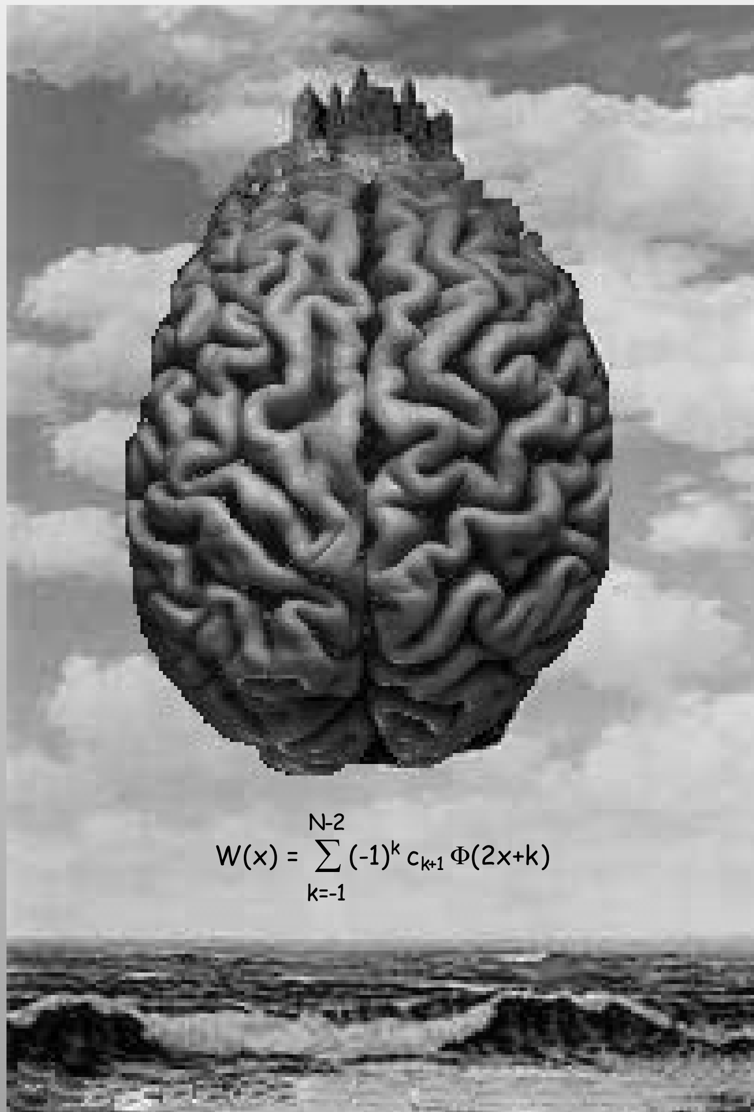
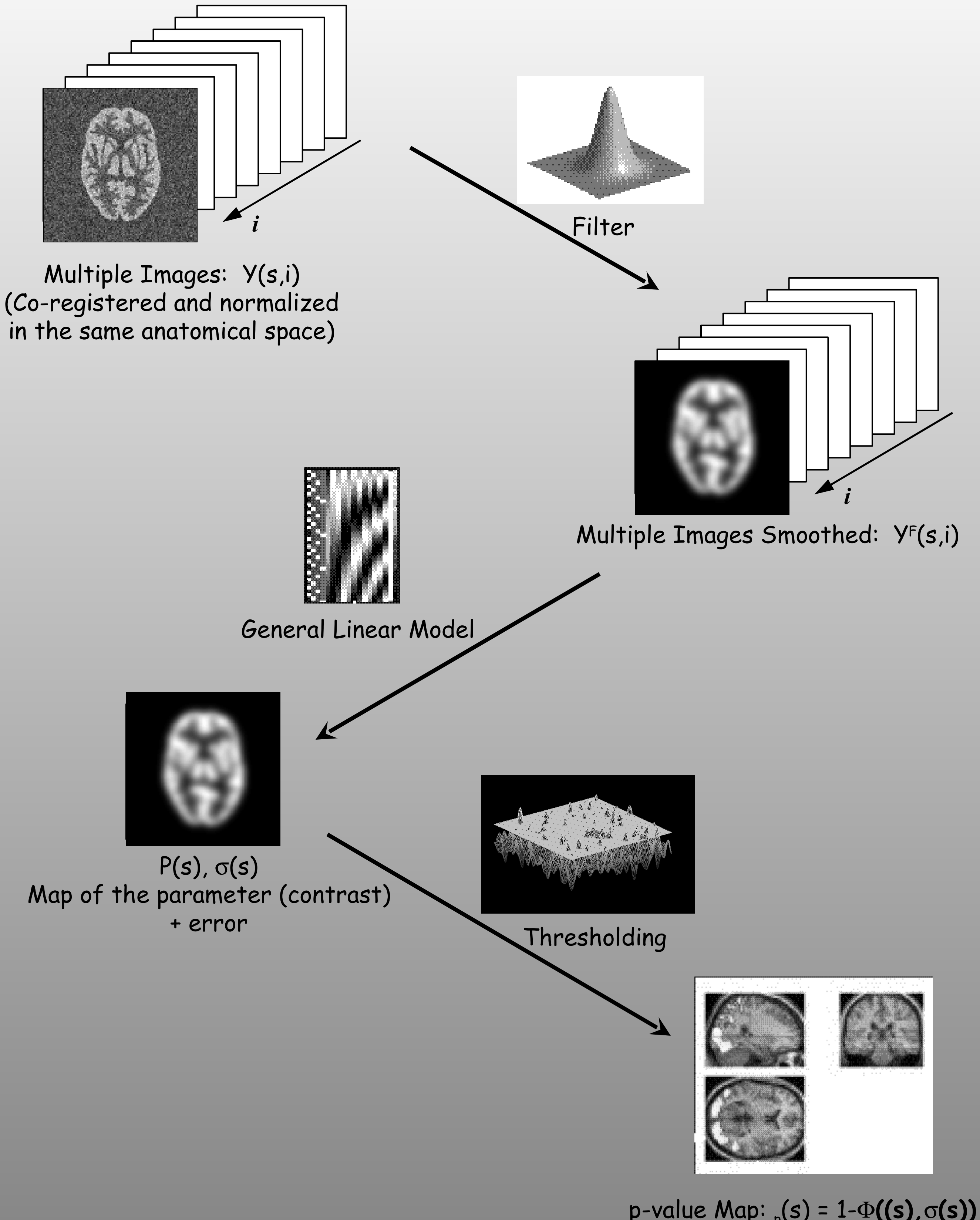
Φ-WAVE



