Permutation goodness of fit test for Poisson distribution

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Abstract

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1. Introduction

The amplification chemistry of absolute quantification in the Digital PCR (dPCR) is orchestrated by well established methods such as PCR or isothermal amplification [1, 2]. But dPCR relies on binary state of positive and negative partitions from a sample. Data fitting to a Poisson distribution is an essential step during analysis. The countable positive independent integer values make the dPCR analysis interesting and the Poisson distribution the obvious choice.

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The target molecule numbers initially in a sample can be determined from the numbers of positive and negative partitions by probability analysis.

There exist other **R** packages for analyse and fit distributions [3].

2. Methods

All functions were implemented in the **R** statistical computing environment as described previously [4]. The permutation goodness of fit test for Poisson distribution (further called PGoF) is based on Chi Square test. The $\hat{\lambda}$ is calculated from counts of positive and negative partitions using following relationship:

$$\hat{\lambda} = -\ln\left(1 - \frac{k}{n}\right) \tag{1}$$

According to the MIQE Guidelines for Digital PCR [5], k is number of positive partitions and n is a total number of partitions. To perform the permutation test, we firstly compute $\hat{\lambda}_R$ for data vector. Next, from the density of Poisson distribution we estimate the chance of having negative partition (no template molecules) or positive partition (more than zero template molecules). Obtained probabilities are used to perform a Chi Square test and the test statistic χ_R is preserved.

Further, we use the $\hat{\lambda}_R$ to generate a large number of n-long sample from Poisson distribution. Each sample is binarized to positive and negative partitions and we perform the exactly the same procedure as for the real sample: we $\hat{\lambda}_P$, estimate probabilities of negative and positive partitions and finally perform the Chi Square test to obtain test statistic χ_P. The p-value of permutation test is defined as:

$$\text{p-value} = \frac{N_{\chi_P > \chi_R}}{N} \tag{2}$$

where $N_{\chi_P > \chi_R}$ is number of times when χ_P was more extreme than χ_R.

In case of very low $\hat{\lambda}_R$, sometimes the $\hat{\lambda}_P$ may be exactly zero. In this case the Chi square test has 0 degrees of freedom.

References

[1] S. Pabinger, S. Rödiger, A. Kriegner, K. Vierlinger, A. Weinhäusel, A survey of tools for the analysis of quantitative PCR (qPCR) data, Biomolecular Detection and Quantification 1 (1) (2014) 23–33. `doi:10.1016/j.bdq.2014.08.002`.
URL `http://www.sciencedirect.com/science/article/pii/S2214753514000059`

[2] A. A. Morley, Digital PCR: A brief history, Biomolecular Detection and Quantification 1 (1) (2014) 1–2. `doi:10.1016/j.bdq.2014.06.001`.
URL `http://www.sciencedirect.com/science/article/pii/S2214753514000023`

[3] M. L. Delignette-Muller, C. Dutang, fitdistrplus: An R package for fitting distributions, Journal of Statistical Software 64 (4) (2015) 1–34.
URL `http://www.jstatsoft.org/v64/i04/`

[4] S. Rödiger, M. Burdukiewicz, K. A. Blagodatskikh, P. Schierack, R as an Environment for the Reproducible Analysis of DNA Amplification Experiments, The R Journal 7 (2) (2015) 127–150.
URL `http://journal.r-project.org/archive/2015-1/RJ-2015-1.pdf`

[5] J. F. Huggett, C. A. Foy, V. Benes, K. Emslie, J. A. Garson, R. Haynes, J. Hellemans, M. Kubista, R. D. Mueller, T. Nolan, M. W. Pfaffl, G. L. Shipley, J. Vandesompele, C. T. Wittwer, S. A. Bustin, The digital MIQE guidelines: Minimum information for publication of quantitative digital PCR experiments, Clinical Chemistry 59 (6) (2013) 892–902. `doi:10.1373/clinchem.2013.206375`.