Using Bayesian priors to improve power of whole brain voxel- and connexelwise inferences

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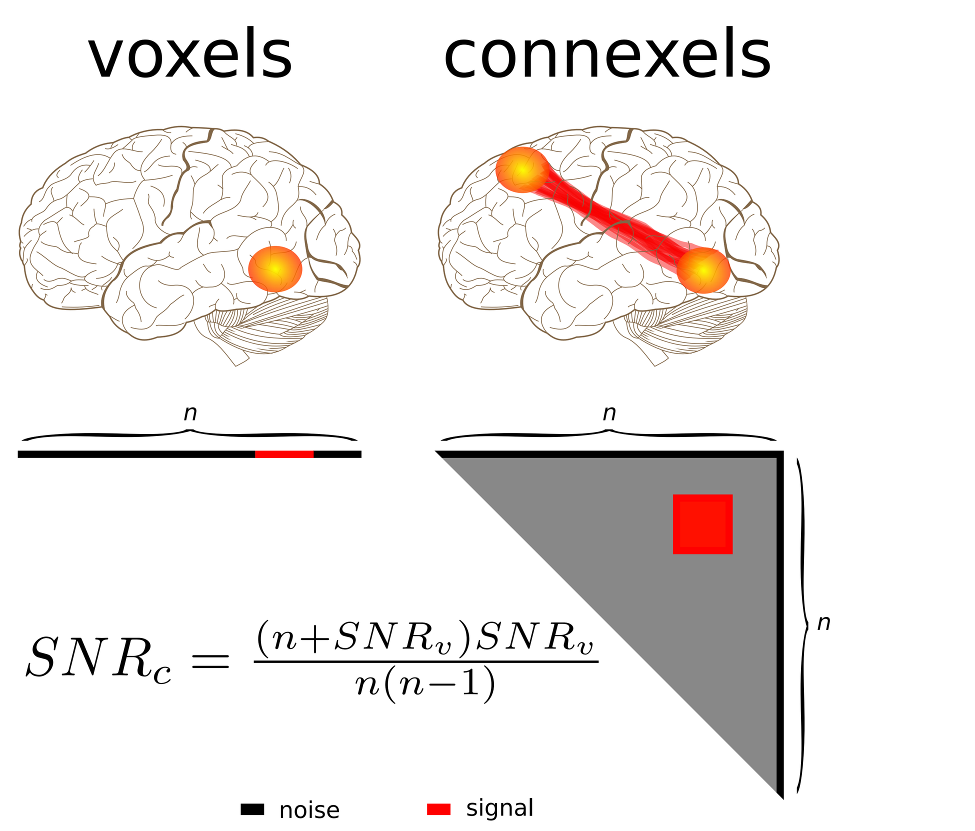
Introduction

- Most neuroimaging studies are underpowered or in other words have small Signal to Noise Ratio (SNR). This is especially true for full brain connexelwise [1] analysis (see Fig. 1).
- A common way of increasing SNR is to restrict the search area with a Region of Interest (ROI).
- ROI definitions have traditionally been binary - discarding uncertainty; potentially missing strong activations outside of the ROI.
- Here we propose a probabilistic approach to ROI analysis - pROI.

1



Left: Symbolic representation of flattened voxels (non-active (black) and active (red)). Right: Connectivity matrix where each point corresponds to one connexel. Below: The relation between SNR in the voxelwise (SNR_v) and connexelwise (SNR_c) cases, where n stands for the number of voxels.

Methods

We propose to formally incorporate prior knowledge into the inference process by using a Bayesian framework. The prior informs the search area, which in turn is subdividedinto noise and signal. Our hierarchical model consists of two levels. On the first level we model two classes corresponding to voxels-/connexels-of-interest or -of-non-interest:

$$p(x|i) = p(m_1|i)p(x|m_1, i) + p(m_2|i)p(x|m_2, i)$$

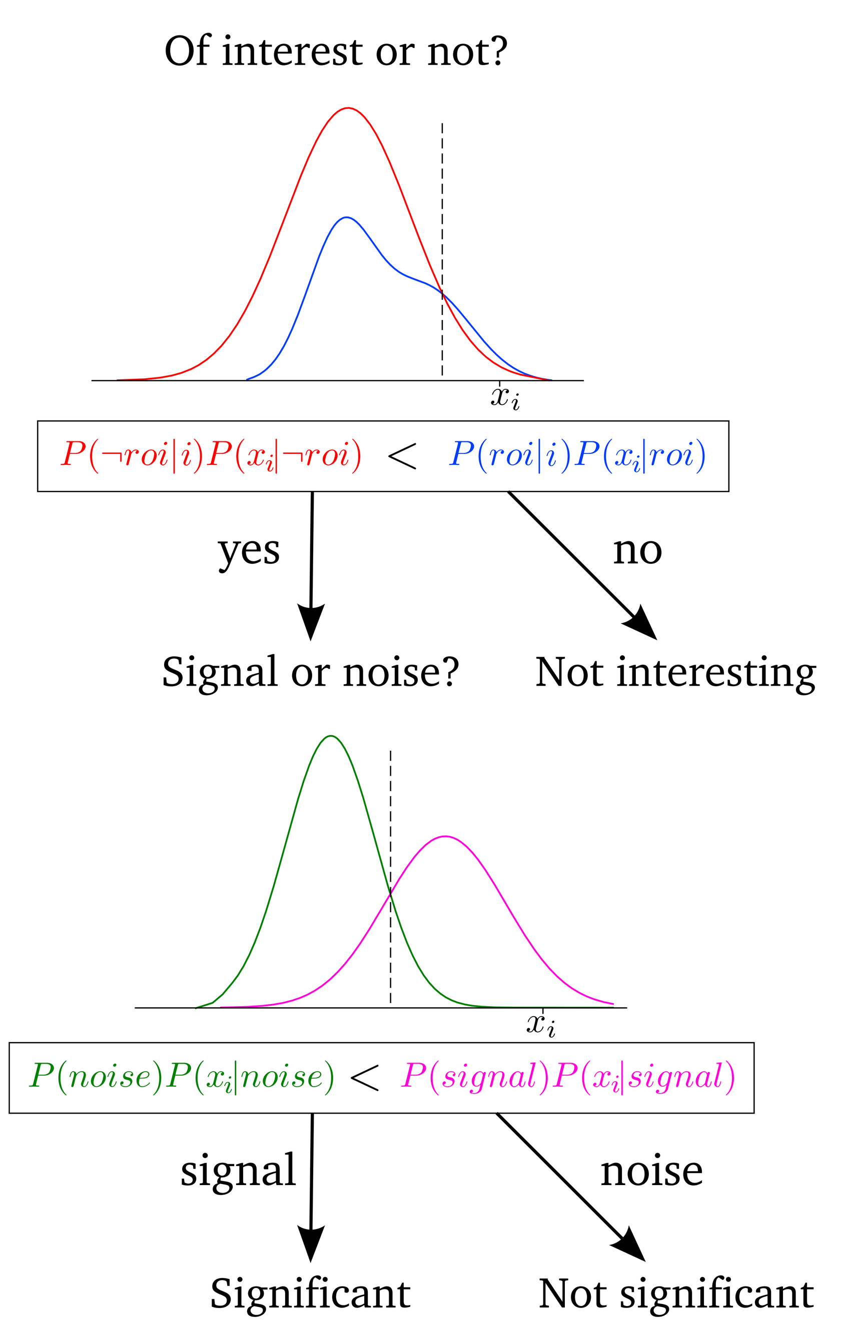
Where $p(m_1|i)$ are the priors on the search areas (or mixing components of the first level). They are different for each location (i), fixed, and set to values based on particular inference assumptions (previous studies, characteristics of different modalities, etc...). On the second level, the voxels-/connexels-of-interest distribution ($p(x|m_1,i)$) is described as a mixture of negative gamma (deactivation), Gaussian (noise), and positive gamma (activation) distributions. The location of the two gamma distribution is tied to the estimated mean of the noise component. This level is identical to the model presented in [2].