Wavelet software for functional imaging

Turkheimer FE, Brett M, Aston JAD and Cunningham VJ

SPM



i
Filter
Multiple Images: Y(s,i)
(Co-registered and normalized
in the same anatomical space)
i
Multiple Images Smoothed: $Y^F(s,i)$
General Linear Model
P(s), σ(s)
Map of the parameter (contrast)
+ error
Thresholding
p-value Map: $_p$(s) = 1-Φ((s),σ(s))

Spatial modeling in SPM

In SPM spatial modeling is performed in 2 steps:

a. Filtering

b. Thresholding

In order to detect patterns of different size and varying spatial distribution, one may either

a. Use different filters

b. Play with the so called "levels of inference" (peaks, clusters,sets).

Gaussian field theory allows the above procedure with a controlled risk of false positives

SPM: Limitations

In order to detect the signal correctly one needs not only a model for the noise (gaussian field theory) but also a model for the signal.

Methods that model only the noise (null distribution) are called “hypothesis testing methods”. They produce a binary answer:

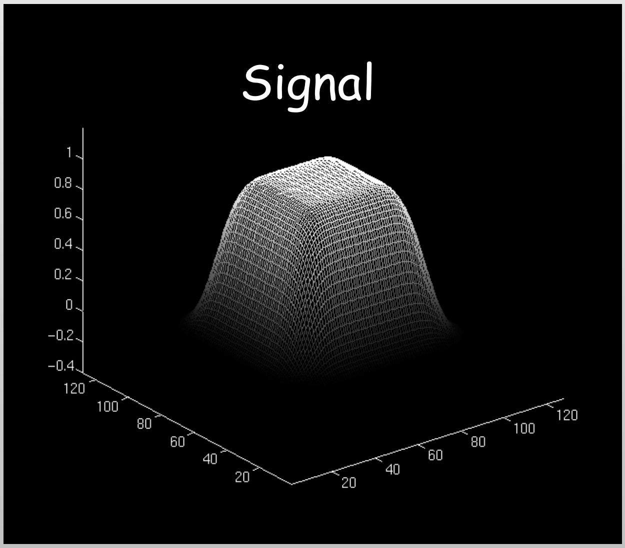
a) pvalue < alfa ----> This is unlikely to be noise

