

Better-Than-Chance Classification for Signal Detection

Jonathan Rosenblatt Roei Gilron Roy Mukamel

August 5, 2016

Abstract

[TODO]

1 Introduction

A common workflow in neuroimaging consists of fitting a classifier, and estimating its predictive accuracy using cross validation. Given that the cross validated accuracy is a random quantity, it is then common to test if the cross validated accuracy is significantly better than chance using a permutation test. Examples in the neuroscientific literature include Golland and Fischl [2003], Pereira et al. [2009], Varoquaux et al. [2016], and especially the recently popularized *multivariate pattern analysis* (MVPA) framework of Kriegeskorte et al. [2006]. This practice is also observed in the genetics literature, but to a lesser extent [Radmacher et al., 2002, Jiang et al., 2008].

To fix ideas, we will adhere to a concrete example. In Gilron et al. [2016], the authors seek to detect brain regions which encode differences between vocal and non-vocal stimuli. Following the MVPA workflow, the localization problem is cast as a supervised learning problem: if the type of the stimulus can be predicted from the spatial activation pattern significantly better than chance, then a region is declared to encode vocal/non-vocal information. We call this an *accuracy test*, a.k.a. *class prediction* in Simon et al. [2003], or *pattern discrimination* in Pereira et al. [2009].

This same signal detection task can be also approached as a two-group multivariate test. Inferring that a region encodes vocal/non-vocal information, is essentially inferring that the spatial distribution of brain activations is different given a vocal/non-vocal stimulus. As put in Pereira et al. [2009]:

... the problem of deciding whether the classifier learned to discriminate the classes can be subsumed into the more general question as to whether there is evidence that the underlying distributions of each class are equal or not.

A practitioner may then call upon a two-group location test such as Hotelling’s T^2 [Anderson, 2003]. Alternatively, if the size of a brain region is too large compared to the number of observations, so that the spatial covariance cannot be fully estimated, then a high dimensional version of Hotelling’s test can be called upon, such as in Schäfer and Strimmer [2005] or Srivastava [2013]. For brevity, and in contrast to *accuracy tests*, we will call these two-sample multivariate tests simply *location tests*, also termed *class comparisons* in Simon et al. [2003].

At this point, it becomes unclear which is preferable: a location test or an accuracy test? The former with a heritage dating back to Hotelling [1931], and the latter being extremely popular, as the 959 citations¹ of Kriegeskorte et al. [2006] suggest.

The comparison between location and accuracy tests was precisely the goal of Ramdas et al. [2016], who compared the T^2 location test to the accuracy of *Fisher’s linear discriminant analysis* classifier (LDA). By comparing the rates of convergence of the powers to 1, Ramdas et al. [2016] concluded that accuracy and location tests are rate equivalent. Judging by convergence rates alone, not much is (asymptotically) lost by using an accuracy test. Asymptotic relative efficiency measures (ARE) are typically used by statisticians to compare between test statistics with similar rates [van der Vaart, 1998].

The ARE between Hotelling’s T^2 (location) test and Fisher’s LDA (accuracy) test in Ramdas et al. [2016] is lower bounded by $\sqrt{2\pi} \approx 2.5$. This means that Fisher’s LDA requires at least 2.5 more samples to achieve the same (asymptotic) power than the T^2 test. In this light, the accuracy test is remarkably inefficient compared to the location test. For comparison, the t-test is only 1.04 more (asymptotically) efficient than Wilcoxon’s rank-sum test [Lehmann, 2009], so that an ARE of 2.5 is strong evidence in favor of the location test.

Before discarding accuracy tests, we recall that Ramdas et al. [2016] analyzed a half-sample holdout. The authors thus conjecture that a leave-one-out approach, which makes more efficient use of the data, may have better performance. On the other hand, the analysis in Ramdas et al. [2016] is asymptotic. This eschews the discrete nature of the accuracy statistic, which will shown to have crucial impact. Since typical sample sizes in neuroscience

¹GoogleScholar. Accessed on Aug 4, 2016.

are not large, we seek to study which test is to be preferred in finite samples? Our conclusion will be quite simple: *location tests almost always have more power than accuracy tests.*

The main argument for our statement rests upon the observation that with typical sample sizes, the accuracy test statistic is highly discrete. Discrete test statistics are known to be conservative [Hemerik and Goeman, 2014], since they are insensitive to mild perturbations of the data, and they cannot exhaust the permissible false positive rate. The degree of discretization is governed by the number of samples. In our neuroscience example from [Gilron et al., 2016], the classification is performed based on 40 trials, so that the test statistic may assume only 40 possible values. This number of examples is not unusual if considering this is the number of subjects, or the number of trial-repeats in an neuroimaging study.

The discretization effect is aggravated if the test statistic is highly concentrated. For an intuition consider the usage of a the *training* accuracy as a test statistic. This is the *resubstitution classification*, and simply means that the accuracy is not cross validated. If the data is high dimensional, the resubstitution accuracy will be very high due to over fitting. In an extreme case, the resubstitution accuracy will be 1 for the observed data, but also for any permutation. The concentration of the resubstitution accuracy near 1, and its discreteness, render this test completely useless, with a power of 0.

