Vector Autoregressive Fractionally Integrated Models to Assess Multiscale Complexity in Cardiovascular and Respiratory Time Series*

Aurora Martins[1], Celestino Amado[1], Ana Paula Rocha[1], Maria Eduarda Silva[2]
Riccardo Pernice[3], Michal Javorka[4] and Luca Faes[3]

***Abstract*— Cardiovascular variability is the result of the activity of several physiological control mechanisms, which involve different variables and operate across multiple time scales encompassing short term dynamics and long range correlations. This study presents a new approach to assess the multiscale complexity of multivariate time series, based on linear parametric models incorporating autoregressive coefficients and fractional integration. The approach extends to the multivariate case recent works introducing a linear parametric representation of multiscale entropy, and is exploited to assess the complexity of cardiovascular and respiratory time series in healthy subjects studied during postural and mental stress.**

I. Introduction

An intrinsic feature of cardiovascular oscillations is their dynamical complexity, which results from the fact that such oscillations reflect the combined activity of several mechanisms of physiological regulation [1]. Since these mechanisms typically operate across multiple temporal scales, e.g. reflecting thermoregulatory or neural parasympathetic and sympathetic control, a surge of interest has recently emerged in methods able to assess the so called multiscale complexity of cardiovascular oscillations. The main approach in this case is multiscale entropy (MSE) [2], which computes the conditional entropy (CE) of an individual time series (typically, heart period (HP) variability) as a function of the time scale at which the series is observed. After its definition, MSE has been refined in order to meet requirements typical of the study of cardiovascular oscillations, such as the joint detection of the complexity of several variables [3] (e.g., besides HRV, also systolic arterial pressure (SAP) or respiratory movements (RESP)) or the detection of complexity from short time series (typically, few hundred beats) [4], [5]. In this context, the present work introduces a novel method to assess multivariate and multiscale complexity of cardiovascular oscillations. The method is based on fitting a multivariate time series with a vector autoregressive fractionally integrated (VARFI) model, and on exploiting the theory of state space models to provide the multiscale representation of the VARFI parameters and obtain from them a multiscale and multivariate measure of complexity. Compared to previous works [3], [4], [5], [6], the proposed VARFI approach allows: (i) to work reliably on short time series thanks to its parametric formulation; (ii) to account for long-range correlations in addition to short-term dynamics thanks to fractional integration; (iii) and to assess the overall complexity of multivariate time series thanks to its vector formulation. Here, it is evaluated on HP, SAP and RESP time series measured in healthy subjects in a resting supine condition and during postural stress induced by head-up tilt and mental stress induced by mental arithmetics.

II. Methods

A complexity measure for a multivariate M-dimensional dynamic process $\mathbf{X} = [X_1, \ldots, X_M]$ is the entropy rate

$$C_{\mathbf{X}} = H(\mathbf{X}_n|\mathbf{X}_n^-) = H(\mathbf{X}_{n+1}^-) - H(\mathbf{X}_n^-) \quad (1)$$

where $\mathbf{X}_n = [X_{1,n}, \ldots, X_{M,n}]$ and $\mathbf{X}_n^- = [\mathbf{X}_{n-1}\mathbf{X}_{n-2}...]$ are the vector variables describing the present and the past states of the process, and $H(\cdot|\cdot)$ and $H(\cdot)$ denote entropy and conditional entropy. If $\mathbf{X}_n$ has a joint Gaussian distribution, it can be described through a vector linear regression model fed by white and uncorrelated innovations $\mathbf{E}_n$, so that the conditional entropy of the present given the past can be expressed analytically in terms of the innovation covariance $\Sigma_{\mathbf{E}}$ as [7]:

$$H(\mathbf{X}_n|\mathbf{X}_n^-) = \frac{1}{2}\ln((2\pi \mathrm{e})^M|\Sigma_{\mathbf{E}}|). \quad (2)$$

In this work we provide an alternative definition of complexity, including in (2) a normalization of the innovation covariance to the process covariance $\Sigma_{\mathbf{X}}$, which is needed to define multiscale complexity where the process covariance changes with the time scale:

$$\overline{C}_{\mathbf{X}} = \frac{1}{2}\ln\left((2\pi \mathrm{e})^M \frac{|\Sigma_{\mathbf{E}}|}{|\Sigma_{\mathbf{X}}|}\right). \quad (3)$$

