

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 very high profile publications in the genetics literature: Golub et al. [1999], Slonim et al. [2000], Radmacher et al. [2002], Mukherjee et al. [2003], Juan and Iba [2004], 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.

Asymptotic relative efficiency measures (ARE) are typically used by statisticians to compare between test statistics with similar rates [van der Vaart, 1998]. Ramdas et al. [2016] derive the asymptotic power functions of the two test statistics, which allow to extract the ARE between Hotelling’s T^2 (location) test and Fisher’s LDA (accuracy) test. Using the Theorem 14.7 in van der Vaart [1998], we deduce that the ARE is lower bounded by $2\pi \approx 6.3$. This means that Fisher’s LDA requires at least 6.3 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

¹GoogleScholar. Accessed on Aug 4, 2016.

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 *resubstitution accuracy* as a test statistic. This statistic 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 a very high dimensional model, the resubstitution accuracy will be 1 for the observed data [McLachlan, 1976, Theorem 1], but also for any permutation. The concentration of resubstitution accuracy near 1, and its discreteness, render this test completely useless, with a power tending to 0 as the dimension of the model grows.

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 Sections 4 and 5, 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) .

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

106 2.1 Candidate Tests

107 The design of a permutation test using the prediction accuracy, requires the
 108 following design choices:

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

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

121 **How to estimate accuracy?** Given a predictor \hat{f} , a natural test statis-
 122 tic is some estimate of its accuracy $T_{\hat{f}}^{acc}$. Complicating matters: very low
 123 accuracies, even 0, is evidence that the classes are separated, and we only
 124 need to invert the predictions. We can thus consider $|T_{\hat{f}}^{acc} - 0.5|$ as the test
 125 statistic. This, however, implies that if the classes are identical, random
 126 guessing has 0.5 accuracy. This is not true if the classes are not balanced.
 127 For unbalanced data the chance level is the probability of the minority class,
 128 we denote by \hat{p}_{min} [Golland et al., 2005, Sec 4.1]. This suggests the following
 129 test statistic $|T_{\hat{f}}^{acc} - \hat{p}_{min}|$. Since we will be aggregating these statistics over
 130 random data sets where \hat{p}_{min} may vary, it seems appropriate to standard-
 131 ize the scale of this statistic. We thus also consider the z-scored accuracy:
 132 $|T_{\hat{f}}^{acc} - \hat{p}_{min}| / \sqrt{\hat{p}_{min}(1 - \hat{p}_{min})}$.

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

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

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

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

166 **How many folds?** Different authors suggest different rules for the num-
167 ber of folds. We will be varying the number of folds. This will affect the
168 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.

174

3 Controlling the False Positive Rate

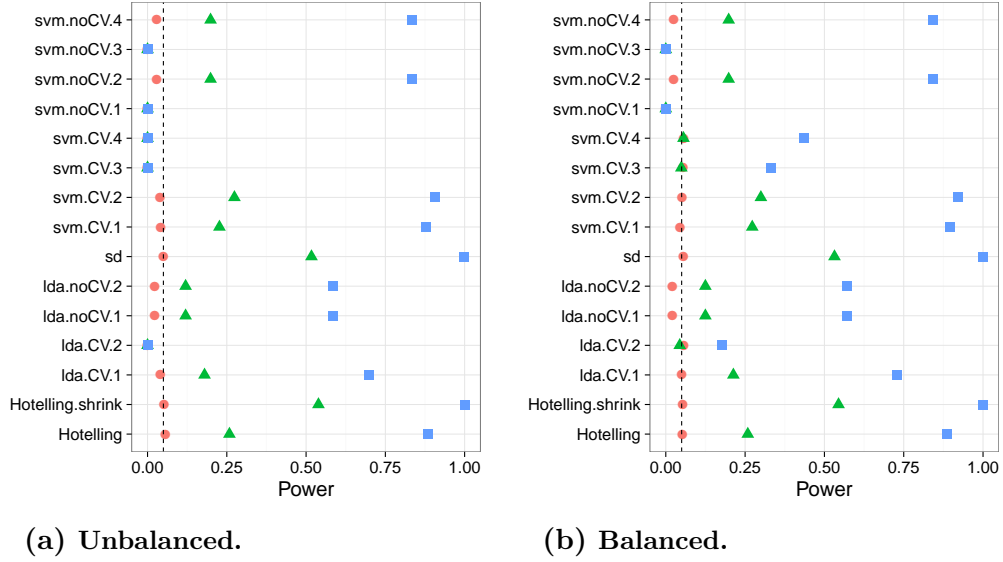
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Figure 1 demonstrates that all of the tests considered conserve the desired 0.05 false positive rate, up to varying levels of conservatism. This can be seen from the fact that the probability of rejection is no larger than 0.05 in the absence of any effect, encoded by a red circle. This is true, in particular