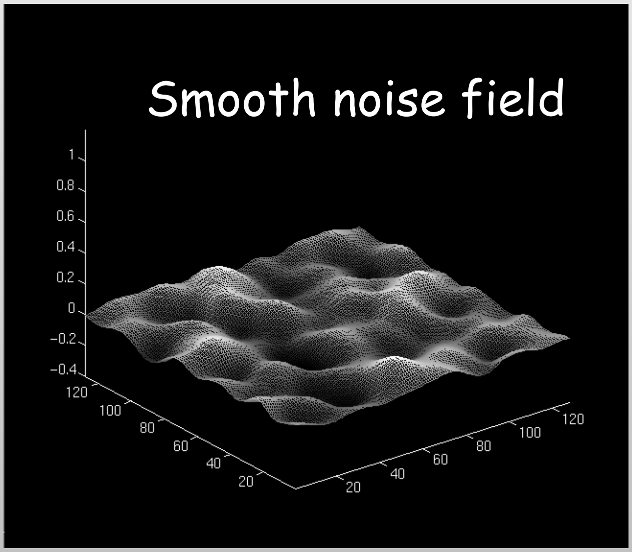
b) pvalue < alfa ----> This is likely to be noise

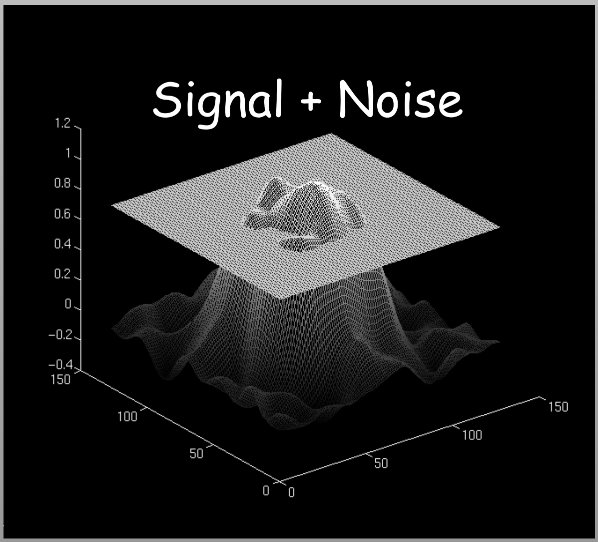
However they are unable to produce an “estimate” of the pattern of the parameter (contrast) of interest

SPM: Limitations (2)

As an example consider the following detection problem







Signal is detected by thresholding. However "detection" does not mean estimation as only the upper part of the signal is recovered that is neither correctly shaped as it is affected by noise fluctuations

Hypothesis testing vs. estimation

There is a technical difference between defining an effect “statistically significant” and “estimating its size with a statistically controlled risk”.

The first method produces only a p-value (or a pattern of p-values). This is equivalent to a statement of the type:

“The probability of this effect to be generated by noise is = pvalue”

The second method produces an effect size (or a pattern of the effect). This is equivalent to a statement of the type:

“The effect is of this size = effect-size with this error = pvalue”

Hypothesis testing vs. estimation (2)

There is also a deep conceptual difference between the two approaches.

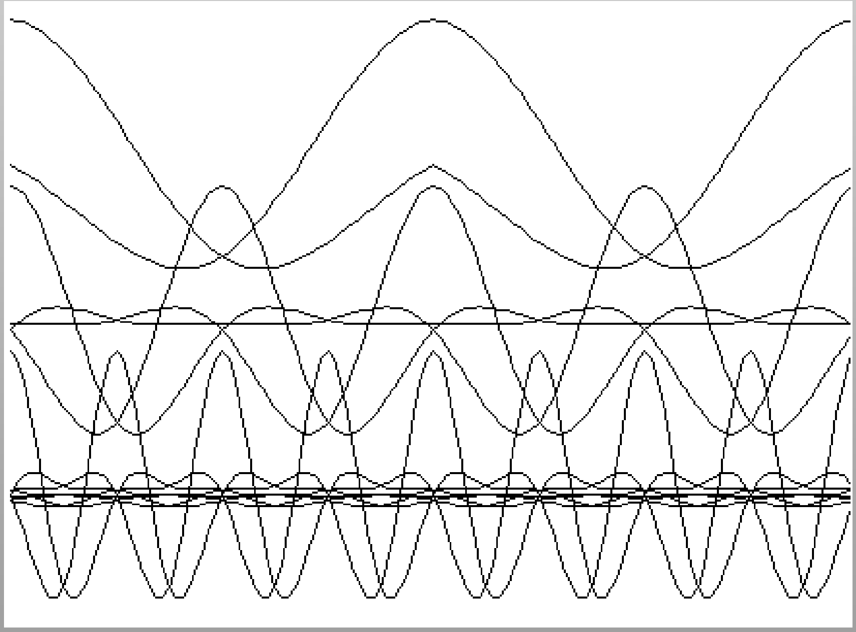
S.C. Pearce* (1993): "... *Also, there should be no suggestion that statistical analyses exist to find significant differences. Experiments are conducted in order to find answers to the questions being asked. Possibly no one doubts that a difference exists. If so, the task is to estimate its size and not to test for its existence. Further, a difference of means may be significant but not important or vice versa...*".

