# Methods of Comparing Digital PCR Experiments

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## Introduction

The outcome of digital PCR (dPCR) experiments are mean copies per partition ($\boldsymbol{\lambda}$). Results are derived from the measured data, an ordered (in one or two dimensions) sequence of positive partitions. The usual analysis involves assumption the template molecules are Poisson distributed among partitions. On this premise, already proposed approaches, based on the confidence intervals (Dube et al., 2008) or uncertainty quantification (Bhat et al., 2009), allow a comparison of experiments.

## Multiple testing scheme

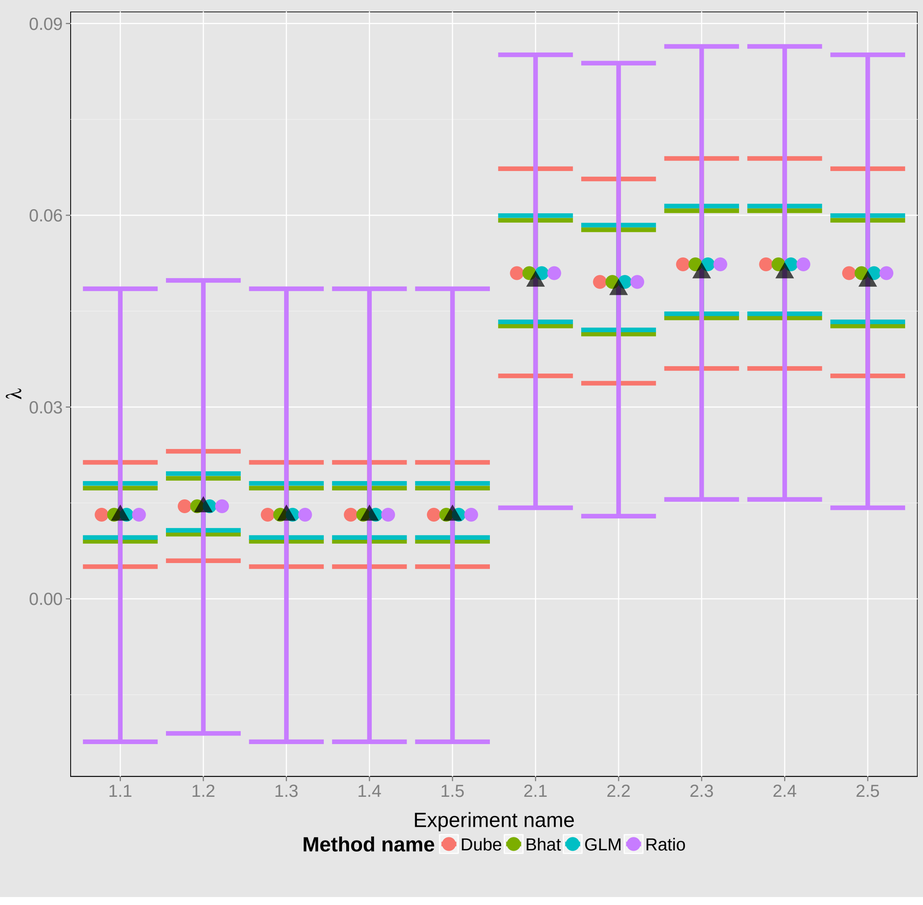
The dPCR experimentes are compared pairwise using the uniformly most powerful (UMP) ratio test (Fay, 2010). Furthermore, computed p-values are adjusted using Benjamini  Hochberg correction (Benjamini and Hochberg, 1995) to control family-wise error rate.

The UMP ratio test has following null-hypothesis:

$$\boldsymbol{H_0} : \frac{\boldsymbol{\lambda_1}}{\boldsymbol{\lambda_2}} = 1 \tag{1}$$

The Wilson's confidence intervals (Brown et al., 2001) are calculated independently for every dPCR experiment. The Dunn - Šidák correction ensures control of the family-wise error rate.

## Possible models




## Evaluation

stuff stuff stuff

## Summary

## Avaibility

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

## Bibliography

Benjamini, Y. and Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, 57(1):289–300.

Bhat, S., Herrmann, J., Armishaw, P., Corbisier, P., and Emslie, K. R. (2009). Single molecule detection in nanofluidic digital array enables accurate measurement of DNA copy number. *Analytical and bioanalytical chemistry*, 394(2):457–467.

Brown, L. D., Cai, T. T., and DasGupta, A. (2001). Interval estimation for a binomial proportion. *Statist. Sci.*, 16(2):101–133.

Dube, S., Qin, J., and Ramakrishnan, R. (2008). Mathematical analysis of copy number variation in a DNA sample using digital PCR on a nanofluidic device. *PloS one*, 3(8):e2876.

Fay, M. (2010). Two-sided exact tests and matching confidence intervals for discrete data. *Proceedings of the National Academy of Sciences of the United States of America*, 2(1):53–58.