To compare the power of accuracy tests and location tests in finite samples, we perform a simulation study of a battery of test statistics. The main findings are reported in Section 4, and the intuition for our findings is provided in Section 6, but first, the problem’s setup.

2 Problem setup

Let $y \in \mathcal{Y}$ be a class encoding. Let $x \in \mathcal{X}$ be a p dimensional feature vector. In our vocal/non-vocal example we have $\mathcal{Y} = \{-1, 1\}$ and p , the number of voxels in a brain region so that $\mathcal{X} = \mathbb{R}^{27}$.

Given n pairs of (x_i, y_i) , typically assumed i.i.d., a location test amounts to testing whether $x|y = 1$ has the the same distribution as $x|y = -1$. I.e., we test if the multivariate voxel activation pattern has the same distribution when given a vocal stimulus, as when given a non-vocal stimulus. An accuracy test amounts to learning a predictive model $\hat{f}(x)$ from some assumed model class $\hat{f} \in \mathcal{F}$. The prediction accuracy, denoted $T_{\hat{f}}^{acc}$, is defined as the probability of a given classifier \hat{f} of making a correct prediction $T_{\hat{f}}^{acc} := Prob(\hat{f}(x) = y)$ when given a randomly drawn data point, (x, y) .

101 A statistically significant “better than chance” estimate of $T_{\hat{f}}^{acc}$ is evidence
 102 that the classes are distinct.

103 2.1 Candidate Tests

104 The design of a permutation test using the prediction accuracy, requires the
 105 following design choices:

- 106 1. How to estimate accuracy?
- 107 2. Is the statistic cross validated or not?
- 108 3. For a K-fold cross validated test statistic: should the data be refolded
 109 in each permutation?
- 110 4. Permute labels of features?
- 111 5. For a K-fold cross validated test statistic: should the data folding bal-
 112 anced (a.k.a. stratified)?
- 113 6. How many folds?

114 We will now address these questions while bearing in mind that unlike the
 115 typical supervised learning setup, we are not interested in an unbiased esti-
 116 mate of the prediction error, but rather in the mere detection of a difference
 117 between two groups.

118 **How to estimate accuracy?** Given a predictor \hat{f} , a natural test statis-
 119 tic is some estimate of its accuracy $T_{\hat{f}}^{acc}$. Complicating matters: very low
 120 accuracies, even 0, is evidence that the classes are separated, and we only
 121 need to invert the predictions. We can thus consider $|T_{\hat{f}}^{acc} - 0.5|$ as the test
 122 statistic. This, however, implies that if the classes are identical, random
 123 guessing has 0.5 accuracy. This is not true if the classes are not balanced.
 124 The chance level in which case is the prevalence of the dominant class, we
 125 denote by \hat{p}_{max} . This suggests the following test statistic $|T_{\hat{f}}^{acc} - \hat{p}_{max}|$. Since
 126 we will be aggregating these statistics over random data sets where the dom-
 127 inant class may have varying frequencies, it seems appropriate to standard-
 128 ize the scale of this statistic. We thus also consider the z-scored accuracy:
 129 $|T_{\hat{f}}^{acc} - \hat{p}_{max}| / \sqrt{\hat{p}_{max}(1 - \hat{p}_{max})}$.

130 **Cross validate or not?** Were we interested in an unbiased estimator of
131 the prediction error, there is no question that some independent validation
132 is in order. Since we are merely interested in detecting a difference between
133 classes, a biased error estimate is not an issue provided that bias is consistent
134 over all permutations. The underlying intuition is that if the exact same
135 computation is performed over all permutations, then a permutation test
136 will be “fair”, i.e., will not inflate the false positive rate. We will thus be
137 considering both cross validated accuracies, and *train* accuracies as our test
138 statistics, a.k.a. *resubstitution classification*.

139 **Refolding?** The standard practice in neuroimaging is to refold the data
140 after each permutation [Pereira et al., 2009]. This is imperative if permuting
141 labels while aiming at balanced data folds. This is not, however, imperative
142 in general. For simplicity, we will adhere to the standard practice of refolding
143 the data within each permutation.

144 **Permute labels of features?** While seemingly identical, the compound-
145 ing of permutations with data foldings renders these two approaches distinct.
146 As an example, consider balanced (stratified) K-fold cross validation where
147 the initial data folding is balanced. After a label permutation, the original
148 folds will probably not be balanced. If the *features* are permuted, then the
149 labels conserve their original fold assignments, and the original folds are bal-
150 anced after each permutation. Since we only report results while refolding
151 the data in each permutation, then the only difference between permuting
152 labels and permuting features seems to be a computational one. We thus
153 adhere to the more common, albeit computationally less efficient practice of
154 permuting labels.

155 **Balanced folding?** As already implied, a standard practice when cross
156 validating is to constrain the data folds to be balanced (i.e. stratified). This
157 is well justified when aiming at unbiased accuracy estimation. This also
158 simplifies matter when aiming at signal detection, as can be seen from the
159 above discussion of the appropriate test statistic. On the other hand, it
160 may complicate matters, as can be seen from the above discussion on label
161 versus feature permutation. We will report results with both balanced and
162 unbalanced data foldings, only to discover, it does not really matter.

