# Sequential rank agreement methods for comparison of ranked lists

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### Abstract

The comparison of alternative rankings of a set of items is a general and common task in applied statistics. Predictor variables are ranked according to magnitude of association with an outcome, prediction models rank subjects according to the personalized risk of an event, and genetic studies rank genes according to their difference in gene expression levels. This article constructs measures of agreement among two or more ordered lists. We use the standard deviation of the ranks to define a measure of agreement that both provides an intuitive interpretation and can be applied to any number of lists even if some or all are incomplete or censored. The approach can identify change-points in the agreement of the lists, and the sequential changes of agreement as a function of the depth of the lists can be compared graphically to a permutation based reference set or evaluated using asymptotic results. The usefulness of these tools are illustrated using gene rankings, and using data from two Danish ovarian cancer studies where we assess the within and between agreement of different statistical classification methods.

Key words: sequential rank agreement, partial ranking, order statistic, gene rankings, methods comparison, variable selection, permutation

## 1 Introduction

Ranking of items or results is common in scientific research and ranked lists occur naturally as the result of many statistical applications. Regression

methods rank predictor variables according to magnitude of their association with an outcome, prediction models rank subjects according to their risk of an event, and genetic studies rank genes according to their difference in gene expression levels across samples.

When several rankings of the same items are available, a common research question is to what extent they agree. In particular, is it possible to identify an optimal rank until which the lists agree on the items? A typical situation arises in high-dimensional genomics studies when several analysis methods are applied to rank a list of genes according to their association with a phenotype, treatment effect or other outcome. A measure of agreement of gene rankings obtained by different methods could often help to identify which genes are worth to pursue in further experiments.

Several approaches exist to measure the "distance" between two ranked lists. Of these, Kendall's $\tau$ (Kendall, 1948) and Spearman's footrule $\rho$ (Spearman, 1910) are among the most well-known, but these measures do not distinguish between agreement in the top versus towards the bottom of the lists and they both provide a single measure of the overall distance. Shieh (1998) proposed a weighted version of Kendall's $\tau$ where each pair of rankings can be assigned different weights, and Yilmaz et al. (2008) proposed the $\tau_{ap}$ which places higher emphasis on the top of the lists. Spearman's footrule uses the ranks of the variables for calculation of the distance and the use of ranks are also employed in the $M$ measure of Bar-Ilan et al. (2006) where the reciprocal rank differences are used to calculate the similarity measure.

Other more recent approaches consider the intersection of lists as the basis for a similarity measure. However, simple intersection also places equal weights on all depths of the list and therefore Fagin et al. (2003) and Webber et al. (2010) proposed weighted intersections which put more emphasis on the top of the lists. Specifically, Webber et al. (2010) define their rank-biased overlap (RBO) by weighting with a converging series to ensure that the top is weighted higher than the potentially non-informative bottom of the lists. It is possible to use the existing methods to calculate agreement of lists until a given depth, i.e., limited to the $d$ items of each list. However, the interpretation may not be straightforward, especially in the case of more than two lists, and they may not accommodate partial rankings.

Very recently, Hall and Schimek (2012) proposed a method for comparing pairwise rankings and derived the asymptotic distribution of the endpoint where the two ranked lists no longer are in agreement. Their approach was based on anchoring one of the two lists and subsequently generating a sequence of 0s and 1s depending on whether the ranks in the second list was close to the rank from the anchored list. Sampath and Verducci (2013) followed up on this idea for pairwise comparison of lists but used penalties

based on a truncated geometric probability instead of a 0-1 process and they evaluated the distribution of the endpoint of agreement by computational approaches. The asymptotic distribution in the Hall and Schimek (2012) paper is based on letting the number of *lists* increase to infinity which is a situation that is only relevant in special cases, whereas the simulation-based null distribution approach of Sampath and Verducci (2013) is guaranteed to work also for small samples.

In this article we introduce sequential rank agreement for measuring agreement among (partially) ranked lists. The general idea is to define agreement based on the sequence of ranks from the first $d$ items in each list. As agreement metric we adapt the limits of agreement known from agreement between quantitative variables (Altman and Bland, 1983; Carstensen, 2010) but any measure for agreement could be essentially be used. Our proposed approach allows us to compare more than two lists simultaneously, it provides a dynamic measure of agreement as a function of the depth in the lists, places high weight on items at the top of the list, accommodates partially observed lists of varying lengths, and has a natural interpretation that directly relates to the ranks. Graphical illustration of sequential rank agreement potentially allows us to infer a change-point, i.e., a list depth where a substantial change in the agreement of the lists occur but we also provide randomization-based graphical tools to compare the observed rank agreement to the expected agreement found in non-informative data. In this sense our approach is a combination and generalization of some of the ideas of Carterette (2009) and Boulesteix and Slawski (2009). The former compares two rankings based on the distance between them as measured by a multivariate Gaussian distribution and the latter presents an overview of approaches for aggregation of ranked lists including bootstrap and leave-one-out jackknife approaches. We show the asymptotic distribution of the endpoint of agreement and discuss how to infer the distribution in small-sample situations using computational methods. This enables us to make inferences about the endpoint of agreement even for situations where there is no actual changepoint present but just a gradual decline in agreement.

The manuscript is organized as follows: In the next section we define sequential rank agreement for multiple ranked lists and discuss how to handle incomplete/censored/partial lists. In section 3 we present and discuss approaches to evaluate the results obtained from sequential rank agreement. Finally we apply the sequential rank agreement to two Danish ovarian cancer studies before we discuss the findings along with possible extensions. The approaches presented in this manuscript are available in the R package `SuperRanker` which can be found on CRAN.

Table 1: Example set of ranked lists. (a) shows the ranked lists of items for each of three lists, (b) presents the ranks obtained by each item in each of the three lists and (c) shows the cumulative set of items up to a given depth in the three lists.

| (a) | | | |
|---|---|---|---|
| Rank | $R_1^{-1}$ | $R_2^{-1}$ | $R_3^{-1}$ |
| 1 | A | A | B |
| 2 | B | C | A |
| 3 | C | D | E |
| 4 | D | B | C |
| 5 | E | E | D |

| (b) | | | |
|---|---|---|---|
| Item | $R_1$ | $R_2$ | $R_3$ |
| A | 1 | 1 | 2 |
| B | 2 | 4 | 1 |
| C | 3 | 2 | 4 |
| D | 4 | 3 | 5 |
| E | 5 | 5 | 3 |

| (c) | |
|---|---|
| Depth | $S_d$ |
| 1 | {A, B} |
| 2 | {A, B, C} |
| 3 | {A, B, C, D, E} |
| 4 | {A, B, C, D, E} |
| 5 | {A, B, C, D, E} |

# 2 Methods

Consider a set of $P$ different items $X = \{X_1, \ldots, X_P\}$ and a ranking function $R : \{X_1, \ldots, X_P\} \to \{1, \ldots, P\}$, such that $R(X_p)$ is the rank of item $X_p$. The inverse mapping $R^{-1}$ gives the item $R^{-1}(r)$ that was assigned to rank $r \in \{1, \ldots, P\}$. An ordered list is the realization of a ranking function $R$ applied to the set of items $X$. Panels (a) and (b) of Table 1 show a schematic example of these mappings. Thus if $R_l^{-1}(1) = X_{34}$ then item $X_{34}$ is ranked first in list $l$ and similarly $R_l(X_{34}) = 1$.