Here, following a parametric approach, we represent the process $\mathbf{X}$ through a VARFI model describing both short-term dynamics and long-range correlations [8]:

$$\mathbf{A}(L)\mathrm{diag}(\nabla^{\mathbf{d}})\mathbf{X}_n = \mathbf{E}_n \quad (4)$$

where L is the back-shift operator ($L^i\mathbf{X}_n = \mathbf{X}_{n-i}$), $\mathbf{A}(L) = \mathbf{I} - \sum_{i=1}^{p} \mathbf{A}_i L^i$ ($\mathbf{I}_M$ is the identity matrix), $\mathbf{A}(L)$ is a vector

*This work was partially supported by UID/MAT/ 00144/2019 (CMUP) and UID/MAT/04106/2019 (CIDMA), which are funded by FCT with national (MEC) and European structural funds through the program FEDER, under PT2020, and project STRIDE-NORTE-01-0145- FEDER-000033 funded by ERDF-NORTE 2020), PRIN 2017 PRJ-0167, "Stochastic forecasting in complex systems", and PON R&I 2014-2020 AIM project no. AIM1851228-2, University of Palermo, Italy.

[1]A. M., C. A. and A. P. R. are with Faculdade de Ciências, Universidade do Porto & CMUP, Portugal
[2]M. E. S. is with Faculdade de Economia, Universidade do Porto & CIDMA, Portugal
[3]R. P. and L. F. are with Department of Engineering, University of Palermo, Italy luca.faes@unipa.it
[4]M. J. is with Department of Physiology, Comenius University in Bratislava, Jessenius Faculty of Medicine & Biomedical Center Martin, Slovakia

autoregressive (VAR) polynomial of order p, and $\text{diag}(\nabla^{\mathbf{d}}) = \text{diag}[(1-L)^{d_i}]$, $i = 1,\dots,M$, where $(1-L)^{d_i}$ is the fractional differencing operator [9]. The parameter $\mathbf{d} = (d_1,\dots,d_M)$ determines the long-term behavior of the process X_i, while the coefficients of $\mathbf{A}(L)$ allow the description of the short-term dynamics.

Then, we identify the VARFI model as described in [5], using the Whittle semiparametric estimator to compute d_i individually for each process X_i and the ordinary least squares to compute the VAR parameters. The estimated VARFI model was approximated with a finite order VAR process, which was represented at any assigned scale τ exploiting the state space method defined in [10]. Finally, the multivariate complexity was computed inserting in (3) the innovation and process covariances derived at scale τ.

III. Application to cardiovascular variability

The proposed method is applied to the time series of HP, SAP and RESP ($\mathbf{X}$ = [RR, SAP, RESP]) (stationary windows of at least 400 beats) measured from 62 healthy subjects (19.5 ± 3.3 years old) in the resting supine position (SU_1), in the upright position (UP) reached through passive head-up tilt, in the recovery supine position (SU_2) and during mental stress induced by mental arithmetics (MA) [11].

Multiscale multivariate complexity was computed comparing the "eVARFI" approach described above, based on VARFI modeling, with the "eVAR" approach, based on pure AR modeling (i.e., $\mathbf{d} = \mathbf{0}$ in (4)). Significant changes in complexity between conditions (SU_1 vs. UP and SU_2 vs. MA) were assessed via a linear mixed-effects model incorporating the fixed-effects condition and scale, and subject-dependent intercept allowing for a random variation between subjects [12]. The estimated marginal means were computed for each difference [13] to evaluate the changes of interest, and a Z-test was applied to check the significance of these difference at a significance level $p < 0.05$.

Figure 1 presents the distributions of the complexity measure computed in the two conditions at different time scales τ. Considering both eVAR and eVARFI estimation, the multivariate complexity measure decreases significantly from SU to UP at scale 1, while no changes are observed at longer time scales. The decrease documents a simplification of the overall dynamics of HP, SAP and RESP, likely as a consequence of the weakening of respiration-related oscillations of HP and SAP which is indeed evident at short time scales during tilt [1], [4]. Here, the similarity between VAR and VARFI identification suggests that the impact of long-range correlations does not change substantially from rest to tilt.

From SU_2 to MA the multivariate complexity increases significantly for eVAR at all scales except 12, but decreases for eVARFI at scales 5 and 12. The increased complexity observed for eVAR at multiple time scales confirms previous results found for HP [4]. On the other hand, the decreased complexity observed using the new VARFI approach suggests that long-range correlations have a bigger impact on the cardiovascular and respiratory dynamics during mental stress. This result confirms the regularizing role of long-range correlations on physiological dynamics [6].

