Estimating the prevalence of 'file drawer' studies in coordinate-based meta-analysis

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Introduction

The 'file drawer' problem is one type of bias in meta-analysis [Easterbrook, 1993]. It refers to research studies that are initiated but are not published due to lack of significance, either by cause of authors' hesitation to submit or perhaps because of rejection by journals that are reluctant to publish negative results [Ioannidis, 2005]. In the field of fMRI, David et al [2013] found evidence of such publication biases, but to date there has been no work on estimating the fundamental 'file drawer' quantity, the number of missing studies.

In this work, we propose a method for estimating the number of non-significant studies omitted from a large cohort of studies, making use of the coordinate data in the BrainMap database [Laird et al, 2005].

Motivating dataset: BrainMap database

BrainMap

- Extensive database consisting of coordinate data obtained from 2562 scientific papers.
- Several experiments (questions) per study.
- Invaluable resource meta-analyses.

A first look at the data

- We consider the 12292 experiments (i.e. contrasts) as the units of observation
- Bar plot shows the empirical distribution of the total number of foci per experiment (Fig. 1; zoom-in show in Fig. 2).
- No zero-foci results.

Objectives

- Estimate the number of unobserved zero-foci studies .
- Use intrinsic statistical characteristics of (non-zero) count data to infer zero counts.
- Account for covariates (e.g. publication year, sample size).

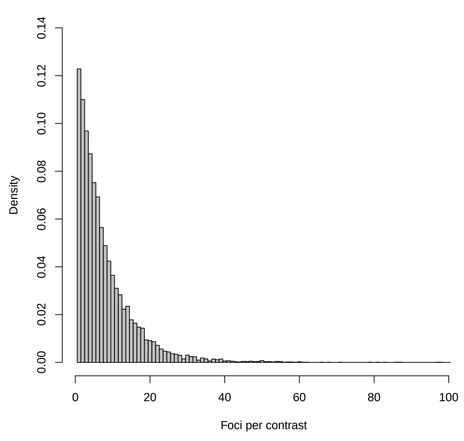


Fig. 1

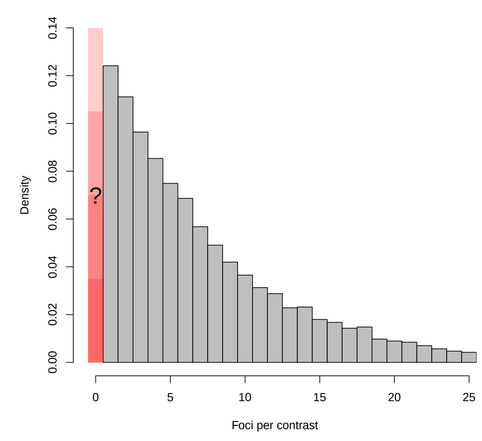


Fig. 2

Methods

Zero-Truncated Modelling

- A zero-truncated count distribution occurs when we restrict the domain of a count distribution $\pi(n \mid \boldsymbol{\theta})$ to the positive integers:

$$\pi_{ZT}(n \mid \boldsymbol{\theta}) = \mathbb{P}(Y = n) = \frac{\pi(n \mid \boldsymbol{\theta})}{1 - \pi(0 \mid \boldsymbol{\theta})}, \quad n = 1, 2, \ldots$$

- Once $\boldsymbol{\theta}$ is estimated, the prevalence of zero-count studies, p_z, can be estimated as:

