

## Stockwell coherence measures resting-state connectivity with low between-session variability

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### Introduction

Analyses of resting-state functional magnetic resonance imaging (fMRI) data typically use approaches that determine the similarity between the time courses of individual image voxels or target regions and reference time courses from seed regions. This can be accomplished either in the time domain (e.g., cross-correlation) or in the frequency domain (e.g., coherence). These approaches assume fMRI signals are stationary over time; however, during a resting-state scan, a subject's rest may become intermittently disrupted due to changes in subject arousal, visual imagery, internal dialogue, etc. [1], which may impact results as well as reduce between-session reproducibility of resting-state connectivity. In this study, we introduce a time-frequency approach based on the Stockwell transform [2] to measure resting-state connectivity and to investigate the effect of imaging repetition time (TR) and scan duration in comparison to cross-correlation and coherence approaches [3].

### Methods:

Four healthy subjects participated in three sessions after providing informed consent. During each session, six 400-second resting-state T2\*-weighted images (GRE-EPI: TE = 30 ms, 24-cm FOV; twenty 5-mm thick slices, 64x64 matrix size) were collected with differing TRs (2 each of 600, 900, 1200 ms) in random order. Additional images were collected during the performance of a bilateral finger movement task (five visually-cued epochs of 20 seconds of self-paced finger movements and 20 seconds of rest). T<sub>1</sub>-weighted anatomical images were also collected. For the fMRI data collected during finger movements, the location of the 300 most significant voxels within left (seed) and right (target) primary sensorimotor cortex was determined using the General Linear Model (FSL: <http://www.fmrib.ox.ac.uk/fsl>). These seed and target regions were then used to extract their average time courses during the resting-state scans. For each TR and for three scan durations (200, 300, and 400 seconds), resting-state connectivity between the seed and target regions was computed using cross-correlation and coherence [3] as well as using Stockwell coherence. To compute Stockwell coherence, first the Stockwell transforms (i.e., temporally resolved frequency spectra) of the seed and target time courses were computed. Similar to the computation of coherence, the Stockwell auto-spectra for the seed and target regions as well as their cross-spectrum were calculated, and the ratio of the square of the cross-spectrum to the product of the auto-spectra was defined as Stockwell coherence. The result is a time-frequency spectrum of coherence. To take full advantage of Stockwell coherence, we recorded the median coherence across time and across the frequency range of 0 to 0.1 Hz rather than the mean, as the median is less sensitive to intermittent disruptions of the resting-state. For each method separately, values of connectivity were entered into a repeated measures ANOVA with session, TR and scan duration as within-subject factors. An alpha level of 0.01 was considered as significant. Also, the inter-session coefficient of variation was computed for all methods and entered into a repeated-measures ANOVA with method, TR, and scan duration as within-subject factors. An alpha level of 0.05 was considered as significant.

### Results:

For cross-correlation, ANOVA revealed a significant session/TR interaction [F(4,12)=5.53; p=0.009]. Hence, there was a difference in cross-correlation estimates of connectivity across sessions, which were dependent on the choice of TR. For coherence, ANOVA revealed a significant session/duration interaction [F(4,12)=58.93; p=0.001]. Hence, there was a difference in coherence estimates of connectivity across sessions, which were dependent on the choice of scan duration. For Stockwell Coherence, ANOVA revealed no significant effects. Hence, there were no differences in Stockwell coherence estimates of connectivity across any of the sessions, TRs, and scan durations. For the coefficients of variation, ANOVA revealed significant effects of method [F(3,9)=5.68; p=0.018] and scan duration [F(2,6)=8.64; p<0.017]. Follow-up t-tests analyses revealed that the coefficient of variation for Stockwell coherence was significantly lower than coherence (p=0.017; see Figure 1), and the coefficient of variation for a scan duration of 400 seconds was significantly lower than for 200 seconds (p=0.046) and 300 seconds (p=0.016).

### Conclusion:

Estimates of resting-state connectivity using Stockwell coherence are not susceptible to changes in TR and scan duration and do not differ between sessions. Cross-correlation and coherence exhibit dependencies on TR and scan duration, respectively. Resting-state connectivity estimated by Stockwell coherence also exhibits a significantly lower coefficient of variation across imaging sessions. Hence, Stockwell coherence is a potentially useful tool for estimations of resting-state connectivity across repeated sessions even in the presence of intermittent disruptions of the resting state.

### References:

- [1] Rogers B, et al. *Magn Reson Imag*. 2007;25:1347-1357.
- [2] Stockwell RG, et al. *IEEE Trans Signal Process* 1996;44:998-1001.
- [3] Sun et al. *Neuroimage* 2004;21:647-658.

