

# Better-Than-Chance Classification for Signal Detection

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## 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 citations<sup>1</sup> 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 as inefficient, we recall that Ramdas et al. [2016] analyzed a *half-sample* holdout. The authors conjectured that a leave-one-out approach, which makes more efficient use of the data, may have better performance. Also, the analysis in Ramdas et al. [2016] is asymptotic. This eschews the discrete nature of the accuracy statistic, which will be shown to have crucial impact. Since typical sample sizes in neuroscience are not large, we seek to study which test is to be preferred in finite samples?

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<sup>1</sup>GoogleScholar. Accessed on Aug 4, 2016.

64 Our conclusion will be quite simple: *location tests almost always have more*  
65 *power than accuracy tests.*

66 The main argument for our statement rests upon the observation that  
67 with typical sample sizes, the accuracy test statistic is highly discrete. Dis-  
68 crete test statistics are known to be conservative [Hemerik and Goeman,  
69 2014], since they are insensitive to mild perturbations of the data, and they  
70 cannot exhaust the permissible false positive rate. The degree of discretiza-  
71 tion is governed by the number of samples. In our neuroscience example  
72 from Gilron et al. [2016], the classification is performed based on 40 trials,  
73 so that the test statistic may assume only 40 possible values. This number  
74 of examples is not unusual if considering this is the number of subjects, or  
75 the number of trial-repeats in an neuroimaging study.

76 The discretization effect is aggravated if the test statistic is highly concen-  
77 trated. For an intuition consider the usage of a the *resubstitution accuracy*  
78 as a test statistic. This statistic simply means that the accuracy is not cross  
79 validated. If the data is high dimensional, the resubstitution accuracy will be  
80 very high due to over fitting [McLACHLAN, 1976, Theorem 1]. In an extreme  
81 case, the resubstitution accuracy will be 1 for the observed data, but also for  
82 any permutation. The concentration of resubstitution accuracy near 1, and  
83 its discreteness, render this test completely useless, with a power of 0.

84 To compare the power of accuracy tests and location tests in finite sam-  
85 ples, we perform a simulation study of a battery of test statistics. The main  
86 findings are reported in Section 4, and the intuition for our findings is pro-  
87 vided in Section 6, but first, the problem’s setup.

## 88 2 Problem setup

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

92 Given  $n$  pairs of  $(x_i, y_i)$ , typically assumed i.i.d., a location test amounts  
93 to testing whether  $x|y = 1$  has the the same distribution as  $x|y = -1$ .  
94 I.e., we test if the multivariate voxel activation pattern has the same dis-  
95 tribution when given a vocal stimulus, as when given a non-vocal stimulus.  
96 An accuracy test amounts to learning a predictive model  $\hat{f}(x)$  from some  
97 assumed model class  $\hat{f} \in \mathcal{F}$ . The prediction accuracy, denoted  $T_{\hat{f}}^{acc}$ , is de-  
98 fined as the probability of a given classifier  $\hat{f}$  of making a correct prediction  
99  $T_{\hat{f}}^{acc} := Prob(\hat{f}(x) = y)$  when given a randomly drawn data point,  $(x, y)$ .  
100 A statistically significant “better than chance” estimate of  $T_{\hat{f}}^{acc}$  is evidence

101 that the classes are distinct.

## 102 2.1 Candidate Tests

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

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

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

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

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

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

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

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

162 **How many folds?** Different authors suggest different rules for the num-  
163 ber of folds. We will be varying the number of folds. This will affect the  
164 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

176 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  
 178 the most conservative tests are the resubstitution accuracy measures. We  
 179 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. The various statistics on the y axis. Their details are given in Table 1. Effects vary over 0 (red circle), 0.25 (green triangle), and 0.5 (blue square). Simulation details in Appendix B. Cross-validation was performed with balanced (stratified) and unbalanced data folding. See sub-captions.*



## 180 4 Power

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

- 185 1. Location tests have more power than accuracy tests in all our configu-  
 186 rations.
- 187 2. The conservativeness decays as the sample grows (Figures 6a, 6b and  
 188 7a), supporting the statement that discretization is responsible for  
 189 power loss.

