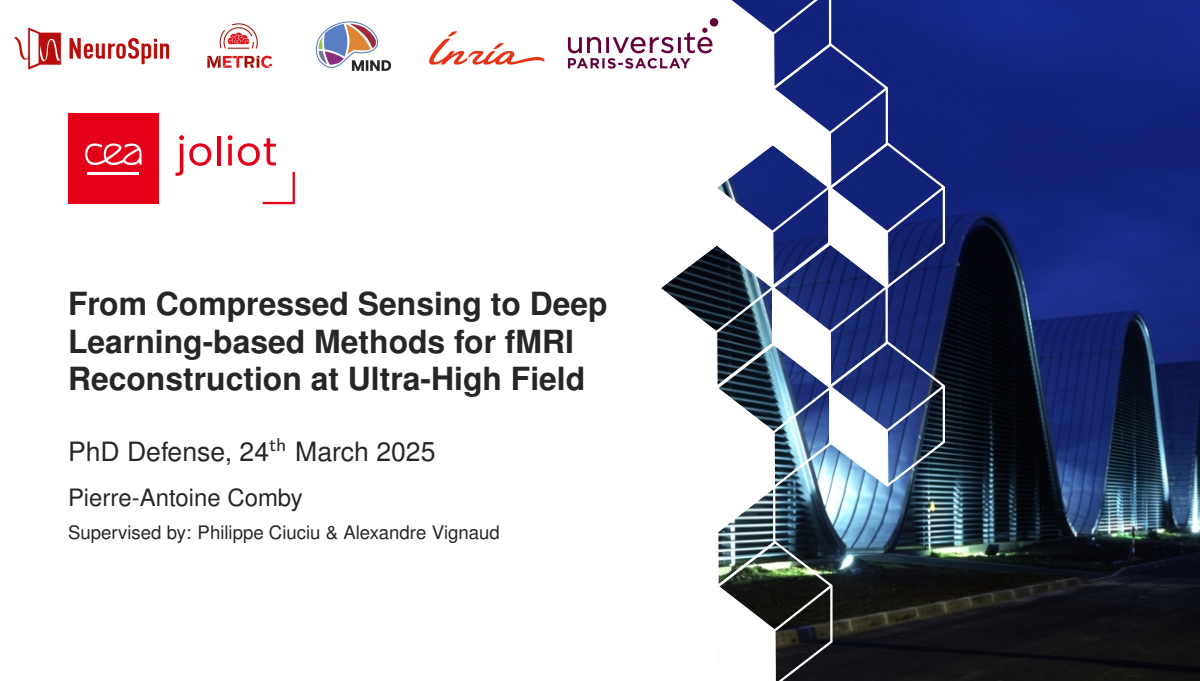




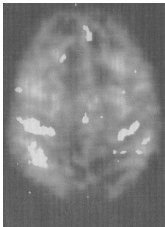
From Compressed Sensing to Deep Learning-based Methods for fMRI Reconstruction at Ultra-High Field

PhD Defense, 24th March 2025
Pierre-Antoine Comby
Supervised by: Philippe Ciuciu & Alexandre Vignaud

1.1/1

1. Good Afternoon Everyone, I am Pierre-Antoine Comby, and today I am deeply honoured to present to you my research work conducted over the past three years entitled:

What is Functional MRI

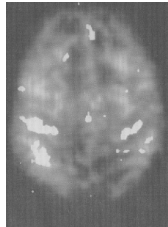


1.5 T, $(4\text{ mm})^3$, 2 s
[Bandettini et al. 1992]

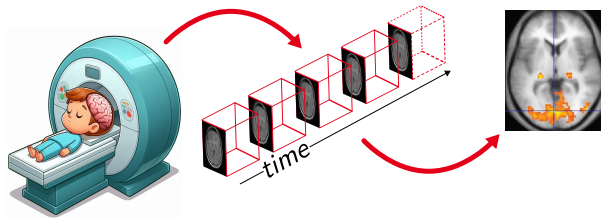
2.1/3 What is Functional MRI

1. A few year before I was born, people discovered that you could WITNESS cerebral activity using an MRI Machine. This open the gates of the fMRI field and provided Neuroscientist with their new favorite tool to explore the mysteries of the Humain Brain.

