- 1 We thank the reviewers for their thoughtful and detailed comments. Brief replies follow below.
- 2 **R1) Input dimensionality:** P-GAMs have similar scaling with the number of input dimensions as traditional GLMs.
- 3 Nonetheless, using P-GAMs makes most sense when the inputs are task or cognitive variables; we don't envision our
- 4 methods being commonly used for estimating V1 RFs. This does not mean that P-GAMs are not generally useful: many
- 5 of the new datasets in systems neuroscience (higher cortices, hippocampus) naturally lend themselves to our analysis.
- 6 Spatio-temporal filters: We chose to include temporal filters only for binary events, which helps interpretability in the
- 7 context of our task. P-GAMs can also model spatio-temporal effects: we simply need to add one extra temporal filter
- for each input dimension, somewhat similar in flavor to the factorization in [Park & Pillow, 2013]. Alternatively, we can
- 9 define 2D nonlinear spatio-temporal filters for each input dimension, each contributing one additive term to the final
- GAM expression. Both versions scale linearly with the number of inputs (with a potentially large hidden constant in the
- second version). We will include examples of this functionality in the new version of the paper (results and code demo).
- Smoothness priors: our current regularizer already encourages smoothness. Incorporating general GP priors seems
- more difficult. GP regression is known to scale unfavorably with the number of inputs, requiring additional structure (e.g.
- 14 Kronecker) to keep computation tractable [Wilson et al, 2014]; even with the extra tricks, GP-based tuning estimates
- are restricted to low dimensional inputs (less than 10, inapplicable to our data, see e.g. [Savin & Tkacik 2016]). A new
- variant of GP-based GAMs may prove competitive [Adam, Durrande & John, 2018] but, to our knowledge, this has not
- yet been adapted to neural tuning estimation. We will cover the GP literature in the discussion.
- Fig1E: shows misses and false positives for detecting whether an input dimension drives neural responses or not.
- 19 Fig3C: We've done additional statistics to disentangle the role of mean firing on tuning and coupling strength. A partial
- 20 correlation analysis confirmed that coupling patterns cannot be trivially explained by differences in mean firing rates.
- 21 **R2) Neural implications:** We could not elaborate on monkey data results due to space limits; journal paper to follow.
- 22 GLM comparison: We chose to compare P-GAMs against a vanilla 'Pillow GLM' instead of a fancier version because
- 23 this is what most neuroscientists end up using in practice; the group sparsity regularization would be closest in aims,
- but, to our knowledge, that has not been extensively applied to real data. We are happy to expand on the links to these
- 25 alternative methods in the introduction/discussion.
- R3) Usability, adapting the code to new datasets: Up to now, we have used the estimator on 3 different datasets (the
- 27 monkey one, rat hippocampus and OFC). The initial P-GAM model specification takes a bit of work on any new dataset,
- but there are relatively few knobs that have to be set by hand (the spline basis); once the model is set, the code runs
- 29 smoothly a rotation student with limited coding background managed to get everything done in a few weeks.
- 30 **ARD:** The ARD regularizer corresponds to a factorized Gaussian prior with β -specific variances (treated as hyperpa-
- 31 rameters). Assuming a 1-to-1 map between parameters and inputs, the prior for irrelevant input dimensions will end up
- sharply concentrated around zero. It is not clear how to do this in the nonlinear case, when several β s are used to model
- 33 each input dimension (one per basis vector). We need some form of group sparsity and traditional ARD can't do that.
- 34 R4) GLM vs P-GAM on real data: we can include GLM filter estimates and additional P-GAM vs. GLM fit quality
- 35 quantification on real data in the supplementary info. Full GLM model comparison is intractable for this dataset so we
- can only do elastic net regularization. In brief, everything is much messier, although some of the trends persist.
- Validation of CIs: Fair enough. We can definitely get bootstrapping-based CIs for artificial data, probably also for
- real units although it may prove too computationally expensive to do extensively. We will add those in the updated
- yersion. Apart from that, please note that the numerical estimates for the type 1 and 2 errors made by our significance
- 40 test (Fig3C) are sensible even if, admittedly, we could only do the validation for artificial data.
- 41 **Utility and relevance:** In practice, there are many experimental scenarios where simple GLMs don't quite suffice; most
- 42 experimentalists will find the technical details too intimidating to attempt complex hierarchical regularization; they also
- 43 often don't have the computational resources to do brute force model comparison for large models. We are providing a
- 44 straightforward and relatively general way to get the job done, one that stays tractable even for large datasets.