In all what follows we consider a fixed set of items and consider the ranking function to be a random variable. Thus, let $R_1(X), \ldots, R_L(X)$, $L \geq 2$, be a sample of $L$ independent identically distributed draws from an unknown probability distribution function $Q$. One aim is then to test how much $Q$ resembles the uniform distribution which assigns probability $1/P!$ to each of the $P!$ different possible rankings.

The agreement of the lists regarding the rank given to an item $X_p$ can be measured by the variance across the lists

$$A(X_p) = \mathbb{E}_Q \left[ (R(X_p) - \mathbb{E}_Q R(X_p))^2 \right] \tag{1}$$
$$= \sum_{r \in \Pi} (r(X_p) - \mathbb{E}_Q R(X_p))^2 Q(r),$$

where $\Pi$ is the set of all permutations of $X$, $Q$ is a probability mass function on $\Pi$, and $\mathbb{E}_Q R(X_p) = \sum_{r \in \Pi} r(X_p) Q(r)$. The empirical counterpart is

$$\widehat{A}_L(X_p) = \frac{1}{L-1} \sum_{i=1}^L (R_i(X_p) - \overline{R}_L(X_p))^2, \quad \overline{R}_L(X_p) = \frac{1}{L} \sum_{i=1}^L R_i(X_p). \tag{2}$$

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For each item, the function $\widehat{A}_L$ has an interpretation as the expected Euclidean distance of the individual rankings from the expected ranking over the $L$ lists, and it corresponds to the same measure that is used in method comparison studies to compute the limits of agreement (Altman and Bland, 1983).

For an integer $1 \leq d \leq P$ we define the expected set of unique items found by merging the first $d$ elements across the possible lists:

$$S(d) = \left\{ X_p; \left( \sum_{r \in \Pi} 1\left( r(X_p) \leq d \right) Q(r) \right) > 0 \right\} \qquad (3)$$

where $1(\cdot)$ denotes the indicator function. The empirical counterpart is the set of unique items ranked less than or equal to $d$ in any of the $L$ lists:

$$\widehat{S}_L(d) = \left\{ X_p; \left( \frac{1}{L} \sum_{l=1}^{L} 1\left( R_l(X_p) \leq d \right) \right) > 0 \right\}, \qquad (4)$$

which is exemplified in Panel (c) of Table 1.

We define the *sequential rank agreement* as the weighted expected agreement of the items found in the set $S(d)$:

$$\mathrm{sra}(d) = \frac{1}{|S(d)|} \sum_{p \in S(d)} A(X_p) \qquad (5)$$

where $|S(d)|$ is the cardinality of the set $S(d)$. The empirical counterpart is equivalently given by

$$\widehat{\mathrm{sra}}_L(d) = \frac{\sum_{\{p \in \widehat{S}_L(d)\}} (L-1) \widehat{A}_L(X_p)}{(L-1)|\widehat{S}_L(d)|} \qquad (6)$$

Values of sra close to zero suggests that the lists agree on the rankings while larger values suggest disagreement. Just like in method comparison studies we prefer smaller limits of agreement because that means that the differences between the methods is small. If the ranked lists are identical then the value of sequential rank agreement will be zero for all depths $d$. The sequential rank agreement is equivalent to the pooled variance of the items found in $S(d)$, and it can be interpreted as the average distance of the individual rankings of the lists from the average ranking for each of the items we have seen until depth $d$. For an easier interpretation we suggest to plot $\sqrt{\widehat{\mathrm{sra}}_L(d)}$ corresponding to the pooled standard deviation.

## 2.1 Agreement among fully observed lists

The simplest case occurs when all $L$ lists are fully observed, *i.e.*, we have observed the rank of all $P$ items for all $L$ lists. Fully observed ranked lists are common and arise, for example, when different statistical analysis methods are applied to a single dataset to produce lists of predictors ranked according to their importance, or if the same analysis method is applied to data from different populations.

With fully observed lists we can plot the sequential rank agreement (5) as a function of depth $d$. An example is seen in top panels of Figure 1 where four analysis methods were used to rank 3051 gene expression values measured on 38 tumor mRNA samples in order to classify between acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) (Golub, 1999). Preprocessing of the gene expression data was done as described in Dudoit et al. (2002) and the four different analysis approaches were: marginal unequal variances two-sample $t$ tests, marginal logistic regression analyses, elastic net logistic regression (Friedman et al., 2010), and marginal maximum information content correlations (MIC) (Reshef et al., 2011). For the first two methods, the genes were ranked according to minimum $p$ value, for logistic regression the genes were ordered by size of the corresponding coefficients (after standardization), and MIC was ordered by absolute correlation which resulted in the top rankings seen in Table 2.

The sequential rank agreement curve plotted in Figure 1 roughly shows how many ranks apart we on average expect the genes found in the top $d$ part of the lists to be for each depth $d$. It can be seen that the sequential rank agreement limits are better towards the top of the lists (smaller values on the $y$ axis) corresponding to *better* agreement than towards the tails of the lists. It is clear from the curve in Figure 1 that there is a substantial drop in agreement even after the first depth. Thus, if we were to restrict attention to a small set of predictors then we would focus on predictors 2124, 829, and 378 as seen in Table 2.