179

180 if: (a) the folds are balanced or not, (b) the tuning parameters of some test
 181 statistic are varied, (d) the number of folds is varied. We also observe that
 182 the most conservative tests are the resubstitution accuracy measures. We
 183 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.



184 4 Power

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

- 189 1. Location tests have more power than accuracy tests in all our configurations.
 190
- 191 2. The conservativeness decays as the sample grows (Figures 8a, 8b and
 192 9a), supporting the statement that discretization is responsible for
 193 power loss.

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

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

214 5 Neuroimaging Example

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

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

²<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.

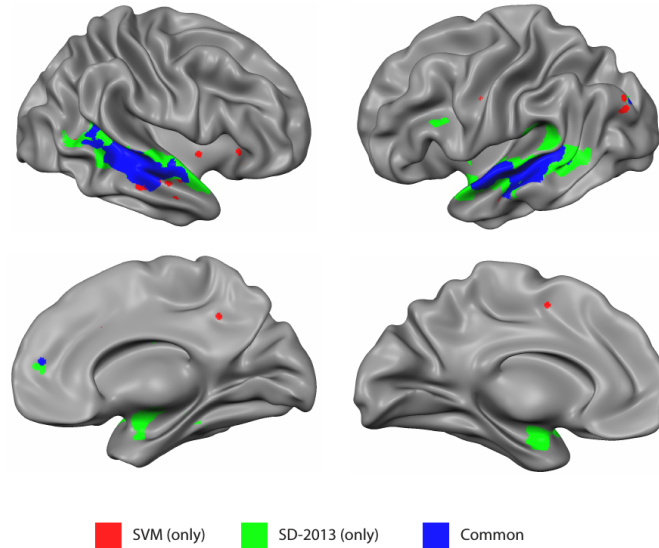


Figure 2: Brain regions encoding information discriminating between vocal and non-vocal stimuli. Map reports the centers of 27-voxel sized spherical regions, as discovered by an accuracy test (*svm.cv.1*), and a location test (*sd*). *svm.cv.1* was computed using 5-fold cross validation, and a cost parameter 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].

236 6 Discussion

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

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

256 6.1 Ease of implementation

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

264 6.2 A good accuracy test

265 In Section 6.4 we discuss cases where an accuracy test cannot replace a
266 location test. For such cases we collect some conclusions from our simulations
267 on the best practices for accuracy tests.

- 268 1. The conservativeness due to discretization decreases with sample size.
- 269 2. Cross validating the accuracy statistic increases power in moderate
270 sample sizes. The power loss due to the holdout inefficiency is smaller

271 than the power loss due to the concentration of the resubstitution ac-
 272 curacy. For large sample sizes, discretization and concentration have
 273 weaker effects, and the cross validated accuracy may be replaced with
 274 the computationally more efficiency resubstitution accuracy.

275 3. Permuting features is easier than permuting labels. It allows to preserve
 276 balanced folds after a permutation without refolding, thus reducing
 277 computational complexity.

278 4. There is no gain in z-scoring the accuracy scores.

279 5. Cross validated accuracy with balanced folds has more power than un-
 280 balanced folds. We currently have no intuition to offer for this phe-
 281 nomenon.

282 6. It is unclear what is the effect of the number of folds. More folds in-
 283 crease power by reducing the number of holdout samples. On the other
 284 hand, it increases the concentration of the accuracy statistic. Com-
 285 pounded with the discreteness of the accuracy statistic, this decreases
 286 power.

287 7. The value of the tuning parameters of a classifier have little to no
 288 effect.

