross-species

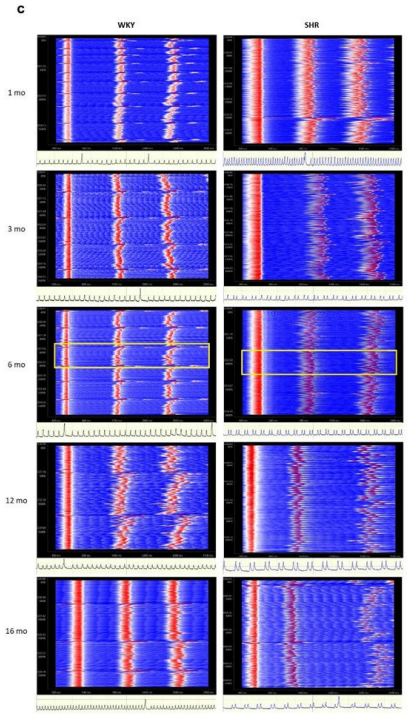

Figure 1: Representative respiratory recordings obtained during anesthesia, presented as carpet plots with corresponding segments of the raw respiratory signal shown below each carpet plot, illustrating strain-specific breathing patterns in WKY and SHR rats. Yellow boxes indicate example carpet plot segments corresponding to the raw traces.

mathematical model. These findings may contribute to the development of methods for monitoring breathing pattern alterations associated with cardiovascular diseases in humans. The cross-species mathematical model may be helpful for early symptoms of primary hypertension and cardiac decompensation in heart failure in V4 population.

Acknowledgements. This work was supported by the National Science Centre (NCN), Poland, grant OPUS 2018/29/B/NZ5/02491.

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Between the Heartbeats: What Heart Rate Variability (HRV) Reveals — From ECG to Smartwatches

Beata Graff

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Heart rate variability (HRV) provides valuable insights into autonomic cardiovascular regulation and reflects the complex mechanisms controlling heart rhythm. This talk will introduce the physiological basis of HRV, key parameters, and current recommendations for its assessment and interpretation. Selected examples from clinical Holter ECG recordings will illustrate how HRV analysis can provide information beyond conventional heart rhythm assessment. Finally, the growing role of wearable devices in HRV monitoring will be discussed, highlighting both their potential and limitations in clinical practice.

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Interactions in a Selected Four-Node Network of Cardiorespiratory Parameters

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This study introduces a network-based view of the spontaneous short-term regulatory mechanisms linking cardiovascular and cardiorespiratory systems across physiological states. Using conditional transfer entropy, we assessed directed interactions among beat-to-beat heart period, arterial pressure, respiration, and arterial compliance variability in 39 healthy subjects during supine rest and orthostatic stress. The analysis confirmed established effects (e.g., reduced respiratory sinus arrhythmia during tilt and increased baroreflex) and revealed additional, less studied compliance-related pathways: tilt-linked changes included weaker influences of heart period and arterial pressure on compliance, stronger causal effects from compliance to arterial pressure, and reduced compliance effects on respiration. By combining model-based and model-free methods, we also identified whether interactions were linear or nonlinear. Overall, the findings highlight arterial compliance as a key driver of cardiovascular coupling and support using direct causality measures to capture the complex origins of short-term cardiovascular oscillations.

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From Understanding to Control: A Dynamical Systems Approach in Physiology

Zoltán Somogyvári[1], in cooperation with Marcell Stippinger[1], Veronika Házi[1,2], Zsigmond Benkő[1], András Telcs[1], Sándor Borbély[3], Ildikó Világi[3], Dániel Fabó[4], Loránt Erőss[4], Paweł Pilarczyk[5], Grzegorz Graff[6], Beata Graff[7]

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I will present results showing how dynamical systems theory has led to new insights into physiological systems through the development of novel data-analysis methods and tools for modifying system dynamics toward more desirable states.

Inferring causal connections in complex physiological systems is a key element in understanding the normal and pathological behavior of observed systems. In recent years, we have developed a new causality analysis method, termed Dimensional Causality (DC), which can detect and distinguish the basic forms of causal relationships between two dynamical systems based on observed time series. DC can detect directed causal connections and circular or bidirectional interactions, and can distinguish these from two unconnected systems driven by a hidden common cause, or confounder. Results of DC analyses will be presented for data ranging from in vitro to in vivo epilepsy experiments, fMRI time series recorded during cognitive tasks,

and interactions within the cardiovascular and pulmonary systems. In these applications, our analysis emphasizes and quantifies the role of hidden, unobservable drivers.

Of course, we would like not only to analyze and understand physiological systems, but also to modify their dynamics, moving them away from pathological behavior toward normal states. I will show how dynamical systems theory can help identify escape routes from pathological dynamics of the epilepsy and, when combined with machine learning, can be used to define optimal stimulation strategies for efficiently terminating epileptic seizures.