If the lists agree on all items then the sequential rank agreement is zero for all depths. Generally, if there are changes in the level of rank agreement then this suggests that there are sets of items that are ranked similarly in all lists and other sets of items that have been assigned vastly different ranks in the lists. In gene association studies we generally expect the agreement among the lists to be better towards the top of the lists and worse towards the end of the lists. In this case the sequential rank agreement curve will start at a low level and then increase until it levels off as seen in Figure 1.
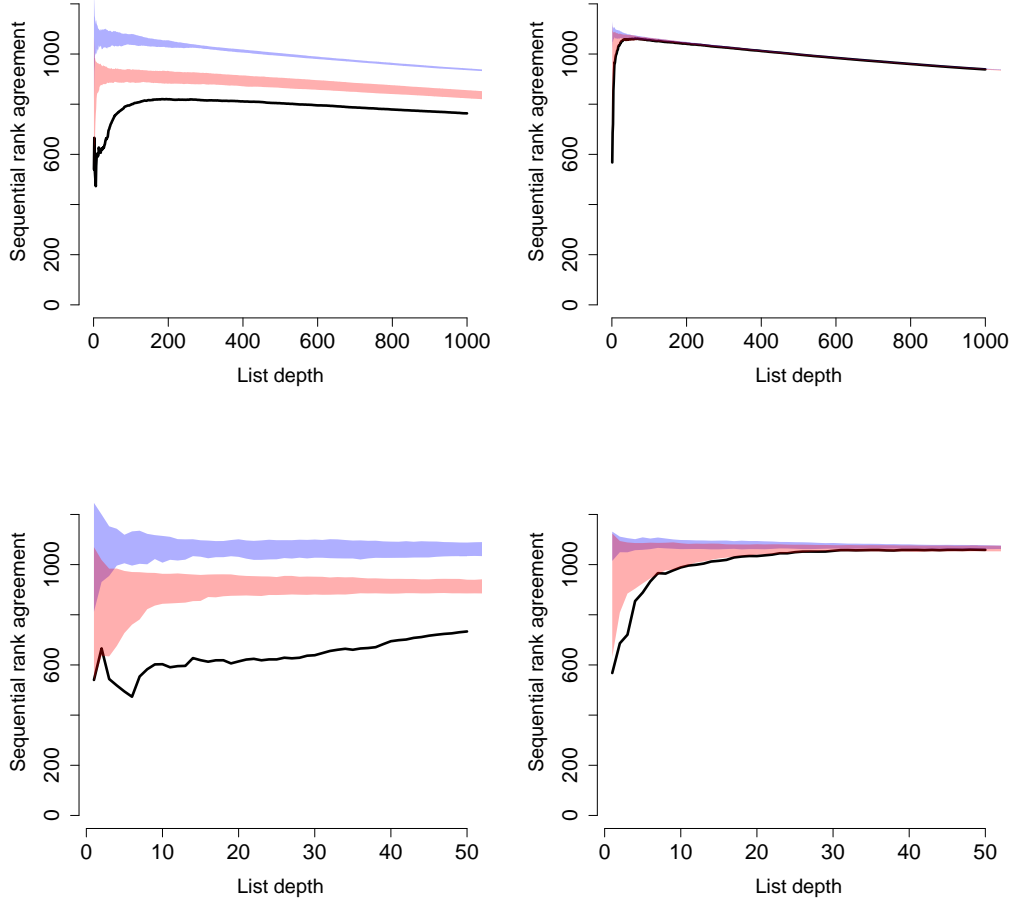
Figure 1: Left panels: Sequential rank agreement for 4 different analysis methods applied to the 3051 genes in the Golub data /black line). Right panels: Corresponding sequential rank agreement for the same data but where only the top 20 ranked items are available and the rest of the items have been censored. The blue and red areas correspond to the independent and randomized reference hypothesis areas, respectively. The bottom plots are identical to the corresponding top plots but have been zoomed in on the first part of the $x$ axis.

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Table 2: Top 10 list of ranked results from the Golub data. Numbers indicate the predictor/gene for the given ranking and method

| Ranking | T | LogReg | ElasticNet | MIC |
|--:|--:|--:|--:|--:|
| 1 | 2124 | 2124 | 829 | 378 |
| 2 | 896 | 896 | 2124 | 829 |
| 3 | 2600 | 829 | 2198 | 896 |
| 4 | 766 | 394 | 1665 | 1037 |
| 5 | 829 | 766 | 1920 | 2124 |
| 6 | 2851 | 2670 | 1042 | 808 |
| 7 | 703 | 2939 | 808 | 108 |
| 8 | 2386 | 2386 | 849 | 515 |
| 9 | 2645 | 1834 | 937 | 2670 |
| 10 | 2002 | 378 | 1995 | 2600 |

## 2.2 Analysis of partial/censored lists

Incomplete or partial lists are a common occurrence that arise, for example, in case of missing data (items), when comparing top $d$ list results from publications, or when some methods only rank a subset of the items. For example, penalized regression based on the Lasso provides a sparse set of predictors that have non-zero coefficients. There is no obvious ordering of the set of predictors whose coefficient has been shrunk to zero and thus we end up with a partial ordering. Incomplete lists also occur when the analyst decides to censor all lists at depth $d$ (*i.e.*, top $d$ lists) such that the measurement of agreement is restricted to the first $d$ elements of each list, or when the analyst only wants to consider the ranking of items that have been found to be statistically significant.

Sequential rank agreement can be generalized to partial lists in the following way. Let $\Lambda_l \subset X$ be the subset of $d_l$ items that have been ranked highest in list $l$. The case where all lists are censored at the same depth $d$ corresponds to $d_1 = \cdots = d_L = d$. For incomplete/censored lists the rank function becomes

$$\widetilde{R}_l(X_p) = \begin{cases} \{R_l(X_p)\} & \text{for } X_p \in \Lambda_l \\ \{d_l + 1, \ldots, P\} & \text{for } X_p \notin \Lambda_l \end{cases} \tag{7}$$

where we only know that the rank for the unobserved items in list $l$ must be larger than the largest rank observed in that list.

The agreement, $A(X_p)$, cannot be computed directly for all predictors in the presence of censored lists because the exact rank for some items will be

unknown. Also, recall that the rankings within a single list are not independent since each rank must appear exactly once in each list. Thus, we cannot simply assign the same number (e.g., the mean of the unassigned ranks) to the censored items since that would result in *less* variation of the ranks and hence less variation of the agreement, and it would artificially introduce a (downward) bias of agreement for items that are censored in multiple lists.

Instead we randomize the ranks $\{d_l + 1, \ldots, P\}$ to the items that do not occur in list $\Lambda_l$. One realization of the $L$ rankings of the set $X$ is obtained by randomizing the missing items of each list. By randomizing a large number of times we can compute (5) for each realization, and then compute the sequential rank agreement as the pointwise (for each depth) average of the rank agreements. The algorithm is described in detail in Algorithm 1.

