

# Open Source Random Matrix Theory Software for the Analysis of Functional Magnetic-Resonance Imaging Examinations

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## BACKGROUND

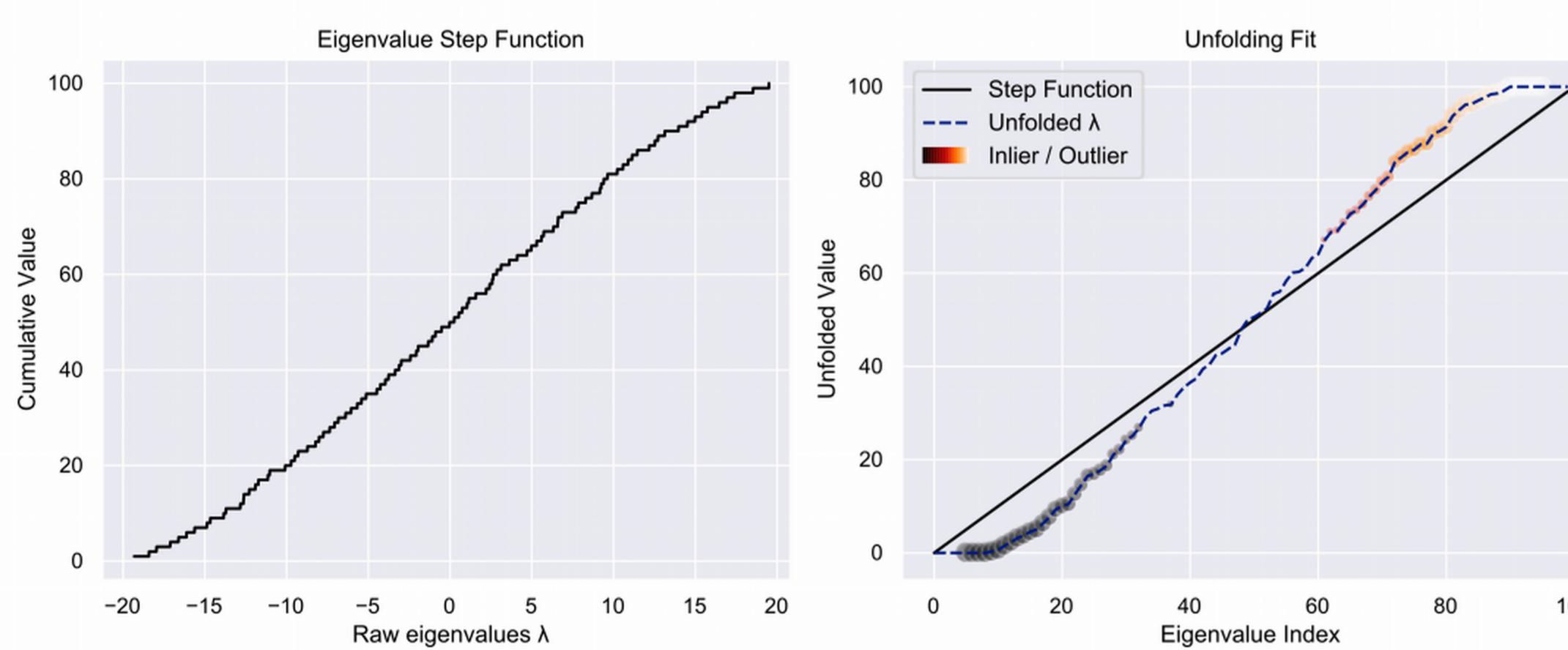
- large systems with complexly interacting individual components are mathematically and computationally intractable to describe completely
- however, the asymptotic behaviour of the eigenvalues of such a system can be described statistically by *Random Matrix Theory* (RMT) [1], [2]
- different systems have different limiting distributions
- we can describe these limiting distributions with statistics called *spectral observables* [2]
- this includes the *spectral rigidity*  $\Delta_3(L)$ :

$$\Delta_3(L) = \left\langle \min_{A,B} \frac{1}{L} \int_c^{c+L} (\eta(\lambda) - A\lambda - B)^2 \right\rangle_c$$

where  $\eta(\lambda)$  is the number of unfolded eigenvalues less than or equal to  $\lambda$ ,  $\langle \cdot \rangle_c$  denotes the average with respect to all starting points  $c$ , and where  $A$  and  $B$  denote the slope and intercept, respectively, of the least squares fit of a straight line to  $\eta(\lambda)$  on  $[c, c + L]$ , [1], [2] and *level number variance*  $\Sigma^2(L)$ :

$$\Sigma^2(L) = \langle \eta^2(L, c) \rangle_c - \langle \eta(L, c) \rangle_c^2$$

where  $\eta(L, c)$  is the number of unfolded eigenvalues in  $[c, c + L]$ , and where  $c$ ,  $L$ , and  $\langle \cdot \rangle_c$  are as above [1], [2]