- 190 3. The power may increase or decrease with the number of folds (Figure 3).  
191 [TODO:effect of n.folds.]
- 192 4. The z-scoring of the accuracies was introduced to deal with unbalanced  
193 foldings. If the z-scoring has any effect at all, it merely kills power.  
194 There is really no reason to use it.
- 195 5. Both accuracy and location tests are inappropriate for scale alternatives  
196 (Figure 5a). This was to be expected and is reported mostly as a sanity  
197 check.
- 198 6. The presence of heavy tails (Figure 5b) may reduce power, but does  
199 not quantitatively change results.
- 200 7. Balanced folding typically has no effect. It increased power only for  
201 the z-scored statistics (Figure 1). This is surprising given they were  
202 precisely designed to deal with the presence of imbalance.
- 203 8. Varying the accuracy test's tuning parameter, such as the cost (i.e.  
204 margins) has no effect on the power of the test.
- 205 9. Correlation between coordinates, mimicking temporal correlation in  
206 fMRI data, has no effect on conclusions, since all test statistics account  
207 for this correlation (Figure 7b).

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

## 211 5 Neuroimaging Example

212 Figure 2 is an application of both a location and an accuracy test to the data  
213 of Pernet et al. [2015]. The authors of Pernet et al. [2015] collected fMRI  
214 data while subjects were exposed to the sounds of human speech (vocal),  
215 and other non-vocal sounds. Each subject was exposed to 20 sounds of each  
216 type, totaling in  $n = 40$  trials in each scan. The study was rather large and  
217 consisted of about 200 subjects. The data was kindly made available by the  
218 authors at the OpenfMRI website<sup>2</sup>.

219 We perform group inference using within-subject permutations using the  
220 pipeline of Stelzer et al. [2013], which was also reported in Gilron et al. [2016].  
221 For completeness, the pipeline is described in Appendix A. To demonstrate

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<sup>2</sup><https://openfmri.org/>



our point, we compare the *sd* location test with the *svm.cv.1* accuracy test (see Table 1 for the definition of these statistics).

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

Having established that accuracy tests are underpowered both in simulation and in application, we wish to identify the conditions under which this 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].*

## 233 6 Discussion

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

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

### 251 6.1 Neyman-Pearson Classification

252 [TODO]

### 253 6.2 A good accuracy test

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

- 257 1. The conservativeness due to discretization decreases with sample size.
- 258 2. Cross-validate. For moderate sample sizes, the power loss due to the  
259 holdout inefficiency is smaller than the power loss due to the concen-  
260 tration of the resubstitution accuracy.
- 261 3. Permuting features is easier than permuting labels. It allows to preserve  
262 balanced folds after a permutation without refolding.
- 263 4. There is no gain in z-scoring the accuracy scores.

- 264 5. Cross validated accuracy with balanced folds has more power than un-  
265 balanced folds. We currently have no intuition to offer for this phe-  
266 nomenon.
- 267 6. It is unclear what is the effect of the number of folds. More folds in-  
268 crease power by reducing the number of holdout samples. On the other  
269 hand, it increases the concentration of the accuracy statistic. Com-  
270 pounded with the discreteness of the accuracy statistic, this decreases  
271 power.
- 272 7. The value of the tuning parameters of a classifier do not matter.

### 273 6.3 Related Literature

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

### 285 6.4 Non-linear predictors

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

### 290 6.5 Reservations

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

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

308 The reservation to the reservation is that the far greater power of the  
 309 location test, certainly in our example, does serve as an empirical evidence  
 310 that changes in location are a prevalent phenomenon.