*Pearce SC. Introduction to Fisher (1925) Statistical Methods for Research Workers. In Kotz S, Johnson NL, Breakthroughs in Statistics. New York: Springer Verlag, Vol II, pp. 60, 1993.

Estimation

In order to estimate a pattern we must have a model for it. The only assumptions that can be made is that PET patterns are smooth, localized, of varying scales.

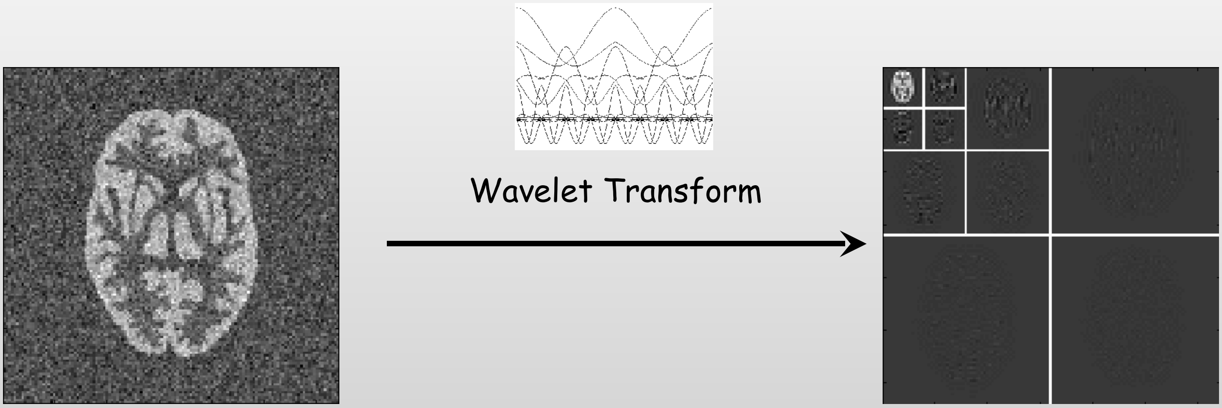
We therefore "fit" the image with a base of wavelet functions:



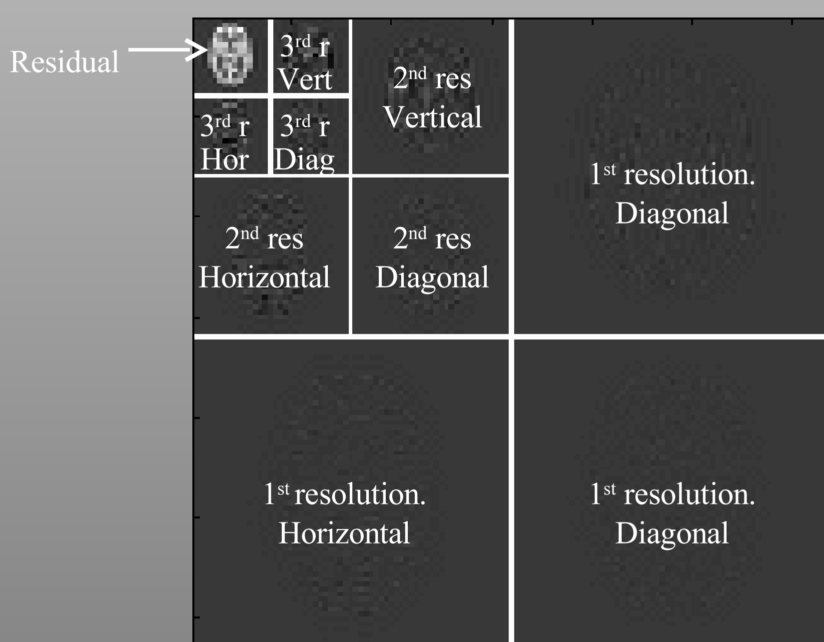
A functional base of Battle-Lemarie wavelets

