Is Human Atrial Fibrillation Stochastic or Deterministic?

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Abstract

The mechanism of atrial fibrillation (AF) maintenance in humans is yet to be determined. It remains controversial whether cardiac fibrillatory dynamics are the result of a deterministic or a stochastic process. Traditional methods to differentiate deterministic from stochastic processes have several limitations and are not reliably applied to short and noisy data obtained during clinical studies. The appearance of missing ordinal patterns (MOP) using the Bandt-Pompe (BP) symbolization is indicative of deterministic dynamics, and is robust to brief time series, and experimental noise. Our aim is to evaluate whether human AF dynamics are the result of a stochastic or a deterministic process. We use 38 intracardiac atrial electrograms during AF from the coronary sinus of 10 patients undergoing catheter ablation of AF. We extract the intervals between consecutive atrial depolarizations (AA interval) and convert the AA interval time series to their BP symbolic representation (embedding dimension 5, time delay 1). We generate the amplitude-adjusted, Fourier-transform surrogate data that have the same frequency spectrum and autocorrelation with the original time series. Using the BP symbolization, we compare the number of MOPs and the rate of MOP decay in the first 1000 timepoints of the original time series with that of the surrogate data. We calculate permutation entropy and permutation statistical complexity, and represent each time series on the causal entropy-complexity plane. We demonstrate that (a) the number of MOP in human AF is significantly higher compared to the surrogate data (range 0-41 vs. 0-13), and (b) the median rate of MOP decay in human AF is significantly lower compared with the surrogate data (6.58x10^-3 vs. 7.59x10^-3, p<0.01). On the causal entropy-complexity plane, human AF is of higher complexity for the same entropy levels compared with the surrogate data. This analysis suggests that human AF dynamics arises from a deterministic process. Our result justifies the development and application of mathematical analysis and modeling tools to enable predictive control of human AF.
Atrial fibrillation (AF) is the most common cardiac arrhythmia in human beings, and is associated with significant morbidity and mortality. The current standard of care is interventional catheter ablation, but the success rate is limited. The major limitation of the current approach to AF is the lack of fundamental understanding of its underlying mechanism. Specifically, it remains unclear whether human AF dynamics are a deterministic or a stochastic process. Here we assess for determinism in human AF by evaluating the properties of the symbolic representation of intracardiac electrical recordings obtained from patients. Specifically, we evaluate (a) the number of the missing ordinal patterns, (b) the rate of missing ordinal pattern decay for increased length of the time series, and (c) the causal-entropy complexity plane of the Bandt-Pompe symbolic representation. When used together, these are powerful tools to detect determinism, even in the presence of experimental noise and brief time series.
I. INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia in humans, with an increasing prevalence that is estimated to rise to 12.1 million in 2030 in the United States, and a significant morbidity and mortality associated with it.\(^1\) AF is characterized by an “irregularly irregular” heart rhythm and a seemingly disorganized activation of the left and right atrium.\(^2\) The current therapeutic approach to AF using interventional catheter ablation has modest efficacy, with recurrence rates up to \(\sim 30\%\).\(^3\)-\(^5\) The main reason for those disappointing clinical outcomes is that, despite the advancement in mapping and catheter ablation technology, the mechanisms of AF maintenance in human are yet to be determined. For example, to describe human AF dynamics, both deterministic\(^6\)-\(^10\) and stochastic\(^11\), \(^12\) models have been developed. It remains controversial whether human AF dynamics results from a deterministic or a stochastic process.\(^13\)-\(^16\)