163 **How many folds?** Different authors suggest different rules for the num-
164 ber of folds. We will be varying the number of folds. This will affect the
165 concentration of permutation distribution of the estimated accuracy, which

will have a crucial effect on the conservativeness of the accuracy test. Our intuition suggests that since more folds imply a less concentrated estimate, then leave-one-out should be the less conservative, and 2-fold should be the most conservative.

The of tests we will be comparing is collected for convenience in Table 1.

Name	Basis	CV	Accuracy	Parameters
Hotelling	Hotelling	—	—	shrink=FALSE
Hotelling.shrink	Hotelling	—	—	shrink=TRUE
lda.CV.1	LDA	TRUE	accuracy	—
lda.CV.2	LDA	TRUE	z-accuracy	—
lda.noCV.1	LDA	FALSE	accuracy	—
lda.noCV.2	LDA	FALSE	z-accuracy	—
sd	SD	—	—	—
svm.CV.1	SVM	TRUE	accuracy	cost=1e1
svm.CV.2	SVM	TRUE	accuracy	cost=1e-1
svm.CV.3	SVM	TRUE	z-accuracy	cost=1e1
svm.CV.4	SVM	TRUE	z-accuracy	cost=1e-1
svm.noCV.1	SVM	FALSE	accuracy	cost=1e1
svm.noCV.2	SVM	FALSE	accuracy	cost=1e-1
svm.noCV.3	SVM	FALSE	z-accuracy	cost=1e1
svm.noCV.4	SVM	FALSE	z-accuracy	cost=1e-1

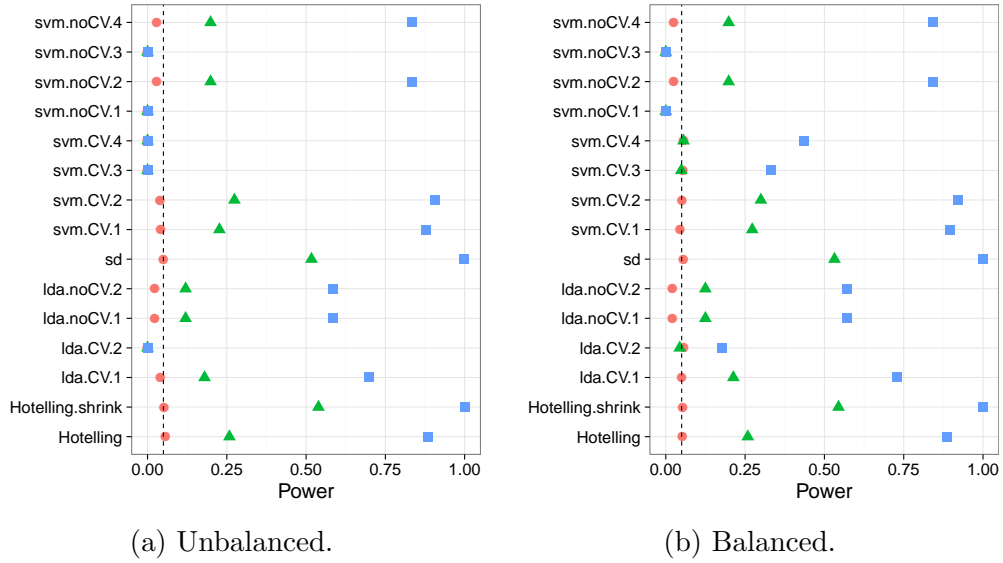
Table 1: This table enumerates the various test statistics we will be studying. Three are location tests: Hotelling, Hotelling.shrink, and sd. *Hotelling* is the classical two-group T^2 statistic. *Hotelling.shrink* is a high dimensional version with the regularized covariance in Schäfer and Strimmer [2005]. *sd* is another high dimensional version of the T^2 , from Srivastava et al. [2013]. The rest of the tests are variations of the linear SVM, and Fisher’s LDA, with varying accuracy measures, cross validated or not, and varying tuning parameters. For example, *svm.CV.4* is a linear SVM, with *libsvm*’s cost parameter set at 0.1, using the cross validated z-scored accuracy ($|T_f^{acc} - \hat{p}_{max}| / \sqrt{\hat{p}_{max}(1 - \hat{p}_{max})}$, see Section 2.1). Another example is *lda.noCV.1*, which is Fisher’s LDA, returning the resubstitution accuracy, without cross validation, and without z-scoring.

3 Controlling the False Positive Rate

Figure 1 demonstrates that all of the tests considered conserve the desired 0.05 false positive rate, up to varying levels of conservatism. This can be seen from the fact that the probability of rejection is no larger than 0.05 in the absence of any effect, encoded by a red circle. This is true, in particular if: (a) the folds are balanced or not, (b) the tuning parameters of some test

177 statistic are varied, (d) the number of folds is varied. We also observe that the
 178 most conservative tests are the accuracy tests that are not cross validated.
 179 We return to this matter in the Discussion.

Figure 1: The power of a permutation test with various test statistics. The power on the x axis. Effect are color and shape coded. They are assumed to be equal in all the 23 dimensions, and vary over 0 (red circle), 0.25 (green triangle), and 0.5 (blue square). The various statistics on the y axis. Their details are given in Table 1. Simulation code available at [TODO].