What is Functional MRI



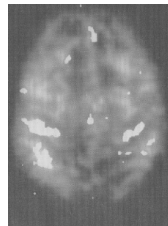
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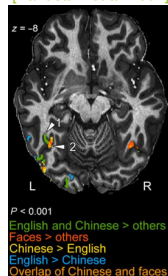
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2. In a Nutshell, fMRI consists in acquiring a sequence of 3D image of the brain to then localize evoked cerebral activity from an external stimulus or spontaneous activity.

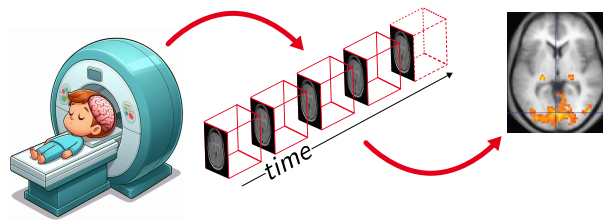
What is Functional MRI



1.5 T, (4 mm)³, 2 s
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7 T, (1.2 mm)³, 2 s
[Zhan et al. 2023]



2.3/3 What is Functional MRI

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2. In a Nutshell, fMRI consists in acquiring a sequence of 3D image of the brain to then localize evoked cerebral activity from an external stimulus or spontaneous activity.
3. 30 years later, with the help of several technological progress it is now possible to explore this activity in greater details, notably using ultra-high magnetic field

However, THREE main challenges are still constraining fMRI studies

The resolution challenge



Challenge 1: Resolution

Spatial resolution

vs temporal resolution

vs brain coverage

vs Signal-to-Noise-Ratio (SNR)



3.1/5 The resolution challenge

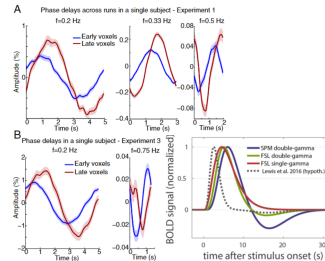
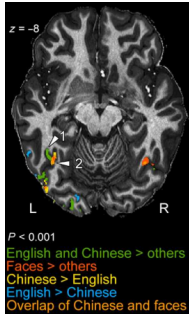
1. The FIRST challenge of fMRI is about the COMPROMISE of spatial temporal resolution

The resolution challenge



Challenge 1: Resolution

Spatial resolution
vs temporal resolution
vs brain coverage
vs Signal-to-Noise-Ratio (SNR)



7 T, (2 mm)³, 10 slices, TR_{vol} = 230 ms
[Lewis et al. 2016]

7 T, (1.2 mm)³, TR_{vol}=2 sec
[Zhan et al. 2023]

3.2/5 The resolution challenge

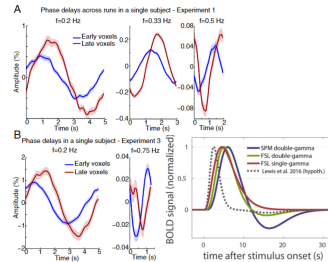
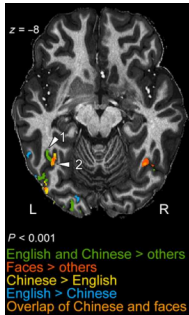
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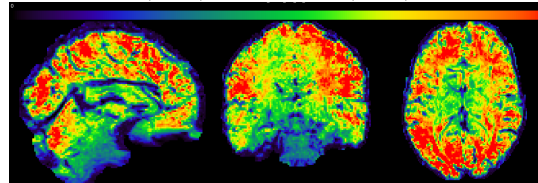
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Signal Quality (temporal SNR)

$$SNR \propto (\Delta r)^3 B_0^\alpha > 1$$

(1.6mm)³, 1.2s, whole brain (3D EPI)