289 It may be possible to alleviate the effect of discretization by appropriate
 290 cross-validation. The discreteness of the accuracy statistic can be “smoothed”
 291 by allowing the test sample to be drawn with replacement. The *bootstrap* may
 292 seem like a candidate approach, but since the original data always serves
 293 as a test set, the accuracy can still only assume $1/n$ values. This is not
 294 the case, however, for the *leave-one-out bootstrap estimator* [Hastie et al.,
 295 2003, Sec 7.11]. It is a simplified version of the *0.632 bootstrap estimator*
 296 [Efron and Tibshirani, 1997], and suffices for our purpose since we are not
 297 interested in unbiased risk estimation, but merely signal detection. The
 298 naming conventions of the bootstrapped estimates are detailed in Table 2.
 299 As seen in Figure 3...

Name	Basis	CV	Accuracy	Parameters
lda.Boot.1	LDA	Bootstrap	accuracy	—
svm.Boot.1	SVM	Bootstrap	accuracy	cost=1e1
svm.Boot.2	SVM	Bootstrap	accuracy	cost=1e-1

Table 2: The same as Table 1 for bootstrapped accuracy estimates.

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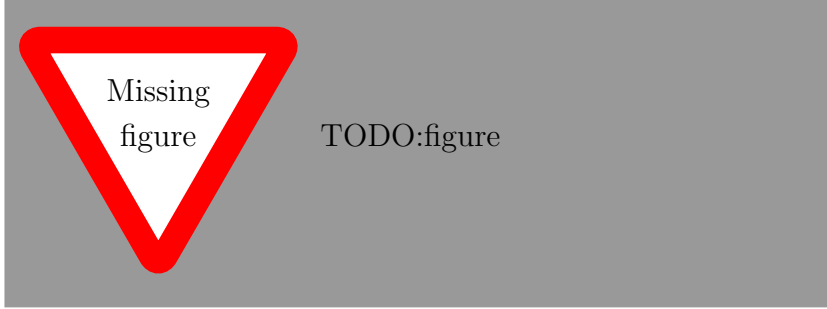


Figure 3: *Bootstrap*

301 6.3 Related Literature

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

313 Golland et al. [2005] study accuracy tests using simulation, real neu-
 314 roimaging and genetic data, and analytically. Their analytic results formalize
 315 our intuition from Section 1 on the effect concentration of the permutatin
 316 p-value: The finite Vapnik–Chervonenkis (VC) dimension requirement (Sec
 317 4.3) prevents the permutation p-value from concentrating. They also find
 318 that the power decreases with the level of discretization of the statistic.
 319 This is seen in their Figure 4, where the size of the test-set, K , governs the
 320 discretization. Since they permute features, and not labels, then all their per-
 321 mutation samples conserve the same balance as the original one, and there
 322 is no issue of refolding.

323 Golland et al. [2005] simulate the power of an accuracy test using a mul-
 324 tivariate Gaussian mixture, with a parameter p governing the separation be-
 325 tween classes. Under their model $(x_i|y_i = 1) \sim p\mathcal{N}(\mu_1, I) + (1 - p)\mathcal{N}(\mu_2, I)$
 326 and $(x_i|y_i = -1) \sim (1 - p)\mathcal{N}(\mu_1, I) + p\mathcal{N}(\mu_2, I)$. Varying p interpolates be-
 327 tween the null distribution ($p = 0.5$) and a location shift model ($p = 0$). We
 328 perform the same simulation as Golland et al. [2005], after reparametrizing p
 329 so that $p = 0$ corresponds to the null model, and $p = 23$ to be comparable to

our other simulations. We find that in this mixture class of models, like the location class of models, a location test has more power than an accuracy test (Figure 4).