180 4 Power

181 Having established that all of the tests in our battery control the false positive rate, it remains to be seen if they have similar power— especially when
 182 comparing the power of location tests to accuracy tests. From the simulation
 183 results reported in Appendix B we collect the following insights:

- 185 1. Location tests have more power than accuracy tests in all our configurations.
 186
- 187 2. The conservativeness decays as the sample grows (Figure 7), supporting
 188 the statement that discretization is responsible for power loss.
- 189 3. The power is may increase or decrease with the number of folds (Figure 3). [TODO:effect of n.folds.]
 190

- 191 4. ... The z-scoring of the accuracies was introduced to deal with unbal-
192 anced foldings. If the z-scoring has any effect at all, it merely kills
193 power. There is really no reason to use it.
- 194 5. Not surprisingly, if the two groups differ in scale, and not in location,
195 then none of the tests is appropriate (Figure 5a).
- 196 6. The presence of heavy tails (Figure 5b) may reduce power, but does
197 not quantitatively change results.
- 198 7. ... [TODO: effect of balancing].
- 199 8. ... [TODO: correlation between voxels].
- 200 9. ... [TODO: effect of tuning parameter].

201 The major insight from simulations is that the use of accuracy tests for
202 signal detection is underpowered compared to location tests. We now verify
203 this finding on a neuroimaging dataset.

204 5 Neuroimaging Example

205 Figure 2 is an application of both a location and an accuracy test to the data
206 of Pernet et al. [2015]. The authors of Pernet et al. [2015] collected fMRI
207 data while subjects were exposed to the sounds of human speech (vocal),
208 and other non-vocal sounds. Each subject was exposed to 20 sounds of each
209 type, totaling in $n = 40$ trials in each scan. The study was rather large and
210 consisted of about 200 subjects. The data was kindly made available by the
211 authors at the OpenfMRI website².

212 We perform group inference using within-subject permutations using the
213 pipeline of Stelzer et al. [2013], which was also reported in Gilron et al. [2016].
214 For completeness, the pipeline is described in Appendix A. To demonstrate
215 our point, we compare the *sd* location test with the *svm.cv.1* accuracy test
216 (see Table 1 for the definition of these statistics).

217 In agreement with our simulation results, the location test (*sd*) discovers
218 more brain regions when compared to an accuracy test (*svm.cv.1*). The
219 former discovers 1,232 regions, while the latter only 441, as depicted in
220 Figure 2. We emphasize that both test statistics were compared with the
221 same permutation scheme, and the same error controls, so that any difference
222 in detections is due to their different power.

²<https://openfmri.org/>

223 Having established that accuracy tests are underpowered both in simula-
 224 tion and in application, we wish to identify the conditions under which this
 225 will occur, and discuss implications on the practice of accuracy tests.



Figure 2: Brain regions encoding information discriminating between vocal and non-vocal stimuli. Map reports the centers of 27-voxel sized spherical regions, as discovered by an accuracy test (*svm.cv.1*), and a location test (*sd*). *svm.cv.1* was computed using 5-fold cross validation, and a cost parameter of 1. Region-wise significance was determined using the permutation scheme of Stelzer et al. [2013], followed by region-wise $FDR \leq 0.05$ control using the Benjamini-Hochberg procedure [Benjamini and Hochberg, 1995]. Number of permutations equals 400. The location test detect 1,232 regions, and the accuracy test 441, 399 of which are common to both. For the details of the analysis see Appendix A and Gilron et al. [2016].

226 6 Discussion

227 We have set out to understand which of the tests is more powerful: the
 228 accuracy test or the location test. Using simulations, we have concluded that
 229 the location tests are preferable. We attribute this to several phenomena:
 230 (a) Discretization introduced in finite samples by the accuracy test statistic.
 231 (b) Inefficient use of the data for the validation holdout set. In our high
 232 dimensional setup, we also confirmed that high-dimensional versions of the T^2
 233 test, such as Srivastava [2013] or Schäfer and Strimmer [2005] are preferable
 234 over the original T^2 .

235 The sensitivity of the power to the number of folds suggests that most
 236 of the power is lost due to the discretization and not to the holdout. The
 237 degree of discretization is governed by the sample size. For this reason, an
 238 asymptotic analysis such as Ramdas et al. [2016] may uncover the holdout
 239 inefficiency, but will not uncover the discretization effect. The practical ad-
 240 vice for the practitioner, is that for the purpose of signal detection, there
 241 is typically a multivariate test (be it a location test or other), that is more
 242 powerful than an accuracy test. There is also a good chance that it would
 243 be easier to implement, since no validation will be involved.

244 6.1 Neyman-Pearson Learning

245 [TODO: optimizing type I or type II errors]. Scott and Nowak [2005]

246 6.2 A good accuracy test

247 In Section 6.5 we discuss cases where an accuracy test cannot replace a
 248 location test. For such cases we collect some conclusions from our simulations
 249 on the best practices for accuracy tests.

