

Quick Permutation Test: feature filtering of n-gram data

Piotr Sobczyk^{1*}, Michał Burdukiewicz², Chris Lauber³, Paweł Mackiewicz²
*Piotr.Sobczyk@pwr.edu.pl

¹Wrocław University of Technology, Department of Mathematics, Poland

²University of Wrocław, Department of Genomics, Poland

³Dresden University of Technology, Institute of Medical Informatics and Biometry, Poland

Introduction

N-grams (k-tuples) are vectors of n characters derived from input sequence(s). They may form continuous sub-sequences or be discontinuous. Another important n-gram parameter is its position. Instead of just counting n-grams, one may want to count how many n-grams occur at a given position in multiple (e.g. related) sequences. Originally developed for natural language processing, n-grams are also used in genomics (Fang et al., 2011), transcriptomics (Wang et al., 2014) and proteomics (Guo et al., 2014).

	P1	P2	P3	P4	P5	P6		1	2	3	4
S1	2	4	3	2	2	1		1	3	1	1
S2	1	2	3	2	1	1		3	2	1	0
S3	1	2	1	1	3	1		4	1	1	0
Sample sequences.							Unigram counts.				

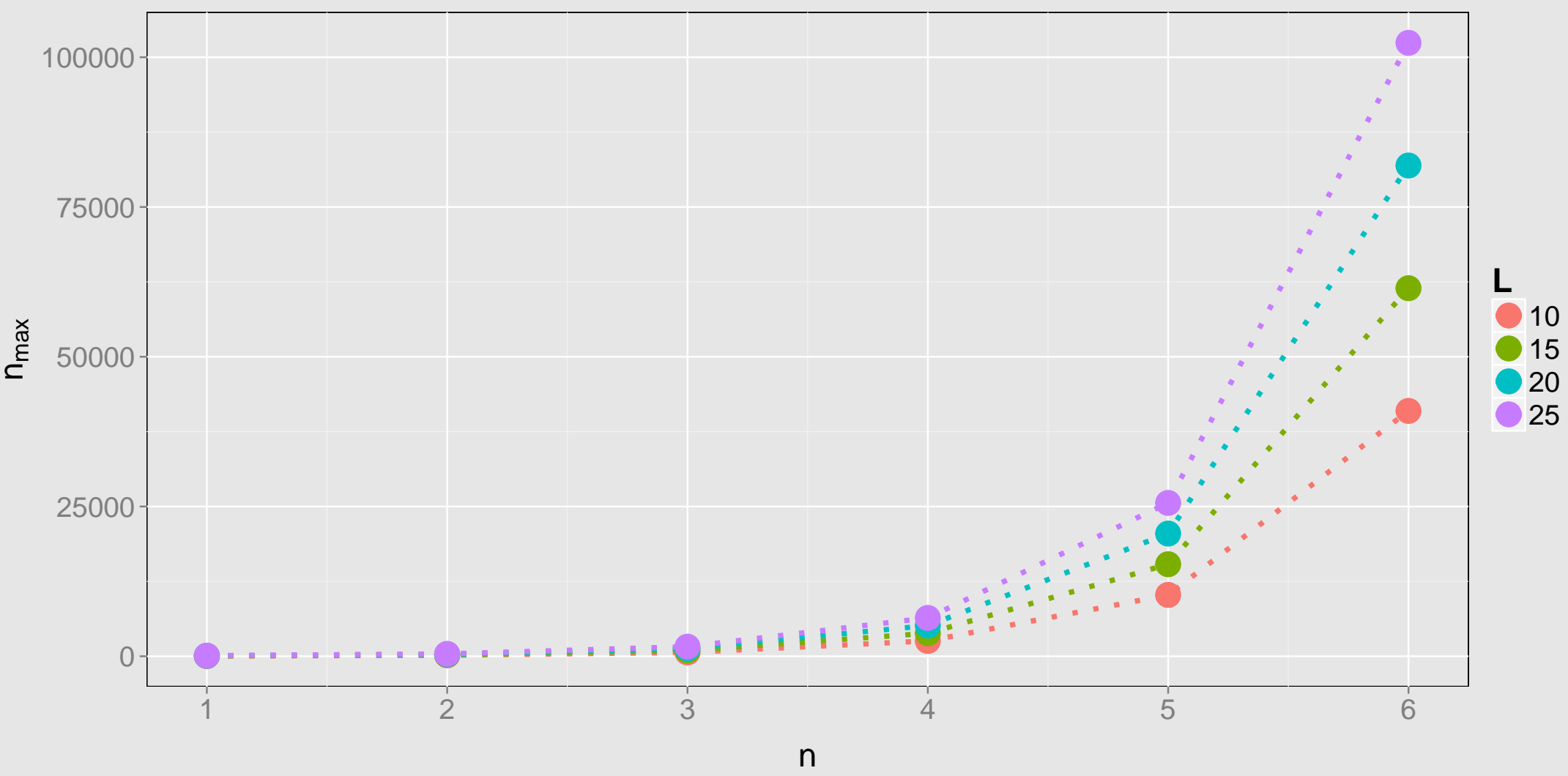
P1	1	P2	1	P3	1	P4	1	P5	1	P6	1	P1	2	P2	2	P3	2	P4	2	P5	2	P6	2	P1	3
0	0	0	0	0	0	1	1	0	0	1	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0
1	0	0	0	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
1	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

