Bivariate temporal orders for causal inference

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Abstract. Causality analysis may be carried out at different levels of detail, e.g. parameter- or temporal-based (both in a global sense). There is hence a need for a local, more distinctive approach, particularly when analyzing data segments. Therefore, the bivariate temporal orders (BTO) estimation was introduced. It uses both ”statistical” and ”causal” approaches, with two different kernels in each (linear modeling and time series distance calculation, for statistical one; and entropy- and integral-approximation-based information geometric causal inference, for causal one). The algorithm was tested on cardiorespiratory data comprising tidal volume and tachogram curves, obtained from elite athletes (supine and standing, static conditions) and a control group (different rates and depths of breathing, while supine). BTO enables to find the local curves of the most optimal shifts between signals (causal vector) and to determine causally stable segments across time. In this context, the causal vectors were determined concerning body position and breathing style changes. The rate of breathing had a greater impact on the causal vector average than does the depth of breathing. The tachogram curve preceded the tidal volume more when breathing was slower. The stability was the highest for the highest breathing rate. The method is implemented in the provided R package and can be also used for other physiological studies or even different research areas.

Keywords: Causality analysis, temporal order, tidal volume, RR intervals, stability, causal vector

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1. Introduction

The network physiology concept is widely accepted \[1\]. It rests on the assumption that several systems are combined in a network of non-linear dependencies with various loops, feedbacks, and delays in transmitting information. The cardiovascular or respiratory systems may be also influenced by many environmental, psychological or demographic factors \[2\].

One of the possible and commonly analyzed combinations is that of respiration and heart activity. Several effects have been introduced and accepted. For instance, sinus respiratory arrhythmia is a phenomenon evident in resting ECG as the effect of successive inspirations and expirations \[3\]. The baroreflex effect is based on adjusting neural responses affecting both heart and respiratory activity \[4\]. Cardiorespiratory coupling holds that heartbeats coincide with the respiratory phases, particularly because of increased sympathetic nervous activity \[5\].

Many mathematical approaches (including ones in the temporal, frequency or information domains) have been proposed to analyze cardiorespiratory relationships. We hypothesized that the parameterization of the cause-and-effect relationships would be valuable. To evaluate different levels of connections, we stated that the analysis should move from general to detailed. It should begin by examining global parameters without considering the impact of time; then delve into temporal relationships and causalities; and end with analysis of narrow time intervals enabling assessment of the stability of causal connections between time segments, e.g., during successive states after an orthostatic maneuver or after significant changes in depth (or rate) of breathing.

The first two approaches have been already utilized \[6,7\]. In the first, the discovery of time-independent causal paths suggested different results depending on the body position. In a supine position, the values of a tidal volume seemed to cause heart activity variation, which affected average heart activity, which finally influenced respiratory timing. For standing, the relation led from normalized respiratory activity variation to average heart activity \[6\].

In the second approach, temporal relationships examined by Granger causality frameworks (with extensions that consider zero-lag effects \[8\]) or Time Series using Restricted Structural Equation Models (TiMINo) \[9\], suggested that the most prominent combination appeared between tachogram (RR intervals curve) and tidal volume signal \[7\].

However, when analyzing signals, instead of beat-by-beat sequences, the results were weak and unstable, an effect of considering relatively long segments of data. On the other hand, temporal causality analyses require minimum lengths of data to work correctly, e.g., by definition and due to the stationarity criterion.

Therefore, as for ambulatory measurements, the physiological states may change across time (even passively). There is a need for a framework to causally examine local, short segments of data and to explore the temporal orders between signals, like tidal volume and tachogram (constituting the main cardiorespiratory relationship).
The introduction of such a technique is hence the main aim of this study. The method can be utilized for stability assessment across time, e.g., by determining the curves of most optimal inter-signal shift relative to different measurement conditions and physiological settings.

2. Materials and Methods

The methodology is divided into four sections: description of the algorithm, surrogate data evaluation, study group specification, and sample analysis of physiological signals.

2.1. Description of the algorithm

The block diagram of the bivariate temporal orders (BTO) estimation is presented in Fig. 1.

The bivariate dataset should be loaded. The first signal (in our case, tachogram estimated as interpolated RR intervals) is kept stationary during the analysis, while another (here, impedance-related tidal volume curve) is shifted in time (backward and forward, in the given range).

