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## Does data preprocessing affect the analysis of couplings in the cardiovascular system?

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Shannon entropy (ShE) is a recognized tool for studying the organization of time series. Transfer entropy (TE) allows the assessment of dependencies between coupled systems. It occurs that both entropies reveal a strong dependence on the preprocessing method used for the signal.

We considered two types of symbolization. The first type refers to the variability of the signal. The second type exposes the trends of dynamics. Both symbolizations were applied to basic physiological signals: the rhythm of heart rate (RR) and systolic blood pressure (SBP) in order to assess the organization of the cardiovascular system. The signals were registered in healthy people during the tilt test (HUT) - a medical procedure often used to evoke autonomic reflexes - here baroreflex, provoked by the sudden change of a body position. Systematic studies were supported by simulations with shuffled data to distinguish the real features of signals from random fluctuations. The obtained results were also confronted with the physiological facts of the cardiovascular response to the HUT test.

We have found that ShE obtained for signals with the preprocessing method based on variability is indistinguishable from ShE obtained from randomly shuffled signals. But when symbolization with coding dynamical trends was used then the expected distinction between real signals (lower entropy) and randomly shuffled signals (higher entropy) occurs.

Also, the high percentage of zero values obtained for TE seems to be the effect of preprocessing.  $TE = 0$  means that studied signals are not coupled (rather rare event) or couplings do not achieve statistical significance. Nevertheless, we found the time periods in the HUT recordings with statistically significant influence of the heart rhythm on the vascular system (so-called, feed-forward baroreflex arm), and the effects of the vascular system on the cardiac system (so-called, feed-back baroreflex arm).

In summary, any inference based on entropy measures must always be supported by the rules used in the preprocessing of data.