### A test procedure for random degeneration of paired rank lists

#### Michael G. Schimek<sup>1,3</sup> Peter Hall<sup>2</sup> Eva Budinská<sup>3</sup>

<sup>1</sup>Medical University of Graz Institute for Medical Informatics, Statistics and Documentation 8036 Graz, Austria, Europe

<sup>2</sup>The University of Melbourne, Australia

<sup>3</sup>Masaryk University, Czech Republic, Europe

MCP 2007 9–11 July 2007, Vienna, Austria



#### The statistical problem

- Assume two assessors (e.g. laboratories, search engines)
- The first assessor ranks N distinct objects according to the extent to which a particular attribute is present
- The ranking is from 1 to N, without ties

#### There are two different situations of interest:

- The second assessor assigns each object to the one or the other of two categories (0-1-decision)
- Intersection of the second assessor also ranks the objects from 1 to N

#### An indicator variable takes $I_i = 1$

if the ranking given by the second assessor to the object ranked *j* by the first is not distant more than m, say, from *j*,

and  $I_j = 0$  otherwise

The  $l_j$ 's form a **data stream** (input of our algorithm)



#### The goal

- In both situations we wish to determine how far into the two rankings one can go before the differences between them degenerate into noise
- This allows us to identify a sequence of objects that is characterized by a high degree of assignment conformity

#### **Typical applications are:**

- Data integration from various 'omic' platforms in molecular research (e.g. microarrays, SNP arrays, microRNA arrays)
- Construction of a meta-search engine for Web applications
- Top-k-list comparisons from data logs on the Web across time (e.g. automatic screening for emerging trends)

inische Universität Gra

### Examples of data streams

#### EXAMPLE 1: DATA STREAM WITH PERFECT OVERLAP IN THE TOP-SET (N=100 OBJECTS)

Assignments	Objects																				
Ranking 1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	 100
Ranking 2	1	2	3	4	5	6	11	9	8	10	18	12	28	17	90	13	21	23	19	14	 87
Indicator	1	1	1	1	1	1	0*	0	0	1	0	1	0	0	0	0	0	0	1	0	 0
	* Point of degeneration																				

#### EXAMPLE 2: DATA STREAM WITHOUT PERFECT OVERLAP IN THE TOP-SET (N=100 OBJECTS)

Assignments	Objects																					
Ranking 1	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 10														100							
Ranking 2	2	1	3	5	4	6	11	9	8	10	18	12	28	17	90	13	21	23	19	14		87
Indicator	0	0	1	0	0	1	0*	0	0	1	0	1	0	0	0	0	0	0	1	0		0
* Is this the point of degeneration?																						



In differential gene expression we usually have results from various biological experiments and/or platforms for

prespecified conditions such as tumor vs. normal (e.g. in tissue)

These results come in **rank lists** of genes (due to criteria such as fold change, multiplicity-controlled p-values, SAM-output) **Our goal** is to consolidate these results **The problem**:

- Usually such lists have limited 'overlap'
- There is no operational concept of list conformity when combining rank lists
- The theory of nonparametric order statistics (random variables) does not really help (due to lack of distributional models)

通りメモトメモン

Let us assume a pairwise consideration of order statistics (e.g. characterizing the rank order of genes resulting from various selection procedures)

- Considerable overlap only for top-ranking objects
- Number of top-ranking objects very small compared to overall number of rank positions
- Even the top-ranked positions can show stochastic fluctuation (no 'perfect' overlap)
- Hard to define an end condition for the set of top-ranking objects
- Need a formal concept to characterize overlap degeneration

### Overall goal and attempts to achieve it

# Aggregation of input information with respect to high conformity

Technically hard to achieve because

- no or little prior information (e.g. in molecular research)
- lack of stochastic concepts that are appropriate
- numerically extremely expensive (combinatorial approaches can be NP hard; see Fagin et al., 2003, SIAM JDM 17, 134-160)

#### Approaches taken so far:

- A similarity score for ordered lists (Yang et al., 2005, JBCB 4, 693-708; Bioconductor package OrderedList)
- Computer-intensive statistics (Cross Entropy Monte Carlo) for rank aggregation (Lin et al., forthcoming)

(人間) (人) (人) (人) (人)