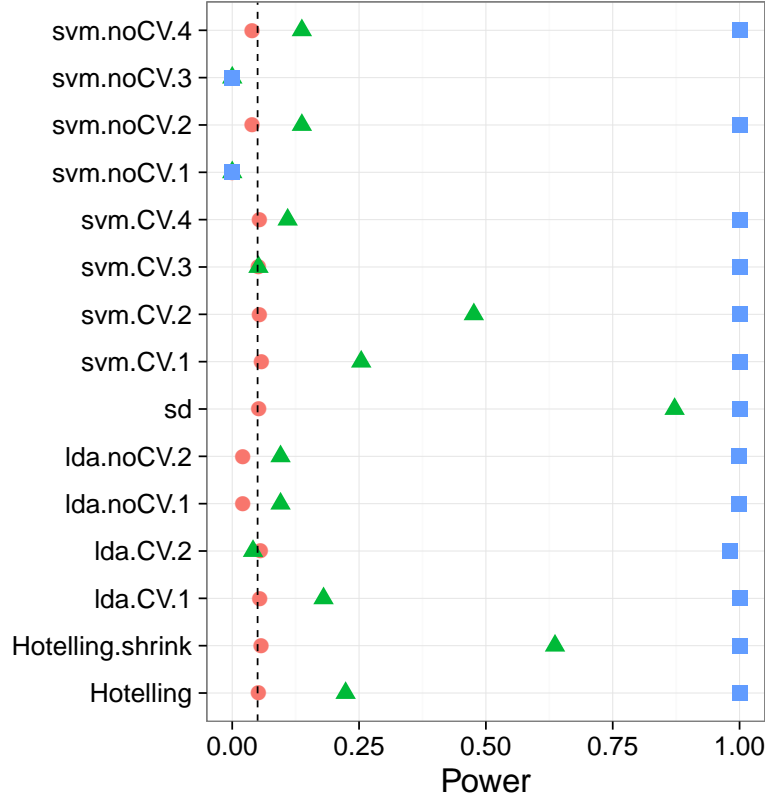


Figure 4: **Mixture:** $\mathbf{x}_i = \chi_i \mu + \eta_i$; $\chi_i = \{-1, 1\}$ and $\text{Prob}(\chi_i = 1) = (1/2 - p)^{y_i^*} (1/2 + p)^{1-y_i^*}$. μ is a p -vector with $3/\sqrt{p}$ in all coordinates. The effect, p , is color and shape coded and varies over 0 (red circle), 1/4 (green triangle) and 1/2 (blue square).

6.4 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, 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 a false argument-accuracy test do not have any more flexibility than location tests. Indeed, it is possible to test for location in the same dimension the classifier is fitted. Gretton et al. [2012] is an example where the test for location is performed in the RKHS of the data. It is also possible to test for the equality of two multivariate distributions without a-priori specifying any a-priori alternative [e.g. Heller et al., 2012]).

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.

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 empirical evidence that changes in location are a prevalent phenomenon.

6.5 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.

And more simply by Frank Harrell in the **CrossValidated** Q&A site³:

... your use of proportion classified correctly as your accuracy score. This is a discontinuous improper scoring rule that can be easily manipulated because it is arbitrary and insensitive.

³<http://stats.stackexchange.com/questions/17408/how-to-assess-statistical-significance-of-the-accuracy-of-a-classifier>.

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.
- B. Efron and R. Tibshirani. Improvements on Cross-Validation: The .632+ Bootstrap Method. *Journal of the American Statistical Association*, 92(438):548–560, June 1997. ISSN 0162-1459. doi: 10.2307/2965703.
- 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.
- P. Golland, F. Liang, S. Mukherjee, and D. Panchenko. Permutation Tests for Classification. In P. Auer and R. Meir, editors, *Learning Theory*, number 3559 in Lecture Notes in Computer Science, pages 501–515. Springer Berlin Heidelberg, June 2005. ISBN 978-3-540-26556-6 978-3-540-31892-7. doi: 10.1007/11503415_34.
- T. R. Golub, D. K. Slonim, P. Tamayo, C. Huard, M. Gaasenbeek, J. P. Mesirov, H. Coller, M. L. Loh, J. R. Downing, M. A. Caligiuri, C. D. Bloomfield, and E. S. Lander. Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring. *Science*, 286(5439):531–537, Oct. 1999. ISSN 0036-8075, 1095-9203. doi: 10.1126/science.286.5439.531.
- 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.
- T. Hastie, R. Tibshirani, and J. Friedman. *The Elements of Statistical Learning*. Springer, July 2003. ISBN 0-387-95284-5.
- R. Heller, Y. Heller, and M. Gorfine. A consistent multivariate test of association based on ranks of distances. *Biometrika*, page ass070, Dec. 2012. ISSN 0006-3444, 1464-3510. doi: 10.1093/biomet/ass070.

