# Generalized Procrustes problem allows to estimate subject-specific functional connectivity in fMRI data

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Advanced methods to explore individual differences

# Overview

# Functional Alignment Problem in a nutshell

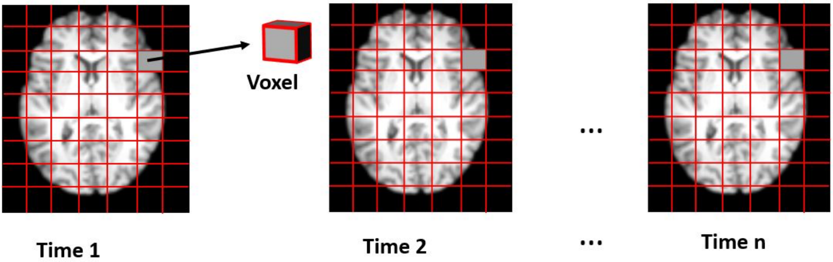
**Multi-subjects** fMRI studies permit to compare studies across subjects, to generalize and to validate the results.

The anatomical and functional structure of brains vary across subjects even in response to identical sensory inputs.

ALIGNMENT STEP

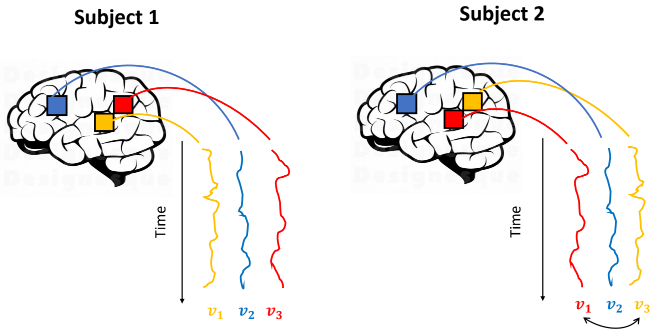
- **Anatomical Alignment** (MNI normalization) [1];
- **Functional Alignment**:
  - Procrustes-based Method [2];
  - Hyperalignment [3].

[1] Jenkinson, M. and Smith, S., (2001) Medical image analysis.
[2] Gower, C., & Dijksterhuis, B., (2004) OUP Oxford.
[3] Haxby et al., (2011) Neuron.




Each subject $i$ is represented by a matrix $\mathbf{X}_i \in \mathbb{R}^{n \times v}$:

- the **rows** represent the **response stimuli activation** of voxels
  → the stimuli are time synchronized
- the **columns** represent the **time series of activation** for each $v$ voxel
  → not assumed to be in correspondence across $N$ subjects.




We can assume that the neural activities in different brains are **noisy rotations of a common space**.

# Procrustes Method

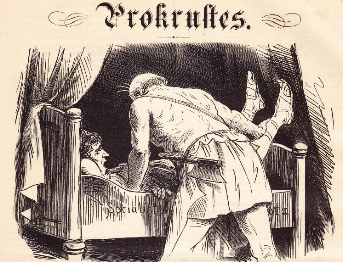
The **Procrustes** method uses **similarity transformation** to match matrices onto the **reference** one as close as possible.

Having $i > 2 \rightarrow$ **Generalized Procrustes Analysis**[4] (GPA):

$$\boxed{\min_{\mathbf{R}_i \in \mathcal{O}(m);\alpha_i \in \mathbb{R}^{>0}} \sum_{i=1}^{N} \|\alpha_i \mathbf{X}_i \mathbf{R}_i - \mathbf{M}\|_F^2}$$

- $\{\boldsymbol{X}_i \in \mathbb{R}^{n \times v}\}_{i=1,\dots,N}$ represent the matrices to be aligned;
- $\boldsymbol{M} \in \mathbb{R}^{n \times v}$ is the configuration reference matrix;
- $\{\boldsymbol{R}_i \in \mathcal{O}(v)\}_{i=1,\dots,N}$ **orthogonal matrix parameters,** $\{\alpha_i \in \mathbb{R}_{>0}\}_{i=1,\dots,N}$ scaling parameters.

[4] Gower, J. C., (1975). Psychometrika.




**IN A NUTSHELL**

Find the **best orthogonal** matrix-transformation that **MINIMIZE THE DISTANCE** between $\mathbf{X}_i$'s and $\mathbf{M}$

**SOLUTION** $\rightarrow \hat{\boldsymbol{R}}_i = \boldsymbol{U}_i \boldsymbol{V}_i^\top$ where $\boldsymbol{X}_i^\top \boldsymbol{M} = \boldsymbol{U}_i \boldsymbol{S}_i \boldsymbol{V}_i^\top$ (SVD).