Parameters of those three distributions (and mixing coefficients) are fitted using a weighted variant of the Expectations-Maximization algorithm [3]: the entire dataset is used but influence of each voxel/connexel on the final mixture is modulated by the $p(m_1|i)$ weight in the E-step:

$$\gamma_{ik} = \frac{p(m_1|i)\pi_k \mathcal{N}(x_i|\mu_k,\sigma_k)}{\sum_{j=1}^{K}\pi_j \mathcal{N}(x_i|\mu_j,\sigma_j)}$$

The actual inference procedure takes two steps (see Fig. 2). First for each voxel/connexel we decide if is ofinterest or non-interest, by comparing the two posterior distributions. For voxels/connexels coming from the of-interest distribution, a similar procedure is used to choose between signal and noise.

2

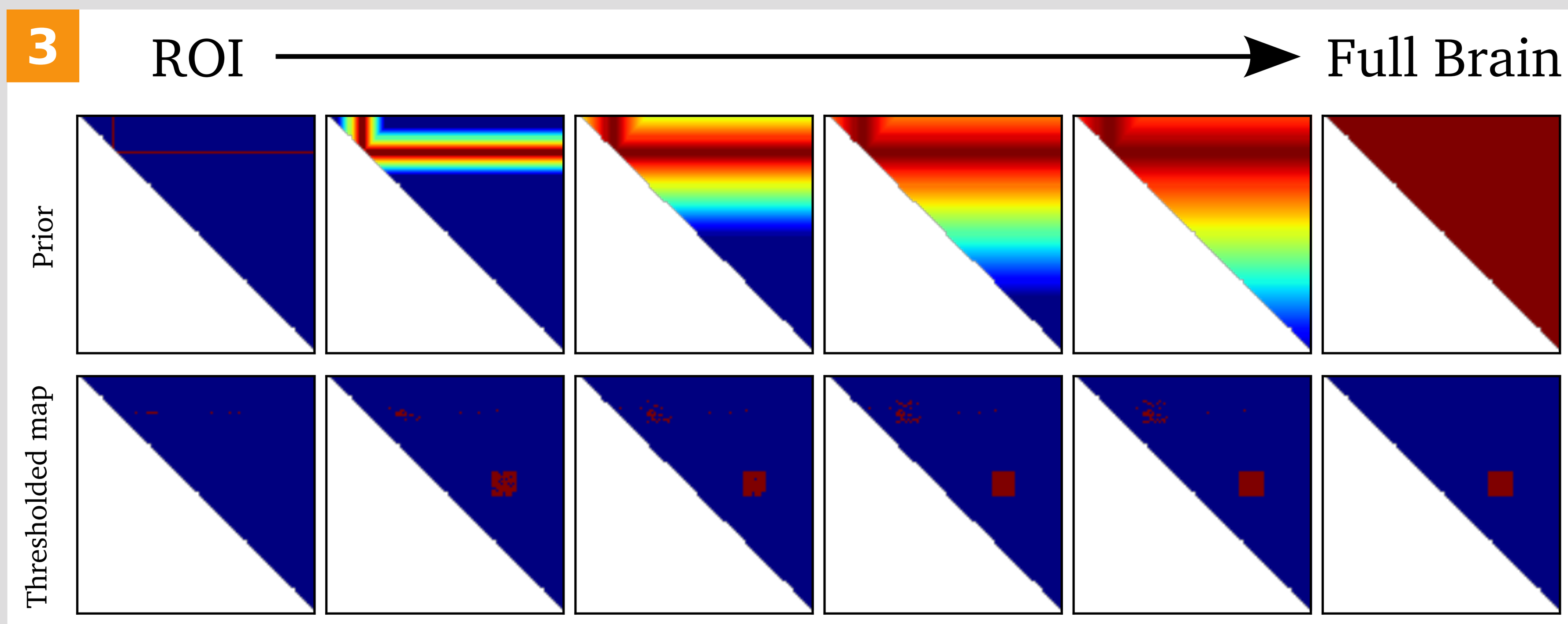


Decision tree within the hierarchical framework. First the fitted distributions are used to classify each voxel/connexel between two categories: "of-interest" or "of-non-interest". In the second step, voxels-/connexels-of-interest are classified as "signal" or "noise".

Results

To evaluate the method we have performed a series of simulations using different prior maps. On a two dimensional 100x100 array two 10x10 sources of signal were placed (see Fig. 3): one weak (effect size 3) and one strong (effect size 9). The "classical ROI" prior fails to find the second signal source, but even the most specific of the non-binary priors (with value 0.005 over the strong signal) does a reasonable job in finding both signals.

