



15th November 2022,
Dear Dr. Giger,

We hope you will consider our manuscript *Random Matrix Theory Tools for the Predictive Analysis of Functional Magnetic Resonance Imaging Examinations* for publication in SPIE Journal of Medical Imaging.

We confirm that this work is original and has not been published elsewhere nor is it currently under consideration for publication elsewhere. However, a poster of limited preliminary results related to this study was presented at the International Symposium for Magnetic Resonance in Medicine 2021 annual conference, and is available in abstract form (Berger, Matharoo and Levman, 2021).

In this paper, we extract a number of eigenvalue-based features inspired by Random Matrix Theory (RMT) from a wide variety of functional magnetic resonance imaging (fMRI) data. We subsequently examine the cross-validated predictive utility of those extracted features on a number of binary classification tasks that can be constructed for each dataset. The predictive utility is examined systematically, in a multiverse-style analysis (Steegen et al., 2016), which reveals the sensitivity of results to various typical preprocessing decisions involved in fMRI and RMT.

This paper is most unique in that it:

1. employs RMT to generate reductions of the full voxelwise fMRI correlation matrix
2. evaluates RMT-related metrics in a cross-validated predictive framework, instead of the more typical descriptive or explanatory frameworks
3. systematically investigates the impact of the various methodological decisions that affect the findings
4. makes all code used in the paper publicly available, including the release of a separate, general, open-source RMT library (DM-Berger, 2022) that will allow RMT metrics to be easily and reproducibly computed on a wide variety of data

Please address all correspondence concerning this manuscript to me at jlevman@stfx.ca.

Thank you for your consideration of this manuscript.

Sincerely,

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DM-Berger (Sept. 2022). *Stfxcutables/empiricalRMT: V1.1.1*. Zenodo. DOI: [10.5281/ZENODO.3820649](https://doi.org/10.5281/ZENODO.3820649).

Berger, Derek, Gurpreet S. Matharoo and Jacob Levman (May 2021). 'Open Source Random Matrix Theory Software for the Analysis of Functional Magnetic-Resonance Imaging Examinations'. In: *ISMRM & SMRT Annual Meeting & Exhibition*. Vancouver, BC, Canada.

Steegen, Sara et al. (Sept. 2016). 'Increasing Transparency Through a Multiverse Analysis'. In: *Perspectives on Psychological Science* 11.5, pp. 702-712. ISSN: 1745-6916, 1745-6924. DOI: [10.1177/1745691616658637](https://doi.org/10.1177/1745691616658637).