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**Algorithm 1** Sequential rank agreement algorithm for censored lists

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1: **procedure** CENSORED RANK AGREEMENT
2:     Let $B$ be the number of permutations to use
3:     **for** each $b \in B$ **do**
4:         **for** each censored list $l \in L$ **do**
5:             Permute the unassigned ranks, $\{d_l + 1, \ldots, P\}$, and assign them randomly to the items *not* found in the list, i.e., $\Lambda^\complement = X \setminus \Lambda_l$. Combine the result with $\Lambda_l$ to fill out the list.
6:         **end for**
7:         Let sra($b$) be the sequential rank agreement computed from the filled out lists.
8:     **end for**
9:     Return element-wise averages across all $B$ permutations of sra($b$).
10: **end procedure**

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The proposed approach is based on two assumptions: 1) that the most interesting items are found in the top of the lists, and 2) that the censored rankings provide so little information that it is reasonable to assume that they can be represented by a random order. The first assumption is justifiable because we have already accepted that it is reasonable to rank the items in the first place. The second assumption is fair in the light of the first assumption provided that we have a "sufficiently large" part of the top of the lists available.

When the two assumptions are satisfied then it is clear that the interesting part of the sequential rank agreement curves is restricted to the depths where the number of censored items is low. Generally, without additional prior knowledge about the distribution of the censored items it seems reasonable to restrict the attention of the sequential rank agreement to depths smaller

than $\max(d_1, \ldots, d_L)$ where at least one list provides an uncensored item.

Like for fully observed lists we generally expect the sequential rank agreement to start low and then increase unless the lists are completely unrelated (in which case the sequential rank agreement will be constant at a high level) or if the lists mostly agree on the ranking (in which case the sequential rank agreement will also be constant but at a low level). For partially ranked lists we also expect a change-point around the depth where the lists are censored. This is an artefact stemming from the fact that we assume that the remainder of the lists can be replaced by a simple permutation of the missing items.

# 3 Evaluating sequential rank agreement

To interpret the sequential rank agreement values we propose two different benchmark values corresponding to two different hypotheses. We wish to determine if we observe better agreement than what would be expected if there were no relevant information available in the data.

The first reference hypothesis is

$$H_0 \quad : \quad \text{The list rankings correspond to completely randomly} \quad (8)$$
$$\text{permuted lists}$$

which not only assumes that there is no information in the data on which the rankings are based but also that the methods are completely independent.

Alternatively, we can remove the restriction on the independence among the methods by only requiring that there is no information in the ranking but that the rankings are all based on applying the method/approaches to the same data

$$\widetilde{H}_0 \quad : \quad \text{The list rankings are based on data containing}$$
$$\text{no association to the outcome.}$$

## 3.1 Permutation-based inference

$H_0$ is a quite unrealistic null hypothesis but we can easily obtain realizations from that null hypothesis simply by permuting the items within each list and then computing the sequential rank agreement for the permuted lists. In the fully observed case each experiment contains $L$ lists of random permutations of the items in $X$. For the censored/partially observed case we first permute the items $X_1, \ldots, X_P$ and then censor list $l$ at $d_l$ (*i.e.*, each list so it has the same number of observed rankings as was observed for list $l$ in the original dataset). The sequential rank agreement curve from the the original lists can

then be compared to, say, the pointwise 95% quantiles of the observed rank agreements obtained under $H_0$.

To obtain the distribution under $\widetilde{H}_0$ the idea is to repeat the ranking procedures for unassociated data many times. Thus, we first permute the outcome variable of the data set on which the rankings are based. This removes any association between the predictor variables and the outcome. Then we apply the methods to the permuted data set to generate $L$ new rankings and subsequently compute the sequential rank agreement. Note that we only permute the outcomes and preserve the structure of the candidate predictors. The randomization approach requires that we have the original data available and as such it may not be possible to evaluate $\widetilde{H}_0$ in all situations.

If the sequential rank agreement for the original data lies substantially below the distribution of the sequential rank agreements obtained under either $H_0$ or $\widetilde{H}_0$ then this suggests that the original ranked lists agree *more* than what we would expect in data with no information, and therefore that the information in the lists is significantly more in agreement than what would be expected.

Figure 1 shows the empirical distributions of sequential rank agreement under $H_0$ and $\widetilde{H}_0$ each based on 400 permutations of the Golub data described in Section 2.1. Not surprisingly, the sequential rank agreement under $\widetilde{H}_0$ is lower than the sequential rank agreement under $H_0$ because the four methods used to rank the data ($t$ test, logistic regression, elastic net, and MIC) generally tend to identify (and rank) similar predictors even if there are only spurious associations. The two bottom panels in Figure 1 also indicate that the observed sequential rank agreement (the black line) is better than what would be expected by chance for data that contain no information since it lies below the reference areas. However, the censored data also suggests that there may be at most 1 or 2 ranked items towards the top of the lists that yield a result better than what would be expected (the bottom-right plot).

It is important to stress that neither $H_0$ nor $\widetilde{H}_0$ are related to questions regarding the association between the outcome and the predictors in the data set. Both hypotheses are purely considering how the rankings agree in a situation where there is no relevant information available in the data used for creating the rankings.

## 3.2 Asymptotic inference of change in agreement

In many applications it is of interest to estimate a list depth which satisfies a change point criterion since that corresponds to a change in agreement among the list ranks. In this section we investigate the theoretical properties

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of our proposed method for this specific task. As in Hall and Schimek (2012) we consider an infinite set of lists and study the asymptotic behaviour for $L \to \infty$. However, we do not allow the length of the lists to change with $L$ because in most applications the lengths of the lists are fixed.

We start by showing that $\widehat{\text{sra}}_L$ is a consistent estimator of sra for $L \to \infty$. The result is stated in Theorem 1.