A fraction of possible unigrams with position information.

Curse of dimensionality

Even when we limit ourselves to only continuous positioned n-grams, feature space grows rapidly with the number of elements in n-gram (n) and length of the sequence (L). Number of possible positioned n-grams:

$$n_{\max} = L \times m^n$$



Feature selecting permutation tests

Model and statistic independent permutation tests can be used to filter features obtained through counting n-grams. During a permutation test class labels are randomly exchanged during computation of significance statistic. p-values are defined as:

$$\text{p-value} = \frac{N_{T_P > T_R}}{N}$$

where $N_{T_P > T_R}$ is number of times when T_P (permuted test statistic) was more extreme than T_R (test statistic for non-permuted data). Permutation tests are computationally expensive (especially precise estimation of low p-values, because the number of permutations is inversely proportional to the interval between p-values).

QuiPT idea

If probability that target equals 1 is p and probability that feature equals 1 is q then we can compute the probability of given observations, eg.

$$P(\text{Target}, \text{Feature}) = (1, 1) = p \cdot q$$

Therefore another view at permutation test is that we get a contingency table, which needs to be tested for independance.

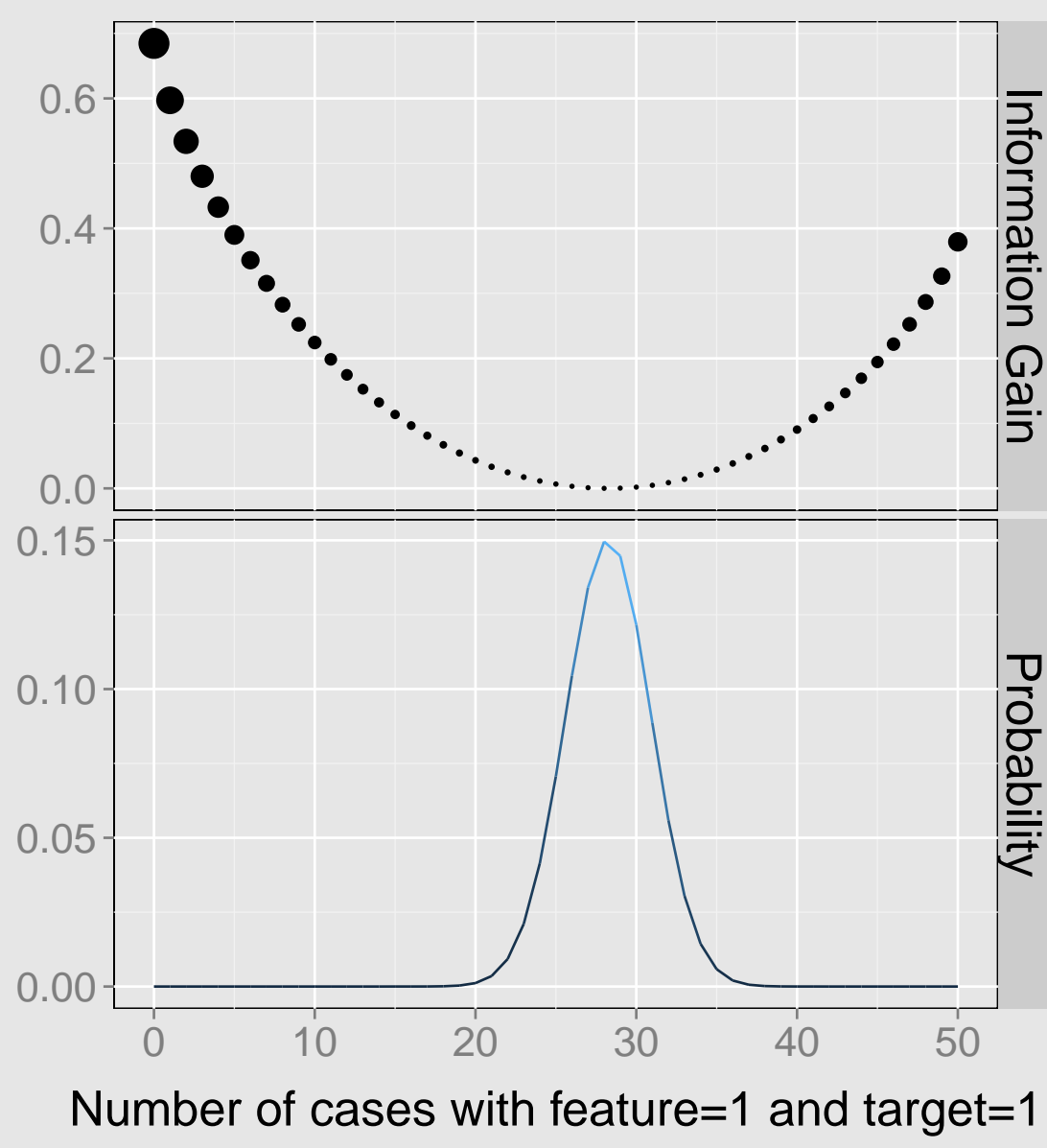
Independence test