## UNFOLDING

- to allow different empirically-derived matrices to be compared, eigenvalues must be “unfolded” [1], [2]
- unfolding smoothly maps the originally observed spectrum  $\lambda_1 \leq \dots \leq \lambda_n$  to the unfolded spectrum  $e_1, \dots, e_n$  such that  $\sum d_i/n \approx 1$  for  $d_i = e_{i+1} - e_i$
- the smoothing function is usually unknown and thus approximated with a polynomial [1]–[3]
- the unfolding method can have serious effects on the resulting statistics [4], [5], so we must be sure that derived RMT statistics are robust to unfolding decisions

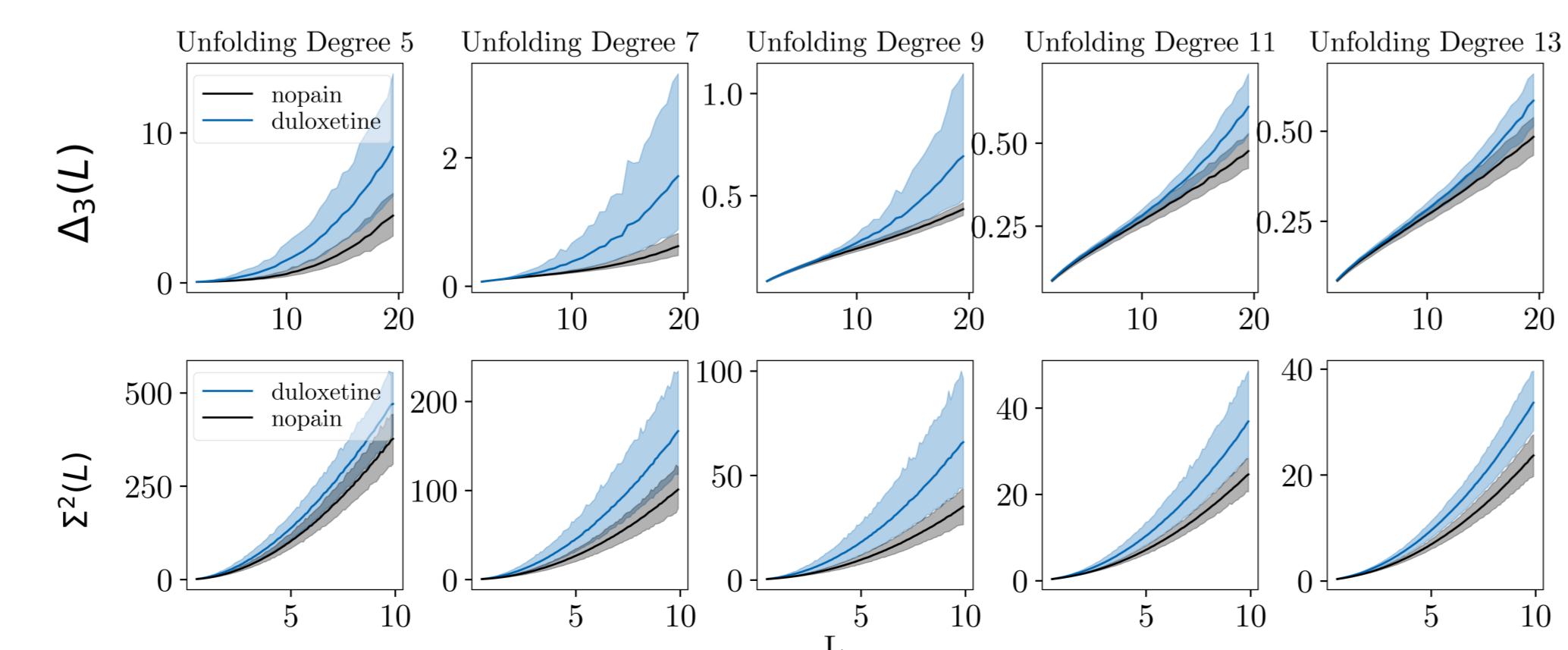
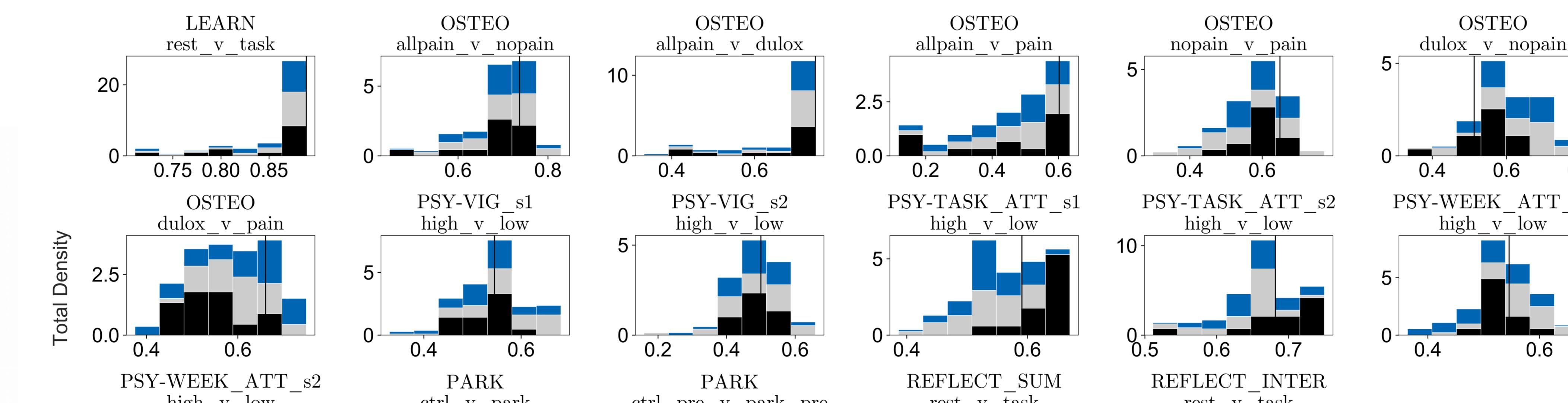
## METHODS AND RESULTS