$$p_z = \frac{\mathbb{P}(Y = 0)}{1 - \mathbb{P}(Y = 0)} \times 100$$

  Interpretation: *the total number of missing experiments per 100 published.*

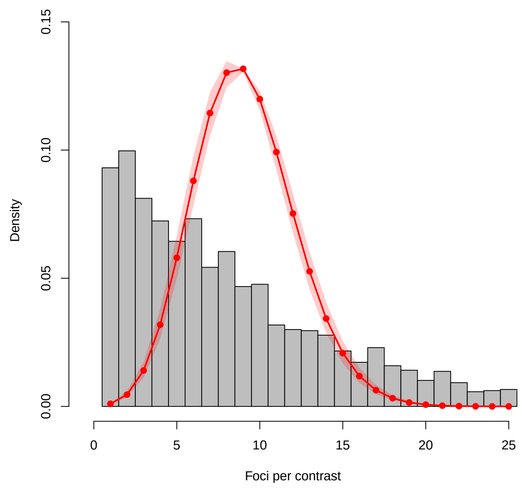
- For the purposes of this work we will assume that $\pi(\cdot)$ is the **Poisson** or **Negative Binomial** probability mass function.
- Study characteristics can be considered as covariates in a Generalised Linear Model:

$$\mathbb{E}[Y_i \mid X] = \exp\left(X^T\beta + \epsilon_i\right),$$

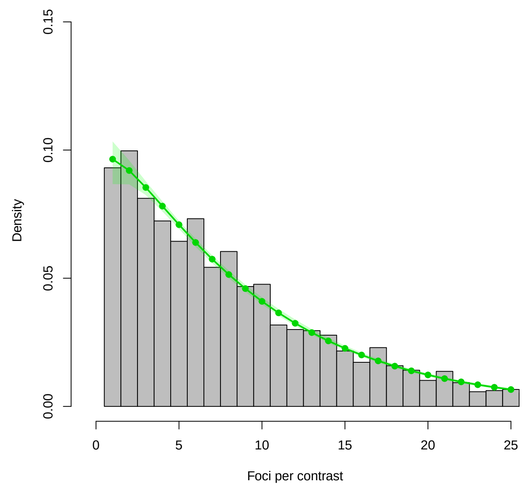
- Covariates used, from BrainMap:
  - ➢ Total number of participants: 1-395 with median 12
  - ➢ Year: 1985-2014 with median 2004
  - ➢ Context: Disease effects, Drug effects, Linguistic effects, Normal Mapping and Other (any other that appears less than 30 times)
  - ➢ Paradigm: 27 levels, e.g. Reward, Face Monitor/Discrimination, Semantic Monitor/Discrimination, n-back.
- To avoid issues with correlated data we randomly choose one contrast from each study.
- Model comparison with the AIC.
- Confidence intervals with the Bootstrap.

Results

- With no covariates, the fit is easily visualised, and the Poisson is seen to be a poor fit, while the Negative Binomial fits well.