## 311 6.6 Ease of implementation

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

## 319 6.7 Epilogue

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

326 The recent popularity of machine learning has resulted in the ex-  
 327 tensive teaching and use of prediction in theoretical and applied  
 328 communities and the relative lack of awareness or popularity of  
 329 the topic of Neyman-Pearson style hypothesis testing in the com-  
 330 puter 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.
- P. Golland and B. Fischl. Permutation tests for classification: towards statistical significance in image-based studies. In *IPMI*, volume 3, pages 330–341. Springer, 2003.
- A. Gretton, K. M. Borgwardt, M. J. Rasch, B. Schölkopf, and A. Smola. A Kernel Two-sample Test. *J. Mach. Learn. Res.*, 13:723–773, Mar. 2012. ISSN 1532-4435.
- J. Hemerik and J. Goeman. Exact testing with random permutations. *arXiv:1411.7565 [math, stat]*, Nov. 2014.
- H. Hotelling. The Generalization of Student’s Ratio. *The Annals of Mathematical Statistics*, 2(3):360–378, Aug. 1931. ISSN 0003-4851, 2168-8990. doi: 10.1214/aoms/1177732979.
- W. Jiang, S. Varma, and R. Simon. Calculating confidence intervals for prediction error in microarray classification using resampling. *Statistical Applications in Genetics and Molecular Biology*, 7(1), 2008.
- N. Kriegeskorte, R. Goebel, and P. Bandettini. Information-based functional brain mapping. *Proceedings of the National Academy of Sciences of the United States of America*, 103(10):3863–3868, July 2006. ISSN 0027-8424, 1091-6490. doi: 10.1073/pnas.0600244103.
- E. L. Lehmann. Parametric versus nonparametrics: two alternative methodologies. *Journal of Nonparametric Statistics*, 21(4):397–405, 2009. ISSN 1048-5252. doi: 10.1080/10485250902842727.
- G. J. McLACHLAN. The bias of the apparent error rate in discriminant analysis. *Biometrika*, 63(2):239–244, Jan. 1976. ISSN 0006-3444, 1464-3510. doi: 10.1093/biomet/63.2.239.

- 365 B. Nadler. Finite sample approximation results for principal component  
366 analysis: A matrix perturbation approach. *The Annals of Statistics*, 36  
367 (6):2791–2817, Dec. 2008. ISSN 0090-5364, 2168-8966. doi: 10.1214/  
368 08-AOS618.
- 369 E. Olivetti, S. Greiner, and P. Avesani. Induction in Neuroscience with  
370 Classification: Issues and Solutions. In G. Langs, I. Rish, M. Grosse-  
371 Wentrup, and B. Murphy, editors, *Machine Learning and Interpretation*  
372 *in Neuroimaging*, number 7263 in Lecture Notes in Computer Science,  
373 pages 42–50. Springer Berlin Heidelberg, 2012. ISBN 978-3-642-34712-2  
374 978-3-642-34713-9. doi: 10.1007/978-3-642-34713-9\_6.
- 375 E. Olivetti, S. Greiner, and P. Avesani. Statistical independence for the  
376 evaluation of classifier-based diagnosis. *Brain Informatics*, 2(1):13–19, Dec.  
377 2014. ISSN 2198-4018, 2198-4026. doi: 10.1007/s40708-014-0007-6.
- 378 F. Pereira, T. Mitchell, and M. Botvinick. Machine learning classifiers and  
379 fMRI: A tutorial overview. *NeuroImage*, 45(1, Supplement 1):S199–S209,  
380 Mar. 2009. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2008.11.007.
- 381 C. R. Pernet, P. McAleer, M. Latinus, K. J. Gorgolewski, I. Charest, P. E. G.  
382 Bestelmeyer, R. H. Watson, D. Fleming, F. Crabbe, M. Valdes-Sosa, and  
383 P. Belin. The human voice areas: Spatial organization and inter-individual  
384 variability in temporal and extra-temporal cortices. *NeuroImage*, 119:164–  
385 174, Oct. 2015. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2015.06.050.
- 386 M. D. Radmacher, L. M. McShane, and R. Simon. A Paradigm for  
387 Class Prediction Using Gene Expression Profiles. *Journal of Computa-*  
388 *tional Biology*, 9(3):505–511, June 2002. ISSN 1066-5277. doi: 10.1089/  
389 106652702760138592.
- 390 A. Ramdas, A. Singh, and L. Wasserman. Classification Accuracy as a Proxy  
391 for Two Sample Testing. *arXiv:1602.02210 [cs, math, stat]*, Feb. 2016.
- 392 J. Schäfer and K. Strimmer. A Shrinkage Approach to Large-Scale Covariance  
393 Matrix Estimation and Implications for Functional Genomics. *Statistical*  
394 *Applications in Genetics and Molecular Biology*, 4(1), Jan. 2005. ISSN  
395 1544-6115. doi: 10.2202/1544-6115.1175.
- 396 C. Scott and R. Nowak. A Neyman-Pearson approach to statistical learning.  
397 *IEEE Transactions on Information Theory*, 51(11):3806–3819, Nov. 2005.  
398 ISSN 0018-9448. doi: 10.1109/TIT.2005.856955.

