

Better-Than-Chance Classification for Signal Detection

Jonathan Rosenblatt Roei Gilron Roy Mukamel

August 4, 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 favour 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 a 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* in Ramdas et al. [2016], and simply means that the accuracy is not cross validated. If the data is high dimensional, the train accuracy will be very high due to over fitting. In an extreme case, the train accuracy will be 1 for the observed data, but also for any permutaiton. The concentration of the train 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

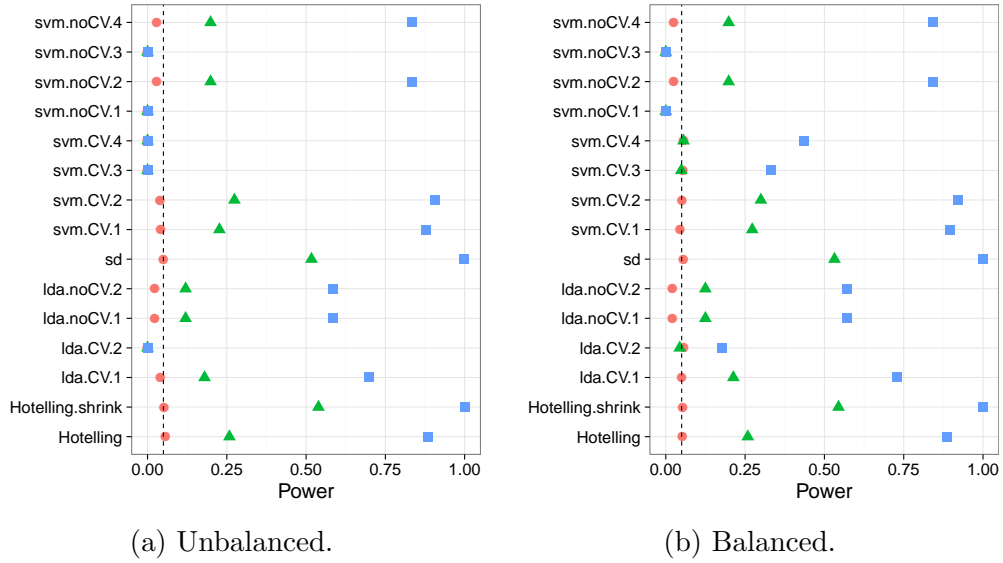
Table 1: This table enumerates the various test statistics we will be studying. Three are location tests: Hotelling, Hotelling.shrink, and sd. *Hotelling* is the classical two-group T^2 statistic. *Hotelling.shrink* is a high dimensional version with the regularized covariance in Schäfer and Strimmer [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 train 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 un-
 192 balanced foldings. In the cases where it has any effect, it merely kills
 193 power. There is really no reason to use it.
- 194 5. ... [TODO: effect of balancing]
- 195 6. ... [TODO: heavy tails]
- 196 7. ... [TODO: signal in scale]
- 197 8. ... [TODO: correlation between voxels]

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

201 5 Neuroimaging Example

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

209 We perform permutation inference using the pipeline of Stelzer et al.
 210 [2013], which was also used in Gilron et al. [2016]. For completeness, the
 211 pipeline is described in Appendix A. To demonstrate our point, we compare
 212 the *sd* location test with the *svm.cv.1* accuracy test (see Table 1 for the
 213 definition of these statistics).

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

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

²<https://openfmri.org/>



Figure 2: Brain regions encoding information discriminating between vocal and non-vocal stimuli. Map reports the centres 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].

6 Discussion

We have set out to understand which of the tests is more powerful: the accuracy test or the location test. Using simulations, we have concluded that the location tests are preferable. We attribute this to the discretization introduced in finite samples by the accuracy test statistic. This also explains why an asymptotic analysis, such as Ramdas et al. [2016], did not find a rate difference. Their results however are limited in that: (a) they are asymptotic, thus eschew the discretization effect. (b) They assume a half-sample holdout, so that half of the data is available for estimation. (c) They assume a linear classifier.

The linear classifier assumption, (c), is immaterial since for every non-linear classifier, one may design a non-linear location test. See ? for an example of a location test in RKHS space. [TODO: relate to large sample simulation] [TODO: discuss ARE, and holdout versus leave one out effect].

237 [TODO: non-linear classification and testing].