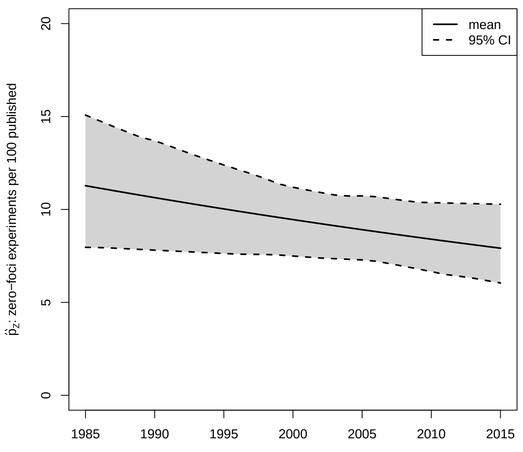


Poisson

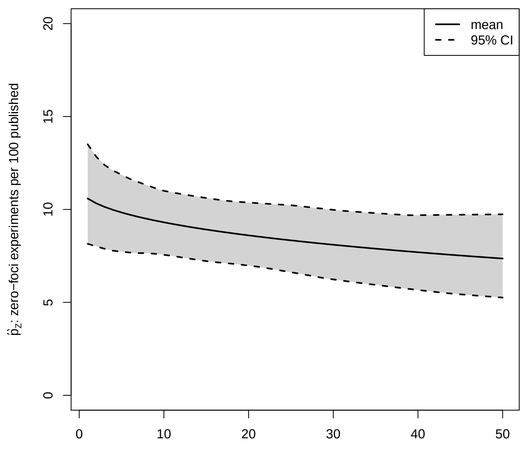


Negative binomial

- Based on AIC, the Negative Binomial GLM fits the data best (**AIC=14164.46**) as compared to the simple Negative Binomial (**AIC=14175.8**), the Poisson GLM (**AIC=21911.07**) and the simple Poisson (**AIC=22379.28**).
- We fit the GLM assuming a Negative Binomial. The model predicts that for the mean sample size and the mean year the prevalence of zero-foci experiments is $\hat{\mathbf{p}}_Z = \mathbf{9.02}$ **(CI** $[\mathbf{7.32}, \mathbf{10.72}]$**)**, averaged across all levels of the factors.
- Each value or level of a covariate implies a different distribution and p_Z. Here we show Bootstrap means and confidence intervals for p_Z as a function of publication year and sample size. Increasing year and study size are associated with reduced missing studies:

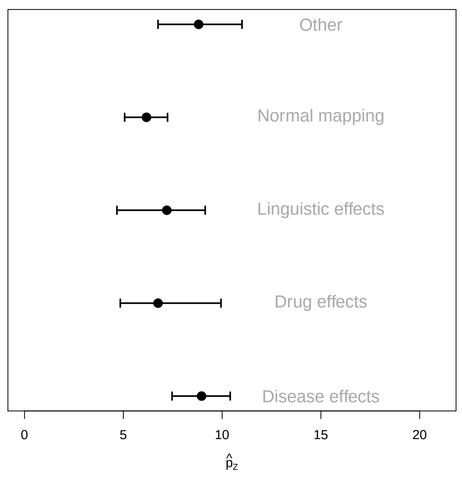


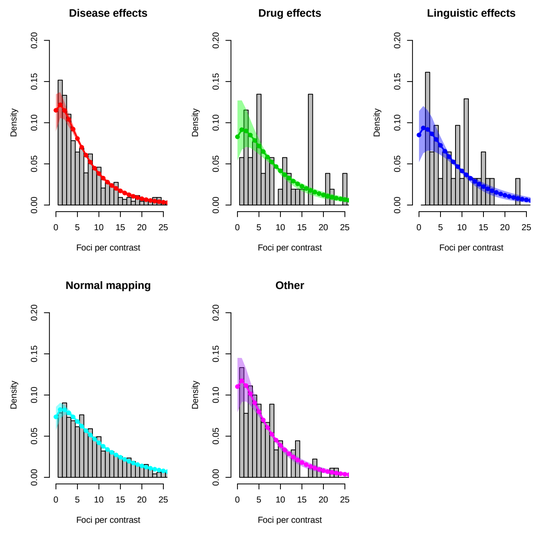
Publication Year



Participants

- For each level of a factor we have fitted values that can be used to generate $\hat{p}_Z$ (below left, mean + Bootstrap CI). Likewise, a given factor level has a predicted distribution (below right). The fewer fewer foci reported, the more likely zero foci are.





Discussion

Conclusion

- Negative Binomial distribution provides a better fit than the Poisson distribution
- Magnitude of zero-foci results varies, but is generally around 10 per 100 experiments. Some of these could be attributed to negative contrasts reported in published papers, but some are surely are never published.
- Covariates are significant (due to large database) but each only have small effect.

Future work

- Include some published studies may indeed report negative results, not registered in BrainMap.
- Bayesian methodologies can allow to account for correlation between the experiments of a given study and maybe some complex censoring mechanisms (e.g. zero-count experiments that are being upgraded).

References

[1] David et al 2013, *PLoS ONE* 8(7): e70104. [2] Easterbrook (1991), *The Lancet* 337: 867-872. [3] Ioannidis (2005), *PLoS Medicine* 2(8): e124. [4] Laird et al (2005), *Neuroinformatics* 3: 65-78. [5] Rigby et al (2005), *Applied Statistics* 54: 507-554.