Both Hyperalignment (sequential version of GPA) and GPA do not a **unique solution** of $\hat{\boldsymbol{R}}_i$:

- **Hyperalignment**'s solutions depend on the order in which individuals are entered into the algorithm;
- **GPA**'s solutions are unique up to rotations.

# ProMises model

We rephrase the Procrustes method as **statistical model** called **ProMises model**[5]:

$$\boxed{\mathbf{X}_i = \alpha_i \mathbf{M}\mathbf{R}_i^\top + \mathbf{E}_i}$$

where $\vec{\boldsymbol{E}}_i \sim \mathcal{N}_{nv}(\vec{0}, \boldsymbol{\Sigma}_v \otimes \boldsymbol{\Sigma}_n)$. We think that also the **anatomical features** are important!

$\boldsymbol{R}_i \sim$ **von Mises-Fisher**[6] distribution with location parameter $\boldsymbol{F} \in \mathbb{R}^{v \times v}$ and concentration parameter $k \in \mathbb{R}_{>0}$, i.e.,

$$\boxed{f(\boldsymbol{R}_i) = C \exp(k\, tr(\boldsymbol{F}^\top \boldsymbol{R}_i))}$$

[5] Andreella, A. & Finos, L., (2022) Psychometrika.
[6] Downs, T. D., (1972) Biometrika.

The regularization leads to a **unique solution** for $\hat{\mathbf{R}}_i$:

$$\boxed{\hat{\boldsymbol{R}}_i = \boldsymbol{U}_i \boldsymbol{V}_i^\top \quad \text{where } \boldsymbol{X}_i^\top \boldsymbol{M} + k\boldsymbol{F} = \boldsymbol{U}_i \boldsymbol{S}_i \boldsymbol{V}_i^\top \ \text{(SVD).}}$$

which combines the columns of $\boldsymbol{X}_i$ to reflect the fMRI data spatial structure → **combine spatially close voxels**:

$$\boxed{\boldsymbol{F} = [\exp(-d_{ij}^2)]}$$

where $d_{ij}$ is the euclidean distance between the 3-D coordinates of voxels $i$ and $j$.

Concluding: The estimation process is computationally heavy, so only ROIs can be aligned