**Theorem 1.** *Assume that $\{R_l(X)\}_{l=1}^L$ are independent draws from a probability distribution $Q$ on the set of lists $\Pi$. Then, $\|\widehat{\text{sra}}_L - \text{sra}\|_\infty = o_P(1)$.*

*Proof.* See Appendix A. ∎

We now define the change point as the first crossing point of the sequential rank agreement and a threshold function $q \colon \{1, \ldots, P\} \mapsto \mathbb{R}_{\geq 0}$. The values of $q$ could be a deterministic constant, or in the experimental setting, for example, the limits-of-agreement obtained in randomly permuted lists corresponding to the null-hypothesis in equation (8). We define the superlevel set of the sequential rank agreement with respect to $q$ as

$$\mathcal{L}(q) = \{d : \text{sra}(d) \geq q(d)\}. \tag{9}$$

A change-point $d^*(q)$ in the list agreement is then defined by the position

$$d^*(q) = \begin{cases} \inf(\mathcal{L}(q)) & |\mathcal{L}(q)| > 0 \\ P & |\mathcal{L}(q)| = 0 \end{cases} \tag{10}$$

corresponding to the first list depth where the sequential rank agreement exceeds the threshold if such a position exists. Otherwise, the full list is in agreement according to $q$ and the change-point is set to the length of the lists. The empirical superlevel set is similarly defined as

$$\widehat{\mathcal{L}}_L(\widehat{q}_L) = \{d : \widehat{\text{sra}}_L(d) \geq \widehat{q}_L(d)\} \tag{11}$$

where we allow the threshold function to depend on the sample size as well. The estimated change-point is therefore

$$\widehat{d_L^*}(\widehat{q}_L) = 1(|\widehat{\mathcal{L}}_L(\widehat{q}_L)| > 0)\inf \widehat{\mathcal{L}}_L(\widehat{q}_L) + 1(|\widehat{\mathcal{L}}_L(\widehat{q}_L)| = 0)P. \tag{12}$$

The consistency of the estimated change-point, $\widehat{d_L^*}(\widehat{q}_L)$, follows from Theorem 1 by the following corollary.

**Corollary 1.** *Let $\widehat{q}_L$ be a threshold function such that $\|\widehat{q}_L - q\|_\infty = o_P(1)$ for some limiting function $q$. Then, $\widehat{d_L^*}(\widehat{q}_L) \xrightarrow{P} d^*(q)$ for $L \to \infty$.*

*Proof.* See Appendix B. ■

Corollary 1 indicates that we can use the a threshold function $\widehat{q}_L$ estimated under the null hypothesis as discussed in the previous section as a limiting threshold function for inferring the depth $d$, where the observed sequential rank agreement first crosses the threshold of the null threshold, *i.e.*, the depth until which the observed ranked lists are in better agreement than expected under the null hypothesis. In that sense the threshold function serves the same role as the limits of agreement in method comparison studies, except that the threshold funciton is not constant but can accommodate the changing nature of the number of items used for the computation of the equential rank agreement for a given depth.

In practice we can compute an estimate of the threshold function under the null using the permutation approach sketched in the previous section which makes it relevant even in small sample settings.

# 4    Application to ovarian cancer data

We now consider an application of the sequential rank agreement to two data sets consisting of MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time Of Flight) mass spectra obtained from blood samples from patients with either benign or malignant ovarian tumors. The data sets are sub-samples of the Danish MALOVA and DACOVA study populations.

The MALOVA study is a multidisciplinary Danish study on ovarian cancer (Hogdall et al., 2004) where all Danish women diagnosed with an ovarian tumor and referred for surgery from the participating departments of gynecology were enrolled continuously from December 1994 to May 1999. For the purpose of illustration we use a random sub-sample of 119 patients with a total of 58 patients with malignant ovarian cancers as cases and 61 patients with benign ovarian tumors as controls. The DACOVA study is another multidisciplinary Danish study on ovarian cancer which included about 66% of the female population of Denmark (Bertelsen, 1991). The study aimed to continuously enroll all patients that were referred to surgery of an ovarian tumor clinically suspected to be cancer during the period from 1984 to 1990. Similarly, we use a random sub-sample from the DACOVA study of 113 patients with a total of 54 malignant ovarian cancers and 59 benign ovarian tumors/gynecologic disorders.

Each spectrum consists of 49642 samples over a range of mass-to-charge ratios between 800 to 20000 Dalton which we downsample on an equidistant grid of 5000 points by linear interpolation. We then preprocess the downsampled spectra individually by first removing the slow-varying baseline intensity

with the SNIP algorithm (Ryan et al., 1988) followed by a normalization with respect to the total ion count. Finally, we standardize the 5000 predictors to have column-wise zero mean and unit variance in each data set.

We use the two data sets to illustrate how the sequential rank agreement can be applied in two different scenarios. In the first scenario we assess the agreement of four different statistical classification methods in how they rank the predictors according to their importance for distinguishing benign and malignant tumors. In the second scenario we assess the agreement among rankings of individual predicted risks of having a malignant tumor. The first scenario is relevant in the context of biomarker discovery and the latter is important e.g., when ranking patients according to immediacy of treatment.

Four classification methods are considered: Random Forest (Breiman, 2001) implemented in the R package `randomForest` (Liaw and Wiener, 2002), logistic Lasso (Tibshirani, 1996) and Ridge regression (Segerstedt, 1992) both implemented in the R package `glmnet` (Friedman et al., 2010), and Partial Least Squares Discriminant Analysis (PLS-DA) (Boulesteix, 2004) implemented in the R package `caret` (Kuhn, 2014).

In both scenarios we use the MALOVA data to train the statistical models, and in both situations the agreements are assessed with respect to perturbations of the training data in the following manner. We repeatedly draw a random sub-sample (without replication) consisting of 90% of the MALOVA observations and train the four models on each sub-sample. We use 1000 iterations for the sub-sampling procedure.

All four methods depend on a tuning parameter. The tuning parameter for Lasso and Ridge regression is the degree of penalization, and for PLS-DA it is the number of components (the dimensionality of the subspace). We estimate these separately for each sub-sample by a 20 times repeated 5-fold cross-validation procedure. For the Random Forest we grow a fixed number of 5000 trees and let the tuning parameter be the number of predictors randomly sampled at each split. We estimate this by a binary search with respect to minimizing the Out-of-Bag classification error estimate.

The implementation of Lasso and Ridge regression in the `glmnet` package offers three different cross-validated optimization criteria for the penalty parameter: total deviance, classification accuracy and area under ROC. We apply all three criteria to our data to investigate their effect on the agreements. Note also that the Lasso models produce censored lists depending on the value of the penalty parameter.

## 4.1 Agreement of predictor rankings

For each of the four methods, each of the 1000 models trained on the 1000 sub-samples of the MALOVA data produces a ranking of the 5000 predictors according to their importance for discriminating between the tumor types. For the Random Forest classifier the predictors are ranked according to the Gini index, while for the logistic Lasso and Ridge regression models we order by absolute magnitude of the estimated regression coefficients. For the PLS-DA model the importance of the predictors is based on a weighted sum of the absolute coefficients where the weights are proportional to the reduction in the sums of squares across the components.