- 250 1. The conservativeness due to discretization decreases with sample size.
- 251 2. Cross-validate. For moderate sample sizes, the power loss due to the
 252 holdout inefficiency is smaller than the power loss due to the concen-
 253 tration of the resubstitution accuracy.
- 254 3. Permuting features is easier than permuting labels. It allows to preserve
 255 balanced folds after a permutation without refolding.
- 256 4. There is no gain in z-scoring the accuracy scores.
- 257 5. Cross validated accuracy with balanced folds has more power than un-
 258 balanced folds. We currently have no intuition to offer for this phe-
 259 nomenon.
- 260 6. It is unclear what is the effect of the number of folds. More folds in-
 261 crease power by reducing the number of holdout samples. On the other
 262 hand, it increases the concentration of the accuracy statistic. Com-
 263 pounded with the discreteness of the accuracy statistic, this decreases
 264 power.
- 265 7. The value of the tuning parameters of a classifier do not matter.

6.3 Related Literature

Olivetti et al. [2012] and Olivetti et al. [2014] also looked into a similar problem as we do, namely, what is the preferred accuracy test? They propose a new test they call an *independence test*, and demonstrate by simulation that it has more power than other accuracy tests, and can deal with non-balanced data sets. We did not include this test in the battery we compared, but we note the following: (a) The independence test of Olivetti et al. [2012] relies on a discrete test statistic. This means that in the cases that the accuracy test is called upon for discriminating populations, it will probably be underpowered compared to location tests. (b) In contrast with the underlying motivation of Olivetti et al. [2012]’s independence test, we did not find that balancing the data folds is crucial for an accuracy test.

6.4 Non-linear predictors

It may be argued that accuracy tests permits the separation between classes in high dimensions, such as in *reproducing kernel Hilbert spaces* (RKHS) by using non-linear predictors. This is immaterial since group tests can also be performed in higher dimensions (see Gretton et al. [2012]).

6.5 Reservations

Some reservations to the generality of our findings are in order. Firstly, not all accuracy tests are concerned with signal detection. Indeed, it is possible that the purpose of the test is not to detect a difference between classes, but to actually test the performance of a particular classifier. Examples include brain decoding for machine interfaces, and clinical diagnosis, where the presence of a medical condition is “predicted” from imaging data. [e.g. Olivetti et al., 2012, Wager et al., 2013]

Secondly, not all signals are manifested in a shift of the null distribution. Our focus on location tests is misleading. Perhaps Simon et al. [2003]’s *class comparison* is a more appropriate name, in that it does not only imply a shift alternative. Indeed, one may consider signal, i.e. effects, as a change in scale, such as the *spiked covariance* model. In this case, other-than-Hotelling type tests are appropriate [e.g. Nadler, 2008]. Tests have been proposed even when the nature of the difference between populations is left unspecified [e.g. Gretton et al., 2012]. The fact that in our neuroimaging example (Section 5) some brain regions were detected with the accuracy test, and not the location test, is consistent with this observation.

The reservation to the reservation is that the far greater power of the

location test, certainly in our example, does serve as an empirical evidence that changes in location are a prevalent phenomenon.

6.6 Ease of implementation

A very important point is the ease of implementation. The need for cross validation of the accuracy test greatly increases its computational complexity. Moreover, anyone who has actually implemented tests with discrete statistics, will attest they are considerably harder to implement. This is because their unforgiveness to the type of inequality. Indeed, mistakenly replacing a weak inequality with a strong inequality in one's program may considerably change the results. This is not the case for continuous test statistics.

6.7 Epilogue

Given all the above, we find the popularity of accuracy tests quite puzzling. We believe this is due to a reversal of the inference cascade. Researchers first fit a classifier, and then ask if the classes are any different. Were they to start by asking if classes are any different, and only then try to classify, then location tests would naturally arise as the preferred method. As put by Ramdas et al. [2016]:

The recent popularity of machine learning has resulted in the extensive teaching and use of prediction in theoretical and applied communities and the relative lack of awareness or popularity of the topic of Neyman-Pearson style hypothesis testing in the computer science and related “data science” communities.

References

- T. W. Anderson. *An Introduction to Multivariate Statistical Analysis*. Wiley-Interscience, Hoboken, NJ, 3 edition edition, July 2003. ISBN 978-0-471-36091-9.
- Y. Benjamini and Y. Hochberg. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *JOURNAL-ROYAL STATISTICAL SOCIETY SERIES B*, 57:289–289, 1995.
- R. Gilron, J. Rosenblatt, O. Koyejo, R. A. Poldrack, and R. Mukamel. Quantifying spatial pattern similarity in multivariate analysis using functional anisotropy. *arXiv:1605.03482 [q-bio]*, May 2016.