Elucidating whether the disorganized dynamics observed in human AF is the result of a deterministic or a stochastic process is essential for a proper physical description of AF. Identifying determinism in AF time series is critically important for understanding the mechanism of, modeling, and predicting AF. Dynamics arising from deterministic processes can be described with relatively few non-linear modes, while dynamics arising from stochastic processes are better described by statistical approaches. Deterministic dynamics is predictable on relatively short time scales and might form stable attracting patterns in the phase space, while stochastic processes are random at any time step and do not form attractors. Discrimination between deterministic and stochastic dynamics can be extremely challenging, especially when the time series under investigation are contaminated with experimental noise, since both processes share many features.\(^17\) Traditional methods for detecting deterministic chaos such as the correlation dimension,\(^18\) Kolmogorov entropy,\(^19\) Lyapunov exponents,\(^20\) nonlinear forecasting models,\(^21\) determinism test,\(^22\) noise titration,\(^23\) and 0–1 test\(^24\) are not readily applicable to biomedical recordings as they are sensitive to experimental noise, require long and/or stationary time series, and/or are sensitive to initial parameter selection. Furthermore, all these tests are not fully reliable and have several limitations.\(^25\)-\(^33\)

Symbolic representation of theoretical and experimentally acquired time series, with ordinal patterns using the Bandt and Pompe’s (BP) methodology has given a new insight in time series characterization and detection of determinism.\(^34\) The emergence of ordinal patterns that never appear in a time series of adequate length (“forbidden ordinal patterns” or FOP) distinguishes deterministic processes from uncorrelated stochastic processes.\(^34\)-\(^37\) Amigó et al. demonstrated that the decay rate of the missing ordinal patterns (MOP) as a function of the time series length can be used to distinguish deterministic from stochastic processes in relatively short and noisy time series.\(^35\), \(^36\), \(^38\) The term MOP over FOP is preferred in analysis of time series contaminated with experimental noise, since all ordinal patterns will eventually emerge if these time series are of adequate length, and thus are not truly “forbidden” but “missing” in a specific time series length segment. Furthermore, the analysis of the BP symbolic representation has been extended
by linking it to the causal entropy-complexity plane. Calculation of permutation entropy and permutation statistical complexity of the BP symbolic representation of the time series under investigation, and representation of the results on the causal entropy-complexity plane, is a powerful tool for detection of determinism. The causal entropy-complexity plane can discriminate deterministic series contaminated with correlated noise from pure noise with long-term correlations.

The purpose of this study is to assess whether human AF dynamics is the result of a deterministic or a stochastic process using the Bandt-Pompe symbolization, and assessing MOP and the symbolic time series representation on the entropy-complexity plane. Our hypothesis is that human AF is a deterministic rather than a stochastic process and that evidence of determinism can be detected in AF time series. To test our hypothesis, we record intracardiac bipolar atrial electrograms of AF from the coronary sinus of patients referred for catheter ablation of AF. We extract the intervals between consecutive atrial depolarizations (AA interval) as representative of the local atrial macroscopic dynamics. We generate the amplitude-adjusted, Fourier-transform (AAFT) surrogate data that have the same frequency spectrum and autocorrelation with the original time series. We construct the BP symbolic representation of the AA interval time series and the surrogate data, and compare the number of MOP and the rate of MOP decay. The null hypothesis is that the AA time series is a rescaled Gaussian linear stochastic process, and thus the number of MOP and rate of MOP decay will be the same between AA time series and surrogate data. If the null hypothesis is rejected, then the system is nonlinear deterministic. We also calculate permutation entropy and permutation statistical complexity of the BP symbolic representation of AA time series and surrogate data, and plot the results on the causal entropy-complexity plane.