The right panel of Figure 2 shows the sequential rank agreement of the estimated importance of the 5000 predictors. For clarity of presentation we zoom in on the agreement up to list depth 600. At deeper list depths all agreement curves are approximately constant.
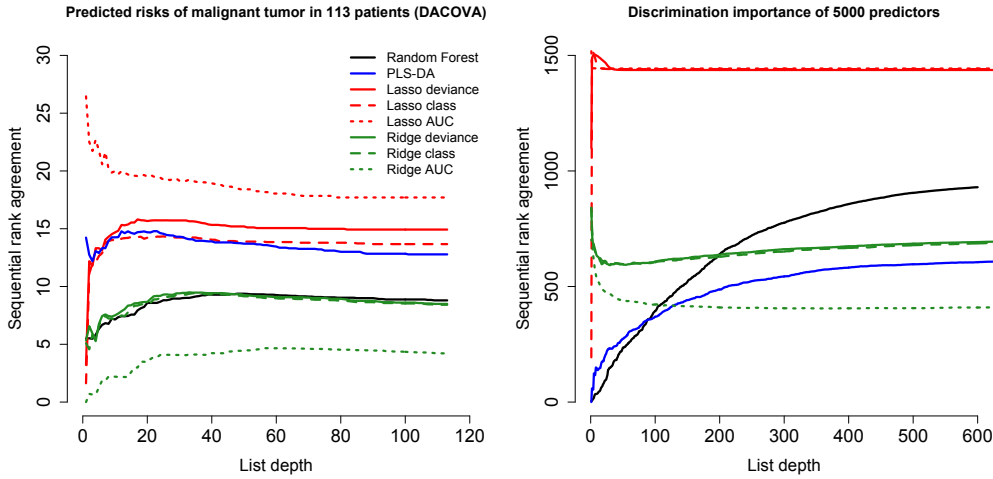


Figure 2: Left panel: Sequential rank agreement of 1000 rankings of the predicted risks of malignant tumor. For each method the different rankings were obtained by first training models in 1000 random sub-samples of the MALOVA data and then predicting the risk of malignant tumor in the 113 DACOVA patients. Right panel: Sequential rank agreement of 1000 rankings of the 5000 predictors. The rankings were obtained from the same 1000 trained models.

For most of the sequential rank agreement curves we see, as expected, that they start low, indicating good agreement, followed by an increase until they approximately become constant. This has the interpretation that the

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agreement across the different sub-samples is higher in the top as compared to the tail of the lists for all these classification methods. The change-points where the curves become approximately constant are the list depths where the ranks of the remaining items become close to uniformly random.

A not expected shape of the agreement curves is seen for the Ridge models for all three tuning criteria. They all show higher disagreement in the top of the lists followed by a decrease. The reason behind this behavior is rather subtle. Looking at the distribution of the absolute value of the regression coefficients we see that a large proportion of them are numerically very close to zero and have almost equal absolute value. This is a general feature of the Ridge models in this data set and seen for all the 1000 trained models. This implies that when predictors are ranked according to the magnitude of their coefficients, their actual order becomes more uncertain and more close to a random permutation. This problem can be alleviated by truncating all predictors with absolute coefficient values below a given threshold thereby introducing an artificial censoring of the lists. For the Ridge models tuned with the deviance criterion, Figure 3 (left) shows the the sequential rank agreement where for each of the 1000 trained models the predictors were artificially censored when their absolute coefficient value was lower than the 0.1% quantile of the 5000 absolute coefficient values. The curve was calculated using Algorithm 1 with $B = 1000$ and $P = 5000$. The corresponding curve from Figure 2 (right panel) is shown for comparison. Even though the number of censored predictors is very small compared to the total number of predictors, the effect on the sequential rank agreement is substantial and with the artificial censoring the shape of the curves is as expected, starting low and then increasing.

Looking at the agreement curves for the Lasso models in Figure 2 (right) we clearly see the effect of the sparsity inducing penalization giving rise to censored lists. These curves were similarly calculated using 1 and 1000 random permutations. Under the deviance optimization criterion the median number of non-zero coefficients was 33 (range 16 to 50) and for the class accuracy criterion 14 (range 4 to 56). These values correspond to the list depths where the agreement curves become constant as a result of the subsequent censoring.

## 4.2    Agreement of individual risk predictions

To assess the stability of the individual risk predictions we apply the predictors from the DACOVA data set to each of the models. The predicted probabilities are then ranked in decreasing order such that the patients with the highest risk of a malignant tumor appears in the top of the list. Figure 2

(left) shows the sequential rank agreement separately for each method, based on the 1000 risk predictions obtained from the models trained in the same 1000 random sub-samples of the MALOVA data.

Most curves start low and then increase indicating higher agreement among high risk patients. This is expected if we rank the individuals according to highest risk of disease. However, it is also expected that individuals with very low risk also show high agreement. In this case we order the patients according to (high) risk prediction but we could essentially also have reversed the order to identify the patients that have low risk prediction.

An exception is the risk prediction agreement for the Lasso tuned with the AUC criterion which shows very low agreement among the high values of the predicted risks. The reason is that optimizing the penalty parameter with respect to the AUC criterion tends to favor a very high penalty value causing only a single predictor to be selected in each of the 1000 iterations. This results in a lack of generalizability to the DACOVA data which gives rise to the higher disagreement in the predicted risks. In the extreme case where the penalty becomes so high that none of the predictors are selected by the Lasso, the sequential rank agreement for the predicted probabilities becomes undefined since all the ranks will be ties.
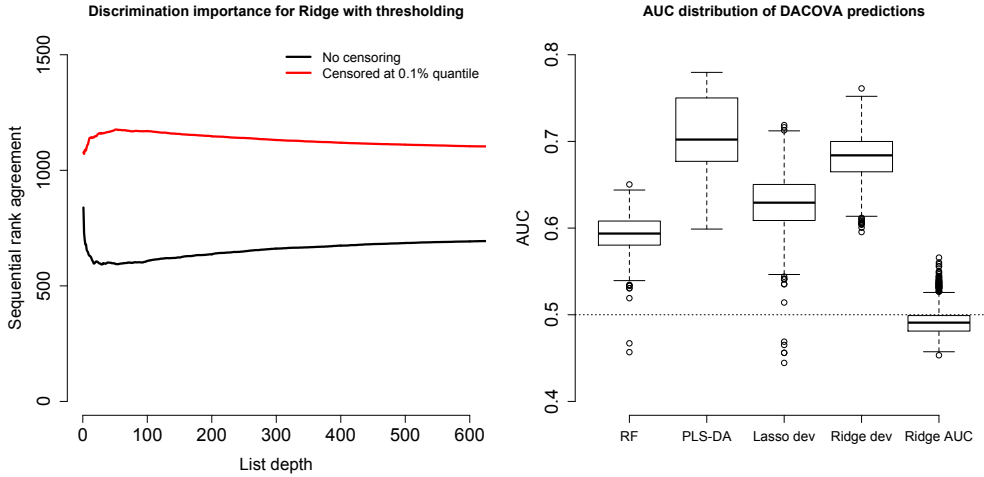


Figure 3: Left panel: Sequential rank agreement for Ridge regression obtained by artificially censoring predictors when their absolute coefficient values are lower than the 0.1% quantile. Right panel: Box plots of AUC values across the 1000 sub-samples with respect to the known class labels of the DACOVA data.