- 412 J. Hemerik and J. Goeman. Exact testing with random permutations.
413 *arXiv:1411.7565 [math, stat]*, Nov. 2014.
- 414 H. Hotelling. The Generalization of Student’s Ratio. *The Annals of Math-*
415 *ematical Statistics*, 2(3):360–378, Aug. 1931. ISSN 0003-4851, 2168-8990.
416 doi: 10.1214/aoms/1177732979.
- 417 W. Jiang, S. Varma, and R. Simon. Calculating confidence intervals for
418 prediction error in microarray classification using resampling. *Statistical*
419 *Applications in Genetics and Molecular Biology*, 7(1), 2008.
- 420 L. Juan and H. Iba. Prediction of tumor outcome based on gene expression
421 data. *Wuhan University Journal of Natural Sciences*, 9(2):177–182, Mar.
422 2004. ISSN 1007-1202, 1993-4998. doi: 10.1007/BF02830598.
- 423 N. Kriegeskorte, R. Goebel, and P. Bandettini. Information-based functional
424 brain mapping. *Proceedings of the National Academy of Sciences of the*
425 *United States of America*, 103(10):3863–3868, July 2006. ISSN 0027-8424,
426 1091-6490. doi: 10.1073/pnas.0600244103.
- 427 E. L. Lehmann. Parametric versus nonparametrics: two alternative method-
428 ologies. *Journal of Nonparametric Statistics*, 21(4):397–405, 2009. ISSN
429 1048-5252. doi: 10.1080/10485250902842727.
- 430 G. J. McLachlan. The bias of the apparent error rate in discriminant analysis.
431 *Biometrika*, 63(2):239–244, Jan. 1976. ISSN 0006-3444, 1464-3510. doi:
432 10.1093/biomet/63.2.239.
- 433 S. Mukherjee, P. Tamayo, S. Rogers, R. Rifkin, A. Engle, C. Campbell,
434 T. R. Golub, and J. P. Mesirov. Estimating dataset size requirements
435 for classifying DNA microarray data. *Journal of Computational Biology:*
436 *A Journal of Computational Molecular Cell Biology*, 10(2):119–142, 2003.
437 ISSN 1066-5277. doi: 10.1089/10665270321825928.
- 438 E. Olivetti, S. Greiner, and P. Avesani. Induction in Neuroscience with
439 Classification: Issues and Solutions. In G. Langs, I. Rish, M. Grosse-
440 Wentrup, and B. Murphy, editors, *Machine Learning and Interpretation*
441 *in Neuroimaging*, number 7263 in Lecture Notes in Computer Science,
442 pages 42–50. Springer Berlin Heidelberg, 2012. ISBN 978-3-642-34712-2
443 978-3-642-34713-9. doi: 10.1007/978-3-642-34713-9_6.
- 444 E. Olivetti, S. Greiner, and P. Avesani. Statistical independence for the
445 evaluation of classifier-based diagnosis. *Brain Informatics*, 2(1):13–19, Dec.
446 2014. ISSN 2198-4018, 2198-4026. doi: 10.1007/s40708-014-0007-6.