There are several input parameters that define the entire setup:

- method - determines which kernel will be used (linear modeling, time series distance, or entropy- and integral-approximation-based information geometric causal inference (IGCI); further explained below);
- scaling - states the standardization type: 0 - no standardization, 1 - uniform standardization, or 2 - Gaussian standardization;
- threshold - the level at which the estimate of the parameter is excluded when determining the curve of maximum or minimum values (for linear modeling and time series distance kernels, respectively); for IGCI kernels, the threshold level for presenting values in the output figure;
- length of signal segment to analyze per loop iteration (the same length for both signals; should not exceed the length of the entire signal);
- maximum shift in time - determines how far the second signal may be moved backwards and forwards; the range does not need to be symmetrical to zero shift (the value should not exceed half of the length of the iteration segment so that the analyzed signals do not overlap);
- time resolution of signal segments’ centers - specifies the resolution of the output figure’s X axis (how frequently the center of the first signal is chosen);
- time resolution of shifts - specifies the resolution of the output figure’s Y axis (how many time shifts of the second signal are tested, between the maximum backward and maximum forward shifts);
- other - when a more sophisticated time series distance method is selected (described in the R package manual - S1 supplementary material).
Data 1 (e.g. tachogram) stands still during analysis
Data 2 (e.g. tidal volume) is being moved during analysis

Main loop for each point of the signal and shift applied to second one

Selection of signals’ parts

Scaling (if chosen)

Statistical approaches

Linear modeling kernel (LM)

Time series distance kernel (TD)
- Manhattan
- STS
- Fourier
- …

Causal approaches

IGCI with entropy estimator
IGCI with integral approximation estimator

Estimation of the main parameter (depending on the method)

Determining the curve of maximum or minimum values (for linear modeling or time series distance kernels, respectively)

Creating the final figure and accompanying data frames

Inputs

Settings
- method
- scaling
- threshold
- length of the signal
- maximal shift in both sides
- time resolution of points
- time resolution of shifts

Outputs

Parameters in an array form
(points vs shifts vs parameters value)

Parameters in an data frame form
(clear column names)

Figure prepared using ggplot function

The curve of maximum or minimum values (only for LM and TD kernels)

**Figure 1.** The general scheme of the BTO algorithm, as implemented in the R package.
The main loop of the analysis is carried out for each point of the first signal with a shift applied to the second signal (according to the set resolutions). In the first step, the vector of shifts (making up the Y-axis of the output figure) and the vector of signal centers (making up the X-axis) are prepared. Then follows selection of the signal parts to be analyzed during each iteration. Next, if scaling was selected, it is performed.

The mathematical interpretation of the main output calculation is divided into statistical and causal approaches. The former is called so because its kernel includes no causal paradigm. The parameter to be visualized is the adjusted-R-squared measure of the linear model between the two signals’ segments for the linear modeling kernel (this is chosen as a more robust parameter than Pearson’s correlation coefficient); or the time series distance measure (e.g. Manhattan or Fourier).

For the latter, two IGCI methods with different estimators (entropy and integral-approximation) are used [10, 11]. The approach is based on the analysis of conditional distributions and is relatively convenient for visual purposes, as a single parameter is returned (originally, a negative value suggests an \( X \rightarrow Y \) relation; positive - the opposite).

After all iterations, the matrix is filled and may be presented in the graph. In order to facilitate the extended interpretation of the relationships’ stabilities, the shape of the maximum and minimum values obtained for each point in time is recognized for use with by the linear modeling and time series distance methods, respectively. If a threshold was chosen, only the values (respectively) above or below the threshold produce those curves.

Finally, the algorithm can present its outputs. The parameters (in array and data frame forms), a ggplot-based figure variable (ready to be visualized in R) and the curve of maximum or minimum values, hereafter the ”causal vector”, are returned (only for statistical approaches).

The color palette is selected so that the maximum/minimum values are marked in blue (red areas are for the opposite, for statistical approaches). On the other hand, positive values from the causal approaches (blue) indicate that the second signal is ”later” than the first (the first is regarded as a cause of the second).

The method is implemented as an R package supplementing the paper. The main ”installer” and the CRAN-compatible manual are available on the author’s website [12]. The package uses external R packages: ggplot2 [13], quantmod [14], seewave [15], signal [16], and TSdist [17].