This can be efficiently done by using the wavelet transform

The Wavelet Transform

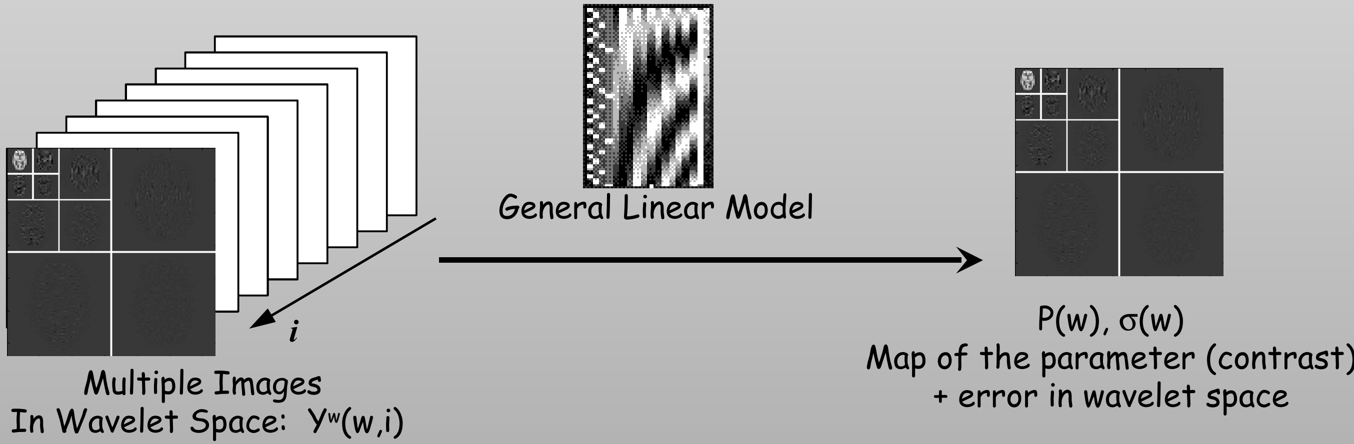


The wavelet transform is a filtering operation. The output is a map of coefficients that has the same size of the original image.
Each coefficient represents a certain wavelet of a certain scale in a certain position in a certain direction (horizontal, vertical,diagonal)



GLM in Wavelet Space

As in SPM we can then apply the GLM to the series of scan. Here the statistical modeling is not applied to each pixel but to each wavelet coefficient.

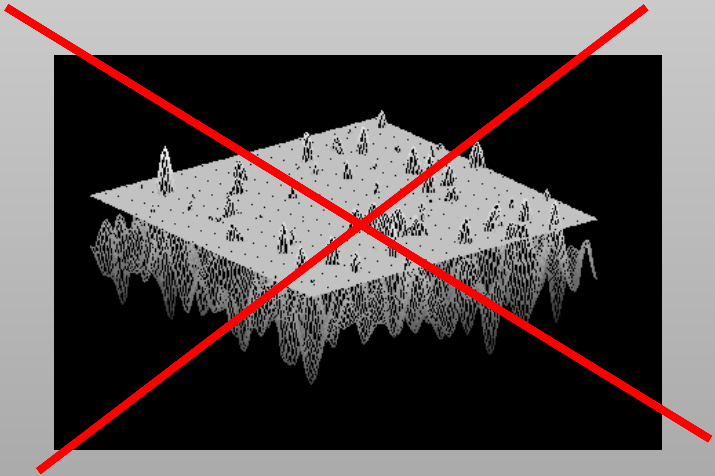


For the contrast of interest we obtain a map of sizes & errors in wavelet space.
The statistical scores for thresholding can be obtained, as in SPM analysis, as:

$$Z = \text{size}/\text{error}$$

Filtering in Wavelet Space

The wavelet transform fits smooth functions to smooth signal and noise. This generates coefficients that are independent. Therefore filtering can be done with standard procedures



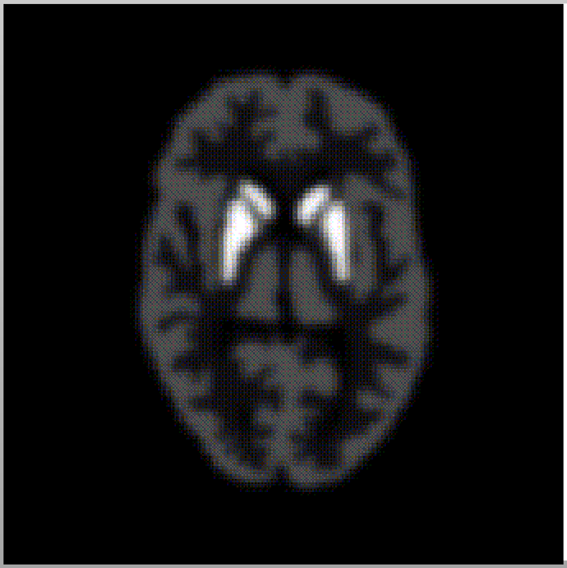
There is no need for gaussian field theory with related assumptions, limitations etc.