- 399 R. Simon, M. D. Radmacher, K. Dobbin, and L. M. McShane. Pitfalls in the  
400 Use of DNA Microarray Data for Diagnostic and Prognostic Classification.  
401 *Journal of the National Cancer Institute*, 95(1):14–18, Jan. 2003. ISSN  
402 0027-8874, 1460-2105. doi: 10.1093/jnci/95.1.14.
- 403 M. S. Srivastava. On testing the equality of mean vectors in high dimension.  
404 *Acta et Commentationes Universitatis Tartuensis de Mathematica*, 17(1):  
405 31–56, June 2013. ISSN 2228-4699. doi: 10.12697/ACUTM.2013.17.03.
- 406 M. S. Srivastava, S. Katayama, and Y. Kano. A two sample test in high  
407 dimensional data. *Journal of Multivariate Analysis*, 114:349–358, Feb.  
408 2013. ISSN 0047-259X. doi: 10.1016/j.jmva.2012.08.014.
- 409 J. Stelzer, Y. Chen, and R. Turner. Statistical inference and multiple test-  
410 ing correction in classification-based multi-voxel pattern analysis (MVPA):  
411 Random permutations and cluster size control. *NeuroImage*, 65:69–82, Jan.  
412 2013. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2012.09.063.
- 413 A. W. van der Vaart. *Asymptotic Statistics*. Cambridge University Press,  
414 Cambridge, UK ; New York, NY, USA, Oct. 1998. ISBN 978-0-521-49603-  
415 2.
- 416 G. Varoquaux, P. R. Raamana, D. Engemann, A. Hoyos-Idrobo, Y. Schwartz,  
417 and B. Thirion. Assessing and tuning brain decoders: cross-validation,  
418 caveats, and guidelines. working paper or preprint, June 2016.
- 419 T. D. Wager, L. Y. Atlas, M. A. Lindquist, M. Roy, C.-W. Woo, and E. Kross.  
420 An fMRI-Based Neurologic Signature of Physical Pain. *New England Jour-  
421 nal of Medicine*, 368(15):1388–1397, Apr. 2013. ISSN 0028-4793. doi:  
422 10.1056/NEJMoA1204471.