ID	FOV (mm)	Dimensions	Voxel Size (mm)	TR	Volumes / Time
PSYCH	192	128×128×70	1.5×1.5×1.5	3.0	300 / 15
OSTEO	-	64×64×36	3.4×3.4×3.0	2.5	300 / 12.5
REFLECT	210	72×72×46	3.0×3.0×3.0	3.0	204 / 10.2
	240	64×64×33	3.8×3.8×3.8	2.0	260 / 8.7
PARK	240×240×129	80×80×43	3.0×3.0×3.0	2.4	149 / 5.96
LEARN	-	64×64×36	3.0×3.0×3.0	2.0	195 / 6.5

PSYCH: resting-state fMRI (rs-fMRI) where subjects differ in trait and task attention and vigilance [7]  
 OSTEO: rs-fMRI for controls or subjects with osteopathic pain given duloxetine or placebo [8]  
 REFLECT: fMRI recorded during various introspective and reflective memory tasks [9]  
 PARK: fMRI of controls vs. individuals with Parkinson's during Attention Network task [10]  
 LEARN: task fMRI (learning to memorize and recognize complex images) vs rs-fMRI [11]

**Table I.** ID = Identifier for paper. FOV = Field of View. TR = Time of Repetition (seconds). Time = total duration (minutes) of each scan. Dimensions listed as M × N × P, indicate P slices with dimensions M × N.

We collect a wide variety of fMRI datasets (above) from the OpenNeuro platform [6]. Eigenvalues are extracted from the voxelwise correlation matrix of each scan, and subject-level RMT metrics (e.g. eigenvalues, spectral rigidity, level variance) are compared across various subgroups (brief details above) to investigate the general applicability of RMT. We then attempt to predict subgroup membership (using various standard classifiers) using these extracted RMT metrics to assess their predictive utility. To ensure results are robust to the unfolding procedure, we compute all statistics for multiple polynomial unfolding degrees.



Across a wide variety datasets and subgroup comparisons, we find RMT-inspired metrics often have utility in predicting subgroup membership (stacked histogram above: “Guess” line indicates accuracy of a dummy classifier always predicting membership in the largest group). This was most strongly the case in the OSTEO dataset for distinguishing controls from those prescribed duloxetine (above, top right panel). In this subgroup comparison, we see that the spectral rigidity and level variance curves for these two subgroups show strong separation (left plots).

## DISCUSSION AND LIMITATIONS

RMT provides a novel way to examine and describe the functional connectivity patterns in fMRI scans. Our preliminary results suggest that the eigenvalues extracted from the voxelwise correlation matrix could have potential in characterizing differences between individuals and different psychological and physiological states.

Given the novelty of RMT, it is not yet clear to what extent RMT metrics are sensitive to different pre-processing steps, scan parameters, and other analytical decisions. We compute correlations over voxels, but other studies have used larger anatomical regions of interest [12], [13].

## OPEN SOURCE CODE

We release open source Python code for performing unfolding, computing spectral observables, and efficiently extracting eigenvalues from large matrices to allow others to replicate and/or extend RMT to a wider variety of empirical domains [12].

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