

# Quick Permutation Test: feature filtering of n-gram data

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## 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 proteomics, genomics (Fang et al., 2011) and transcriptomics.

	P1	P2	P3	P4	P5	P6
S1	3	1	1	2	3	2
S2	3	3	4	4	4	2
S3	3	4	4	4	3	3

Sample sequences.

	1	2	3	4
2	2	2	2	0
0	1	2	3	
0	0	3	3	

Unigram counts.

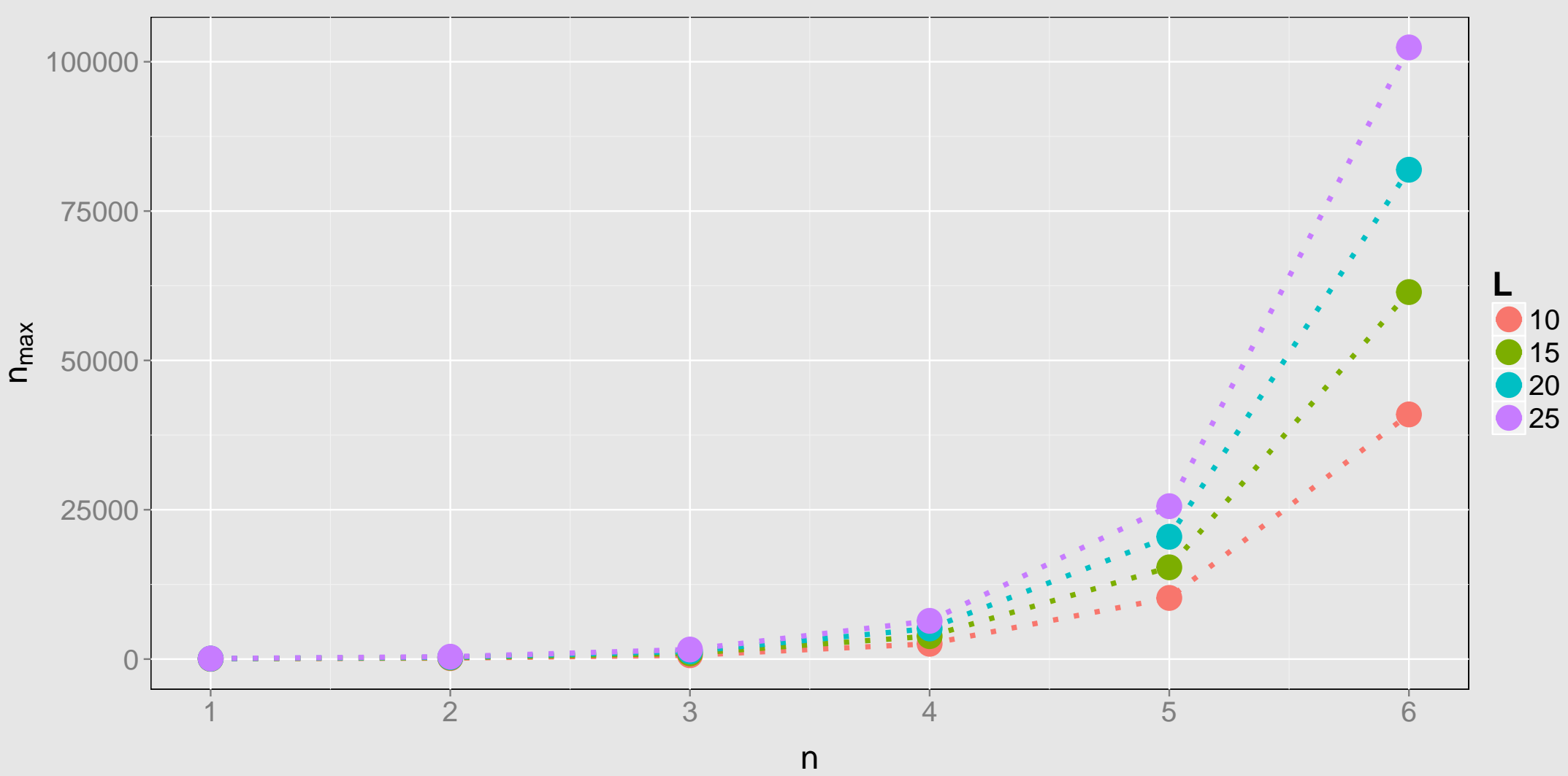
P1.1	P2.1	P3.1	P4.1	P5.1	P6.1	P1.2	P2.2	P3.2	P4.2	P5.2	P6.2	P1.3
0	1	1	0	0	0	0	0	0	1	0	1	1
0	0	0	0	0	0	0	0	0	0	0	1	1
0	0	0	0	0	0	0	0	0	0	0	0	1

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.