### Our approach

We apply a **statistical approach** taking advantage of the theoretical concept of 'moderate deviations' (for this mathematical concept see e.g. Donoho et al., 1995, JRSS, B 57, 301-369)

- We are not aiming at an overall score or global rank aggregation
- We reduce the input information to a sequence of indicator variables with respect to the concordance of paired ranks
- Our focus is the **selection of a set of top-ranked objects** based on paired information
- We allow for the realistic setting of irregular rankings (fuzzy instead of perfect overlap)
- We even allow for very small numbers of top-ranking objects compared to the overall number of objects

ヨト・モラト

We develop a methodology that allows us to test for random degeneration of paired rank information This is equivalent to the identification of that point where the data stream degenerates into noise Basic assumptions

- For the estimation of the point of degeneration into noise we assume independent **Bernoulli random variables**
- There are **no ties** in the rankings
- Under the condition of a general decrease of the probability for concordance of rankings with increasing distance from the top rank a formal inference model can be developed
- Moderate deviation arguments are suitable for testing in a sequence of indicator values (data stream)

<回>< 回> < 回> < 回>

### Our methodology continued

- The 2nd assessor, like the 1st, ranks the objects  $o_1, \ldots, o_N$  from 1 to N ( $j = 1, \ldots, N$ )
- Indicator I<sub>j</sub> = 1 if the ranking given by the 2nd assessor to the object ranked j by the 1st is not distant more than m from j, and I<sub>j</sub> = 0 otherwise
- Can symmetrise this definition by asking that both, or at least one, of the two distances not exceed 1
- Taking m = 0, symmetry already prevails, but then we have to adjust for irregular rankings
- Several 'regularization' (tuning) parameters are introduced to account for the closeness of the assessors' rankings and the degree of randomness in the assignments



イロト イポト イヨト イヨト

We shall assume that the Bernoulli random variables  $I_j$  are **independent**, somewhat a simplification

Note: The additional complication of modelling dependence in the nonstationary sequence of 0's and 1's would not pay off for our purposes

Our model:

**Independent Bernoulli random variables**  $I_1, \ldots, I_N$  are observed, with  $p_j \ge \frac{1}{2}$  for each  $j \le j_{0-2}$ ,  $p_{j_0-1} > \frac{1}{2}$ , and  $p_j = \frac{1}{2}$  for  $j > j_0$ 

From this information we wish to estimate the value of  $j_0$  (point of degeneration into noise)

The 'general decrease' of  $p_j$  for increasing j, implied by this condition, need not be monotone

In some circumstances the threshold  $\frac{1}{2}$  should be replaced by a different value

## Algorithm

- Consists of an ordered sequence of 'test stages'  $s_1, s_2, \ldots$
- Stage  $s_k$  terminates a distance  $J_{s_k}$  into the sequence  $I_1, \ldots, I_N$
- When k is odd,  $J_{s_k}$  is a potential lower bound to  $j_0$
- Can show that when k = 1, the probability that  $J_{s_{2k-1}}$  is a lower bound for  $j_0$  is approximately equal to 1 under our model (analogous for each  $k \ge 1$ )
- Stage s<sub>k</sub> starts by drawing a 'pilot sample' of size ν, consisting of the set of values l<sub>j</sub> for which j is among the first ν indices to the right of J<sub>s<sub>k-1</sub></sub> rν, if k is odd, or to the left of J<sub>s<sub>k-1</sub></sub> + rν, if k is even (r > 1 fixed)
- The sequence of consecutive steps that leads from
   J<sub>s<sub>k</sub></sub> ± rν to J<sub>s<sub>k</sub></sub> is called the 'test stream' for stage s<sub>k</sub>

zinische Universität Gra

イロト イポト イヨト イヨト

### Algorithm continued: inference

- Pilot sample size to construct  $\hat{\rho}_j^+ = \frac{1}{\nu} \sum_{\ell=j}^{j+\nu-1} I_\ell$  and  $\hat{\rho}_j^- = \frac{1}{\nu} \sum_{\ell=j-\nu+1}^{j} I_\ell$
- These quantities represent estimates of p<sub>j</sub> computed from the ν data pairs l<sub>ℓ</sub> for which ℓ lies immediately to the right of j, or immediately to the left, respectively
- Pilot sample size v can be interpreted as smoothing parameter (choice is critical; see simulations)
- Choose the constant C > 0 so that  $z_{\nu} \equiv (C \nu^{-1} \log \nu)^{\frac{1}{2}}$  is a moderate-deviation bound for testing the null hypothesis  $H_0$  that  $p_k = \frac{1}{2}$  for  $\nu$  consecutive values of k, versus the alternative  $H_1$  that  $p_k > \frac{1}{2}$  for at least one of the values of k
- Assuming that  $H_0$  applies to the  $\nu$  consecutive values of k in the respective series we reject  $H_0$  if and only if  $\hat{p}_j^{\pm} \frac{1}{2} > z_{\nu}$