2.2. Surrogate data

Three types of surrogate data were prepared to test and evaluate the outputs based on different cases:

- Noiseless static (0.2167Hz, 13 periods per minute) sinus signals (imitating breathing), shifted by 1/6 of the period (770ms).
The same sinus signals, with added static Gaussian noise (mean value of zero and standard deviation of 15% for the first signal and 18% for the second).

Dynamic sinus signals with the same noise levels as in the previous case, and different base settings for each minute:
- 1st minute: 0.133 Hz, 8 periods / min, shifted by 1/14 of the period (536 ms);
- 2nd minute: 0.167 Hz, 10 periods / min, 1/18 shift (333 ms);
- 3rd minute: 0.200 Hz, 12 periods / min, 1/22 shift (227 ms); and
- 4th minute: 0.267 Hz, 16 periods / min, 1/10 shift (375 ms).

The greatest mismatch occurs at the end of the second minute.

In all cases, we assumed the synchronicity of the data, as this is expected in the physiological signals while breathing phasing is treated as a trigger for heart rhythm changes (respiratory sinus arrhythmia). All signals were created assuming a sampling frequency of 25 Hz and 4 minutes of recording (6000 samples). Then, we tested the BTO estimation algorithm using the following settings:

- LM, TD-Manhattan and TD-Fourier kernels;
- without thresholds;
- with Gaussian standardization;
- segment length - 10 seconds;
- maximal shift in both directions - 2 seconds;
- time resolution of points - 25 points (1 second);
- time resolution of shifts - 1 points (0.04 seconds);

2.3. Study group and measurements

For physiological analysis, we used data from:

- a group of 10 elite athletes (A) - 4 minutes of registrations for supine and standing body positions, with unconstrained and free breathing protocols (sample choice from the study group described in [6,7]);
- a control group of 10 subjects (B) - following a constrained breathing procedure consisting of 12 breaths (6 normal, then 6 deep) each at rates of 6, 10, and 15 breaths per minute (BPM).

Both study groups are demographically described in Table 1.

Single-lead ECG and impedance pneumography signals were acquired using our prototype, Pneumonitor 2 [18]. The tachogram was calculated from the ECG signal after the signal’s non-linear detrending for baseline alignment and identification of R peaks based on the Pan-Tompkins algorithm. A tidal-volume-related impedance signal was obtained without calibration (this is based on the confirmed observation that linear fitting provides the best agreement between the impedance signal and the reference, pneumotachometry [19]). The sampling frequency was reduced from the original 250 Hz to 25 Hz for computational reasons.
Table 1. The demographic summary of both study groups.

| Group     | A       | B       |
|-----------|---------|---------|
| Count     | 10      | 10      |
| Sex       | 5F & 5M | 3F & 7M |
| Weight [kg]| 68.5 ± 15.3 | 72.9 ± 13.2 |
| Height [cm]| 179.5 ± 12.6 | 176.2 ± 7.2 |

2.4. Sequence of physiological signal analysis

The main objective of this part of the analysis is to present the sample executions of the algorithm and analytical/interpretative opportunities behind it. Therefore, the section is not adjusted to provide general medical conclusions.

In the first step, the BTO estimation (using both statistical approaches) helped to find the course of a causal vector (its value and stable segments over time) with and without manual and arbitrary thresholds. Then, the course could be analyzed in relation to body positions and changes in breathing style, to determine how they affect the relationships (whether relationship direction, intensity, or other aspects change).

During the analysis, average and standard deviation values of the estimated causal vector were calculated for supine/standing body positions in Group A, and for different depths and rates of breathing in Group B, without a threshold. Then, the same parameters, along with the duration of the longest stable part and the ratio of the duration to that of the signal, were determined while applying thresholds of:

- 0.90 for the Linear Modeling kernel.
- 0.15 for the TD Manhattan kernel.
- 0.15 for the TD Fourier kernel.

Next, causal-based BTO estimation was performed to analyze the course within particular shift slices to assess the complexity of signals’ dynamic differences during physiological state changes.

Average and standard deviation values at each zero-shift slice were calculated for supine/standing body positions in Group A and for different depths and rates of breathing in Group B, with a 0.25 threshold (the absolute values below the threshold were treated as ”not assigned”). All data presented in the Results section for this approach comes from the integral approximation estimator.

In all cases, the settings were the same as for the surrogate data analysis, except for the thresholds.