3.3/5 The resolution challenge

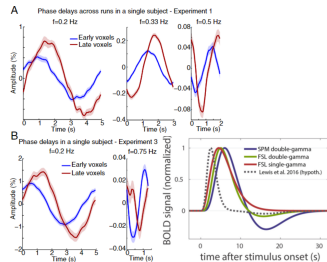
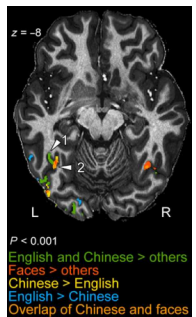
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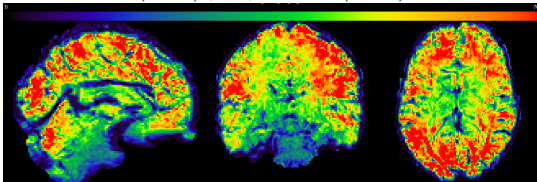
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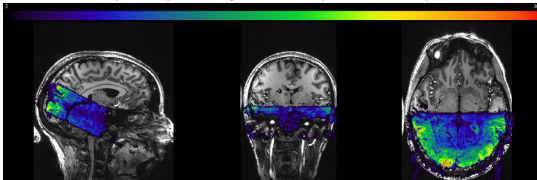
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(1.6mm)³, 1.2s, whole brain (3D EPI)



(0.8mm)³, 2.5s, partial brain (3D EPI+CAIPI)



Courtesy of Redouane Jamil

3.4/5 The resolution challenge

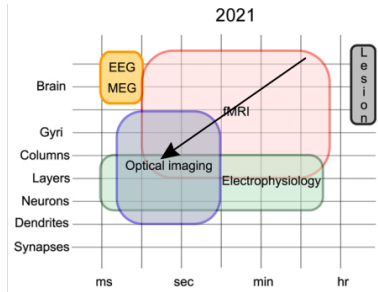
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The resolution challenge



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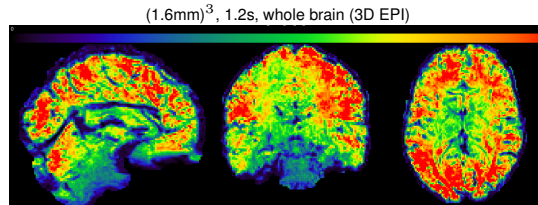
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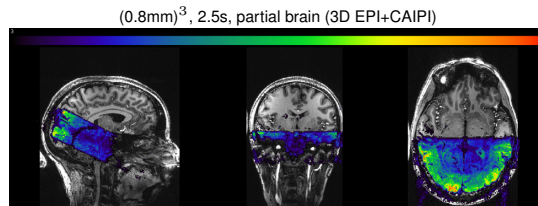
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4. BUT, by dividing the voxel length by 2, and thus the volume by 8 to MAINTAIN suitable signal quality it is required to increase the temporal resolution and reduce the field of view. And even in this case, the signal quality is reduced.
5. To reach deeper insight on the brain, we DO NEED to tackle this challenge! HOWEVER, getting higher resolution fMRI data will be DEFEATED by the two other challenges

The Reproducibility challenge



Challenge 2:

Lack of perfect reproducibility of brain activity

- Despite controlled and careful design of paradigms

4.1/4 The Reproducibility challenge

1. The second challenge of fMRI concern the reproducibility.

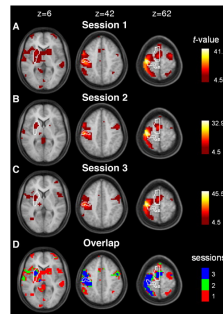
The Reproducibility challenge



Challenge 2:

Lack of perfect reproducibility of brain activity

- Despite controlled and careful design of paradigms
- Intra subject variability [Zandbelt et al. 2008; Dehaene-Lambertz et al. 2006; Bennett and Miller 2010; Badillo et al. 2013; Nakuci et al. 2023]



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4.2/4 The Reproducibility challenge

1. The second challenge of fMRI concern the reproducibility.
2. Indeed, humans are not machines, and we can't RESET them to repeat the same fMRI experiment multiple times, and we get INTRA-subject variability