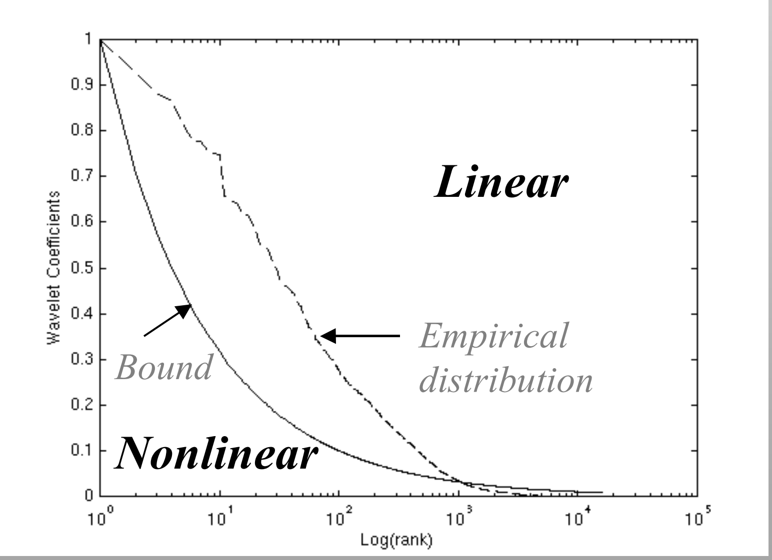
Linear and Nonlinear Filters

Classic theory of estimation of a multivariate normal vector provides an alternative between:

1) Nonlinear (thresholding) filters : optimal for very sparse vectors of coefficients

2) Linear (shrinkage) filters: optimal for less sparse vectors





The bound between the two is of the form: $k^{-0.5}$ where k is the index of the ranked coefficients.

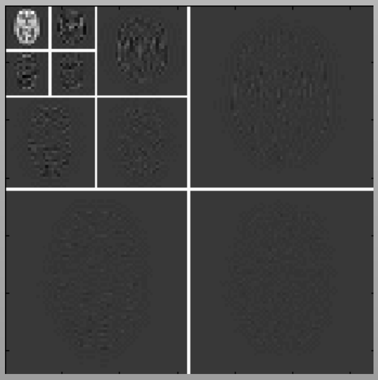
Typical PET patterns have wavelet representations whose sparsity is not constrained by this bound.

Reconstruction

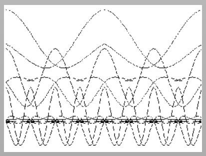
The aim is to obtain a map of the effect (contrast) of interest. Therefore we re-obtain from the filtered coefficients their original size:

$$\text{size} = Z_{\text{thresholded}} * \text{error}$$

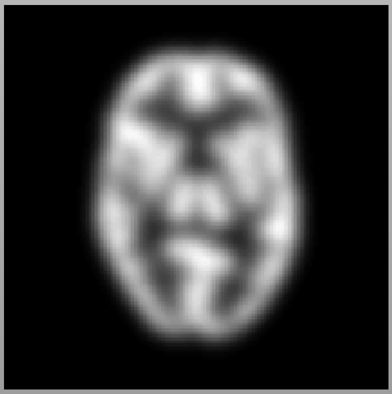
Then the inverse wavelet transform is applied to obtain the filtered map.