3. Results

Like the Materials and Methods section, Results is divided into subsections, presenting the sample results of the surrogate data analysis with its general interpretation, and the
outcomes with regards to physiological signals measured from the athletes and controls (with the reference to previous findings).

3.1. Surrogate data analysis and general interpretation of the results

Figure 2 presents 9 outputs for 3 types of surrogate data (noiseless static sinus in the first column; noisy static sinus in the second; dynamic noisy sinus in the third). Rows (labeled in graph titles) correspond to methods.

For the third, dynamic surrogate data set, average values of the causal vector curves are presented in Table 2 along with the reference signals’ shift.

For the linear modeling kernel, the setting of the right shift range is crucial. If the range is too wide, the impact of consecutive periods will be visible. For noisy signals, it may distort the BTO estimation and prevent establishment of the right causal vector curve. This issue is not present for the TD kernels.

In general, the black line, representing the curve of the causal vector, should be non-dashed (in the case, where a threshold is used) and near-parallel to the X-axis. In
Table 2. The average values of the causal vector curves for the dynamic surrogate data set; shift resolution is 40 ms; TD - time-series distance measure.

| Minute | Reference  | Linear modeling | TD Manhattan | TD Fourier |
|--------|------------|-----------------|--------------|------------|
| 1      | 536 ms     | 523 ms          | 516 ms       | 523 ms     |
| 2      | 333 ms     | 333 ms          | 333 ms       | 333 ms     |
| 3      | 227 ms     | 241 ms          | 223 ms       | 241 ms     |
| 4      | 375 ms     | 203 ms          | 377 ms       | 378 ms     |

such fragments of the signal, the relation may be considered stable.

The narrower the blue area is, the more coherent the calculation. The area’s width is a function of the signal-to-noise ratio and the signals’ regularity.

In turn, step changes in the course of the maximum values may reflect extrinsic changes in the study conditions.

The same analysis may be carried out for causal approaches, without causal vector determination; however, it performs better for more irregular data, such as physiological data.

3.2. Evaluation of physiological signals

Table 3 gathers the means and standard deviations of the causal vector in Group A for both supine and standing body positions without a threshold, for linear modeling, TD Manhattan, and TD Fourier kernels. Table 4 collects these results (mean and SD of causal vector, duration of the longest stable part and ratio of the duration to that of the signal) after applying a threshold only to the TD Manhattan method.

The overall average for BTO estimation without a threshold for supine body position was 302 ms for LM, 456 ms for TD Manhattan, and 469 ms for TD Fourier; for standing: −2 ms, 251 ms, and 239 ms, respectively. Respiratory sinus arrhythmia seems to be present, particularly for the supine body position. The standard deviations are much greater for the standing body position, for which the relation between tidal volume curve and tachogram appears to be more "independent". There are relatively few, and short, fragments of constant causal vectors between signals. Those suggest greater variability, perhaps even complexity of the relationships, and more difficult causal inference.

When applying arbitrary thresholds, stable parts of the causal vectors were determined. Standard deviations decreased. In 2 of the 10 participants in Group A, there was no value below the threshold for the supine body position; likewise for 4 of 10 for standing. The mean causal vectors were 571 ms and 431 ms for supine and standing body positions, respectively.

Sample visual results for very regular signals recorded for a supine position (small SD) are shown in Figure 3 and for less regular signals obtained during standing (greater SD) - in Figure 4. In both cases, thresholds were applied.
Table 3. Summary of mean values and standard deviations for each participant for both supine and standing body positions, for statistical approaches of BTO estimation (Linear Modeling, TD Manhattan and TD Fourier), without any threshold, all for Group A. A minus means that the tidal volume curve is ahead of the tachogram. All values are presented as mean ± SD, in milliseconds.