⟶ **Semi-orthogonal transformation** on $\boxed{\mathbf{X}_i}$

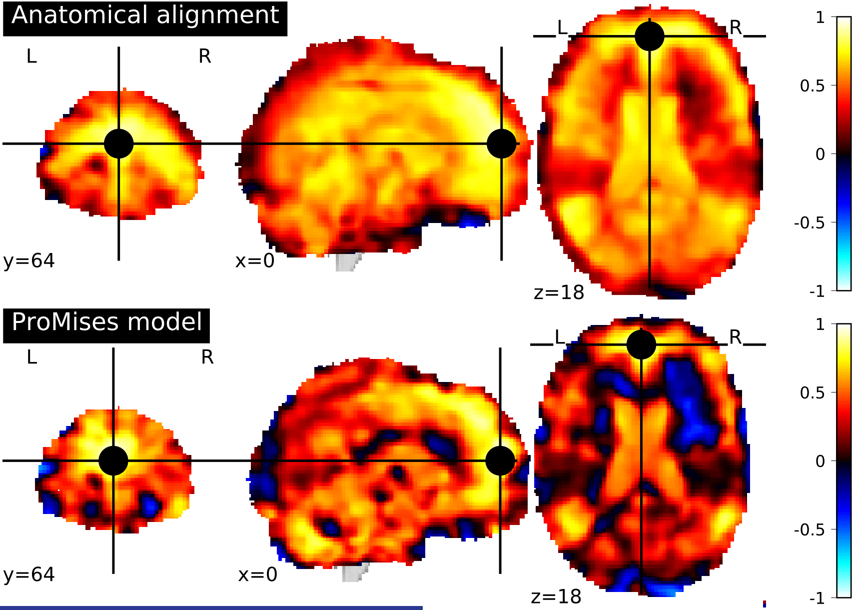
# fMRI Application

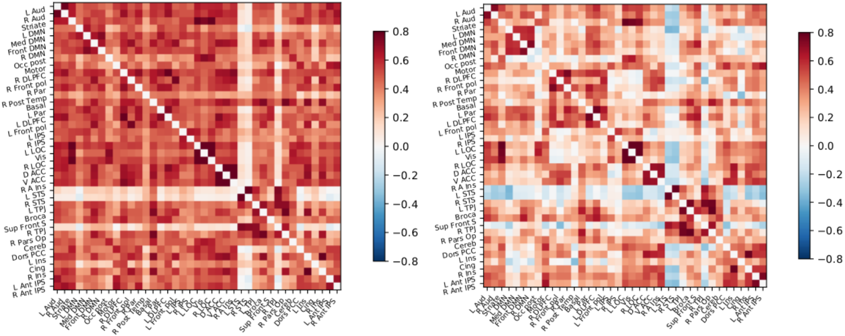
We align the brain images from Pernet et al. (2015)[7] of 18 subjects passively listening to vocal, i.e., speech, and non-vocal sounds.

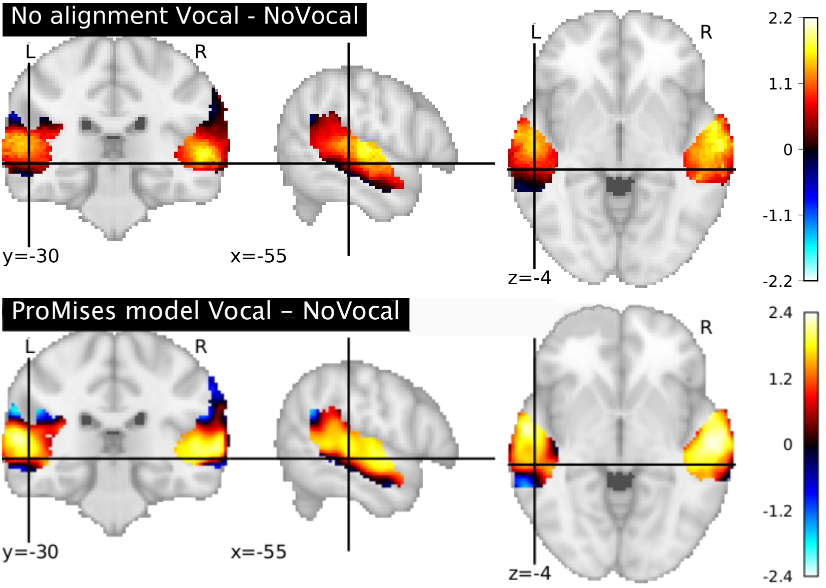
After the $\mathbf{X}_i$ matrices' alignment:

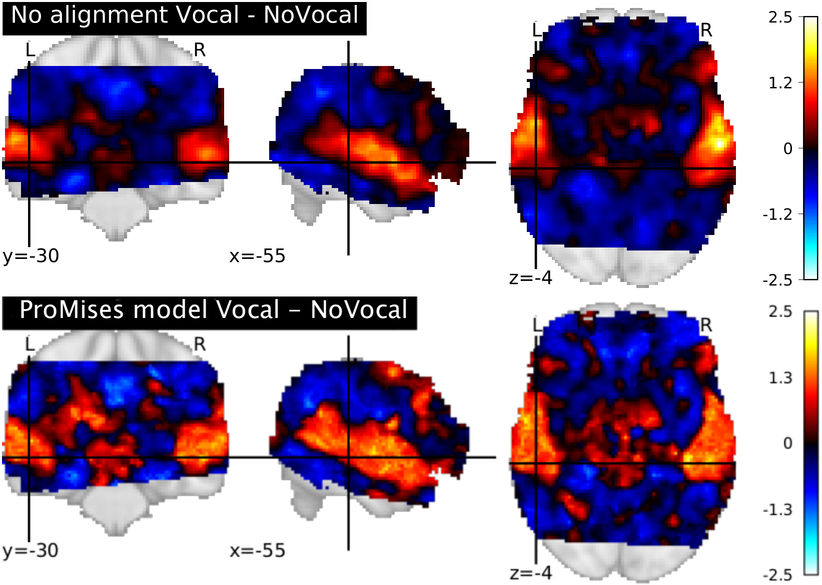
- **Seed-based correlation analysis**;
- **ROI correlation analysis**;
- **Statistical Parametric Mapping**.

