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. 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
S1	3	4	2	2	1	1
S2	2	2	2	1	4	1
S3	3	1	4	2	4	3

Sample sequences.

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

Unigram counts.

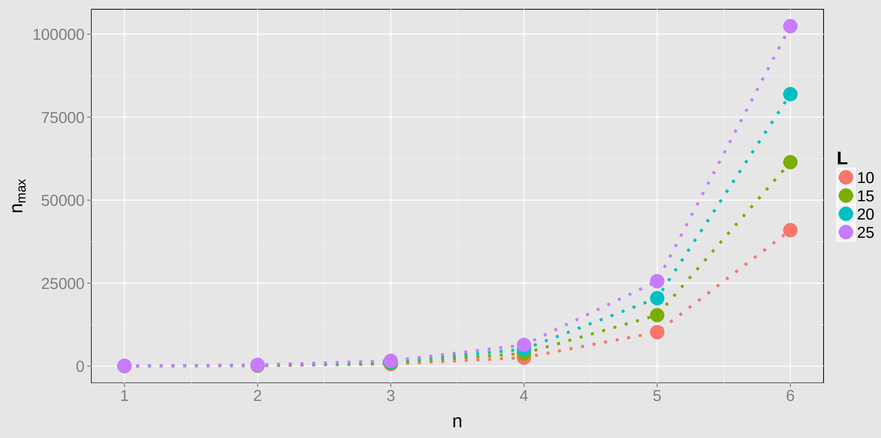
P1_1	P2_1	P3_1	P4_1	P5_1	P6_1	P1_2	P2_2	P3_2	P4_2	P5_2	P6_2	P1_3
0	0	0	0	1	1	0	0	1	1	0	0	1
0	0	0	1	0	1	1	1	1	0	0	0	0
0	1	0	0	0	0	0	0	0	1	0	0	1

A fraction of possible unigrams with position information.

Curse of dimensionality

Even when we limit ourselves to only continuous positioned n-grams, build on $\boldsymbol{m}$ possible characters, feature space growths rapidly with the number of elements in n-gram ($\boldsymbol{n}$) and length of the sequence ($\boldsymbol{L}$).
Number of possible positioned n-grams:

$$\boldsymbol{n}_{\text{max}} = \boldsymbol{L} \times \boldsymbol{m}^{\boldsymbol{n}}$$



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 $\boldsymbol{N_{T_P > T_R}}$ is number of times when $\boldsymbol{T_P}$ (permuted test statistic) was more extreme than $\boldsymbol{T_R}$ (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

In each permutation, for every observation, there are four possible results.

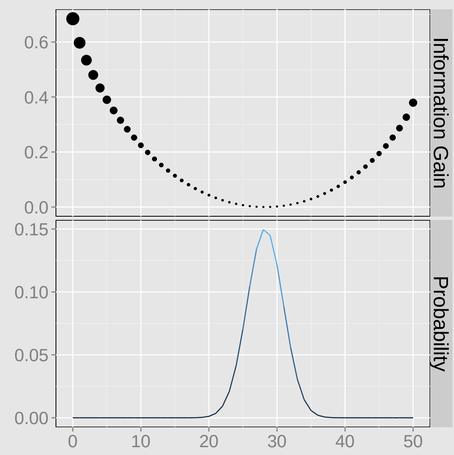
$$\boldsymbol{P(Target, Feature) = (1,1)) = p \cdot q}$$
$$\boldsymbol{P(Target, Feature) = (1,0)) = p \cdot (1-q)}$$
$$\boldsymbol{P(Target, Feature) = (0,1)) = (1-p) \cdot q}$$
$$\boldsymbol{P(Target, Feature) = (0,0)) = (1-p) \cdot (1-q)}$$

Where $\boldsymbol{p}$ and $\boldsymbol{q}$ are fractions of positive observations in target and feature respectively. Another view at permutation test is therefore that we get a contingency table, which is to be tested for independance. Computing probability of such a table with two constraints, $\boldsymbol{n_{1,\cdot} = n_{1,1} + n_{1,0}}$ and $\boldsymbol{n_{\cdot,1} = n_{1,1} + n_{0,1}}$, and conditioning on $\boldsymbol{n_{1,1}}$, leads to hypergeometric distribution. $\boldsymbol{n_{i,j}}$ denotes number of observations for which $\boldsymbol{(Target, Feature) = (i,j)}$
This is in fact exact two-sided Fisher's test (Lehmann, 1986). Information Gain is a way of deciding how strong is the evidence against independance.

Computational cost

The cost of performing QuiPT is equal to computing Information Gain and probability of occurence for $\boldsymbol{n_{1,1} + n_{0,1}}$ 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 $\boldsymbol{0.05 \times 10^{-5}}$. 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.
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 $\boldsymbol{10^5}$ permutations.

Contingency table representation

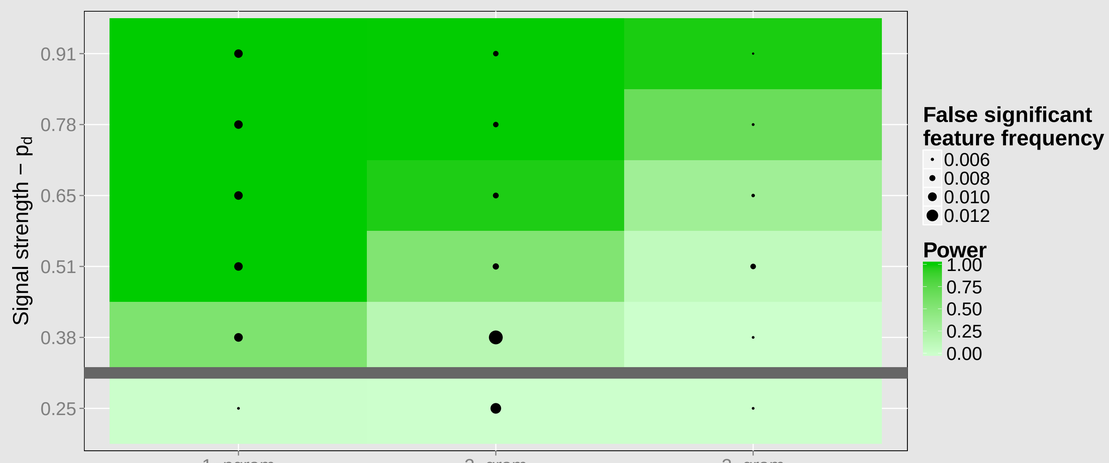


	Target	Feature	Freq
1	0	0	40
2	1	0	10
3	0	1	25
4	1	1	40

Simulation scheme - genomics

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 nucletoide has probabilitiy of occurence $\boldsymbol{p_d = 0.25}$. Other nucleotides have probability of occurence $\boldsymbol{p_o = (1 - p_d)/3}$.
4. Perform QuiPT (Information Gain) and choose significant features (with p-value $\boldsymbol{< 0.001}$).
5. Iterate steps 1-4 over other values of $\boldsymbol{p_d}$ - 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.

Avaibility

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

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