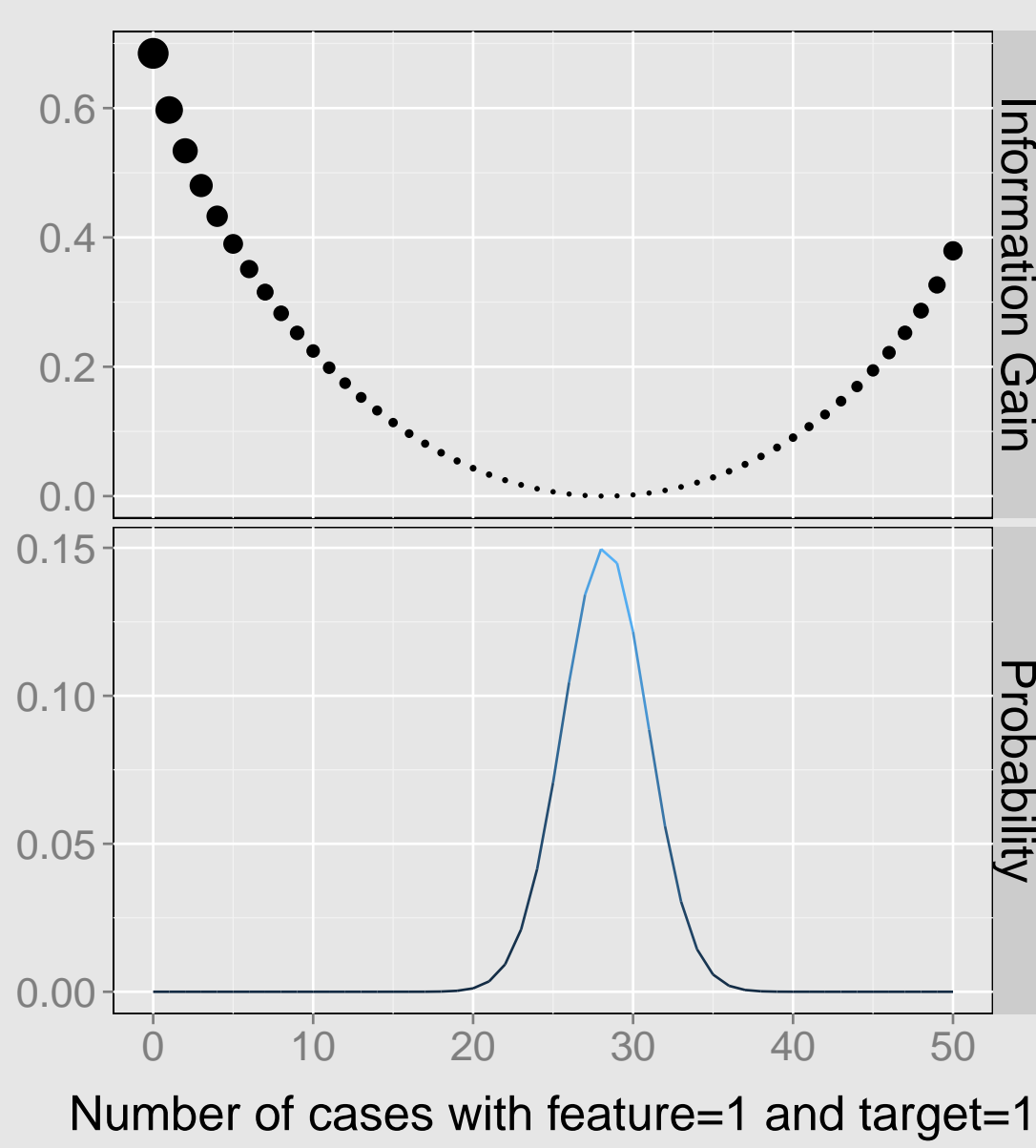
## Independence test

$F(n_{1,1}, n_{1,0}, n_{0,1}, n_{0,0}) = \binom{n}{n_{1,1}} (p \cdot q)^{n_{1,1}} \binom{n-n_{1,1}}{n_{1,0}} (p \cdot (1-q))^{n_{1,0}} \binom{n-n_{1,1}-n_{1,0}}{n_{0,1}} ((1-p) \cdot q)^{n_{0,1}} \binom{n-n_{1,1}-n_{1,0}-n_{0,1}}{n_{0,0}} ((1-p) \cdot (1-q))^{n_{0,0}}$   
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  $0.05 \times 10^{-5}$ . 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.