3



Simulation results. Two sources of were used signal: one weak and one strong (left) and set of prior maps (top row right): one representing classical (binary) ROI approach (with the ROI encompassing the weak signal), one representing whole-brain analysis, and four non-binary priors. The "classical ROI" prior misses the strong signal, while the "whole-brain" prior barely finds the weak signal. Only an 'in between' pROI which focuses on the right location, but gives small (but non-zero) chance of finding signal outside of this spot, manages to strike a balance delineating both sources of signal.

We apply the pROI method to thresholding an fMRI dataset acquired during performance of an emotional task. Subjects were exposed to negative and neutral visual imagery with varying uncertainty of the nature of the next stimulus. The prior was generated using the NeuroSynth database (based on the term "emotion" [4]). In comparison to whole-brain analysis, the thresholded map obtained using the pROI delineated activation in the amygdala in voxels that were significant, taking into account their high probability of involvment (Fig 4)

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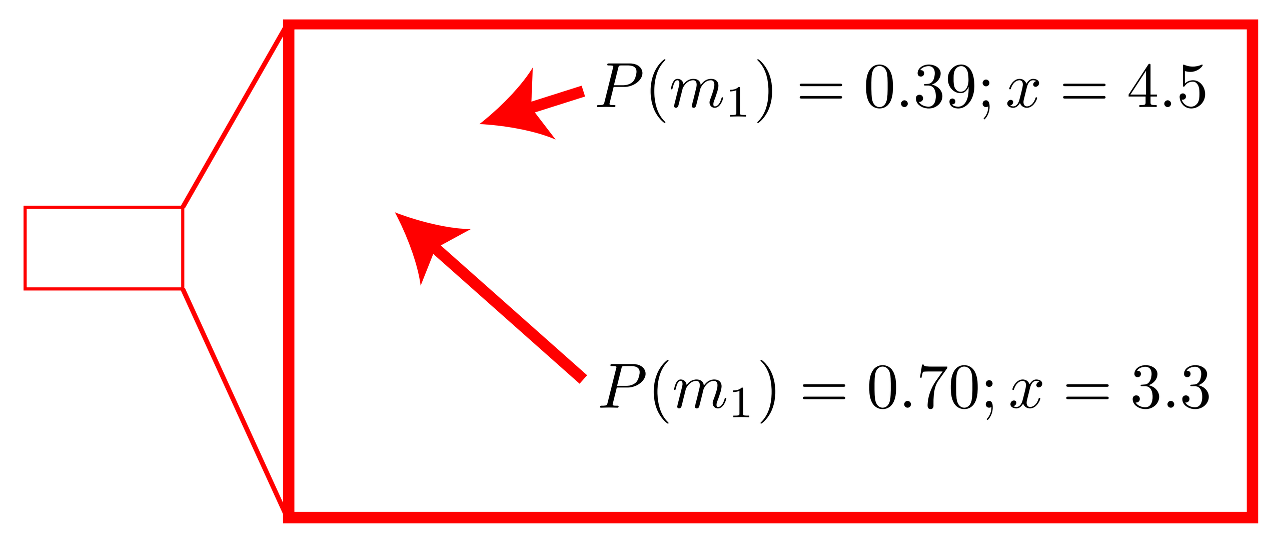

Experiment with emotion task based fMRI. Statistical map was thresholded using full brain non-informative binary prior (transparent blue) and prior based on the "emotion" term in the NeuroSynth database (light green). The NeuroSynth based prior presented cleaner maps. Some voxel were significant only when using one of the priors due to combination of prior probability at given point and value of the statistic (see arrows).

Discussion

- We propose a Bayesian framework for performing ROI analysis with non binary priors
- pROI enable researchers to explicitly encode the uncertainty about search space
- Different sources of priors can be used ans should be investigated in the future: tissue probability maps, results from different modalities, literature reviews
- Due to its modular design, the proposed framework is flexible: second level model can be replaced with Markov Random Field or Kernel Density estimation
- Proof of concept code is available at: https://github.com/chrisfilo/Adaptive-Thresholding/

References

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