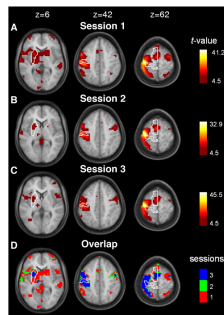
The Reproducibility challenge



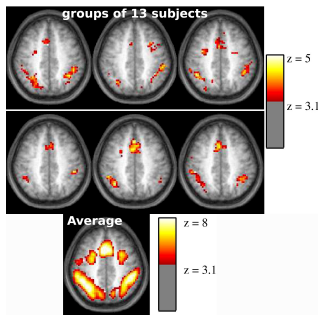
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Lack of perfect reproducibility of brain activity

- Despite controlled and careful design of paradigms
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- 🎯 Average effect, loss of spatial specificity



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4.3/4 The Reproducibility challenge

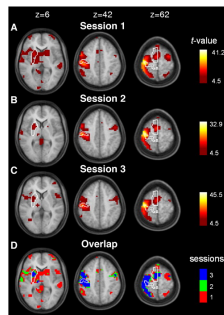
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The Reproducibility challenge

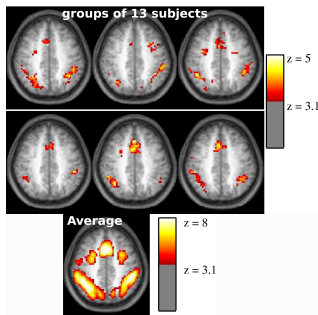


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Lack of perfect reproducibility of brain activity



[Zandbelt et al. 2008]



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- Inter subject variability [Thirion et al. 2007; Poline et al. 2010; Badillo et al. 2013]
 - 🎯 Average effect, loss of spatial specificity
- Noise
 - Many experiments required

4.4/4 The Reproducibility challenge

1. The second challenge of fMRI concern the reproducibility.
2. Indeed, humans are not machines, and we can't RESET them to repeat the same fMRI experiment multiple times, and we get INTRA-subject variability
3. Furthermore, INTER-subject variability is also an issue, as every brain is ever so slightly DIFFERENT.
4. Measurements are also corrupted by NOISE, and multiple acquisition of fMRI data are required to gain enough statistical SIGNIFICANCE. This brings us to our third challenge:

The Quality Challenge



Challenge 3: Quality

Image Quality vs Statistical performances

5.1/4 The Quality Challenge

1. The third and last challenge on fMRI is a more technical one regarding the quality of the data.

The Quality Challenge



Challenge 3: Quality

Image Quality vs Statistical performances

- A compromise between



Resolution

and



Reproducibility

5.2/4 The Quality Challenge

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2. High Res fMRI goes on par with a high image quality, but this may LIMITS the EXTRACTION of statistically significant EFFECTS from the data.

The Quality Challenge

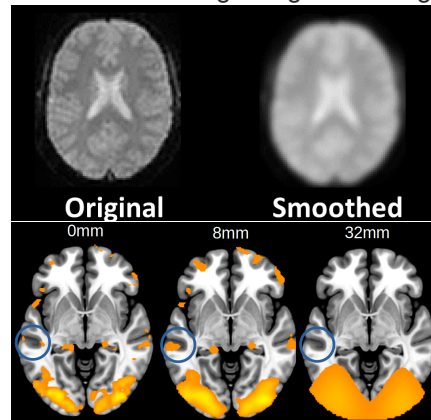


Challenge 3: Quality

Image Quality vs Statistical performances

- A compromise between  **Resolution** and  **Reproducibility**
- fMRI data processing can be more an art than a science

Statistics boosting using smoothing:



<https://martynmcfarquhar.github.io/NCCN-IA-fMRIPreProcessing>

5.3/4 The Quality Challenge

1. The third and last challenge on fMRI is a more technical one regarding the quality of the data.
2. High Res fMRI goes on par with a high image quality, but this may LIMITS the EXTRACTION of statistically significant EFFECTS from the data.
3. A typical example is the effect of spatial smoothing on the detection of statistical maps. The WAY in which the fMRI DATA is PROCESSED has a significant IMPACT on the insight it can provide. For Instance, the SMOOTHING kernel width can boost or delete detected brain activity