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Cerebrovascular Interactions in Relation to Orthostatic Syncope

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Cerebrovascular regulation maintains stable cerebral blood flow (CBF) via cerebral autoregulation (CA) during mean arterial pressure (MAP) fluctuations. This closed-loop interaction between MAP and mean CBF velocity (MCBFV, measured via transcranial Doppler) is widely investigated using time-domain and spectral Granger causality. Crucially, postural challenge impairs CA in subjects prone to orthostatic syncope, thus underscoring the need for efficient predictors of fainting and more severe cardiovascular events in pathological cohorts.

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Methods for Analyzing Cardiovascular Signal Asymmetry in Healthy Individuals and Patients with OSA

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This study aims to evaluate the application of the Makowiec Generalised Asymmetry Index (MI) to cardiovascular signal analysis in healthy individuals and patients with obstructive sleep apnea (OSA). Time series of RR intervals and systolic blood pressure (SBP) were analyzed by examining the distributions of MI values and comparing the resulting parameters between the study groups.

The analysis will be extended to account for respiratory phase. RR and SBP values will be assigned to separate datasets corresponding to inspiration and expiration, and the MI will be calculated independently for each phase. This approach will let us assess how respiratory phase affects signal asymmetry and evaluate its usefulness in cardiovascular signal analysis.

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Hierarchically-Organized Interactions in Dynamic Physiological Networks

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In Network Physiology, the human organism is modeled as a complex network of interacting organ systems. While traditional approaches focus on pairwise interactions and time-domain analysis, these methods often fail to capture the full complexity of physiological regulation. This research addresses these limitations by investigating how multi-organ regulation emerges from high-order interactions (involving more than two nodes) and by shifting the focus to frequency-specific mechanisms. Exploring these distinct oscillations and multi-node synergies sheds new light on the hidden modalities of signal cooperation in both healthy and pathological conditions.

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Dimensional Causality: Revealing Hidden Shared Drivers in Cardiovascular Recordings

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HUN-REN Wigner Research Centre for Physics, Department of Computational Sciences, Budapest, Hungary Dimensional Causality (DC) is a method for revealing causal connections between recorded signals with a focus on identifying hidden common drivers [1]. The state variable of the original system are reconstructed from the recorded signal with time delay embedding. In this reconstructed space our method measures the dimension of individual signals and their joint embedding to infer the probability of each possible causal connection based on the data.

We apply DC to two physiological datasets. The first, featured in the ESGCO challenge [2], consists of beat-to-beat cardiovascular, cerebrovascular, and respiratory signals recorded in healthy controls and individuals prone to postural syncope, during rest, early head-up tilt, and prolonged tilt phases of the head-up tilt test. Our results reveal that hidden common drivers dominate the inferred interaction structure in most cases, highlighting the importance of accounting for latent confounding influences in physiological causality analysis. Orthostatic stress induced substantial reorganization of the interaction network, with stronger bidirectional cardiovascular coupling in healthy subjects. In syncope-prone patients, altered coupling patterns suggested impaired autonomic and cerebrovascular regulation.

The second dataset, recorded at the Medical University of Gdańsk, contains instantaneous blood pressure, beat-to-beat heart rate derived from ECG and respiration. We observe that the dimension of the respiratory dynamics differs significantly between the two groups. The dimension of respiration is lower in individuals with disease, and in parallel, the joint dimension of respiration/blood pressure (BP) and respiration/heart rate (HR) also decreased. In the disease group, these suggest altered causal relationships: instead of a hidden common cause connecting the subsystems their cardiovascular signals (BP, HR) drive respiration more directly. Further analysis requires moving from pairwise causal analysis to describing a network with multiple hidden causes.

Our findings demonstrate the usefulness of dimensional causality analysis for uncovering complex hidden interactions in cardio-respiratory dynamics.

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Entropy-Based Indices in the Analysis of Age-Related Changes in Heart Rate–Blood Pressure Coupling

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Our research focuses on exploring the potential of entropy-based indices for the analysis of cardiovascular interactions. As a first step, we investigate whether these measures can capture age-related differences in heart rate-blood pressure coupling. ECG and continuous non-invasive blood pressure recordings from the PhysioNet Autonomic Aging database were analysed for two groups of healthy participants aged 25-29 and 50-54 years. After signal-quality assessment and preprocessing, 10-minute segments were used to derive RR intervals and corresponding systolic blood pressure values, which were then transformed into ordinal patterns. Classical heart rate variability measures were used as a reference, while mutual information (MI) and transcript mutual information (TMI) were explored to characterize dependence and directional information exchange between RR and blood pressure series. Preliminary results indicate lower heart rate variability in the older group, together with weaker short-delay RR-BP dependence and a lower BP-to-RR directional TMI value. These findings motivate further investigation of the physiological interpretation and robustness of entropy-based measures of cardiovascular coupling.