## 423 A Analysis pipeline

424 Here is the analysis pipeline of Stelzer et al. [2013] we for the auditory data in  
 425 Gilron et al. [2016]. Denoting by  $i = 1, \dots, I$  the subject index,  $v = 1, \dots, V$   
 426 the voxel index, and  $s = 1, \dots, S$  the permutation index. Since regions<sup>3</sup> are  
 427 centered around a unique voxel, the voxel index  $v$  also serves as a unique  
 428 region index. Algorithm 1 computes a region-wise test statistic, which is  
 429 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
```

---

<sup>3</sup>*searchlight* or *sphere* in the MVPA parlance



## 432 B Simulation Details

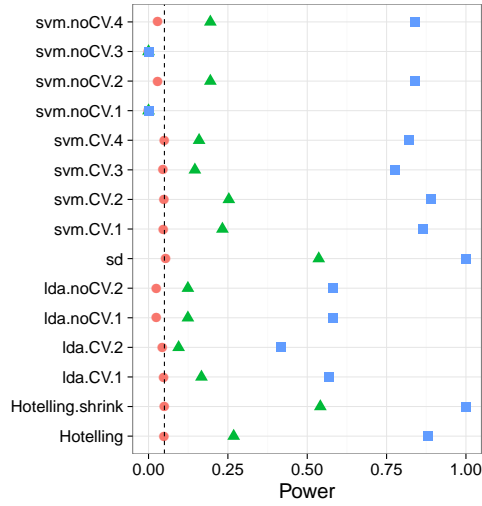
433 The following details are common to all the reported simulations, unless stated  
434 otherwise in a figure’s caption. The R code for the simulations can be found  
435 in [TODO].

436 Each simulation is based on 4,000 replications. In each replication, we  
437 generate  $n$  i.i.d. samples from a shift model  $\mathbf{x}_i = \mu \mathbf{y}_i^* + \eta_i$ . Where  $y_i^* = \{0, 1\}$   
438 is the class of subject  $i$  in dummy coding. Recalling that  $y_i = \{-1, 1\}$  is the  
439 class in effect coding, then clearly  $y_i = 2y_i^* - 1$ . The noise is distributed as  
440  $\eta_i \sim \mathcal{N}_p(0, \Sigma)$ . The sample size  $n = 40$ . The dimension of the data is  $p = 23$ .  
441 The covariance  $\Sigma = I$ . Effects, i.e. shifts  $\mu$ , are equal coordinate  $p$ -vectors  
442 with coordinates that vary over  $\mu \in \{0, 1/4, 1/2\}$ .

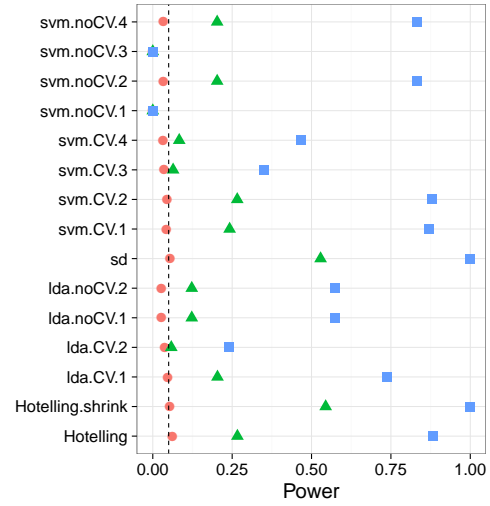
443 Having generated the data, we compute each of the test statistics in Ta-  
444 ble 1. For test statistics that require data folding, we used 8 folds. We then  
445 compute a permutation p-value by permuting the class labels, and recomput-  
