

## Cluster extent inference revisited: quantification and localization of brain activity

Jelle Goeman<sup>1</sup>, Wouter Weeda<sup>2</sup>, Ramin Monajemi<sup>1</sup> Xu Chen<sup>1,2</sup> Paweł Górecki<sup>3</sup>

<sup>1</sup>Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands

<sup>2</sup>Methodology and Statistics, Leiden University, Leiden, The Netherlands

<sup>3</sup>Mathematics, Informatics and Mechanics, University of Warsaw, Warsaw, Poland

E-mail for correspondence: [j.j.goeman@lumc.nl](mailto:j.j.goeman@lumc.nl)

**Abstract:** Cluster inference based on spatial extent thresholding is the most popular analysis method for finding activated brain areas in neuroimaging. However, the method has several well-known issues. While powerful for finding brain regions with some activation, the method as currently defined does not allow any further quantification or localization of signal. In this paper we repair this gap. We show that cluster-extent inference can be used (1.) to infer the presence of signal in anatomical regions of interest and (2.) to quantify the percentage of active voxels in any cluster or region of interest. These additional inferences come for free, i.e. they do not require any further adjustment of the alpha-level of tests, while retaining full familywise error control. We achieve this extension of the possibilities of cluster inference by an embedding of the method into a closed testing procedure, and solving the graph-theoretic  $k$ -separator problem that results from this embedding. The new method can be used in combination with random field theory or permutations. We demonstrate the usefulness of the method in a large-scale application to neuroimaging data from the Neurovault database.

**Key words:** fMRI; Spatial specificity paradox; Closed testing; Familywise error rate