II. METHODS

A. Intracardiac Recordings

We enrolled 10 patients who were referred for a standard catheter ablation for symptomatic, drug-refractory AF at the Johns Hopkins Hospital between August 2017 and October 2017. The protocol was approved by the Johns Hopkins Medicine Institutional Review Board and all participants provided written informed consent. All patients underwent pre-procedural transesophageal echocardiogram to rule out intracardiac thrombus. A 5-Fr decapolar catheter (Dynamic Tip 2-5-2 Boston Scientific, Marlborough, MA; inter-electrode distance 2 mm between poles and 5 mm between bipolar pairs) was introduced from the right femoral vein into the coronary sinus. In one patient that presented in sinus rhythm, AF was induced by burst pacing. Induced AF was mapped after > 15 min. Intracardiac bipolar electrograms during AF using 3-5 pairs of two immediately adjacent electrodes were recorded at the sampling frequency.
of 977 Hz for the duration of 1.88 to 3.26 minutes by the standard clinical electrophysiology recording system (CardioLab, GE Healthcare, Waukesha, WI). The surface 12-lead electrocardiogram was also recorded simultaneously. We filtered the recorded time series and removed the ventricular signals as previously described41 (Figure 1). We excluded from analysis recordings with high levels of noise that preclude visual identification of atrial signals. Finally, we included a total of 38 intracardiac recordings, as adjudicated by two clinical cardiac electrophysiologists. We defined the atrial depolarization as any peak exceeding 0.02 mV in amplitude located at least 102 msec away from the prior peak, which is shorter than the atrial effective refractory period in all cases. We confirmed the accurate identification of atrial depolarization with visual inspection of all detected peaks and we made adjustments on the peak detection thresholds, if necessary, to ensure accurate identification of atrial depolarization. We defined the AA interval as the time interval between two consecutive atrial depolarizations.

B. Surrogate Data

The BP symbolization has been used in an AAFT surrogate data framework for the detection of non-linear determinism in both theoretical and experimental time series. The presence of a higher number of MOP in the time series under examination and AAFT surrogate data and
for a time series, and for \( D=5 \) all possible ordinal patterns are depicted in Figure 2. Ordinal patterns that have not appeared in a length \( L \) of time series are called missing ordinal patterns (MOP).  

Amigó et al. demonstrated that the rate of decay of MOP for increasing \( L \) can be used to discriminate deterministic time series contaminated with noise from pure uncorrelated noise. Specifically, the number of MOP decays exponentially with increasing \( L \) and the rate of decay is significantly different from that of uncorrelated stochastic processes. MOPs can be used to detect determinism even in the setting of irregular-sampling, missing data, and timing jitter. MOPs have been used to detect determinism in financial time series and epileptic brain states. A major limitation of this method is the inability to differentiate deterministic processes from stochastic processes that exhibit long-term correlations. Specifically, the persistence of MOP is not necessarily a signature of underlying determinism, because this same persistence is found in stochastic time series with long term correlation structures. To overcome this limitation, Kulp used AAFT surrogate data and the BP MOP paradigm, to detect non-linear determinism in both theoretical and experimental deterministic time series and distinguish them from correlated stochastic time series.

For the purposes of our analysis we used the first 1,000 time steps (= 1,000 atrial depolarizations) of the AA time series and surrogate data, to ensure that the analyzed time series will be of the same length. We used \( D = 5 \) and \( \tau = 1 \) to assure adequate sampling of the time series \([1000 > (5+1)! = 720]\). We calculate the number of MOP. Subsequently, for each time
series, we calculated the rate of MOP decay for increasing length \( L \) (\( 5 \leq L \leq 1000 \)) by fitting an exponential function of the type:

\[
MOP(L) = MOP_0 e^{-bL}, \quad 5 \leq L \leq 1000 \tag{1}
\]

Here, \( MOP(L) \) is the number of MOP at time series length \( L \), \( MOP_0 \) is the number of missing patterns at \( L=5 \) and \( b \) is the time constant for the exponential decay and represents the decay of MOPs. Smaller values of \( b \) mean slower decay and are consistent with deterministic over stochastic time series.\(^{36,38}\) We compared the number of MOP and the rate of MOP decay in the AA time series and surrogate data using the Mann-Whitney U statistical test. If the number of MOP is higher and the rate of MOP decay is lower in the AA time series compared to surrogate data we then reject the null hypothesis that the AA time series is a rescaled Gaussian linear stochastic process, and the AA time series are nonlinear deterministic.\(^{42}\) The probability of falsely rejecting the null hypothesis is equal to the two-sided p-value derived from the Mann-Whitney U test.