### Algorithm continued: inference and tuning

- Under  $H_0$ , the variance of  $\hat{p}_i^{\pm}$  equals  $(4\nu)^{-1}$
- Therefore we should take C > <sup>1</sup>/<sub>4</sub> if we are to control moderate deviations
- Can be compared with the construction of thresholds for wavelet expansions under moderate-deviation arguments
- The test results depend on the choice of the tuning parameters, i.e. r, C, ν, and m
- Because our mathematical model can never be more than an approximation to the complex decision problem an iterative algorithm was developed (adjusting for irregularity)
- A prototype is implemented in the statistical computing environment R

・ 同 ト ・ ヨ ト ・ ヨ ト

### Simulation outline and results

#### Goal was to study the role of tuning parameters

- Length of paired rank list N = 1000
- Two segments variable in length, separated by j<sub>0</sub>, point of degeneration into noise
- $p.seg1 \in [0.6, 0.7, 0.8, 0.9, 1], p.seg2 \in [0.1, 0.2, 0.3]$
- $C \in [0.251, 0.3, 0.35, 0.4, 0.45, 0.50, \dots, 1]$
- $j \in [10, 20, 30, 40, 50, 100, 150, 200, 250, \dots, 500]$
- $\nu \in [10, 20, 30, 40, 50, 100, 150, 200, 250, 300, 350, 400]$

#### Main results

- C compensates for poor segment separability:  $0.25 < C \le 0.4$  is best choice
- The pilot sample size  $\nu$  should be approximately  $2 * j_0$
- Technical constant r can be fixed to, say, r = 1.2
- Choice of  $\nu$  much more critical than of C

(B)

# Typical simulation result: influence of $\nu$ and C on $\hat{j}_0$



2.segm.comp.j to C by v. N=1000 p.seg1=0.8 p.seg2=0.1 j=150 r=1.2

Schimek, M. G. et al. Random degeneration of paired rank lists

### Microarray data and results

**Breast cancer data** due to Sørlie et al. (2001, PNAS 98, 10869-10874)

- N = 500 genes selected by SAM
- 7 samples hybridized on different microarray platforms, we selected 2 of them (30 resp. 40 arrays)
- Input are 2 rank lists of differentially expressed genes

Goal is to estimate the point of degeneration into noise and a set of genes that is supported by both platforms User has to specify distance parameter *m* (exploratory plot of the maximal proportions of ones for the range 5 to 500) Results

- Exploratory plot hints at *m* = 20
- Pilot sample size  $\nu = 10$  and  $C \in [0.251, 0.3, 0.35, 0.4]$ resulted in a **point of degeneration**  $\hat{j}_0 = 22$
- The set size is  $\hat{j}_0 1 + m = 41$  objects (genes)

### Microarray data: exploratory plot for *m* selection



#### Maximas of probabilities for all m.dist for Sorlie dataset

Schimek, M. G. et al. Random degeneration of paired rank lists

# Microarray data: influence of $\nu$ and C on $\hat{j}_0$



comp.j to C by v. m.dist=20j.pos22

Schimek, M. G. et al. Random degeneration of paired rank lists

### Summary

#### • Our iterative algorithm

- works perfectly well for regular rankings
- works well even for irregular rankings
- selects top ranking sets well even when they are small compared to the overall number of objects
- is computationally highly efficient
- is not too sensitive to the choice of tuning parameters (apart from  $\nu$  and *m* for real data)
- is promising for real rank list data of unknown structure

#### Future research needs to address

- the problem of objective choice of the smoothing parameter ν (much more critical than choice of C)
- the situation of more than two assessors (a generalization of our algorithm is feasible)
- the problem of missing rankings

(日)、
(1)(