On the pros and cons of using temporal derivatives to assess brain functional connectivity

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Abstract

The study of correlations between brain regions in functional magnetic resonance imaging (fMRI) is an important chapter of the analysis of large-scale brain spatiotemporal dynamics. In particular, novel methods suited to extract **dynamic changes in mutual correlations** are needed. Here we scrutinize a recently reported metric dubbed "Multiplication of Temporal Derivatives" (MTD) [1].

We compare it with the sliding window Pearson correlation (SWPC) of the raw time series in several stationary and non-stationary set-ups, including: simulated autoregressive models with a step change in their coupling, surrogates [2] with realistic spectral and covariance properties and a step change in their cross- and autocovariance, and a realistic stationary network detection (with the use of gold standard simulated data [3]).

Along the way we discover that **cross-correlations are tied to their autocorrelations** for fMRI time series of brain regions. We solve simple autoregressive models to provide mathematical grounds for that behaviour.

Formulation

The MTD measure of dynamic functional correlations is defined in [1]:

$$ds_{it} = s_{it+1} - s_{it} \tag{1}$$

$$MTD_{ijt} = \frac{ds_{it} ds_{jt}}{\bar{\sigma}_i \bar{\sigma}_j} \tag{2}$$

$$SMA_{ijt} = \frac{1}{2w+1} \sum_{t'=t-w}^{t+w} MTD_{ijt'} = \frac{1}{2w+1} \sum_{t'=t-w}^{t+w} \frac{ds_{it'}}{\bar{\sigma}_i} \frac{ds_{jt'}}{\bar{\sigma}_j}, \tag{3}$$

where $2w+1$ equals to the number of samples considered in a temporal window $[t-w, t+w]$, s_i is an i-th time series, and $\bar{\sigma}_i$ is the standard deviation of the entire ds_i series.

Intuitions: theory and reality

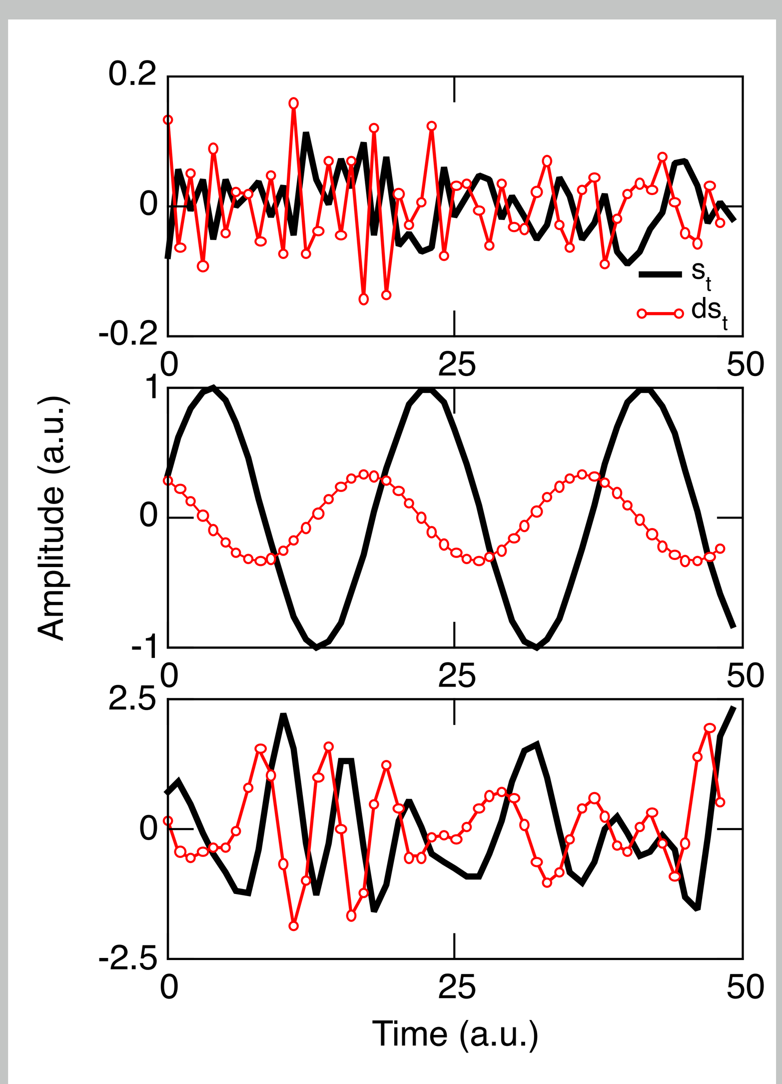

Fig. 1 Simple examples of raw time series s_t (black) and its series of derivatives ds_t (red) for a Gaussian (top), a sinusoid (middle), and a typical brain BOLD (bottom) time series.