**D. Causal Entropy-Complexity Plane**

Each time series \( X \) is represented on the causal entropy-complexity plane \( \mathcal{H}[P] \times C_{JS}[P] \) as a point \( (\mathcal{H}[P], C_{JS}[P]) \).\(^{17,39}\) Here \( \mathcal{H}[P] \) is the permutation entropy and \( C_{JS}[P] \) the permutation statistical complexity of the probability distribution \( P \), of the observed ordinal patterns \( \pi \) in the time series \( X \).\(^{17,39}\) Calculation of permutation entropy and permutation statistical complexity are described in detail in *Supplemental Materials (Appendix B)*. Shannon entropy-based measures quantify the information content, or uncertainty, associated with the physical process described by \( P \),\(^{54}\) but do not quantify the degree of structure or patterns of the process.\(^{55}\) Measures of statistical complexity are necessary to capture the organizational properties of the process\(^{56}\), to detect essential details of the dynamics, and to differentiate different degrees of periodicity and chaos.\(^{57}\) The BP symbolization takes into account the time-causality in the derivation of the probability distribution \( P \) associated to the time series under investigation.\(^{34}\)

The causal entropy-complexity plane of the BP symbolic representation of a time series has been used to detect determinism in time series\(^{17}\) and to distinguish deterministic time series contaminated with correlated noise from purely correlated noise.\(^{39}\) Specifically, deterministic time series, even if contaminated with correlated noise (of various intensity and strength of correlation), maintain higher complexity levels for the same entropy levels on \( \mathcal{H}[P] \times C_{JS}[P] \) plane.\(^{39}\) Because the probability distribution is derived from the Bandt and Pompe methodology, all the advantages associated with it, including simplicity, low computational cost, robustness, and invariance with respect to monotonous transformations, are inherited by the \( \mathcal{H}[P] \times C_{JS}[P] \) plane analysis.
For the purposes of our study we estimated the permutation entropy and permutation statistical complexity for each AA time series and surrogate data. We plot each time series as a point on the $\mathcal{H} [P] \times C_{JS}[P]$ plane. To statistically compare the position of the two curves on the $\mathcal{H} [P] \times C_{JS}[P]$ plane we fitted a separate quadratic regression curve to the points derived from the AA time series and the points derived from the AAFT surrogate data using a least squares technique. If the fitted curve of the AA time series follows a higher complexity trajectory compared to the fitted curve of the surrogate data, we reject the null hypothesis that the AA time series is a rescaled Gaussian linear stochastic process, and the AA time series are nonlinear deterministic. The probability of falsely rejecting the null hypothesis is equal to the two-sided p-value comparing the regression coefficients of the AA time series to the AAFT surrogate data.

The goodness-of-fit of the linear regression was assessed with the coefficient of determination of the regression model. The coefficient of determination, is the proportion of the variance of $C_{JS}[P]$ that is predictable from $\mathcal{H}[P]$. A coefficient of determination of $>90\%$ indicates that the model fits the data very well and a coefficient of determination of $100\%$ indicates that the model fits the data perfectly.

**Figure 3:** Examples of processed intracardiac recordings, corresponding AA time series and surrogate data from 5 patients. Each row represents one bipolar recording from different patient. The first column shows the first 2 seconds of the intracardiac bipolar electrograms. Second column shows the AA interval of the first 1000 atrial depolarizations (dark green). Third column shows the AAFT surrogate data derived from the AA series of the second column (dark red). Fourth column shows the AA time series (dark green) superimposed to surrogate data time series (dark red) to facilitate visual comparison.
III. RESULTS