## Validation procedure

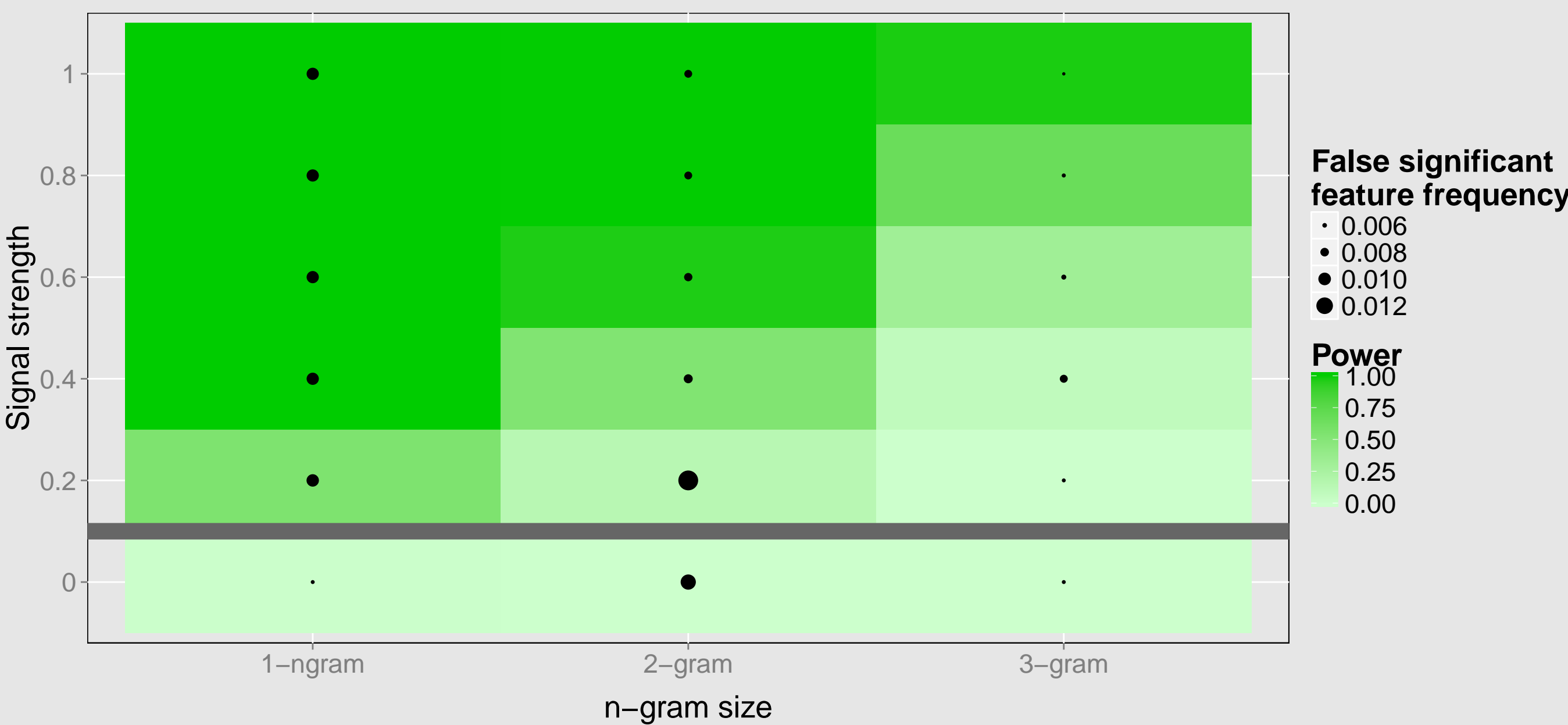


	Target	Feature	Freq
1	0	0	40
2	1	0	10
3	0	1	25
4	1	1	40

## 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 occurrence  $p_d = 0.25$ . Other nucleotides have probability of occurrence  $p_o = (1 - p_d)/3$ .
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.

## Availability

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). Meinfox 2.0: gene methylation and cancer relation extraction from biomedical literature. *BMC Bioinformatics*, 12(1):471.