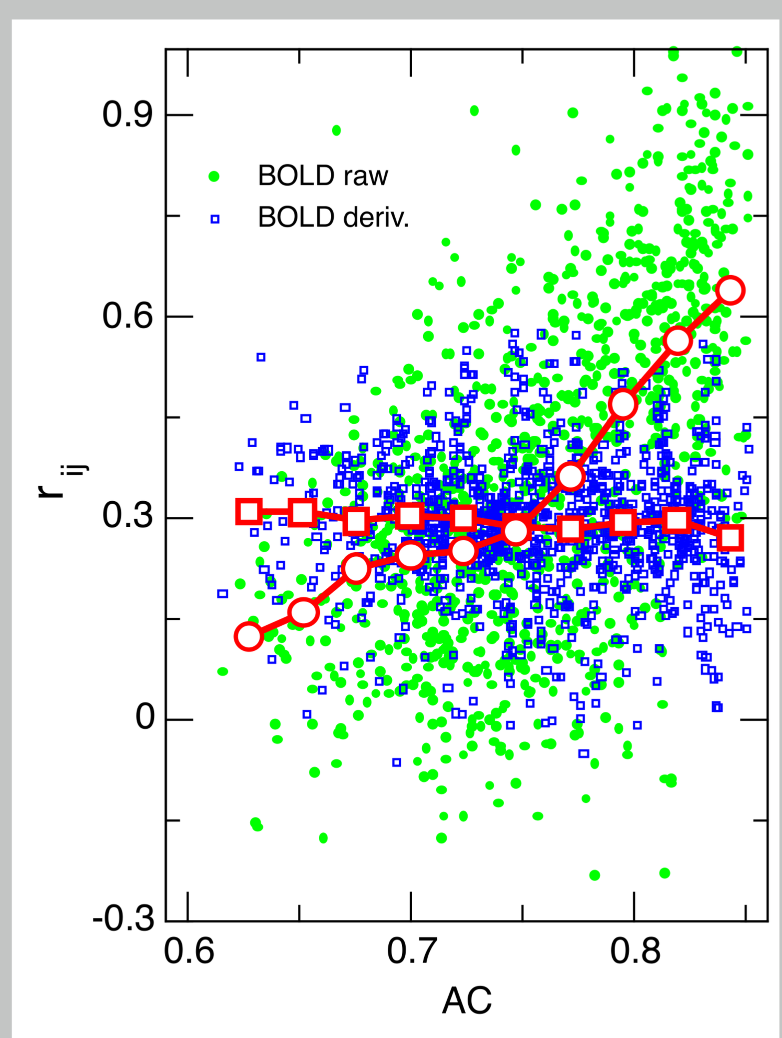

Fig. 2 Each dot represents the cross-correlation (r_{ij}) of two BOLD time series versus the average autocorrelation value (AC) of the pair (small filled green circles for raw BOLD and open squares for derivatives; red big circles denote binned averages for raw signal and squares for derivatives).

References

[1] JM Shine, O Koyejo, PT Bell, et al., *Estimation of dynamic functional connectivity using multiplication of temporal derivatives*, Neuroimage, 122 (2015) 399-407

[2] T.O. Laumann, A.Z. Snyder, A. Mitra, et al., *On the stability of BOLD fMRI correlations*, Cerebr. Cortex, 27 (2017) 4719-4732

[3] S.M. Smith, K.L. Miller, G. Salimi-Khorshidi, et al., *Network modelling methods for FMRI*, Neuroimage, 54 (2011) 875-891

[4] JK Ochab, W Tarnowski, MA Nowak, DR Chialvo, *On the pros and cons of using temporal derivatives to assess brain functional connectivity*, NeuroImage, 184 (2019) 577-585.