446 ing each test statistic. We perform 400 such permutations. We then reject  
447 the  $\mu_i = 0$  null hypothesis if the permutation p-value is smaller than 0.05.  
448 The reported power is the proportion of replication where the permutation  
449 p-value falls below 0.05.

## C Simulation Results

Figure 3: *Simulation details in Appendix B except the changes in the sub-captions.*

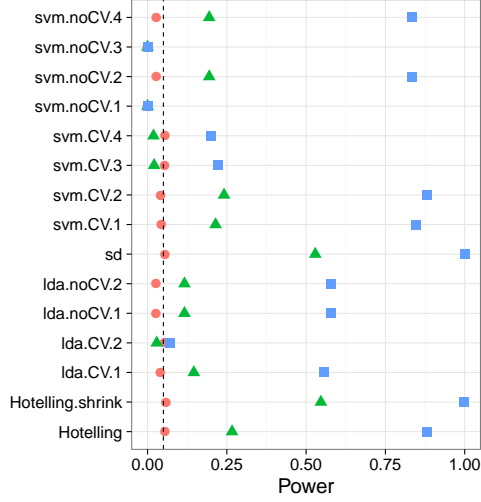


(a) 2-fold cross validation.  
Balanced folding.

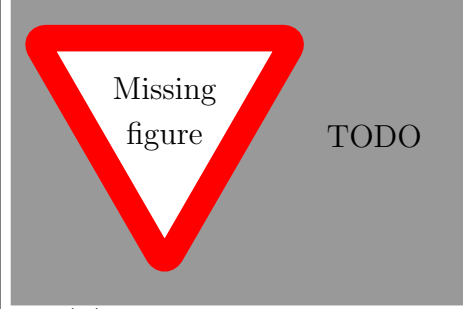


(b) 20-fold cross validation.  
Balanced folding

Figure 4: *Simulation details in Appendix B except the changes in the sub-captions.*

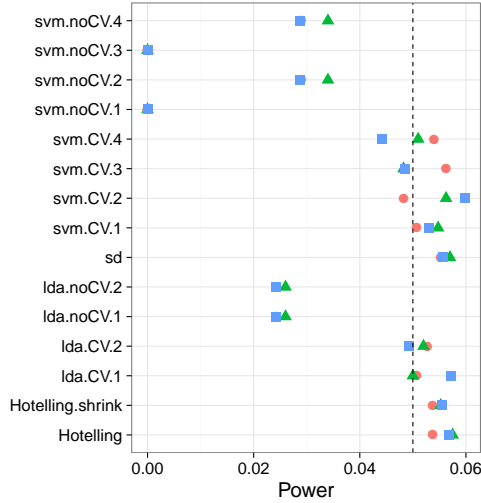


(a) **2-fold** cross validation.  
Unbalanced folding.

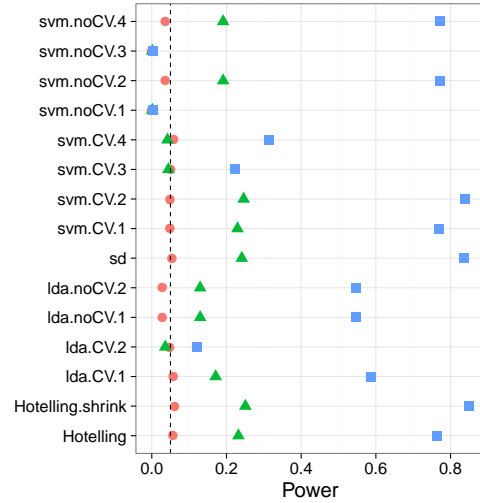


(b) **20-fold** cross validation.  
Unbalanced folding.

Figure 5: *Simulation details in Appendix B except the changes in the sub-captions.*

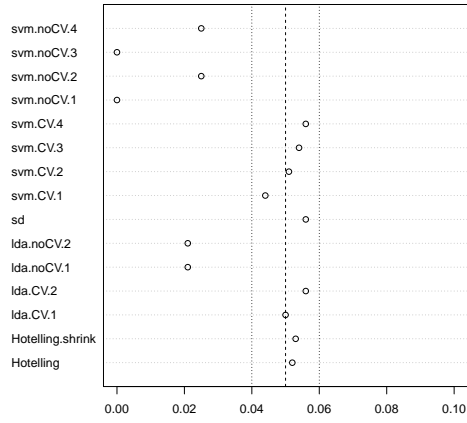


(a) **Scale Change:**  $\mathbf{x}_i = \eta_i * \mu^{\mathbf{y}_i^*}$   
so that the effect are a scale  
change.

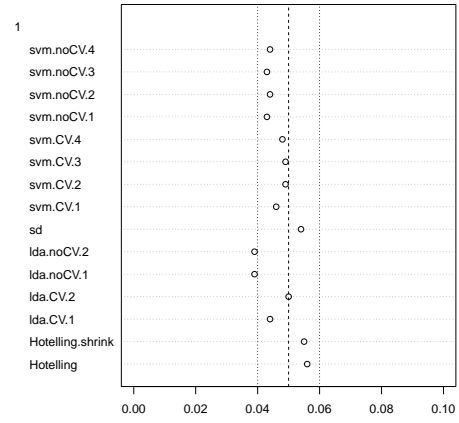


(b) **Heavytailed:**  $\eta_i$  is not  
 $p$ -variate Gaussian, but rather  
 $p$ -variate  $t$ , with  $df = 3$ .

Figure 6: *Simulation details in Appendix B except the changes in the sub-captions.*

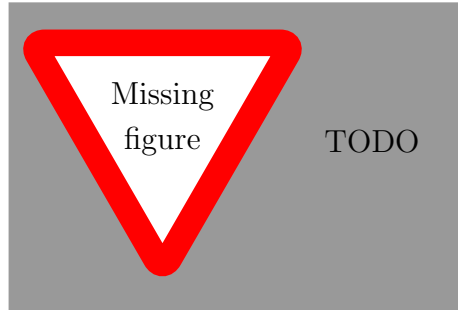


(a) **Low-Dimension:** False positive rates for  $n = 40$ .



(b) **High-Dimension:** False positive rates for  $n = 400$ .

*Figure 7: Simulation details in Appendix B except the changes in the sub-captions.*



(a) **High-Dimension, local alternative:**  $n = 400$ ,  
 $\mu \in \frac{\sqrt{40}}{\sqrt{400}} \times \{0, 1/4, 1/2\}$ .



(b) **AR(1) dependence:**  
 $\Sigma_{k,l} = \rho^{|k-l|}; \rho = 0.8$ .