- 334 P. Golland and B. Fischl. Permutation tests for classification: towards statis-
335 tical significance in image-based studies. In *IPMI*, volume 3, pages 330–341.
336 Springer, 2003.
- 337 A. Gretton, K. M. Borgwardt, M. J. Rasch, B. Schölkopf, and A. Smola. A
338 Kernel Two-sample Test. *J. Mach. Learn. Res.*, 13:723–773, Mar. 2012.
339 ISSN 1532-4435.
- 340 J. Hemerik and J. Goeman. Exact testing with random permutations.
341 *arXiv:1411.7565 [math, stat]*, Nov. 2014.
- 342 H. Hotelling. The Generalization of Student’s Ratio. *The Annals of Math-*
343 *ematical Statistics*, 2(3):360–378, Aug. 1931. ISSN 0003-4851, 2168-8990.
344 doi: 10.1214/aoms/1177732979.
- 345 W. Jiang, S. Varma, and R. Simon. Calculating confidence intervals for
346 prediction error in microarray classification using resampling. *Statistical*
347 *Applications in Genetics and Molecular Biology*, 7(1), 2008.
- 348 N. Kriegeskorte, R. Goebel, and P. Bandettini. Information-based functional
349 brain mapping. *Proceedings of the National Academy of Sciences of the*
350 *United States of America*, 103(10):3863–3868, July 2006. ISSN 0027-8424,
351 1091-6490. doi: 10.1073/pnas.0600244103.
- 352 E. L. Lehmann. Parametric versus nonparametrics: two alternative method-
353 ologies. *Journal of Nonparametric Statistics*, 21(4):397–405, 2009. ISSN
354 1048-5252. doi: 10.1080/10485250902842727.
- 355 B. Nadler. Finite sample approximation results for principal component
356 analysis: A matrix perturbation approach. *The Annals of Statistics*, 36
357 (6):2791–2817, Dec. 2008. ISSN 0090-5364, 2168-8966. doi: 10.1214/
358 08-AOS618.
- 359 E. Olivetti, S. Greiner, and P. Avesani. Induction in Neuroscience with
360 Classification: Issues and Solutions. In G. Langs, I. Rish, M. Grosse-
361 Wentrup, and B. Murphy, editors, *Machine Learning and Interpretation*
362 *in Neuroimaging*, number 7263 in Lecture Notes in Computer Science,
363 pages 42–50. Springer Berlin Heidelberg, 2012. ISBN 978-3-642-34712-2
364 978-3-642-34713-9. doi: 10.1007/978-3-642-34713-9_6.
- 365 E. Olivetti, S. Greiner, and P. Avesani. Statistical independence for the
366 evaluation of classifier-based diagnosis. *Brain Informatics*, 2(1):13–19, Dec.
367 2014. ISSN 2198-4018, 2198-4026. doi: 10.1007/s40708-014-0007-6.

- 368 F. Pereira, T. Mitchell, and M. Botvinick. Machine learning classifiers and
369 fMRI: A tutorial overview. *NeuroImage*, 45(1, Supplement 1):S199–S209,
370 Mar. 2009. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2008.11.007.
- 371 C. R. Pernet, P. McAleer, M. Latinus, K. J. Gorgolewski, I. Charest, P. E. G.
372 Bestelmeyer, R. H. Watson, D. Fleming, F. Crabbe, M. Valdes-Sosa, and
373 P. Belin. The human voice areas: Spatial organization and inter-individual
374 variability in temporal and extra-temporal cortices. *NeuroImage*, 119:164–
375 174, Oct. 2015. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2015.06.050.
- 376 M. D. Radmacher, L. M. McShane, and R. Simon. A Paradigm for
377 Class Prediction Using Gene Expression Profiles. *Journal of Computa-*
378 *tional Biology*, 9(3):505–511, June 2002. ISSN 1066-5277. doi: 10.1089/
379 106652702760138592.
- 380 A. Ramdas, A. Singh, and L. Wasserman. Classification Accuracy as a Proxy
381 for Two Sample Testing. *arXiv:1602.02210 [cs, math, stat]*, Feb. 2016.
- 382 J. Schäfer and K. Strimmer. A Shrinkage Approach to Large-Scale Covariance
383 Matrix Estimation and Implications for Functional Genomics. *Statistical*
384 *Applications in Genetics and Molecular Biology*, 4(1), Jan. 2005. ISSN
385 1544-6115. doi: 10.2202/1544-6115.1175.
- 386 C. Scott and R. Nowak. A Neyman-Pearson approach to statistical learning.
387 *IEEE Transactions on Information Theory*, 51(11):3806–3819, Nov. 2005.
388 ISSN 0018-9448. doi: 10.1109/TIT.2005.856955.
- 389 R. Simon, M. D. Radmacher, K. Dobbin, and L. M. McShane. Pitfalls in the
390 Use of DNA Microarray Data for Diagnostic and Prognostic Classification.
391 *Journal of the National Cancer Institute*, 95(1):14–18, Jan. 2003. ISSN
392 0027-8874, 1460-2105. doi: 10.1093/jnci/95.1.14.
- 393 M. S. Srivastava. On testing the equality of mean vectors in high dimension.
394 *Acta et Commentationes Universitatis Tartuensis de Mathematica*, 17(1):
395 31–56, June 2013. ISSN 2228-4699. doi: 10.12697/ACUTM.2013.17.03.
- 396 M. S. Srivastava, S. Katayama, and Y. Kano. A two sample test in high
397 dimensional data. *Journal of Multivariate Analysis*, 114:349–358, Feb.
398 2013. ISSN 0047-259X. doi: 10.1016/j.jmva.2012.08.014.
- 399 J. Stelzer, Y. Chen, and R. Turner. Statistical inference and multiple test-
400 ing correction in classification-based multi-voxel pattern analysis (MVPA):
401 Random permutations and cluster size control. *NeuroImage*, 65:69–82, Jan.
402 2013. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2012.09.063.