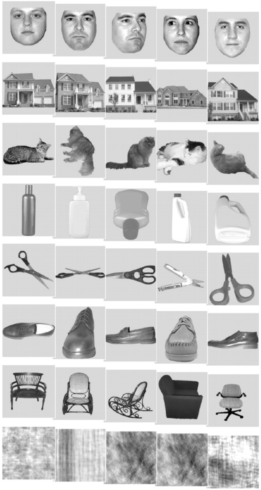
[7] https://openneuro.org/datasets/ds000158/versions/1.0.0


Anatomical alignment
L
R
y=64
x=0
z=18
1
0.5
0
-0.5
-1
ProMises model
L
R
y=64
x=0
z=18
1
0.5
0
-0.5
-1


L Aud
R Aud
Striate
L DMN
Med DMN
Front DMN
R DMN
Occ post
Motor
R DLPFC
R Front pol
R Par
R Post Temp
Basal
L Par
L DLPFC
L Front pol
L IPS
R IPS
L LOC
Vis
R LOC
D ACC
V ACC
R A Ins
L STS
R STS
L TPJ
Broca
Sup Front S
R TPJ
R Pars Op
Cereb
Dors PCC
L Ins
Cing
R Ins
L Ant IPS
R Ant IPS
0.8
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6
−0.8

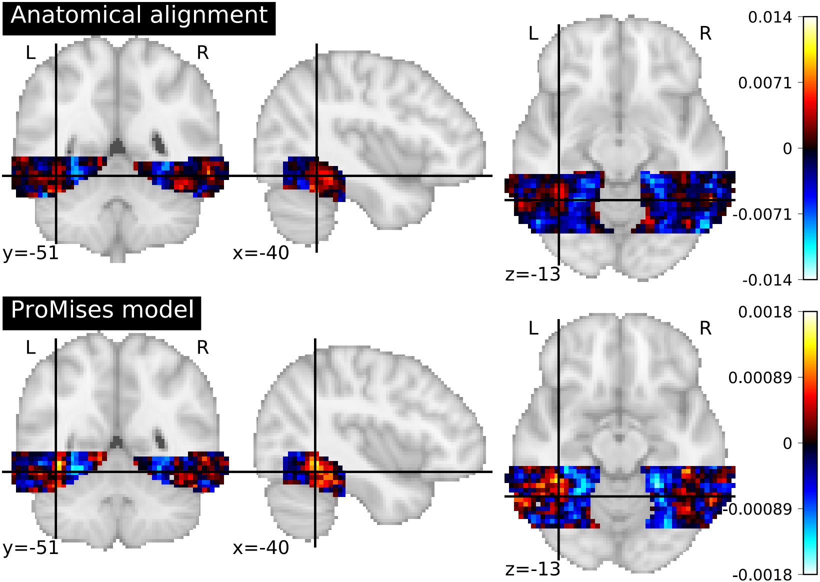

No alignment Vocal - NoVocal
L
R
y=-30
x=-55
L
R
z=-4
2.2
1.1
0
-1.1
-2.2
ProMises model Vocal – NoVocal
L
R
y=-30
x=-55
R
z=-4
2.4
1.2
0
-1.2
-2.4

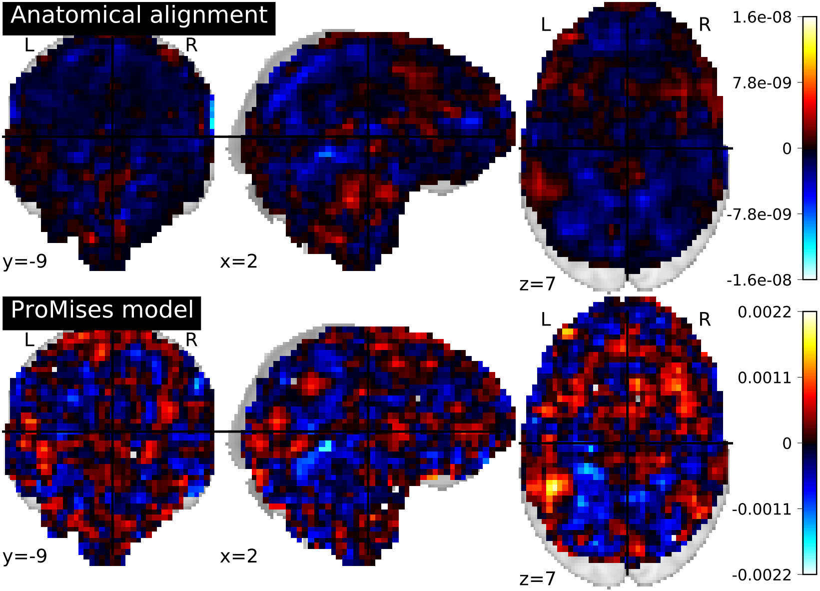

No alignment Vocal - NoVocal
L
R
y=-30
x=-55
z=-4
2.5
1.2
0
-1.2
-2.5
ProMises model Vocal – NoVocal
L
R
y=-30
x=-55
z=-4
2.5
1.3
0
-1.3
-2.5



- We align the images of the **Ventral Temporal Cortex** and **whole brain** from Haxby et. al (2001)[8] of 10 subjects watching static, grey-scale images of faces and objects;
- The **Multi-class Linear Support Vector Machine** is used as classifier with leave one out subject cross-validation.