- 447 F. Pereira, T. Mitchell, and M. Botvinick. Machine learning classifiers and
448 fMRI: A tutorial overview. *NeuroImage*, 45(1, Supplement 1):S199–S209,
449 Mar. 2009. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2008.11.007.
- 450 C. R. Pernet, P. McAleer, M. Latinus, K. J. Gorgolewski, I. Charest, P. E. G.
451 Bestelmeyer, R. H. Watson, D. Fleming, F. Crabbe, M. Valdes-Sosa, and
452 P. Belin. The human voice areas: Spatial organization and inter-individual
453 variability in temporal and extra-temporal cortices. *NeuroImage*, 119:164–
454 174, Oct. 2015. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2015.06.050.
- 455 M. D. Radmacher, L. M. McShane, and R. Simon. A Paradigm for
456 Class Prediction Using Gene Expression Profiles. *Journal of Computa-
457 tional Biology*, 9(3):505–511, June 2002. ISSN 1066-5277. doi: 10.1089/
458 106652702760138592.
- 459 A. Ramdas, A. Singh, and L. Wasserman. Classification Accuracy as a Proxy
460 for Two Sample Testing. *arXiv:1602.02210 [cs, math, stat]*, Feb. 2016.
- 461 J. Schäfer and K. Strimmer. A Shrinkage Approach to Large-Scale Covariance
462 Matrix Estimation and Implications for Functional Genomics. *Statistical
463 Applications in Genetics and Molecular Biology*, 4(1), Jan. 2005. ISSN
464 1544-6115. doi: 10.2202/1544-6115.1175.
- 465 R. Simon, M. D. Radmacher, K. Dobbin, and L. M. McShane. Pitfalls in the
466 Use of DNA Microarray Data for Diagnostic and Prognostic Classification.
467 *Journal of the National Cancer Institute*, 95(1):14–18, Jan. 2003. ISSN
468 0027-8874, 1460-2105. doi: 10.1093/jnci/95.1.14.
- 469 D. K. Slonim, P. Tamayo, J. P. Mesirov, T. R. Golub, and E. S. Lander. Class
470 Prediction and Discovery Using Gene Expression Data. In *Proceedings of
471 the Fourth Annual International Conference on Computational Molecular
472 Biology*, RECOMB ’00, pages 263–272, New York, NY, USA, 2000. ACM.
473 ISBN 978-1-58113-186-4. doi: 10.1145/332306.332564.
- 474 M. S. Srivastava. On testing the equality of mean vectors in high dimension.
475 *Acta et Commentationes Universitatis Tartuensis de Mathematica*, 17(1):
476 31–56, June 2013. ISSN 2228-4699. doi: 10.12697/ACUTM.2013.17.03.
- 477 M. S. Srivastava, S. Katayama, and Y. Kano. A two sample test in high
478 dimensional data. *Journal of Multivariate Analysis*, 114:349–358, Feb.
479 2013. ISSN 0047-259X. doi: 10.1016/j.jmva.2012.08.014.
- 480 J. Stelzer, Y. Chen, and R. Turner. Statistical inference and multiple test-
481 ing correction in classification-based multi-voxel pattern analysis (MVPA):

- 482 Random permutations and cluster size control. *NeuroImage*, 65:69–82, Jan.
483 2013. ISSN 1053-8119. doi: 10.1016/j.neuroimage.2012.09.063.
- 484 A. W. van der Vaart. *Asymptotic Statistics*. Cambridge University Press,
485 Cambridge, UK ; New York, NY, USA, Oct. 1998. ISBN 978-0-521-49603-
486 2.
- 487 G. Varoquaux, P. R. Raamana, D. Engemann, A. Hoyos-Idrobo, Y. Schwartz,
488 and B. Thirion. Assessing and tuning brain decoders: cross-validation,
489 caveats, and guidelines. working paper or preprint, June 2016.
- 490 T. D. Wager, L. Y. Atlas, M. A. Lindquist, M. Roy, C.-W. Woo, and E. Kross.
491 An fMRI-Based Neurologic Signature of Physical Pain. *New England Jour-*
492 *nal of Medicine*, 368(15):1388–1397, Apr. 2013. ISSN 0028-4793. doi:
493 10.1056/NEJMoa1204471.

