

1 We thank the reviewers for their positive, kind, and constructive feedback! The two main points of criticism concerned
2 (1) the lack of neuroscience background information, and (2) missing discussion and comparison to prior work. Due to
3 page limitations, these points were insufficiently addressed. In a revision, we will provide additional details here as well
4 as more citations concerning prior work in TDA and neuroscience.

5 **Differences/comparison to previous work:** We are the first TDA paper to work *directly* with fMRI input data (using
6 cubical complexes). Prior work uses auxiliary representations such as networks extracted from correlation matrices [2, 7].
7 Moreover, previous studies often use other measuring modalities such as structural MRI for anatomical analyses [1], or
8 diffusion MRI/DTI for studying white matter integrity [2]. Our cubical persistence formulation is the first of its kind in
9 the context of functional MRI measuring brain activity during a movie-watching task. We will make this delineation
10 more clear in a revision.

11 Inspired by this feedback, we also prepared experiments using a more con-
12 ventional formulation of TDA methods based on correlation graphs of the
13 data, which we created from correlation matrices using a correlation distance
14 filtration [3] (terminology follows the paper; time-based: TT-TDA; voxel-
15 based, parcellated: PP-TDA). The new values in the table are **highlighted**; the
16 remaining rows are duplicated from the table in the paper. We observe that
17 the time-based correlation matrix/graph is improved by topological feature
18 extraction, while the voxel-based (parcellated) correlations are not improved.
19 This demonstrates the advantage of using the input data directly, instead of
20 requiring auxiliary representations.

Method	BM	OM	XM
BASELINE-TT	0.09	0.02	0.24
BASELINE-PP	0.41	0.40	0.40
SRM	0.44	—	—
TT-TDA	0.16	0.08	0.24
PP-TDA	0.19	0.24	0.23
$\ \mathcal{D}\ _1$	0.46	0.67	0.48
$\ \mathcal{D}\ _\infty$	0.61	0.77	0.73

Performance of baselines, **standard TDA** approaches, and our method for the age prediction task.

21 **Reviewer 1:** Thank you very much for your exuberant feedback, we really
22 appreciate it! Concerning the weaknesses that you mentioned: indeed, there
23 is no direct ‘link’ between our approach and classical approaches; however, our topological features ‘live’ in the original
24 space of the data and can be localised [5, 8], i.e. endowed with a minimal geometry. Other topological approaches,
25 which use correlation graphs as intermediaries, do not have features that directly relate back to the data. We plan to
26 explore this in the future and we are convinced that our approach will also open up other avenues of inquiry. We will
27 also run our approach on synthetically-generated data sets [4] for verification and validation (in order to study the
28 limitations of our approach).

29 **Reviewer 3:** Thank you very much for your positive feedback! Concerning the weakness that you mentioned, please
30 see our general points above—in a revision, we will delineate this work better from related papers. Thanks for the links
31 to additional papers; we will cite and discuss them accordingly. • *Dimensions of the data:* Thanks for highlighting this;
32 we will add it to the paper! The 4D volume of each participant has dimensions $65 \times 77 \times 60 \times 168$ (as described in the
33 paper, we are not considering all 168 time steps). • *Neuroscience background:* We will add an appropriate section to the
34 paper or the supplemental materials. • *Contributions:* We are the first work utilising cubical persistent homology in the
35 context of fMRI. We use theoretical tools with a strong mathematical foundation and apply them in a novel way. This
36 results in *dynamic* representations (previous work only considered static representations), the brain state trajectories,
37 whose calculation combines topological features with the diffusion geometry method PHATE [6], yielding a novel set
38 of features that were previously not considered in the literature. As we show in the paper, these trajectories are capable
39 of capturing the dynamics of cognition. We will emphasise these contributions more in the revision.

40 **Reviewer 4** Thank you very much for your constructive feedback! We will delineate our work (novel cubical persistence
41 calculations) better from existing work (requiring auxiliary representations such as networks). • *Generalisability:* While
42 we focussed on one data set for this initial submission, our method can be applied to *any* neuroimaging data set. A key
43 feature is its abstraction—as we show in the prediction task, this may help counteract noise and intra-subject variability.
44 We are convinced that other applications in neuroscience, using metrics other than age prediction, can benefit from our
45 approach (which is why we will make all code available). Thus, we think that our work paves the way for a different
46 sort of topology-based neuroscience methods that are based on *direct* feature extractions from the data. We will explore
47 the feasibility of our work on other modalities (such as EEG) in the future (presently, they are out of scope for this
48 work). • *Time series visualisation:* We will extend the description of this approach and provide examples.

49 [1] M. K. Chung et al. Persistence diagrams of cortical surface data. In *Information Processing in Medical Imaging*, pages 386–397. Springer, 2009.
50 [2] M. K. Chung et al. Persistent homological sparse network approach to detecting white matter abnormality in maltreated children: MRI and DTI multimodal study.
51 In *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2013*, pages 300–307. Springer, 2013.
52 [3] M. K. Chung et al. Topological distances between brain networks. In *Connectomics in NeuroImaging*, pages 161–170, 2017.
53 [4] C. T. Ellis et al. Facilitating open-science with realistic fMRI simulation: validation and application. *PeerJ*, 8:e8564, 2020.
54 [5] J. Erickson and K. Whittlesey. Greedy optimal homotopy and homology generators. In *Proc. SODA*, pages 1038–1046. SIAM, 2005.
55 [6] K. R. Moon et al. Visualizing structure and transitions in high-dimensional biological data. *Nature Biotechnology*, 37(12):1482–1492, 2019.
56 [7] M. Saggari et al. Towards a new approach to reveal dynamical organization of the brain using topological data analysis. *Nature Communications*, 9(1):1399, 2018.
57 [8] A. Zomorodian and G. Carlsson. Localized homology. *Computational Geometry*, 41(3):126–148, 2008.