A. Intracardiac Recordings and Surrogate Data

Figure 3 shows the intracardiac bipolar electrograms, the AA time series, and the corresponding surrogate data obtained from five patients. Each atrial depolarization in the bipolar electrograms contained 2-4 sharp, high-frequency deflections, although the exact morphology of the atrial electrograms varied among patients, leads, and atrial depolarizations. The bipolar electrograms contained the electrical activity of various frequency and amplitude, which represents local fragmented electrical activity, far field signals, and/or noise. Those are inherently passed on to the AA time series. Overall, the AA time series showed the stereotypical “irregularly irregular” interval behavior of AF. The length of the AA time series was 1,026 to 1,297 time steps. We used only the first 1,000 time steps for analysis to allow comparative assessments among different patients. The mean (± standard deviation) AA interval of the original AA time series was 168.4 ± 32 ms (25th -75th percentile was 150.5 - 183.2 ms). The mean AA interval of the AAFT surrogate data was 168.2 ± 31 ms (25th -75th percentile was 151.5 - 182.2 ms), which was similar to that of the original AA time series. This is consistent with the AAFT surrogate data design described above.

Figure 4: Frequency histograms of the number of missing ordinal patterns that emerge in the experimental AA time series data (blue) and the surrogate data (red). The number of missing ordinal pattern in the experimental time series is lower than that of the surrogate data suggesting that AF dynamics are deterministic.
B. Missing Ordinal Patterns and Rate of Missing Ordinal Pattern Decay

The mean (± standard deviation), the median, and the range of the number of MOP in the AA time series was 2.8±7.3, 1, and 0 - 41 (25th-75th percentile range: 0 - 2), respectively. The number of MOP in the AA time series was significantly higher than the number of MOP in the AAFT surrogate data that had a mean of 0.89±2.2, a median of 0, and a range of 0 - 13 (25th-75th percentile range: 0 – 1). The frequency histogram of the number of MOP for the AA time series and the AAFT surrogate data is shown in Figure 4. The p-value from the Mann-Whitney U comparing the number of MOP in the AA time series and the AAFT surrogate data was 0.010. This indicates that the null hypothesis was rejected, therefore the AA time series is a result of a nonlinear deterministic process with 99% confidence.

The mean, the median and the range of the time constant of MOP decay of the AA time series as defined by (1) was 6.58×10⁻³ ± 1.89×10⁻³, 6.58×10⁻³, and 5.33×10⁻³ - 7.88×10⁻³ (25th-75th percentile range), respectively. The time constant of MOP decay in the AA time series was significantly lower than the time constant of MOP decay of the AAFT surrogate data that had a mean of 7.37×10⁻³ ± 1.17×10⁻³, a median of 7.59×10⁻³, and a 25th-75th percentile range of 6.78×10⁻³ - 8.15×10⁻³. An example of the MOP decay with increasing time series length is shown in Figure 5A: graph demonstrating an example of the exponential decay of the number of missing ordinal patterns with increasing length of the time series. This graph is created from data from one patient. Experimental AA time series are shown in blue and surrogate data is shown with red. Figure 5B: frequency histograms of missing ordinal patterns decay time constant observed in the experimental AA time series data (blue) and the surrogate data (red). The rate of missing ordinal pattern decay in the experimental time series is lower than that of the surrogate data suggesting that AF dynamics are deterministic.
in Figure 5a. The frequency histogram of the time constant of MOP decay for the AA time series and the AAFT surrogate data is shown in Figure 5b. The p-value from the Mann-Whitney U comparing the time constant of MOP decay in the AA time series and the AAFT surrogate data was 0.009. This indicates that the null hypothesis was rejected, therefore the AA time series is a result of a nonlinear deterministic process with >99% confidence.

C. Causal Entropy-Complexity Plane

Representation of the AA time series and the AAFT surrogate data over the causal entropy-complexity plane is shown on Figure 6. The lines represent the fitted least-square quadratic regression curve and the shaded areas the corresponding 95% confidence intervals of the AA time series and the AAFT surrogate data. The coefficient of determination of the quadratic model was 99.9%. The quadratic function fitted to the AA time series showed a trajectory in higher complexity levels compared to that of the AAFT surrogate data. The quadratic term for the surrogate data was larger by 0.041 (p = 0.005, 95% confidence interval 0.013 - 0.069), and the linear term was smaller by 0.040 (p = 0.004, 95% confidence interval -0.067 - -0.013). There was no difference in the intercept between the AA time series and the AAFT surrogate data. These p-values and confidence intervals suggest that the AA time series has a significantly higher
complexity than the AAFT surrogate data. This indicates that the null hypothesis was rejected, therefore the AA time series is a result of a nonlinear deterministic process with >99% confidence.