238 Olivetti et al. [2012] and Olivetti et al. [2014] also looked into a similar
239 problem as we do, namely, what is the preferred accuracy test? They propose
240 a new test they call an *independence test*, and demonstrate by simulation that
241 it has more power than other accuracy tests, and can deal with non-balanced
242 data sets. We did not include this test in the battery we compared, but we
243 note the following: (a) The independence test of Olivetti et al. [2012] relies
244 on a discrete test statistic. This means that in the cases that the accuracy
245 test is called upon for discriminating populations, it will probably be under-
246 powered compared to location tests. (b) The problem of the accuracy test
247 with unbalanced data-sets, which motivates Olivetti et al. [2012]’s indepen-
248 dence test, can also be remedied by replacing the accuracy statistic with its
249 z-score, as suggested in Section 2.1.

250 At this point some reservations to the generality of our findings are in
251 order. Firstly, not all accuracy tests are concerned with signal detection.
252 Indeed, it is possible that the purpose of the test is not to detect a difference
253 between classes, but to actually test if a particular classifier is better than
254 chance. This would be the case in decoding applications, like brain-machine
255 interfaces, where the localization of a signal is not enough. Clinical diagnosis is
256 another application, where the presence of a medical condition is “predicted”
257 from imaging data. [e.g. Olivetti et al., 2012, Wager et al., 2013]

258 Secondly, not all signals are manifested in a shift of the null distribution.
259 Put differently, the preferred alternative to an accuracy test is not always a
260 location test. Indeed, one may consider signal, i.e. effects, as a change in
261 scale, such as the *spiked covariance* model. In this case, other-than-Hotelling
262 type tests are appropriate [TODO: cite change in covariance alternative].
263 Tests have been proposed even when the nature of the difference between
264 populations is left unspecified [e.g. ?]. The fact that in our neuroimaging
265 example (Section 5) some brain regions were detected with the accuracy test,
266 and not the location test, is consistent with this observation. On the other
267 hand, the far greater power of the location test, certainly in our example,
268 does serve as empirical evidence that changes in location are a prevalent
269 phenomenon. [TODO: signal in scale? heavy tails?]

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

277 Given all the above, we find the popularity of accuracy tests quite puz-

278 zling. We believe this is due to a reversal of the inference cascade. Re-
 279 searchers first fit a classifier, and then ask if the classes are any different.
 280 Were they to start by asking if classes are any different, and only then try
 281 to classify, then location tests would naturally arise as the preferred method.
 282 As put by Ramdas et al. [2016]:

283 The recent popularity of machine learning has resulted in the ex-
 284 tensive teaching and use of prediction in theoretical and applied
 285 communities and the relative lack of awareness or popularity of
 286 the topic of Neyman-Pearson style hypothesis testing in the com-
 287 puter science and related “data science” communities.

288 References

- 289 T. W. Anderson. *An Introduction to Multivariate Statistical Analysis*. Wiley-
 290 Interscience, Hoboken, NJ, 3 edition edition, July 2003. ISBN 978-0-471-
 291 36091-9.
- 292 Y. Benjamini and Y. Hochberg. Controlling the false discovery rate: a prac-
 293 tical and powerful approach to multiple testing. *JOURNAL-ROYAL STA-*
 294 *TISTICAL SOCIETY SERIES B*, 57:289–289, 1995.
- 295 R. Gilron, J. Rosenblatt, O. Koyejo, R. A. Poldrack, and R. Mukamel. Quan-
 296 tifying spatial pattern similarity in multivariate analysis using functional
 297 anisotropy. *arXiv:1605.03482 [q-bio]*, May 2016.
- 298 P. Golland and B. Fischl. Permutation tests for classification: towards statis-
 299 tical significance in image-based studies. In *IPMI*, volume 3, pages 330–341.
 300 Springer, 2003.
- 301 J. Hemerik and J. Goeman. Exact testing with random permutations.
 302 *arXiv:1411.7565 [math, stat]*, Nov. 2014.
- 303 H. Hotelling. The Generalization of Student’s Ratio. *The Annals of Math-*
 304 *ematical Statistics*, 2(3):360–378, Aug. 1931. ISSN 0003-4851, 2168-8990.
 305 doi: 10.1214/aoms/1177732979.
- 306 W. Jiang, S. Varma, and R. Simon. Calculating confidence intervals for
 307 prediction error in microarray classification using resampling. *Statistical*
 308 *Applications in Genetics and Molecular Biology*, 7(1), 2008.
- 309 N. Kriegeskorte, R. Goebel, and P. Bandettini. Information-based functional
 310 brain mapping. *Proceedings of the National Academy of Sciences of the*