$P^F(w)$, $\sigma(w)$
Filtered Map of the parameter (contrast) in wavelet space

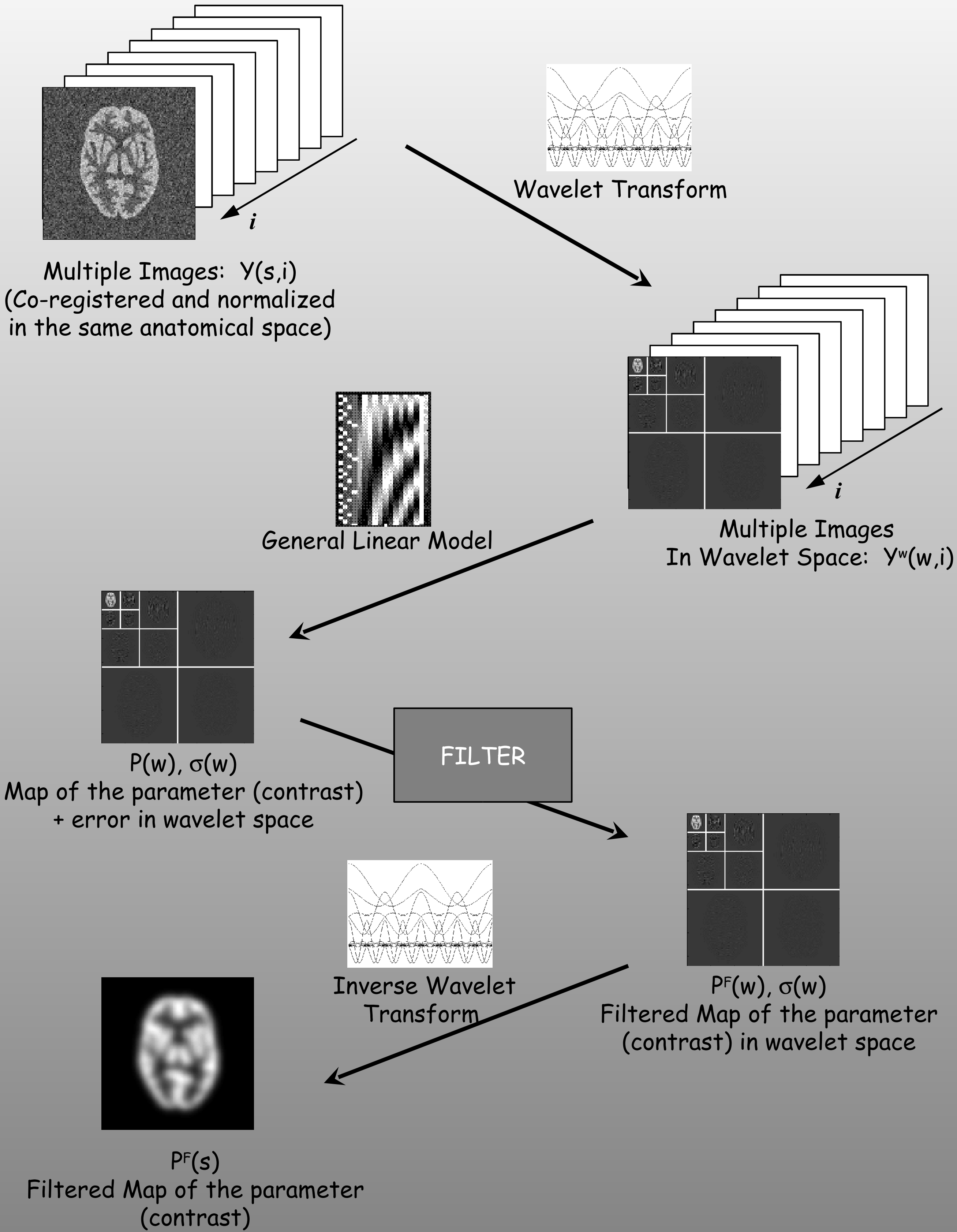


Inverse Wavelet Transform



$P^F(s)$
Filtered Map of the parameter (contrast)

Φ-WAVE



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Wavelet Transform
Multiple Images: Y(s,i)
(Co-registered and normalized
in the same anatomical space)
General Linear Model
i
Multiple Images
In Wavelet Space: Yʷ(w,i)
P(w), σ(w)
Map of the parameter (contrast)
+ error in wavelet space
FILTER
Inverse Wavelet
Transform
Pᶠ(w), σ(w)
Filtered Map of the parameter
(contrast) in wavelet space
Pᶠ(s)
Filtered Map of the parameter
(contrast)

Validation

Although extensive work has been carried out for validation of WT methods in tomography it is of interest to verify the assumptions behind the thresholding procedure. In particular, the use of GLM and relative Bonferroni adjustment are appropriate only if the noise processes of the set W(s,i) strictly match the independent normal noise conditions in wavelet space.

Null experiment:
Correspondence was verified by resampling from a null set (all images in the same condition) two groups of scans each time and then running a statistical comparison between them. Since no difference is expected, rejection rates should match the theoretical error rates.

Null Experiment

The null dataset was composed by the scans in activation state of a previously published protocol where changes in cerebral blood flow (CBF) were measured with H_2O^{15} and PET (Brett et al., 1998)*.