IV. DISCUSSION

A. Main Findings

Our findings indicate that human AF is the result of a deterministic, rather than of a stochastic process. The MOP analysis using BP symbolization is robust to clinical time series that are inherently noisy, and can be applied even in the setting of irregular-sampling, missing data, and timing jitter. The limitation of the MOP analysis to differentiate determinism from highly correlated noise is complemented by the causal entropy-complexity plane analysis and the use of AAFT surrogate data. Analysis of the intracardiac data with both methodologies yielded consistent results that AF time series are non-linear deterministic with >99% confidence.

B. Determinism of Atrial Fibrillation

To our knowledge, this is the first study to demonstrate determinism of human AF using the BP methodology. The MOP analysis has been used to evaluate the determinism of heart rate variability which reflects the autonomic function rather than cardiac dynamics, but it has never been applied to human AF. Our findings help to improve our understanding of human AF at multiple levels. For example, our results validate the effort to develop a non-linear deterministic model to simulate AF. In addition, our results justify the use of nonlinear dynamical tools to describe AF properties. Furthermore, our result suggests that the dynamical behavior of AF is theoretically predictable, at least on short time scales, while on longer time scales AF has the potential to form attractors in a phase-space that could be used for long-term statistical predictions. Moreover, our result indicates that AF can potentially be controlled because it is deterministic.

In light of the pool of the literature evaluating the determinism in human AF, our work is highlighted by the application of novel methodology to address the limitations of earlier studies. To date, there are only three studies available that directly evaluated the determinism of human AF, and their conclusions were conflicting. Two of those studies (n=5 and 7) found determinism in AF, and the other study failed to demonstrate determinism (n=9). In those earlier studies, the methods to detect determinism in human AF included Poincaré plot analysis, Grassberger-Procaccia correlation dimension, correlation entropy, coarse-grained correlation dimension and coarse-grained correlation entropy, Lyapunov exponent, Kolmogorov entropy, and Lempel-Ziv complexity. All of those methods are limited by the sensitivity to experimental noise, low robustness with shorter durations of time series, and the sensitivity to initial parameter selection. In addition, the Grassberger-Procaccia method and Lyapunov exponents could falsely
classify highly correlated stochastic time series as deterministic. The critical strength of our work is that we used a combination of the BP symbolization with the Amigó methodology and the causal entropy-complexity plane, both of which are robust against all of those limitations. Importantly, the two separate methods showed consistent results. Another strength of our work is that we used the AAFT surrogate data. Only one of the earlier studies described above used a surrogate data framework. The use of surrogate data is critical for accurate evaluation of time series that have the potential to be contaminated by noise. The AAFT surrogate data have been used with the BP MOP paradigm successfully, in both theoretical and experimental settings. We used the causal entropy-complexity plane of the BP symbolization of the AA time series and the AAFT surrogate data to differentiate deterministic time series from highly correlated noise. In addition, we used rigorous statistical analyses to quantify the confidence of our findings using a relatively large sample size.

Last, several studies provide indirect evidence of determinism in AF. For example, simulation studies suggest that AF may arise through a quasiperiodic transition to chaos, and conversion from AF to atrial flutter is a phase transition. In human AF, spatiotemporal organization of atrial electrical activity has been demonstrated. In addition, human AF had higher values of several nonlinear parameters such as Lyapunov exponent, Kolmogorov entropy, and Lempel-Ziv complexity compared to human typical atrial flutter. However, an additional strength of our work is that it provides direct evidence of determinism in AF.