The Quality Challenge

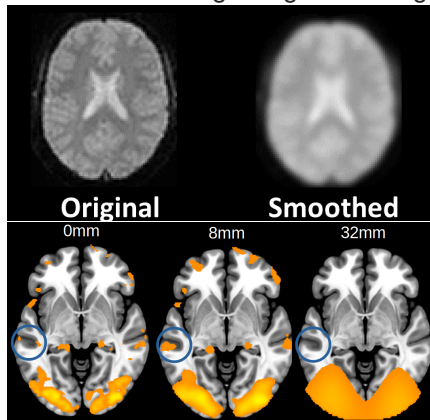


Challenge 3: Quality

Image Quality vs Statistical performances

- A compromise between **Resolution** and **Reproducibility**
- fMRI data processing can be more an art than a science
- Did my processing invent or forget activation?
✗ No ground truth to validate

Statistics boosting using smoothing:



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5.4/4 The Quality Challenge

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3. A typical example is the effect of spatial smoothing on the detection of statistical maps. The WAY in which the fMRI DATA is PROCESSED has a significant IMPACT on the insight it can provide.
For Instance, the SMOOTHING kernel width can boost or delete detected brain activity
4. Finally, a CRUCIAL regarding the production of fMRI results is whether or not our processing of the data invented or forgot some cerebral activity. WITHOUT a GROUND-TRUTH, we CANNOT get CERTAINTY on the PERFORMANCE of our METHODS.

Outline



Resolution



Reproducibility



Quality

6.1/6 Outline In this thesis, we will contribute to push the limits further on these three challenges.

1. First, I will go into greater details on how these challenges arise and how the community is currently tackling them

Outline



Resolution



Reproducibility



Quality

0. What can we already do about these challenges?

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1. First, I will go into greater details on how these challenges arise and how the community is currently tackling them
2. Then, I will present my first contribution to the field, which is about using image denoising to boost the quality and resolution of fMRI data

Outline



Resolution



Reproducibility



Quality

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1. First contribution:

Using image denoising to boost  Quality &  Resolution



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Outline



Resolution



Reproducibility



Quality

0. What can we already do about these challenges?

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Using image denoising to boost  Quality &  Resolution

2. Second contribution:

Building a ground truth for  Quality &  Reproducibility



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Outline



Resolution



Reproducibility



Quality

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Deep learning for fMRI reconstruction?



Quality



Reproducibility



Resolution



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5. Finally, I will conclude and show some perspectives that this work has opened

Outline



Resolution



Reproducibility



Quality

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Quality



Reproducibility



Resolution

4. Conclusion & perspectives

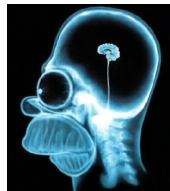


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0. What can we already do about these challenges?



MRI: Brain Anatomy



fMRI: Brain functions

7.1/1 BOIRE DE L'EAU, RESPIRE

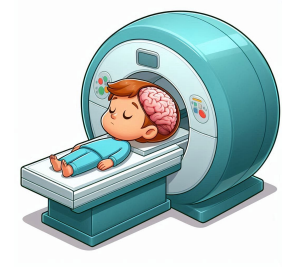
1. So first, let's start with how these challenges are tackled