Autoregressive models: not enough but explain a lot

We can derive and compute analytically Pearson correlation (and correlation of the derivative) of AR(1) process

$$\begin{aligned} x_{1t} &= a_1 x_{1,t-1} + a_2 x_{2t-1} + \xi_{1t}, \\ x_{2t} &= a_1 x_{2,t-1} + a_2 x_{1t-1} + \xi_{2t}, \end{aligned} \tag{4}$$

knowing its parameters a_1 and a_2 (their range is limited by $|a_1| + |a_2| < 1$), where ξ_{it} are uncorrelated. Consequently, we can predict the average behaviour of SWPC and MTD for a range of parameters within that model, as well as we can reverse-engineer the real data, designing a model that exhibits specific Pearson correlations.

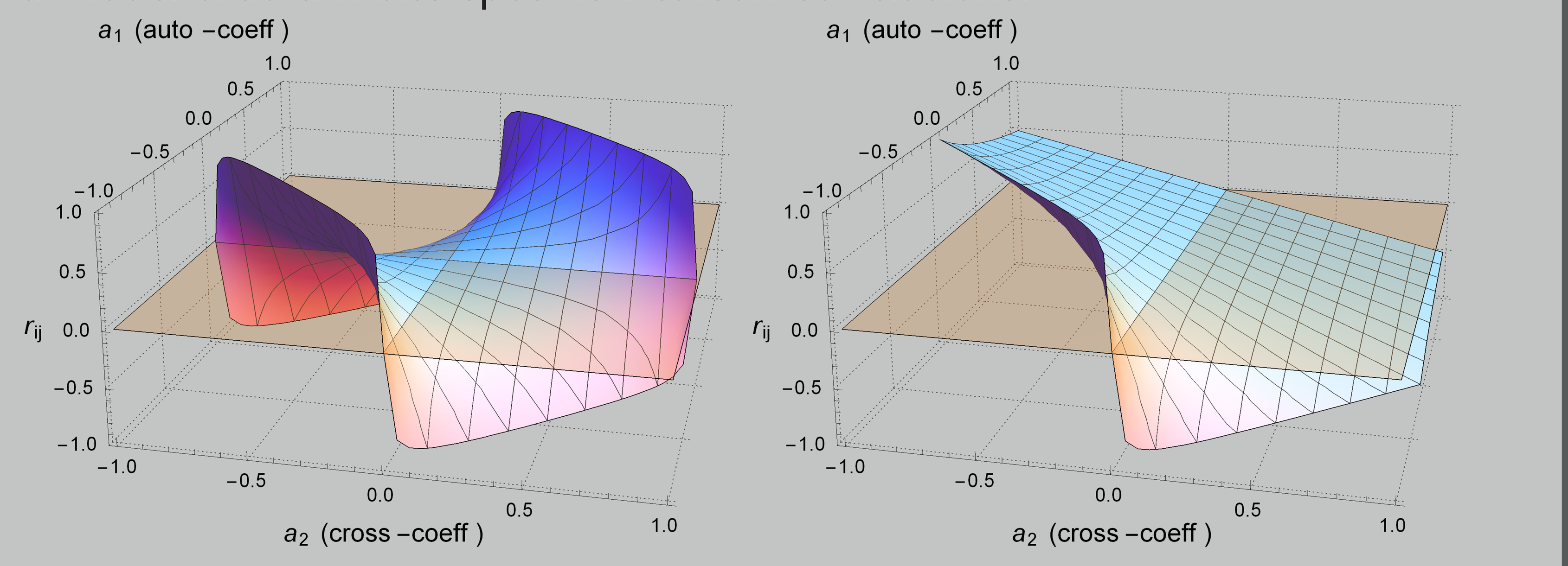

Fig. 3 Dependence of cross-correlations r_{ij} on parameters of the AR(1) model. **Left:** raw signals. **Right:** derivatives.

Dynamic correlations

Can derivatives enhance detection of an abrupt change in functional correlations between two regions of interest (ROI) or change of the whole functional network?