C. Limitations

Our findings may be applicable only to the location of the catheter-based intracardiac recordings of AF. For example, our data derived exclusively from the coronary sinus, which is anatomically adjacent to the inferior aspect of the left atrium. It is possible that intracardiac measurements from other parts of the left atrium or the right atrium may have led to a different result. However, we chose to use the electrograms from the coronary sinus because its anatomical structure allows persistent stabilization of the measurement catheter for the entire duration of measurements to minimize motion-induced noise in the beating human heart.

D. Conclusions

Analysis of human AF using missing ordinal patterns and the causal entropy-complexity plane of the Bandt-Pompe symbolization, in a surrogate data framework, suggests that it is driven by a deterministic process. Our results justify the development and application of mathematical analysis and deterministic modeling tools to enable predictive control of human AF.
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Appendix A. The Bandt-Pompe Symbolization

Let $X = \{x_n: n = 1, 2, \ldots, N\}$ be the one-dimensional time series under investigation with length $N$. To define ordinal patterns $\pi$ of length $D$ ($D \in \mathbb{N}$) and embedding delay $\tau$ ($\tau \in \mathbb{N}$) we first assign to each time a $D$-dimensional vector with the values of the time series $X$ at times $n, n-1, \ldots, n-(D-1)\tau$, such as:

$$(X) \mapsto (x_{n-(D-1)\tau}, x_{n-(D-2)\tau}, \ldots, x_{n-1\tau}, x_n) \quad (S1)$$

We then assign to each vector the permutation $\pi = (r_0, r_1, \ldots, r_{D-1})$ of $\{0, 1, \ldots, D-1\}$ such that $x_{n-r_{D-1}} \leq x_{n-r_{D-2}} \leq \cdots \leq x_{n-r_0}$. To get a unique correspondence of $\pi$ to the vector defined in $(S1)$ we set $r_i < r_{i-1}$ if $x_{n-r_i} = x_{n-r_{i-1}}$. For example, the ordinal pattern with $D=5$ and $\tau=1$ of the first vector [as defined in $(S1)$] of the sample AA time series shown in Figure 3 (202.6, 133.1, 169.9, 192.4, 180.1) would be the pattern $(5,1,2,4,3)$. The set of all possible permutations $(r_0, r_1, \ldots, r_{D-1})$ of $\{0, 1, \ldots, D-1\}$ is $S_D$, and for $D=5$ all possible ordinal patterns are depicted in Figure 2. The subset of $S_D$ that appears in the orbits of $X$ is called allowed or admissible ordinal patterns for $X$, while the subset of $S_D$ that never appears in the orbits of $X$ is called forbidden ordinal patterns (FOP) for $X$. With $|\cdot|$ denoting the cardinality of a set, the number of FOP is defined as:

$|\{\pi \in S_D: \pi \text{ forbidden for } X\}| = |S_D| - |\{\pi \in S_D: \pi \text{ admissible for } X\}| \quad (S2)$

The length $N$ of the time series under investigation should be $N \gg D! + D - 1$ and preferably $N \geq (D+1)!$ to avoid undersampling and allow for true FOP to emerge.\textsuperscript{38} For practical purposes Bandt and Pompe suggest to estimate the frequency of ordinal patterns using $3 \leq D \leq 7$ and time lag $\tau = 1$.\textsuperscript{34} In deterministic time series FOP emerge, while in stochastic time series all ordinal patterns are admissible. In deterministic time series contaminated with noise all ordinal patterns are admissible, if the length of the time series is adequate, and thus determinism cannot be ascertained by pure observation for the emergence of FOPs. However, at any given length $L$ ($D \leq L \leq N$) of the time series, ordinal patterns might have not appeared yet. Ordinal patterns that have not appeared in a length $L$ of time series are called missing ordinal patterns (MOP).\textsuperscript{35,36,46} The existence of a non-observed ordinal pattern does not qualify it as “forbidden”, but only as “missing”, and this is due to the finite length $L$. 