$F(n_{1,1}, n_{1,0}, n_{0,1}, n_{0,0}) = \binom{n}{n_{1,1}} (p \cdot q)^{n_{1,1}} \binom{n-n_{1,1}}{n_{1,0}} (p \cdot (1-q))^{n_{1,0}} \binom{n-n_{1,1}-n_{1,0}}{n_{0,1}} ((1-p) \cdot q)^{n_{0,1}} \binom{n-n_{1,1}-n_{1,0}-n_{0,1}}{n_{0,0}} ((1-p) \cdot (1-q))^{n_{0,0}}$
This distribution comes with two constraints: $n_{1,\cdot} = n_{1,1} + n_{1,0}$ and $n_{\cdot,1} = n_{1,1} + n_{0,1}$. Thus, conditioning on $n_{1,1}$, we get hypergeometric distribution.
This is in fact exact two-sided Fisher's test. Information Gain is used here as a way of deciding which contingency tables are more extreme.

Computational cost

The cost of performing QuiPT is equal to computing Information Gain and probability of occurence for $n_{1,1} + n_{0,1}$ contingency tables. Suppose we consider 6-grams build on sequences of length 25 build of four characters. Then there are around 100,000 n-grams, features to test. This means that for Benjamini-Hochberg procedure, we need to calculate p-values with accuracy of 0.05×10^{-5} . This requires at least 2 million permutations. Each permutation, apart from reshuffling labels, requires computation of IG. Since n-gram features are very sparse vectors, QuiPT needs to evaluate only few contingency tables.
The relative difference in speed between QuiPT and normal permutation tests depends on several factors, as number of permutations and input data. For example, for simulation scheme presented below, QuiPT was on average 93 times faster than normal permutation test with 10^5 permutations.