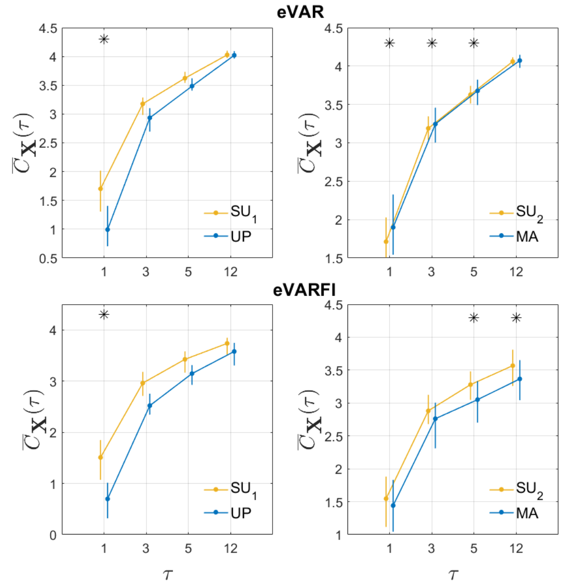

Fig. 1: Median and quartiles of the multiscale complexity measure $\overline{C}_{\mathbf{X}}(\tau)$ computed through eVAR and eVARFI approaches during postural (SU_1 vs. UP, left) and mental stress (SU_2 vs. MA, right). * indicate significant differences between conditions.

References

[1] M. A. Cohen, and A. J. Taylor, "Short-term cardiovascular oscillations in man: measuring and modelling the physiologies", *J. Physiol.*, vol. 542, no. 3, pp. 669-683, 2002.

[2] M. Costa, A. L. Goldberger, and C. K. Peng, "Multiscale entropy analysis of complex physiologic time series", *Phys. Rev. Lett.*, vol. 89, no. 6, pp. 068102, 2002.

[3] M. U. Ahmed, and D. P. Mandic, "Multivariate multiscale entropy analysis", *IEEE Sig. Proc. Lett.*, vol. 19, no.2, pp. 91-94, 2011

[4] L. Faes, A. Porta, M. Javorka, and G. Nollo, "Efficient computation of multiscale entropy over short biomedical time series based on linear state-space models", *Complexity*, vol. 2017, pp. 1768264, 2017.

[5] L. Faes, M. A. Pereira, M. E. Silva, R. Pernice, A. Busacca, M. Javorka, and A. P. Rocha, "'Multiscale information storage of linear long-range correlated stochastic processes"', *Phys. Rev. E*, vol. 99, no. 3, pp. 032115, 2019.

[6] W. Xiong, L. Faes, and P. Ivanov, "Entropy measures, entropy estimators, and their performance in quantifying complex dynamics: Effects of artifacts, nonstationarity, and long-range correlations", *Phys. Rev. E*, vol. 95, pp. 062114, 2017.

[7] A. B. Barrett, L. Barnett, and A. K. Seth, "Multivariate Granger causality and generalized variance", *Phys. Rev. E*,, vol. 81, pp. 041907, 2010.

[8] W. J. Tsay, "Maximum likelihood estimation of stationary multivariate ARFIMA processes", *J. Stat. Comp. Sim.*, vol. 80, pp. 729–745, 2010.

[9] J. Beran, Y. Feng, S. Ghosh, and R. Kulik, "Statistics for Long-Memory Processes: Probabilistic Properties and Statistical Methods", Springer, 2012.

[10] L. Faes, S. Stramaglia, G. Nollo, D. Marinazzo, "Multiscale Granger causality", *Phys. Rev. E*, vol. 96, pp. 042150, 2017.

[11] M. Javorka, B. Czippelova, Z. Turianikova, Z. Lazarova, I. Tonhajzerova, and L. Faes, "Causal analysis of short-term cardiovascular variability: state-dependent contribution of feedback and feedforward mechanisms", *Med. Biol. Eng. Comput.*, vol. 55, pp. 179–190, 2017.

[12] J. Pinheiro, D. Bates, "Mixed-Effects Models in S and S-PLUS", Springer, 2000.

[13] S. R. Searle, F. M. Speed, and G. A. Milliken, Population Marginal Means in the Linear Model : An Alternative to Least Squares Means, The American Statistician, vol. 34, pp. 216–221, 1980