- 311 *United States of America*, 103(10):3863–3868, July 2006. ISSN 0027-8424,
312 1091-6490. doi: 10.1073/pnas.0600244103.
- 313 E. L. Lehmann. Parametric versus nonparametrics: two alternative method-
314 ologies. *Journal of Nonparametric Statistics*, 21(4):397–405, 2009. ISSN
315 1048-5252. doi: 10.1080/10485250902842727.
- 316 E. Olivetti, S. Greiner, and P. Avesani. Induction in Neuroscience with
317 Classification: Issues and Solutions. In G. Langs, I. Rish, M. Grosse-
318 Wentrup, and B. Murphy, editors, *Machine Learning and Interpretation*
319 *in Neuroimaging*, number 7263 in Lecture Notes in Computer Science,
320 pages 42–50. Springer Berlin Heidelberg, 2012. ISBN 978-3-642-34712-2
321 978-3-642-34713-9. doi: 10.1007/978-3-642-34713-9_6.
- 322 E. Olivetti, S. Greiner, and P. Avesani. Statistical independence for the
323 evaluation of classifier-based diagnosis. *Brain Informatics*, 2(1):13–19, Dec.
324 2014. ISSN 2198-4018, 2198-4026. doi: 10.1007/s40708-014-0007-6.
- 325 F. Pereira, T. Mitchell, and M. Botvinick. Machine learning classifiers and
326 fMRI: A tutorial overview. *NeuroImage*, 45(1, Supplement 1):S199–S209,
327 Mar. 2009. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2008.11.007.
- 328 C. R. Pernet, P. McAleer, M. Latinus, K. J. Gorgolewski, I. Charest, P. E. G.
329 Bestelmeyer, R. H. Watson, D. Fleming, F. Crabbe, M. Valdes-Sosa, and
330 P. Belin. The human voice areas: Spatial organization and inter-individual
331 variability in temporal and extra-temporal cortices. *NeuroImage*, 119:164–
332 174, Oct. 2015. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2015.06.050.
- 333 M. D. Radmacher, L. M. McShane, and R. Simon. A Paradigm for
334 Class Prediction Using Gene Expression Profiles. *Journal of Computa-*
335 *tional Biology*, 9(3):505–511, June 2002. ISSN 1066-5277. doi: 10.1089/
336 106652702760138592.
- 337 A. Ramdas, A. Singh, and L. Wasserman. Classification Accuracy as a Proxy
338 for Two Sample Testing. *arXiv:1602.02210 [cs, math, stat]*, Feb. 2016.
- 339 J. Schäfer and K. Strimmer. A Shrinkage Approach to Large-Scale Covariance
340 Matrix Estimation and Implications for Functional Genomics. *Statistical*
341 *Applications in Genetics and Molecular Biology*, 4(1), Jan. 2005. ISSN
342 1544-6115. doi: 10.2202/1544-6115.1175.
- 343 R. Simon, M. D. Radmacher, K. Dobbin, and L. M. McShane. Pitfalls in the
344 Use of DNA Microarray Data for Diagnostic and Prognostic Classification.

- 345 *Journal of the National Cancer Institute*, 95(1):14–18, Jan. 2003. ISSN
346 0027-8874, 1460-2105. doi: 10.1093/jnci/95.1.14.
- 347 M. S. Srivastava. On testing the equality of mean vectors in high dimension.
348 *Acta et Commentationes Universitatis Tartuensis de Mathematica*, 17(1):
349 31–56, June 2013. ISSN 2228-4699. doi: 10.12697/ACUTM.2013.17.03.
- 350 M. S. Srivastava, S. Katayama, and Y. Kano. A two sample test in high
351 dimensional data. *Journal of Multivariate Analysis*, 114:349–358, Feb.
352 2013. ISSN 0047-259X. doi: 10.1016/j.jmva.2012.08.014.
- 353 J. Stelzer, Y. Chen, and R. Turner. Statistical inference and multiple test-
354 ing correction in classification-based multi-voxel pattern analysis (MVPA):
355 Random permutations and cluster size control. *NeuroImage*, 65:69–82, Jan.
356 2013. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2012.09.063.
- 357 A. W. van der Vaart. *Asymptotic Statistics*. Cambridge University Press,
358 Cambridge, UK ; New York, NY, USA, Oct. 1998. ISBN 978-0-521-49603-
359 2.
- 360 G. Varoquaux, P. R. Raamana, D. Engemann, A. Hoyos-Idrobo, Y. Schwartz,
361 and B. Thirion. Assessing and tuning brain decoders: cross-validation,
362 caveats, and guidelines. working paper or preprint, June 2016.
- 363 T. D. Wager, L. Y. Atlas, M. A. Lindquist, M. Roy, C.-W. Woo, and E. Kross.
364 An fMRI-Based Neurologic Signature of Physical Pain. *New England Jour-
365 nal of Medicine*, 368(15):1388–1397, Apr. 2013. ISSN 0028-4793. doi:
366 10.1056/NEJMoA1204471.