| Participant | Position | Linear modeling | TD Manhattan | TD Fourier |
|-------------|----------|-----------------|--------------|------------|
| 1           | Supine   | 446 ± 517       | 493 ± 366    | 511 ± 372  |
|             | Standing | 55 ± 1284       | 24 ± 1057    | 42 ± 1016  |
| 2           | Supine   | 99 ± 1202       | 192 ± 191    | 181 ± 153  |
|             | Standing | −266 ± 1310     | 35 ± 1016    | 66 ± 1016  |
| 3           | Supine   | 719 ± 710       | 851 ± 350    | 864 ± 349  |
|             | Standing | 337 ± 704       | 487 ± 527    | 487 ± 490  |
| 4           | Supine   | 1304 ± 961      | 1337 ± 855   | 1339 ± 911 |
|             | Standing | −70 ± 1949      | 1909 ± 300   | 1933 ± 219 |
| 5           | Supine   | 45 ± 1337       | 310 ± 1050   | 436 ± 978  |
|             | Standing | −496 ± 1365     | 374 ± 994    | 369 ± 983  |
| 6           | Supine   | 582 ± 1222      | 1185 ± 497   | 1209 ± 497 |
|             | Standing | 128 ± 1412      | 1075 ± 698   | 1120 ± 682 |
| 7           | Supine   | −263 ± 1115     | −84 ± 297    | −101 ± 226 |
|             | Standing | 245 ± 1289      | −79 ± 1135   | −132 ± 1208|
| 8           | Supine   | −100 ± 1341     | 46 ± 949     | −4 ± 1016  |
|             | Standing | −92 ± 1375      | −160 ± 1207  | −333 ± 1166|
| 9           | Supine   | 68 ± 768        | 328 ± 263    | 328 ± 257  |
|             | Standing | 21 ± 1175       | −768 ± 483   | −775 ± 491 |
| 10          | Supine   | 122 ± 1090      | −94 ± 475    | −76 ± 453  |
|             | Standing | 119 ± 1195      | −384 ± 587   | −389 ± 545 |

Next, the mean and standard deviation were calculated for the TD Manhattan kernel (with threshold) for different breathing rates and depths (in Group B), and are shown in Table 5. For the 6 BPM breathing rates, an extended range of shifts was applied.

The results suggest the rate of breathing has a greater impact on the mean value of the causal vector (without considering the threshold) than the depth of breathing. The averages (each calculated as a mean of all values in the table for particular column) for Group B are 2484 ms, 841 ms, and 313 ms, for 6, 10, and 15 BPM, respectively.

As the breathing cycle durations are 10s, 6s, and 4s for those rates, it appears that the most optimal shifts are about 24.8%, 14.0%, and 7.9% of the cycle length, respectively.

Interestingly, the RR interval curve precedes the tidal volume more when breathing is slower. On the other hand, the stability of the relation is highest for the quickest breathing rate (standard deviations are smallest).
Table 4. Summary of the mean and standard deviation, duration of the longest stable part, and ratio of the duration to the duration of the signal, for each participant for both supine and standing body positions, for the TD Manhattan kernel, with a 0.15 threshold, all for Group A. Dashes mean that no value below the threshold was found.

| Participant | Position | Mean ± SD [ms] | Longest [sec] | Ratio [%] |
|-------------|----------|----------------|---------------|-----------|
| 1           | Supine   | 369 ± 137      | 52            | 60.8      |
|             | Standing | −114 ± 356     | 9             | 9.3       |
| 2           | Supine   | −              | −             | 0.0       |
|             | Standing | 360 ± 301      | 3             | 1.3       |
| 3           | Supine   | 878 ± 288      | 17            | 32.6      |
|             | Standing | 491 ± 399      | 15            | 26.4      |
| 4           | Supine   | 1382 ± 840     | 11            | 15.0      |
|             | Standing | 1755 ± 389     | 11            | 15.0      |
| 5           | Supine   | −              | −             | 0.0       |
|             | Standing | −              | −             | 0.0       |
| 6           | Supine   | 1194 ± 465     | 8             | 18.1      |
|             | Standing | 854 ± 513      | 7             | 8.8       |
| 7           | Supine   | −133 ± 108     | 5             | 4.0       |
|             | Standing | −              | −             | 0.0       |
| 8           | Supine   | 600 \(1\) point | 1             | 0.4       |
|             | Standing | −              | −             | 0.0       |
| 9           | Supine   | 364 ± 206      | 8             | 14.5      |
|             | Standing | −763 ± 285     | 9             | 5.3       |
| 10          | Supine   | −86 ± 143      | 5             | 3.1       |
|             | Standing | −              | −             | 0.0       |

Sample visual results for the entire breathing protocol are shown in Figure 5 (a threshold of 0.15 for the TD Manhattan kernel was used).

Then, the causal approaches were tested in both groups. In each case, the integral approximation estimator was used. Sample BTO estimation results for the signals acquired from a Group A participant (#1) in a supine body position and a Group B participant (#7) (presented earlier) are shown in Figure 6. The summary for the zero shift is presented in Table 6. In both cases, no threshold was used.