- 403 A. W. van der Vaart. *Asymptotic Statistics*. Cambridge University Press,
404 Cambridge, UK ; New York, NY, USA, Oct. 1998. ISBN 978-0-521-49603-
405 2.
- 406 G. Varoquaux, P. R. Raamana, D. Engemann, A. Hoyos-Idrobo, Y. Schwartz,
407 and B. Thirion. Assessing and tuning brain decoders: cross-validation,
408 caveats, and guidelines. working paper or preprint, June 2016.
- 409 T. D. Wager, L. Y. Atlas, M. A. Lindquist, M. Roy, C.-W. Woo, and E. Kross.
410 An fMRI-Based Neurologic Signature of Physical Pain. *New England Jour-*
411 *nal of Medicine*, 368(15):1388–1397, Apr. 2013. ISSN 0028-4793. doi:
412 10.1056/NEJMoa1204471.

413 A Analysis pipeline

414 Here is the analysis pipeline of Stelzer et al. [2013] we for the auditory data in
 415 Gilron et al. [2016]. Denoting by $i = 1, \dots, I$ the subject index, $v = 1, \dots, V$
 416 the voxel index, and $s = 1, \dots, S$ the permutation index. Since regions³ are
 417 centered around a unique voxel, the voxel index v also serves as a unique
 418 region index. Algorithm 1 computes a region-wise test statistic, which is
 419 compared to its permutation null distribution computed by Algorithm 2.

Algorithm 1: Compute a group parametric map.

Data: fMRI scans, and experimental design.
Result: Brain map of group statistics: $\{\bar{T}_v\}_{v=1}^V$

```

1 for  $v \in 1, \dots, V$  do
2   for  $i \in 1, \dots, I$  do
3      $T_{i,v} \leftarrow$  test statistic for subject  $i$  in a region centered at  $v$ .
4    $\bar{T}_v \leftarrow \frac{1}{I} \sum_{i=1}^I T_{i,v}$ .
```

Algorithm 2: Compute a permutation p-value map.

Data: fMRI scans of 20 subjects, experimental design.
Result: Brain map of permutation p-values: $\{p_v\}_{v=1}^V$

```

1 for  $s \in 1, \dots, S$  do
2   permute labels;
3    $\bar{T}_v^s \leftarrow$  parametric map
```

³*searchlight* or *sphere* in the MVPA parlance

B Simulations

Figure 3: [TODO].

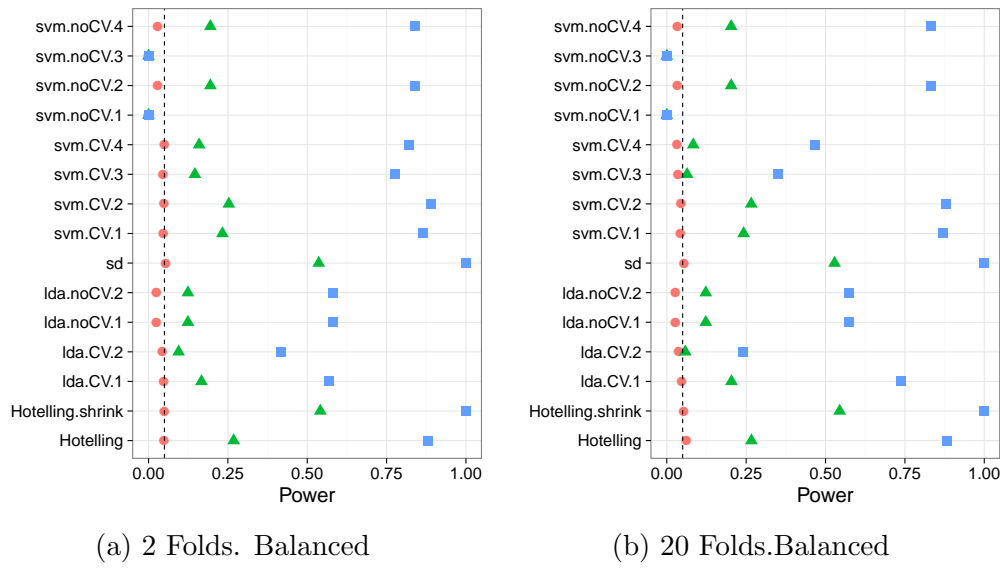


Figure 4: [TODO].

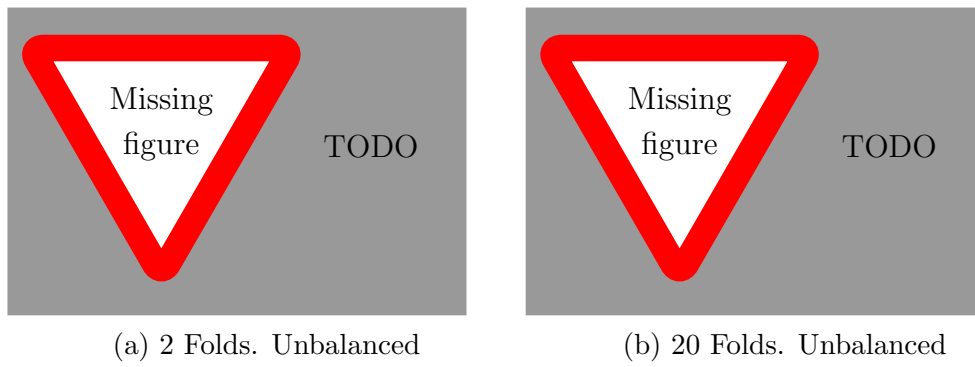


Figure 5: [TODO].