367 A Analysis pipeline

368 Here is the analysis pipeline of Stelzer et al. [2013] we for the auditory data in
 369 Gilron et al. [2016]. Denoting by $i = 1, \dots, I$ the subject index, $v = 1, \dots, V$
 370 the voxel index, and $s = 1, \dots, S$ the permutation index. Since regions³ are
 371 centred around a unique voxel, the voxel index v also serves as a unique
 372 region index. Algorithm 1 computes a region-wise test statistic, which is
 373 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

376 **B Simulations**

Figure 3: [TODO].

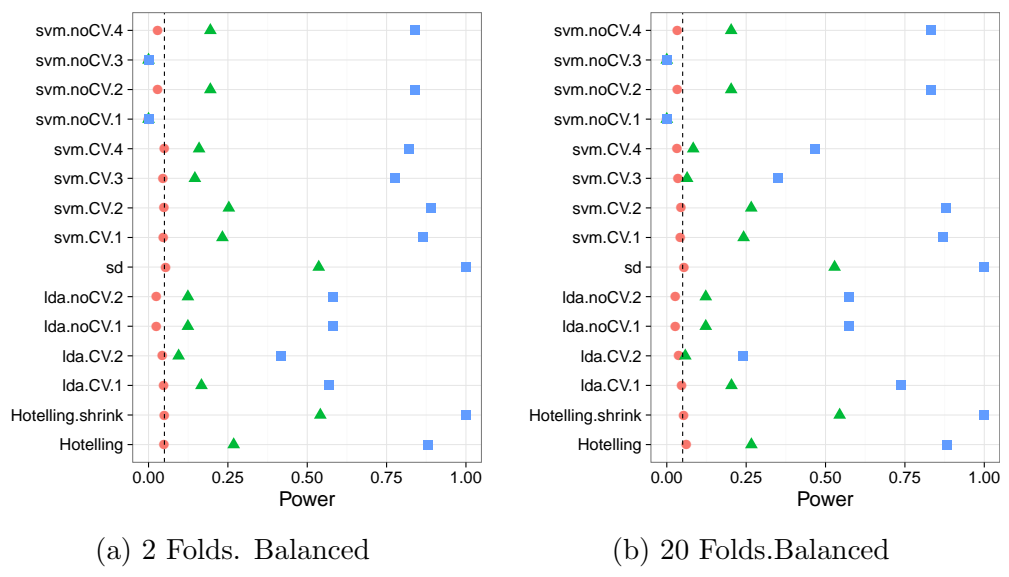


Figure 4: [TODO].

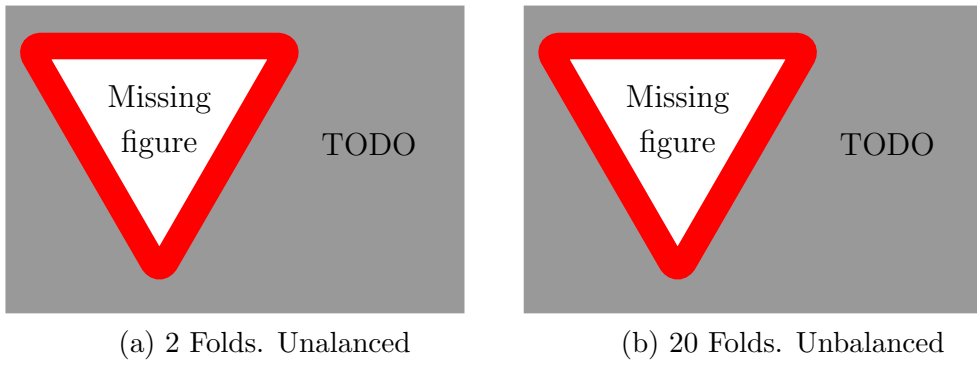


Figure 5: [TODO].