Comparing the left and right panels of Figure 2 it can further be seen that some of the methods show better agreement with respect to the predicted probabilities than for ranking the importance of the predictors and vice versa. Ridge regression shows higher agreement across training sets for the risk predictions than PLS-DA, and PLS-DA shows higher agreement for predictor importance than Ridge regression.

Lasso shows similar agreement for ranking the risk predictions than PLS-DA (unless with the AUC criterion), and poorer agreement for ranking predictors. This reason for the latter is the high auto-correlation between the intensities in the mass spectra which leads to collinearity issues in the regression models. It is well-known that variable selection with the Lasso penalty does not preform very well when the predictors are highly correlated. The collinearity does, however, not affect the agreement of the risk predictions, as seen on the left panel of Figure 2, since it is not so important which specific variable that gets selected from a group of highly correlated predictors when the purpose is risk predictions.

It appears that Ridge regression tuned with the AUC criterion achieves the best performance with respect to the stability of ranking the individual predicted risk probabilities. It must, however, be stressed that the sequential rank agreement in this application is only concerned with the agreement of the risk predictions across sub-samples and not with the actual accuracy of the risk predictions. Thus, we also computed the AUC values for the different models based on the DACOVA data. The distributions across the 1000 sub-samples for a selection of the models is shown in the right panel of Figure 3. Here we see that PLS-DA attains the highest AUC values with a median value of 0.70 while the Ridge model with the AUC criterion attains a median AUC of 0.49. This implies that while Ridge regression optimized with respect to the AUC criterion achieves the best sequential rank agreement, it performs similar to a random coin toss with respect to classifying the DACOVA patients. In practice both concerns are of importance.

# 5   Discussion

In this article we address the problem of comparing ranked lists of the same items. Our proposed method can handle both the situation where the underlying data to generate the ranked lists are available and the situation where the only available data is the actual ranked lists. In addition, censored ranked lists where only the ranks of the top $k$ ranked items are known can be accommodated as well. The proposed agreement measure can be interpreted as the average distance between an item's rank and the average rank assigned to

that item across lists. Thus the measure determines how well the lists agree on the ranks of a specific item.

The sequential rank agreement is extremely versatile. We have shown that it can be used not only to compare ranked lists of items produced from different samples/populations but that it also can be used to study the ranks obtained from different analysis methods on the same data as well as to evaluate the stability of the ranks from a single method by bootstrapping (or sub-sampling) the data repeatedly and comparing the ranks obtained from training the models in the bootstrapped data.

The sequential rank agreement can be used to determine the depth at which the rank agreement becomes too large to be desirable based on prior requirements or acceptable differences, or it can be used to visually determine when the change in agreement becomes too large. In that regard the investigator can have prior limits on the level of agreement that is acceptable.

While the sequential rank agreement is primarily an exploratory tool we have suggested two null hypotheses that can be used to evaluate the sequential rank agreement obtained. Note that none of the two null hypotheses are concerned with the actual "true ranking" but are purely concerned with consistency/stability of the rankings among the lists. As such we cannot determine if the rankings are good but only whether they agree. The sequential rank agreement curve can be compared visually to the curves obtained under either of the null distributions and simple point-wise $p$-values can be obtained for each depth by counting the number of sequential rank agreements under the null hypothesis that is less than or equal to the observed rank agreement. Two simple extensions can be pursued to make more formal uniform tests: one would be to use a Kolmogorov-Smirnov-like test and use the largest difference between the variance-weighted sequential rank agreement curve and the mean null rank agreement curve as a test statistic. Alternatively, a change-point analysis could be made on the sequential rank agreement in order to determine the depths at which there are "jumps" in the rank agreement. These jumps would correspond to depths for which the agreement among the lists was substantially worse and could serve as indicators for when the lists no longer agree sufficiently satisfactory.

Finally, we have — whenever possible — used all available ranks from the lists. We could choose to censor the rankings of all the items that were deemed not to be significant if information on both rankings and the corresponding evidence for significance was available. That would ensure that there would be put less emphasis on the agreement of the non-significant items and it would be easier to identify a change in agreement among the items that were deemed to be relevant. In our application section we have successfully introduced such an artificial censoring for the predictor rankings

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obtained with ridge regression.

We note that the sequential rank agreement is still marred by problems that generally apply to ranking of items and/or individuals. Collinearity in particular can be a huge problem when bootstrapping data or when comparing different analysis methods. For example, marginal analyses where each item is analyzed separately will assign similar ranks to two highly correlated predictors while methods that provide a sparse solution such as the Lasso will just rank one of the two predictors high while the other might have a very low rank. Thus in such a scenario we would expect low agreement of the rankings from Lasso and marginal analyses simply because of the way correlated predictors are handled. This is not a shortcoming of the sequential rank agreement but is a problem general to all ranked lists.

Another caveat with the way the sequential rank agreement is defined is the use of the standard deviation to measure agreement. The standard deviation is an integral part of the limits-of-agreement as discussed by Altman and Bland (1983). However, the standard deviation can also be unstable when the number of observations is low and alternative measures such as the median absolute deviance may prove more stable in some situations. However, the current definition using the standard deviation is analogous to the approach used for agreement in method comparison studies so we have used that.

In conclusion we have introduced a method for evaluation of ranked (partial/censored) lists that can be easily interpreted and that can be applied to a large number of situations. The method presented here can be adapted further by using it to compare and classify statistical analysis methods that agree on the rankings they provide or by using the rank agreement to optimize a hyper-parameter in, say, elastic net regularized regression where the rank agreement is used to determine the mixing proportion between the $L_1$ and the $L_2$ penalty. We will be investigating these extensions further in the future.