494 A Analysis pipeline

495 Here is the analysis pipeline of Stelzer et al. [2013] we for the auditory data in
 496 Gilron et al. [2016]. Denoting by $i = 1, \dots, I$ the subject index, $v = 1, \dots, V$
 497 the voxel index, and $s = 1, \dots, S$ the permutation index. Since regions⁴ are
 498 centered around a unique voxel, the voxel index v also serves as a unique
 499 region index. Algorithm 1 computes a region-wise test statistic, which is
 500 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
```

⁴*searchlight* or *sphere* in the MVPA parlance

503 B Simulation Details

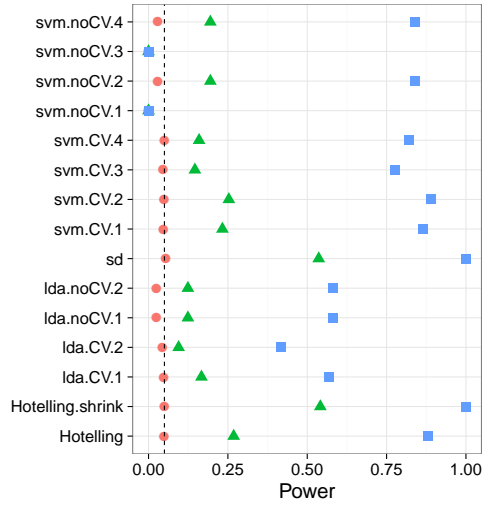
504 The following details are common to all the reported simulations, unless stated
505 otherwise in a figure’s caption. The R code for the simulations can be found
506 in [TODO].

507 Each simulation is based on 4,000 replications. In each replication, we
508 generate n i.i.d. samples from a shift model $\mathbf{x}_i = \mu \mathbf{y}_i^* + \eta_i$. Where $y_i^* = \{0, 1\}$
509 is the class of subject i in dummy coding. Recalling that $y_i = \{-1, 1\}$ is the
510 class in effect coding, then clearly $y_i = 2y_i^* - 1$. The noise is distributed as
511 $\eta_i \sim \mathcal{N}_p(0, \Sigma)$. The sample size $n = 40$. The dimension of the data is $p = 23$.