Contingency table representation

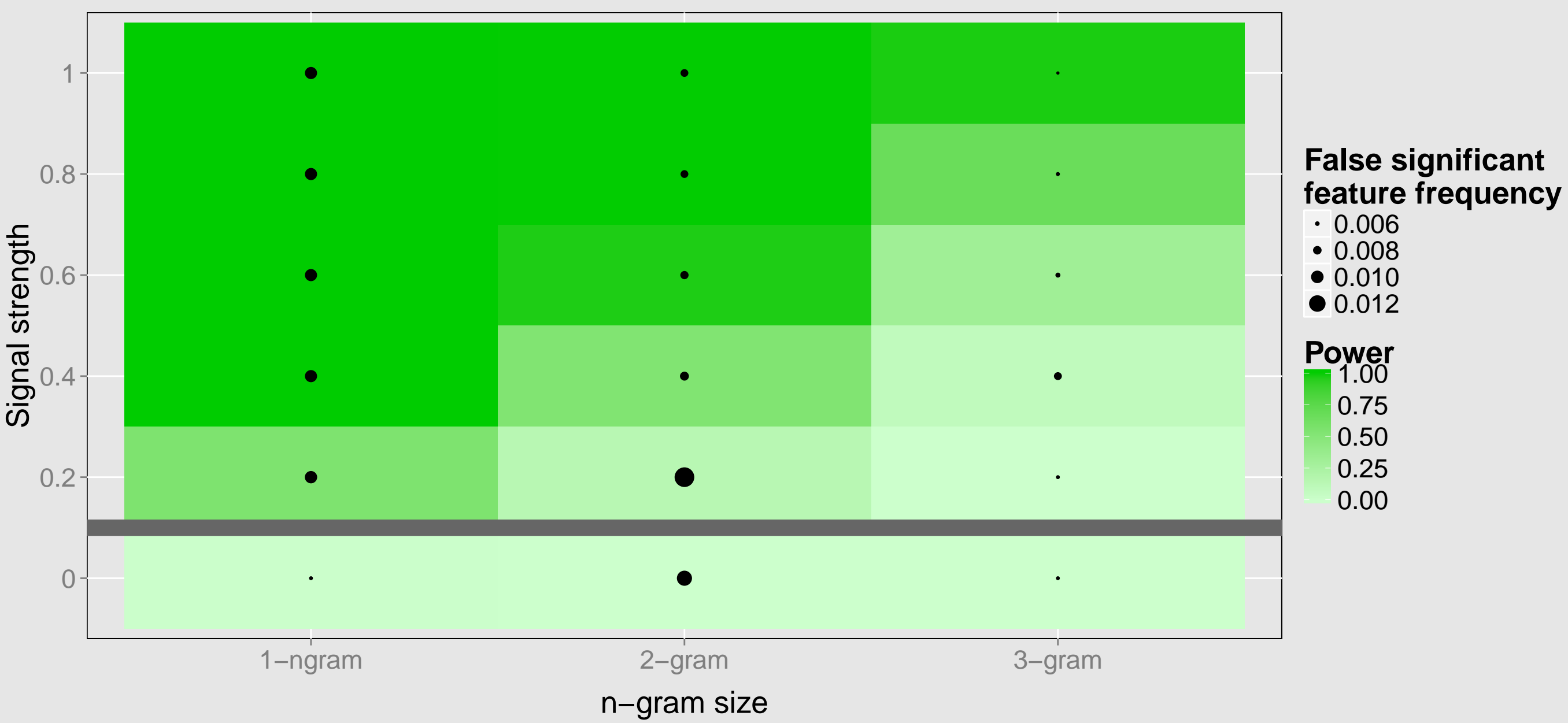


	Target	Feature	Freq
1	0	0	40
2	1	0	10
3	0	1	25
4	1	1	40

Simulation scheme

1. Random 4000 sequences (20 nucleotides each). The half of the sequences has label 0.
2. Choose a single position between 3 and 18 (to avoid border cases).
3. Resample nucleotides at chosen position. The dominant nucleotide has probability of occurence $p_d = 0.25$. Other nucleotides have probability of occurence $p_o = (1 - p_d)/3$.
4. Perform QuiPT (Information Gain) and choose significant features (with p-value < 0.001).
5. Iterate steps 1-4 over other values of p_d - 0.38, 0.51, 0.65, 0.78, 0.91.
6. Repeat steps 1-5 200 times.

Power and False discoveries



Summary

Quick permutation test is a powerful and quick equivalent of permutation test in binary feature-binary target testing scenario.

Avaiability

biogram R package:
<http://cran.r-project.org/web/packages/biogram/>

Bibliography

Fang, Y.-C., Lai, P.-T., Dai, H.-J., and Hsu, W.-L. (2011). Meinfoxtext 2.0: gene methylation and cancer relation extraction from biomedical literature. *BMC Bioinformatics*, 12(1):471.
Guo, S.-H., Deng, E.-Z., Xu, L.-Q., Ding, H., Lin, H., Chen, W., and Chou, K.-C. (2014). inuc-psekcnc: a sequence-based predictor for predicting nucleosome positioning in genomes with pseudo k-tuple nucleotide composition. *Bioinformatics*, 30(11):1522–1529.
Wang, Y., Liu, L., Chen, L., Chen, T., and Sun, F. (2014). Comparison of metatranscriptomic samples based on *italic*₂k-i/*italic*₂tuple frequencies. *PLoS ONE*, 9(1):e84348.