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Appendix B. Permutation Entropy and Permutation Statistical Complexity

To calculate the permutation entropy, we first derive the probability distribution \( P \) of the BP ordinal patterns \( P = \{p(\pi)\} \); \( p(\pi) \) can be easily calculated as the relative frequency that each pattern \( \pi \) is observed in the time series (S3):

\[
p(\pi) = \frac{|\{x | x \leq L - D + 1; (x), \text{has type } \pi\}|}{L - D + 1} \quad (S3)
\]

Here the operator \(| \cdot |\) denotes set cardinality, \( D \) is the length of the ordinal pattern and \( L \) is the length of the time series under investigation. Shannon entropy of the probability distribution \( P \) is defined as:

\[
H_S[P] = - \sum_{\pi=1}^{D!} p(\pi) \ln[p(\pi)] \quad (S4)
\]

The normalized Shannon entropy of the probability distribution \( P \) is defined as \( H[P] = H_S[P]/H_{S,\text{max}} \), where \( H_{S,\text{max}} = H_S[P_u] \) and \( P_u \) is the uniform distribution with \( D! \) elements such as \( P_u = \{ \frac{1}{D!}, \ldots, \frac{1}{D!} \} \) that results in \( H_{S,\text{max}} = \ln D! \), and thus:

\[
H[P] = - \frac{1}{\ln D!} \sum_{\pi=1}^{D!} p(\pi) \ln[p(\pi)], \quad 0 \leq H[P] \leq 1 \quad (S5)
\]

Shannon entropy is a measure of information content, or uncertainty associated with the physical process described by \( P \).\(^{54}\) When the probability distribution \( P \) is derived from the BP symbolic representation, \( H[P] \) is called permutation entropy.

Shannon entropy however does not quantify the degree of structure or patterns of a process.\(^{55}\) Measures or statistical complexity are necessary to capture the organizational properties of a process.\(^{56}\) The MPR-statistical complexity was introduced by Rosso et al. as an effective statistical complexity measure that can be used to detect essential details of the dynamics and differentiate different degrees of periodicity and chaos.\(^{57}\) The MPR-statistical complexity can be easily calculated as the product\(^{63}\)

\[
C_{JS}[P] = Qf[P, P_u] \cdot H[P] \quad (S6)
\]

Where:

\[
Qf[P, P_u] = Q_0 \cdot J[P, P_u] \quad (S7)
\]

\[
J[P, P_u] = H_S\left[\frac{P + P_u}{2}\right] - \frac{H_S[P]}{2} - \frac{H_S[P_u]}{2} \quad (S8)
\]
\[ Q_0 = -2 \left\{ \frac{D! + 1}{D!} \ln(D! + 1) - 2 \ln(2D!) + \ln(D!) \right\}^{-1} \quad (S9) \]

Here, \( \mathcal{H} [P] \) is the permutation entropy of the probability distribution \( P \) as defined in (S5), and \( Q_J[P, P_u] \) is a disequilibrium term. \( Q_J[P, P_u] \) is defined in (S7) as the Jensen-Shannon divergence \( \mathcal{I}[P, P_u] \) between the probability distribution \( P \) of the BP ordinal patterns observed in the time series and the \( P_u \) uniform distribution (S8), normalized by a constant \( Q_0 \). The Jensen–Shannon divergence, quantifies the difference between two probability distributions, and is especially useful to compare the symbol-composition of different time series.\(^{64}\) The normalization constant \( Q_0 \) is equal to the inverse of the maximum value of \( \mathcal{I}[P, P_u] \) (S9). Statistical complexity measures provide an additional insight into the nature of probability distribution of the system under investigation, in a way that cannot be captured in pure entropic measures.\(^{17,56}\) Statistical complexity measure uncover information related to the correlational structure between the components of the physical process under study.\(^{65}\) When the probability distribution \( P \) is derived from the BP symbolic \( C_{JS}[P] \) is called permutation statistical complexity.
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