For the regular curves in Group A, the advantage of the case where the heart curves seems to cause the respiratory are better visible than for the breathing protocol in Group B. For participant #7, blue coloring even suggests the opposite relationship. This is true for almost all shifts in the considered range.
Figure 3. Sample BTO estimation for very regular signals acquired from one supine Group A participant (#1).

Figure 4. The sample BTO estimation for less regular signals acquired from another, standing, Group A participant (#3).
Table 5. Summary of mean and standard deviation values, for each Group B participant, for every combination of breathing depth (normal and deep) and breathing rate (6, 10, and 15 breaths per minute, BPM), for the TD Manhattan kernel, without a threshold.

| Participant | Depth | 6 BPM      | 10 BPM     | 15 BPM     |
|------------|-------|------------|------------|------------|
| 1          | Normal| 2140 ± 974 | 656 ± 328  | 253 ± 303  |
|            | Deep  | 2490 ± 369 | 608 ± 211  | 120 ± 80   |
| 2          | Normal| 1828 ± 583 | 523 ± 402  | 27 ± 198   |
|            | Deep  | 2090 ± 270 | 949 ± 1126 | 104 ± 49   |
| 3          | Normal| 2799 ± 746 | 863 ± 357  | 813 ± 1307 |
|            | Deep  | 2976 ± 998 | 1509 ± 1202| 896 ± 239  |
| 4          | Normal| 2753 ± 524 | 1043 ± 399 | 510 ± 429  |
|            | Deep  | 2412 ± 343 | 664 ± 788  | 258 ± 255  |
| 5          | Normal| 1985 ± 184 | 829 ± 375  | −2 ± 278   |
|            | Deep  | 2583 ± 380 | 783 ± 236  | 11 ± 162   |
| 6          | Normal| 3543 ± 690 | 696 ± 220  | 106 ± 385  |
|            | Deep  | 2845 ± 529 | 663 ± 123  | 131 ± 107  |
| 7          | Normal| 2527 ± 543 | 318 ± 888  | −82 ± 212  |
|            | Deep  | 1782 ± 452 | 238 ± 208  | −94 ± 45   |
| 8          | Normal| 3160 ± 282 | 1154 ± 275 | 562 ± 227  |
|            | Deep  | 2929 ± 239 | 1203 ± 278 | 397 ± 134  |
| 9          | Normal| 1402 ± 466 | 1108 ± 238 | 216 ± 242  |
|            | Deep  | 2260 ± 345 | 748 ± 150  | 526 ± 192  |
| 10         | Normal| 2555 ± 297 | 1102 ± 378 | 822 ± 240  |
|            | Deep  | 2621 ± 458 | 1171 ± 225 | 689 ± 245  |

Table 6. The summary statistics of the BTO estimation using the causal IGCI approach with the integral approximation estimator, without a threshold, for both groups and every condition. Positive values mean that the RR interval seems to cause tidal volume curve. The greater the absolute value, the stronger the “causal” connection.

| Group | Condition       | Statistics |
|-------|----------------|------------|
| A     | Supine         | 0.41 ± 0.68|
|       | Standing       | 0.35 ± 0.84|
| B     | Normal 6 BPM   | −0.07 ± 0.60|
|       | Deep 6 BPM     | 0.33 ± 0.61|
|       | Normal 10 BPM  | 0.03 ± 0.42|
|       | Deep 10 BPM    | −0.09 ± 0.40|
|       | Normal 15 BPM  | 0.04 ± 0.40|
|       | Deep 15 BPM    | 0.03 ± 0.33|
**Figure 5.** Sample BTO estimation for the whole protocol acquired from a Group B participant (#7); using only the TD Manhattan kernel with threshold, with shifts from $-2s$ to $5s$. For the last part of the signal (15 BPM breathing rate), the second period appears to decrease the distance between the analyzed tidal volume and tachogram curves for shifts close to $5s$.