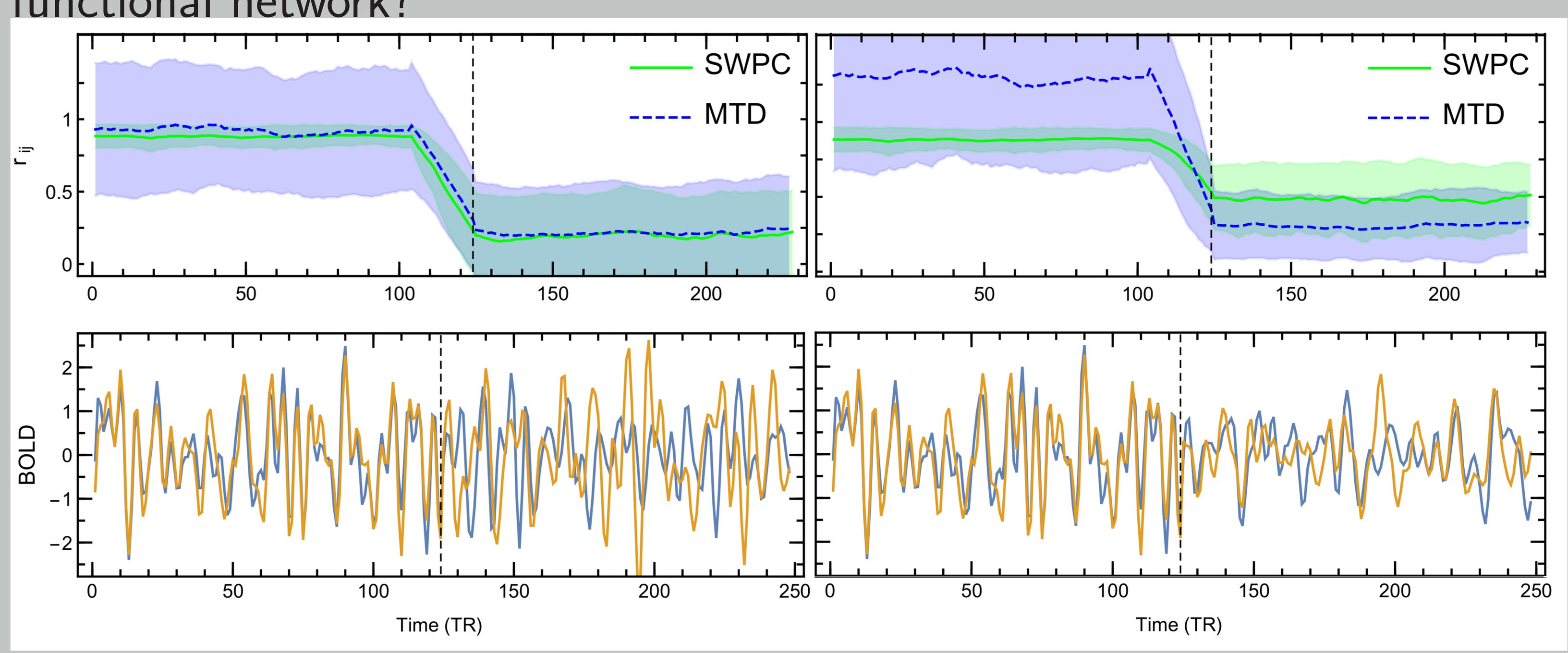

Fig. 4 Simulation of a sudden change (dashed vertical line) in covariance using surrogate [2] times series. **Left:** cross-correlation ↘ **0.2**, autocorrelation≈ **1**. **Right:** cross-correlation drops ↘ **0.2** and autocorrelation ↘ **0.4**. **Top:** correlations. **Bottom:** time series of two selected ROI.

Conclusions

The formal comparison of MTD with Pearson correlation of the derivatives reveals only negligible differences. There are no evident mathematical advantages of the MTD metric over commonly used correlation methods.

Does differentiation help? It depends:

- centering and windowed standardization decrease uncertainty of correlations
- differences: decrease signal-to-noise ratio
- differences: enhance stationarity, not affected by low frequency drifts
- differences: have lower sensitivity to autocorrelations (but worse than raw series for high autocorrelations)

The relation between cross- and autocorrelation is relevant to the occurrence of false positives in real networks, because similar autocorrelations of any two regions do not necessarily result from their actual structural connectivity or functional correlation.

Acknowledgments

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