[8] https://openneuro.org/datasets/ds000105/versions/00001


Anatomical alignment
L
R
y=-51
x=-40
z=-13
0.014
0.0071
0
-0.0071
-0.014
ProMises model
L
R
y=-51
x=-40
z=-13
0.0018
0.00089
0
-0.00089
-0.0018


Anatomical alignment
L
R
y=-9
x=2
L
R
z=7
1.6e-08
7.8e-09
0
-7.8e-09
-1.6e-08
ProMises model
L
R
y=-9
x=2
L
R
z=7
0.0022
0.0011
0
-0.0011
-0.0022

- **ProMises Model** gives us a set of orthogonal matrices, one for each subject.
- We can use these matrices to understand underlying clusters,
- associating also some available covariates.

We align the brain images from Smeets et al. (2013)[8] of 29 subjects watching food and no-food images.

After that, the **multidimensional scaling** is applied on the $\mathbf{R}_i$ pairwise distance matrix.

[8] https://openneuro.org/datasets/ds000157/versions/00001

Multidimensional scaling technique [9] reduces the data dimensions using **dissimilarity** information of pairs of objects, $\{\boldsymbol{R}_i\}_{i=1,\ldots,29}$ in our case.

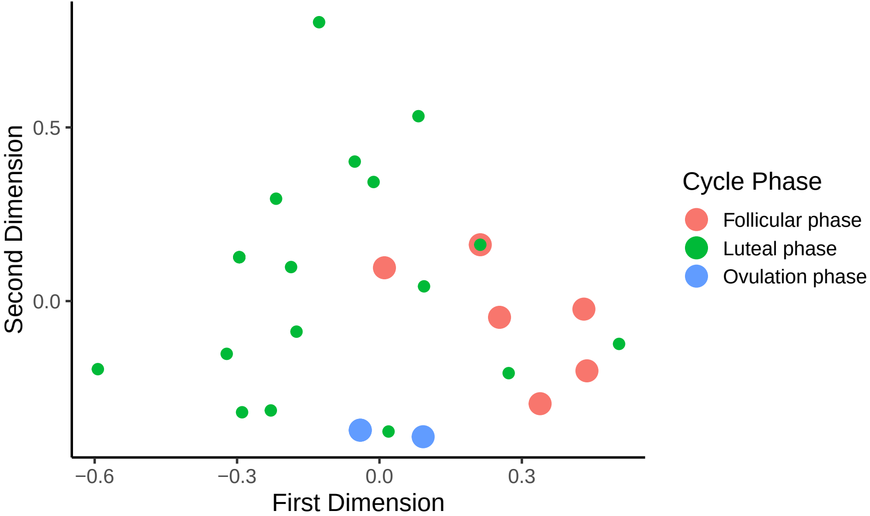
Having 29 subjects, we analyze the dissimilarity matrix $\Delta$ with dimensions $29 \times 29$ where $\delta_{ij} = ||\boldsymbol{R}_i - \boldsymbol{R}_j||_F$ and $i, j \in \{1, \ldots, 29\}$.

Multidimensional scaling then find a lower dimensional configuration $\boldsymbol{X}$ such that the following relations are satisfied as well as possible:

$$f(\delta_{ij}) \approx d_{ij}(\boldsymbol{X})$$

where $f(\cdot)$ stands for some transformation, in our case a spline transformation.

[9] Torgerson. (1958).


Second Dimension
0.5
0.0
−0.6
−0.3
0.0
0.3
First Dimension
Cycle Phase
Follicular phase
Luteal phase
Ovulation phase

The **ProMises Model**:

- leads to a **unique** solution of the transformation → unique representation/interpretation of the final result;
- allows alignment of the **whole brain**;
- exploits the information of voxels' **spatial position**;
- yields more **reliable** measures of individual differences both:
  1. by reducing confounds from topographic idiosyncrasies;
  2. by capturing variation around shared functional and anatomical response across individuals;
- allows to find **groups** of individuals sharing patterns of neural brain activation.

You can find the `Python` module and the `R` package on my GitHub profile `https://github.com/angeella`.