- ECAT 953B scanner

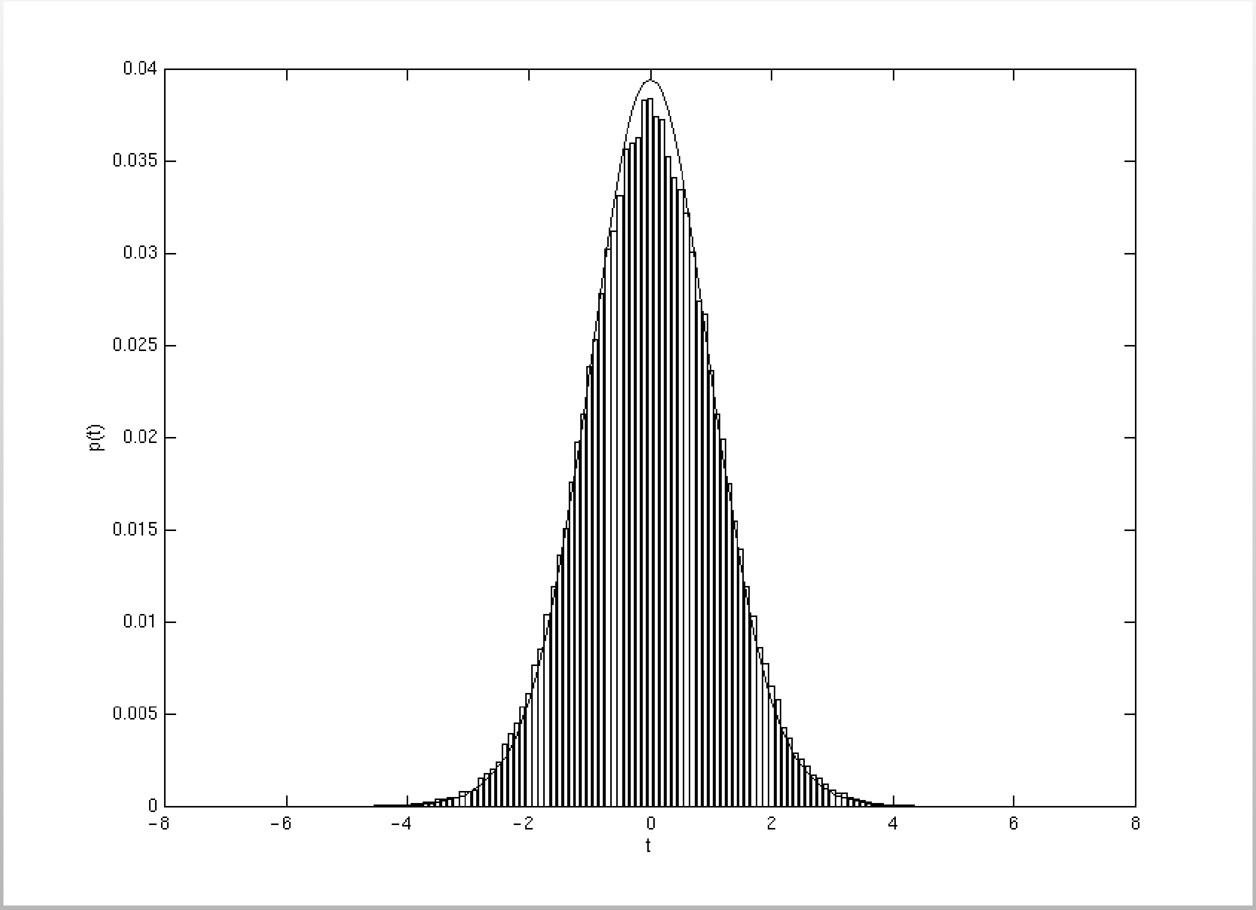
- The null set Y(s,i) consisted in data from 8 subjects, 5 frames each.

- Images coregistered and normalized using SPM99 (Functional Imaging Laboratory)

- GLM with 8 subjects factors plus 8 subject specific covariates to normalize each scan to its global counts (23 degrees of freedom)

*Brett M., Stein JF, Brooks DJ. The role of the premotor cortex in imitated and conditional praxis. Neuroimage 1998; 7(4): S978

Null Experiment:results

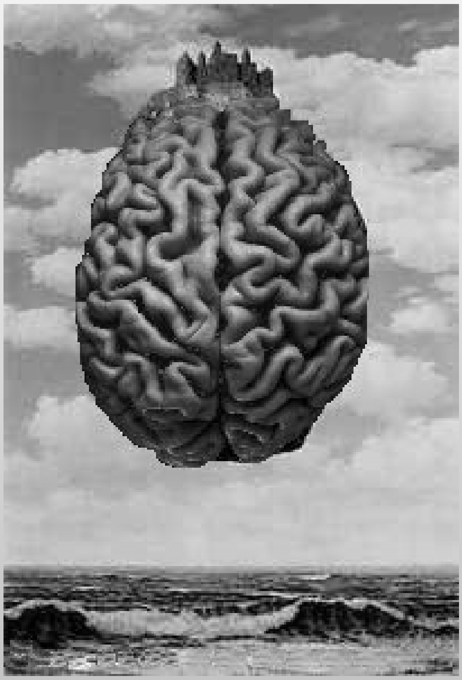


Distribution of wavelet scores computed from one of the null-datasets obtained by random assignment of 40 scans acquired in the same experimental conditions in two simulated experimental groups of 20. The figure displays the empirical distribution of studentized wavelet coefficients superimposed with the expected distribution, a standard Student t-distribution with 23 degrees of freedom.

Specificity of wavelet filter with Bonferroni correction for all 100 repetitions matched theoretical expectations. Values were was as follows (error rates ± 90% confidence interval):

Nominal Level	α = 0.1	α = 0.05	α=0.01
Estimates (Randomization)	0.087 (±0.016)	0.045 (±0.011)	0.012 (±0.005)

Φ-WAVE SOFTWARE



Input:	- Normalized SPM files
	- No additional processing required
Interface:	Same Model and Contrast Manager of SPM99
Status:	Beta version available for internal testing