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# A Proof of Theorem 1

We start by defining the following cadlag function

$$N(p;d) = \sum_{s=1}^{p} 1\left(Q(R(X_s) \le d) > 0\right), \quad p = 1, \ldots, P \tag{13}$$

which runs through the list elements in an arbitrary order and counts how many list elements have a strictly positive probability to have rank less than or equal to $d$ under the probability measure $Q$. Note that the cardinality of the set $S(d)$ in equation (3) is equal to the counting process evaluated at the last element: $|S(d)| = N(P;d)$. The empirical counterpart of the counting process is given by

$$\widehat{N}_L(p;d) = \sum_{s=1}^{p} 1\left(\frac{1}{L}\sum_{l=1}^{L} 1(R_l(X_s) \le d) > 0\right) \tag{14}$$

$$= \sum_{s=1}^{p} 1\left(\widehat{Q}_L(R(X_s) \le d) > 0\right).$$

The joint law of the sequence $\{\widehat{N}_L(p;d)\}_{1 \le p \le P}$ is completely determined by the finite set of the jump times of $N(p;d)$. Since $\{1(R_l(X_s) \le d); l = 1, \ldots, L\}$ consists of independent and identically Bernoulli distributed variables with expectation $Q(R(X_s) \le d)$ it follows from the law of large numbers that $\widehat{Q}_L(R(X_p) \le d) \xrightarrow{P} Q(R(X_p) \le d)$ for every $p$ and $d$ as $L \to \infty$. Therefore, we have

$$\sup_{d \in 1,\ldots,P} \sup_{p \in 1,\ldots,P} \left|\widehat{N}_L(p;d) - N(p;d)\right| = o_P(1). \tag{15}$$

The sequential rank agreement given in equation (5) may therefore be rewritten as the following integral with respect to $N$

$$\mathrm{sra}(d) = \int_1^P \frac{A(X_p)}{N(P;d)} \mathrm{d}N(p;d). \tag{16}$$

The empirical sequential rank agreement is similarly given by

$$\widehat{\mathrm{sra}}_L(d) = \int_1^P \frac{\widehat{A}_L(X_p)}{\widehat{N}_L(P;d)} \mathrm{d}\widehat{N}_L(p;d) \tag{17}$$

and it follows that

$$\sup_{d \in 1,\ldots,P} |\widehat{\mathrm{sra}}_L(d) - \mathrm{sra}(d)| \le \sup_{d \in 1,\ldots,P} |U_L(d)| - \sup_{d \in 1,\ldots,P} |V_L(d)| \tag{18}$$

where

$$U_L(d) = \int_1^P \frac{A(X_p)}{N(P;d)} \mathrm{d}\left(\widehat{N}_L(p;d) - N(p;d)\right) \tag{19}$$

$$V_L(d) = \int_1^P \left(\frac{\widehat{A}_L(X_p)}{\widehat{N}_L(P;d)} - \frac{A(X_p)}{N(P;d)}\right) \mathrm{d}\widehat{N}_L(p;d) \tag{20}$$

The conclusion of the proof therefore follows if each of these two terms are uniformly of order $o_P(1)$ in $d$. For the first term we have that

$$|U_L(d)| \le \left(\sup_{p \in 1,\ldots,P} \left|\frac{A(X_p)}{N(P;d)}\right|\right)\left(\widehat{N}_L(p;d) - N(p;d)\right)\Big|_1^P \tag{21}$$

where the second factor is $o_P(1)$ uniformly in $d$ by equation (15). The first factor is $O(1)$ since $N(P;d) > 0$ uniformly in $d$ and because $A(X_p) = O(P^2)$ uniformly in $p$ by the Cauchy-Schwarz inequality. It thus follows that $|U_L(d)| = o_P(1)$ uniformly in $d$.

Similarly we derive an upper bound for $V_L(d)$ by

$$V_L(d) \le \sup_{p \in 1,\ldots,P} \left|\frac{\widehat{A}_L(X_p)}{\widehat{N}_L(P;d)} - \frac{A(X_p)}{N(P;d)}\right| \int_1^P \left|\mathrm{d}\widehat{N}_L(p;d)\right| \tag{22}$$

and it follows directly from the law of large numbers that $\widehat{A_L(X_p)} = A(X_p) + o_P(1)$ uniformly in $p$ since $R_i(X_p)$ in equation (2) for $i = 1,\ldots,L$ are independent and $Q$-identically distributed random variables with finite second moment. Again, $\widehat{N}_L(P;d) = N(P;d) + o_P(1)$ uniformly in $d$ by equation (15) and $N(P;d) > 0$ so by the continuous mapping theorem the first factor in equation (22) is of order $o_P(1)$ uniformly in $p$ and $d$. The result then follows by noting that the second factor is bounded by $P$ uniformly in $d$.

# B  Proof of Corollary 1

Recall that $\mathcal{L}$ is the superlevel set of list positions where the sequential rank agreement exceeds the threshold function $q$. Let $A \triangle B = (A \setminus B) \cup (B \setminus A)$ is the symmetric difference between sets $A$ and $B$. It is then sufficient to show that $|\widehat{\mathcal{L}}_L(\widehat{q}_L) \triangle \mathcal{L}(q)|$ converges to zero in probability as $L \to \infty$. By the triangle inequality we have that

$$\left|\widehat{\mathcal{L}}_L(\widehat{q}_L)\triangle\mathcal{L}(q)\right| = \left|\left(\widehat{\mathcal{L}}_L(\widehat{q}_L)\triangle\widehat{\mathcal{L}}_L(q)\right) \cup \left(\widehat{\mathcal{L}}_L(q)\triangle\mathcal{L}(q)\right)\right| \tag{23}$$

$$\le \left|\widehat{\mathcal{L}}_L(q)\triangle\mathcal{L}(q)\right| + \left|\widehat{\mathcal{L}}_L(\widehat{q}_L)\triangle\widehat{\mathcal{L}}_L(q)\right|$$

Looking at the first term we have

$$\left|\widehat{\mathcal{L}}_L(q)\triangle\mathcal{L}(q)\right| = \sum_{d=1}^{P} |1\left(\widehat{\mathrm{sra}}_L(d) \geq q(d)\right) - 1\left(\mathrm{sra}(d) \geq q(d)\right)| \qquad (24)$$

$$= \qquad\qquad\qquad\qquad\qquad (25)$$

Similarly we have

$$\left|\widehat{\mathcal{L}}_L(\widehat{q}_L)\triangle\widehat{\mathcal{L}}_L(q)\right| = \sum_{d=1}^{P} |1\left(\widehat{\mathrm{sra}}_L(d) \geq \widehat{q}_L(d)\right) - 1\left(\widehat{\mathrm{sra}}_L(d) \geq q(d)\right)| \qquad (26)$$

$$= \qquad\qquad\qquad\qquad\qquad (27)$$

This completes the proof.