**Figure 6.** Sample BTO estimation for the whole protocol, assessed for the signals acquired from a supine Group A participant (#1) and a Group B participant (#7); estimation used an IGCI causal approach with the integral approximation estimator, without a threshold. Blue areas suggest the RR interval to be causing the tidal volume curve, red ones - the opposite relation.
4. Discussion

Causality analysis appears to be a promising tool to extend the classical approaches of cardiorespiratory analysis and enable answers to new physiological questions. For instance, it can be used by practitioners to identify optimal training schedules based on the individual set of parameters and the strengths of cardiorespiratory relationships, to establish sufficient training loads, and to promote desirable progress during a training cycle and high performance during competition [6,7].

However, in a traditional approach, a possible graph of connections is treated rather as an input, "prior information" based on medical knowledge. We would like to emphasize the opposite approach, in which the results of the causality analysis, e.g., a graph, G-causalities, or others, might be used as the input. We call this the "bottom-up" strategy. The training can be designed to achieve optimal parameters. The connections and their directions and strengths may indicate which changes in the training schedule may be applied with the expectation of specific results [6, 7].

A relatively similar approach, though without the causal component, was done for school-aged children by Gasior et al. [20]. HR was found to be the principal predictor of all standard HRV parameters. Hence, the presented analysis may be extended using those observations.

Both cardiac and respiratory signals are very objective (compared to psychological questionnaires), particularly during established tests, like the orthostatic maneuver. This makes the analysis sensitive and reproducible. Different parts of the signal may show different issues, e.g., adaptation, recovery status, etc.

As so-called global methods deal with entire signals, there is a need to supplement the chain of possible levels of analysis with a method that assesses the local temporal orders.

In our opinion, the presented concept may be used primarily to test the temporal stability of relationships. This has already been discussed by Porta et al. [21], in the context of different physiological phenomena. The stability can be described as strong when the course of the causal vector (from statistical approaches) over time is almost constant. Protocol changes, like switching from supine to standing, may be compared with possible changes in explored BTO. Stable connections may also improve the prediction in counterfactual cases [22].

Probably the most interesting finding from the sample analysis is that the precedence of the tachogram curve before the tidal volume curve is relatively greater (while still being synchronized) when the breathing is forced to be slower. This may be connected to the idea of slow breathing as an intervention that subjects may practice to benefit health (particularly cardiovascular) [23]. Here, the relation between depth of breathing and causal vector values appeared insignificant; however, to maintain a lower breathing rate without disturbing respiratory homeostasis, tidal volume must be increased (the relation between temporal and amplitude ventilation coefficients [23]). Moreover, the effects of slow breathing reviewed by Russo et al. appear accessible to...
study using BTO estimation. This issue certainly requires a further look.

In our opinion, various improvements may be further considered, based on the different:

- pre-processing, e.g., non-linear transformations, introducing weights for different depths of shifts;
- post-processing, e.g., analyzing the lengths of series of sub-maximum values during a stable segment of data (red areas in the figures); or
- kernels, e.g., considering Bayesian methods or deep-learning-based approaches.

The most significant limitation of the current version of the algorithm is the bivariate input. If the transition from bivariate (BTO) to multivariate (MTO) estimation is introduced, the range of possible physiological problems that can be covered will be wider.

Other limitations include the adaptation of the currently used kernels to the specific cardiorespiratory data characteristics and the relatively substantial dependence of the results on the input parameter settings.

5. Summary

A technique for exploring bivariate temporal orders (BTO) in physiological data was introduced using the example of cardiorespiratory data (tachogram and tidal volume curves) in two groups (elite athletes and control). Two different approaches (statistical and causal) were proposed. The first uses linear modeling or time series distance calculation. The second, based on information geometric causal inference (IGCI), utilizes two estimators (based on entropy and integral approximation).

The method can be used as a step during causality analysis, as it may show the stability of the temporal orders over time, and also highlight the similar part of the signals (which can be then compared with events in the study protocol).

Respiratory sinus arrhythmia seems to be visible in the results, particularly for the supine body position. The mean causal vector was $571\text{ms}$ for supine and $431\text{ms}$ for standing body positions. The phenomenon is better visible for regular curves in Group A than for the breathing protocol in Group B.

The results also suggested that the rate of breathing has a greater impact on the mean value of the causal vector than does the depth of breathing. Interestingly, the RR interval curve precedes the tidal volume more when breathing is slower. On the other hand, the stability of the relation is the highest for the highest breathing rate.

The R package, supplementing this paper, enables calculation of bivariate temporal orders for different data sets or even different studies and research areas.
Supplementary Materials

S1 - R package (BTO) documentation

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