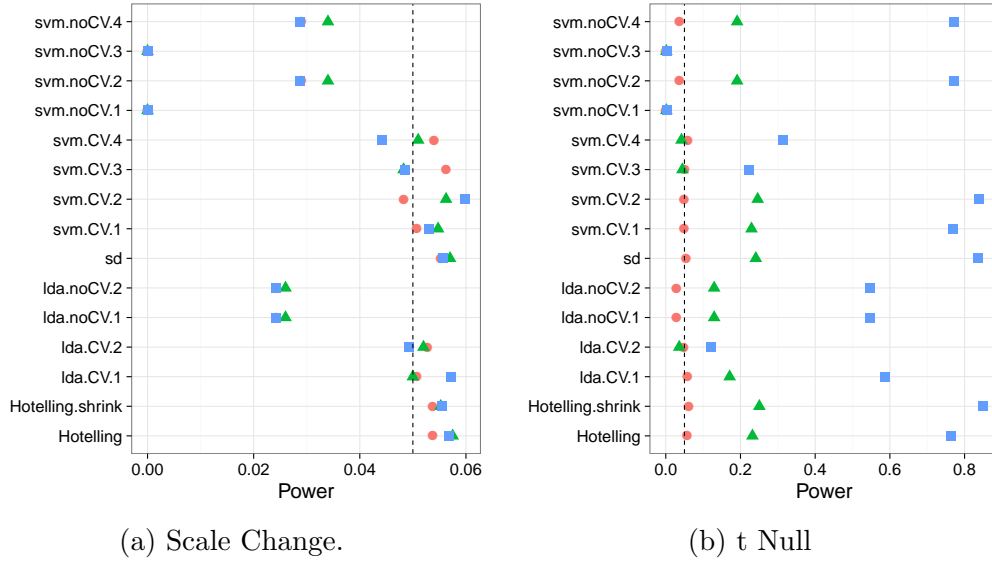


Figure 6: [TODO].

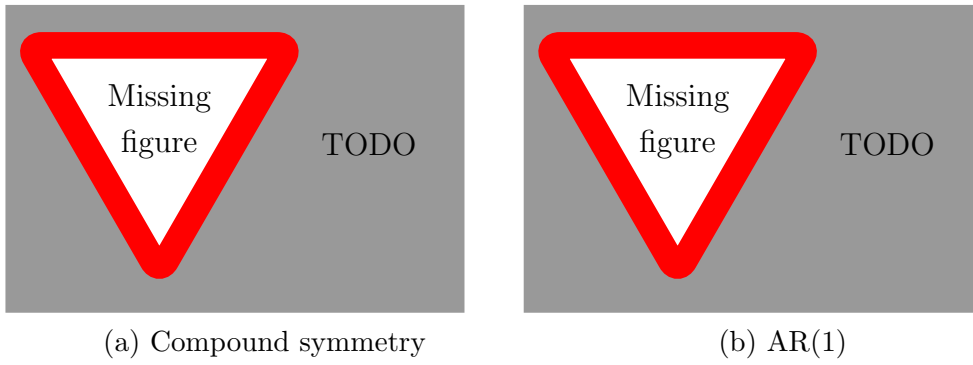


Figure 7: [TODO].

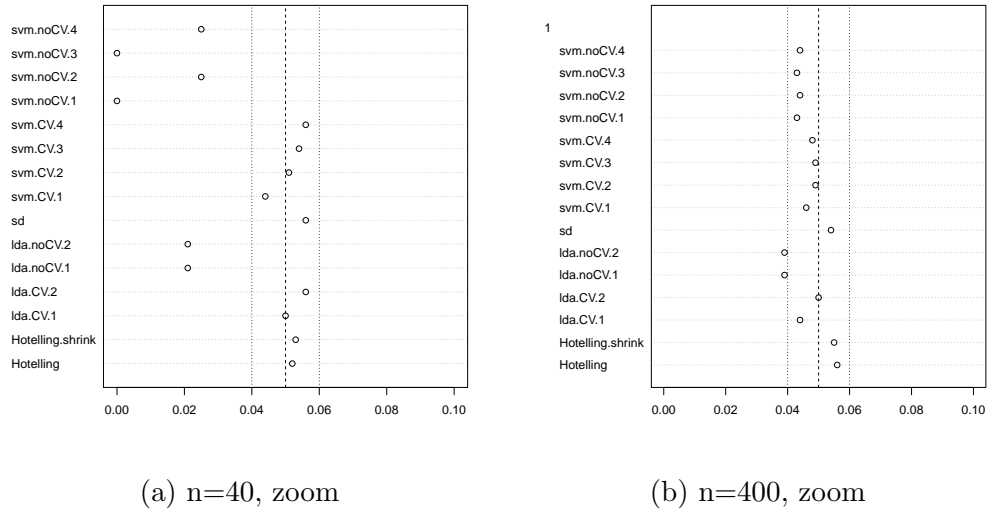


Figure 8: [TODO].