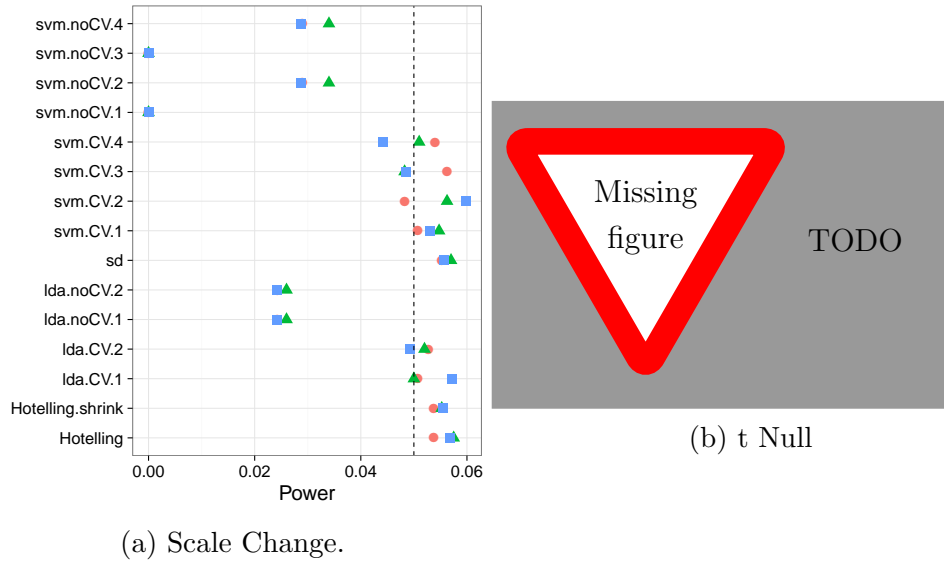


Figure 6: [TODO].

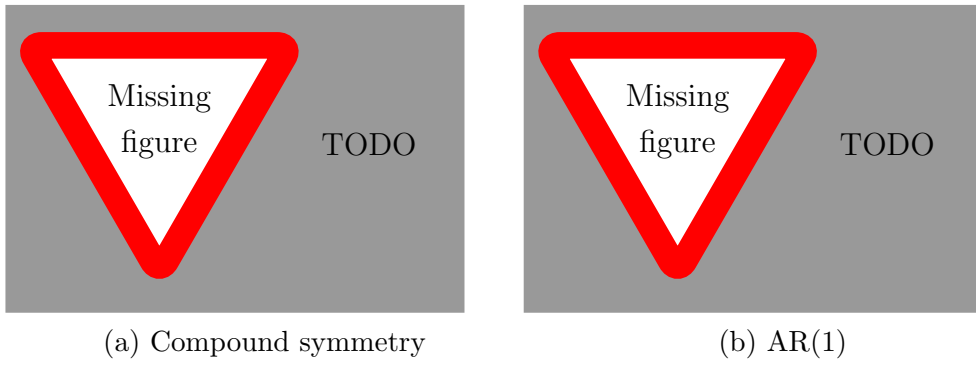


Figure 7: [TODO].

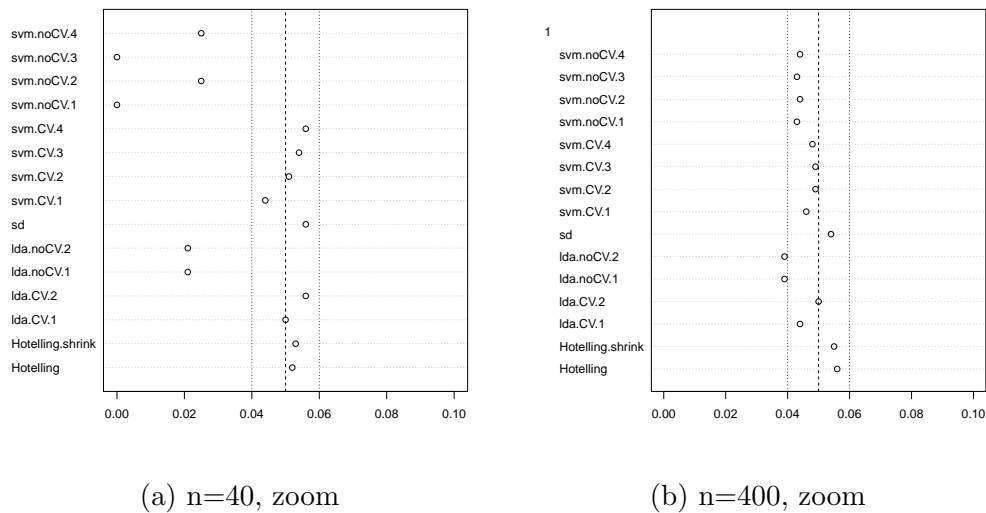


Figure 8: [TODO].