512 The covariance $\Sigma = I$. Effects, i.e. shifts μ , are equal coordinate p -vectors
513 with coordinates that vary over $\mu \in \{0, 1/4, 1/2\}$.

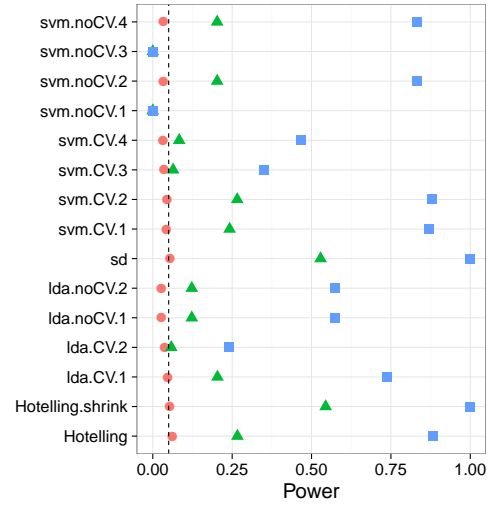
514 Having generated the data, we compute each of the test statistics in Ta-
515 ble 1. For test statistics that require data folding, we used 8 folds. We then
516 compute a permutation p-value by permuting the class labels, and recomput-
517 ing each test statistic. We perform 400 such permutations.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

C Simulation Results

Figure 5: *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 6: *Simulation details in Appendix B except the changes in the sub-captions.*

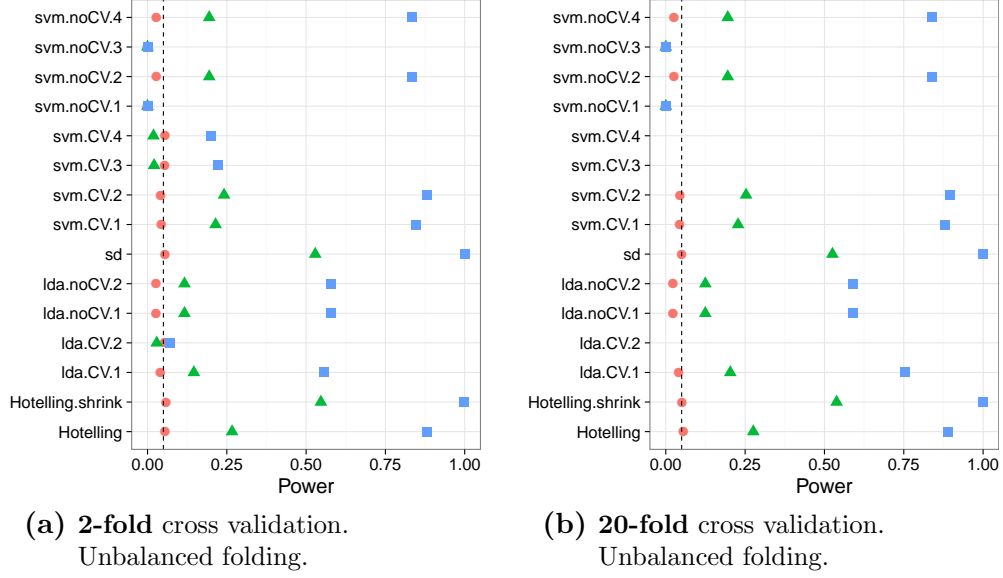


Figure 7: *Simulation details in Appendix B except the changes in the sub-captions.*

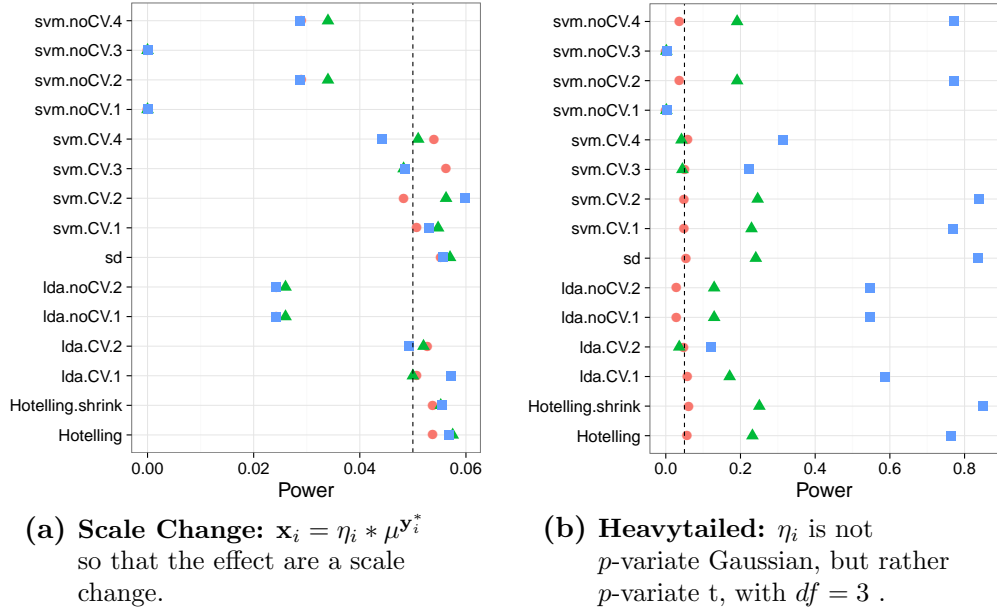
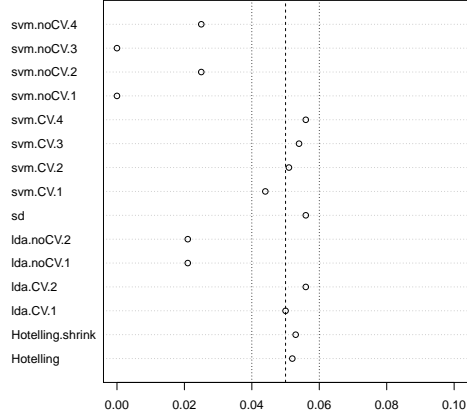
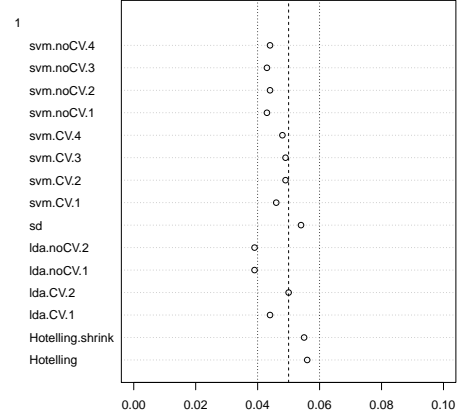


Figure 8: *Simulation details in Appendix B except the changes in the sub-captions.*



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

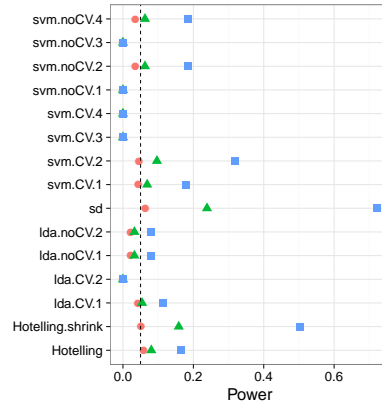


(b) **High-Dimension:** False positive rates for $n = 400$.

Figure 9: *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:**
 $\Sigma_{k,l} = \rho^{|k-l|}; \rho = 0.8$.