Revisiting Multi-Subject Random Effects in fMRI

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Introduction Random Effects analysis has been introduced into fRMI research in order to generalize findings from the study group to the whole population (see Friston et al.2002). Generalizing findings is obviously harder then detecting activation in the study group since in order to be significant, an activation has to be larger then the inter-subject variability which is assessed and controlled for within the study group. Indeed, detected regions are smaller when using random effect analysis versus fixed effects. The statistical assumptions behind the classic random effects model are that the effect is normally distributed over and "activation" refers to a non-null mean effect. We argue this model is unrealistic and conservative compared to the true population variability.

Method Inspired by the Two-Populations model widely used in genetics (Efron2008) and in fMRI (Hartvig and Jensen20 we develop a model for the inter-subject voxel-wise effect as a mixture of two populations: One in which the voxel was activated by the paradigm with a normally distributed effect and a second, in which the voxel is inactive, thus- a null effect. We suggest two justifications for this model: (a) Ill registration might map active and non-active voxel to the same locations. (b) Brain plasticity permits the same anatomical location to serve different functions.

The implementation of the method was done in *R* and included: (a) ML estimation of the parameters of the proposed finite mixture using an EM algorithm over a non-convex constrained parameter space (to solve identifiability issues). (b) Bootstrapping of the estimates' distribution for inference on the number of mixed populations, known to be an analytically unsolved problem (Garel2007) . (c) Optional parallelization of the Bootstrapping using *Condor* and/or the **snow** package.

Results We demonstrate our method on real fMRI dataset of 67 subjects at 60,000 brain locations. We construct estimate maps and p-value maps of the voxel-wise proportion of population responding to an experimental paradigm. Once these have been constructed, we define "activation" as locations where more then a given percentage of the population has been found active. We revisit the activation maps created under the classical definition of activation and compare them to activation found under this new definition to show the power gained using the finite Gaussian mixture.

References

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