Source of fMRI Signal: BOLD Contrast

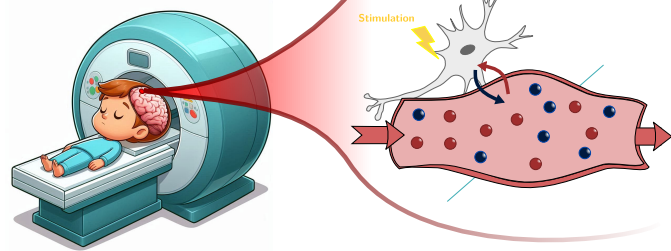


8.1/5 Source of fMRI Signal: BOLD Contrast

1. Let's place ourselves inside an MRI scanner



Source of fMRI Signal: BOLD Contrast



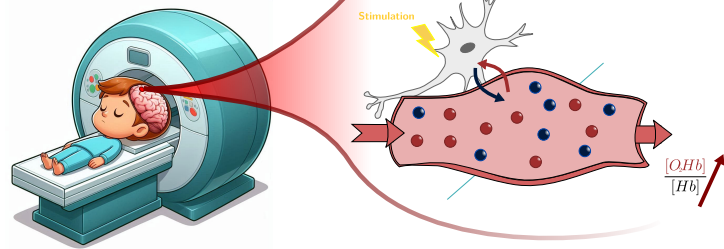
Under a given stimulus:

- Increase in oxygen consumption ($CMRO_2$)
- Increase in cerebral blood flow (CBF)
- Increase in cerebral blood volume (CBV)

8.2/5 Source of fMRI Signal: BOLD Contrast

1. Let's place ourselves inside an MRI scanner
2. When the brain undergoes some activity, it **LOCALLY** increase its consumption of Oxygen as well as the CBF and CBV, through the so-call **NEURO-VASCULAR COUPLING**.

Source of fMRI Signal: BOLD Contrast



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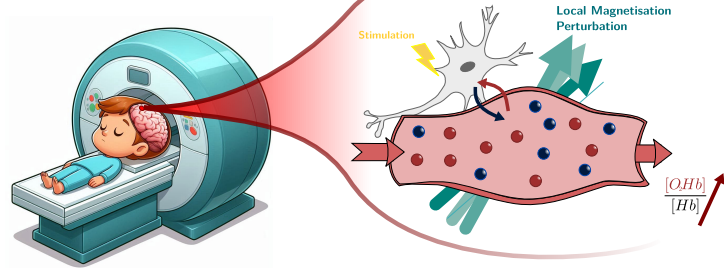
Consequences:

- Ratio $\frac{[O_2Hb]}{[Hb]}$ $\nearrow$

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3. As a consequence, the ratio of Oxyhemoglobin over Deoxyhemoglobin increases

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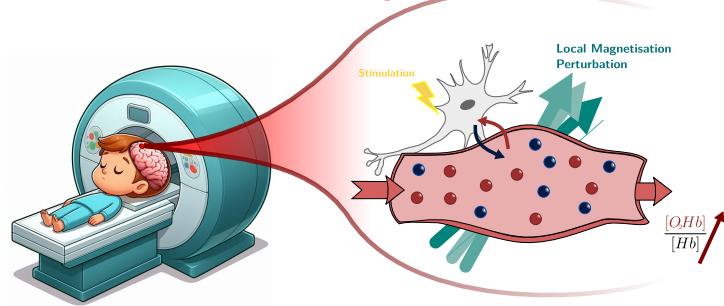
Consequences:

- Ratio $\frac{[O_2Hb]}{[Hb]}$ $\nearrow$
- Local change in magnetic properties of the blood (T_2^* $\nearrow$)

8.4/5 Source of fMRI Signal: BOLD Contrast

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4. And this **INDUCE** a **LOCAL CHANGE** of the T_2^* Parameter, that an MRI scanner can witness as it **LOCALLY** Disturb the Magnetic Field.

Source of fMRI Signal: BOLD Contrast

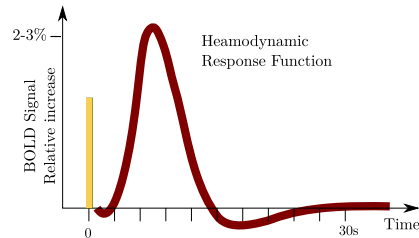


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Consequences:

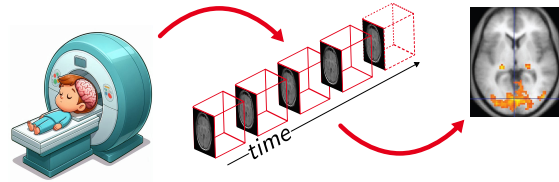
- Ratio $\frac{[O_2Hb]}{[Hb]}$ $\nearrow$
- Local change in magnetic properties of the blood (T_2^* $\nearrow$)
- **Blood Oxygen Level Dependent Contrast (BOLD)**



8.5/5 Source of fMRI Signal: BOLD Contrast

1. Let's place ourselves inside an MRI scanner
2. When the brain undergoes some activity, it **LOCALLY** increase its consumption of Oxygen as well as the CBF and CBV, through the so-call **NEURO-VASCULAR COUPLING**.
3. As a consequence, the ratio of Oxyhemoglobin over Deoxyhemoglobin increases
4. And this **INDUCE** a **LOCAL CHANGE** of the T_2^* Parameter, that an MRI scanner can witness as it **LOCALLY** Disturb the Magnetic Field.
5. Overall, we can witness the cerebral activity through the so-call BOLD Contrast, which manifest itself as a transient increase of a couple of percent in the MR Images. The way the BOLD signal evolved over time after a stimulus is called the Hemodynamic Response Function.

A journey between physics & applied mathematics



9.1/6 A journey between physics & applied mathematics

1. functional MRI extracts the BOLD signal, as a proxy Cerebral activity from a sequence of volume acquired using a MRI Machine.

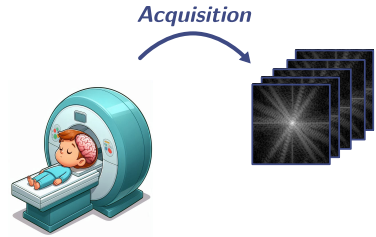
A journey between physics & applied mathematics



9.2/6 A journey between physics & applied mathematics

1. functional MRI extracts the BOLD signal, as a proxy Cerebral activity from a sequence of volume acquired using a MRI Machine.
2. However Extracting the Cerebral activity from the fMRI signal is in fact a long journey

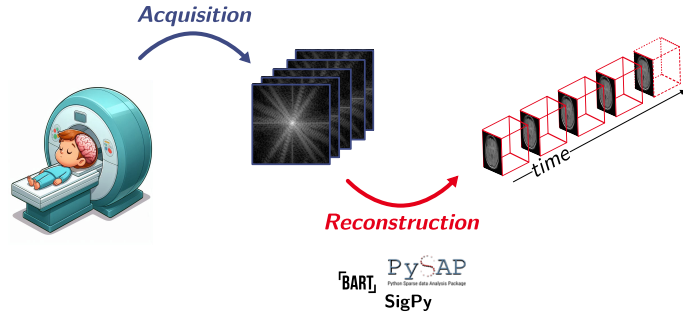
A journey between physics & applied mathematics



9.3/6 A journey between physics & applied mathematics

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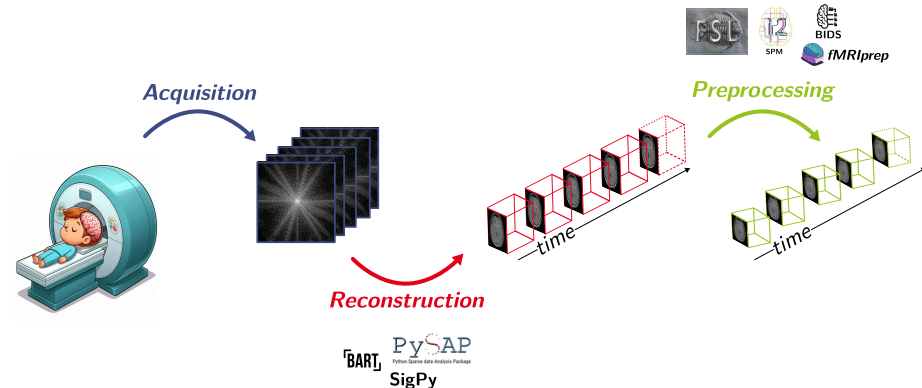
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9.4/6 A journey between physics & applied mathematics

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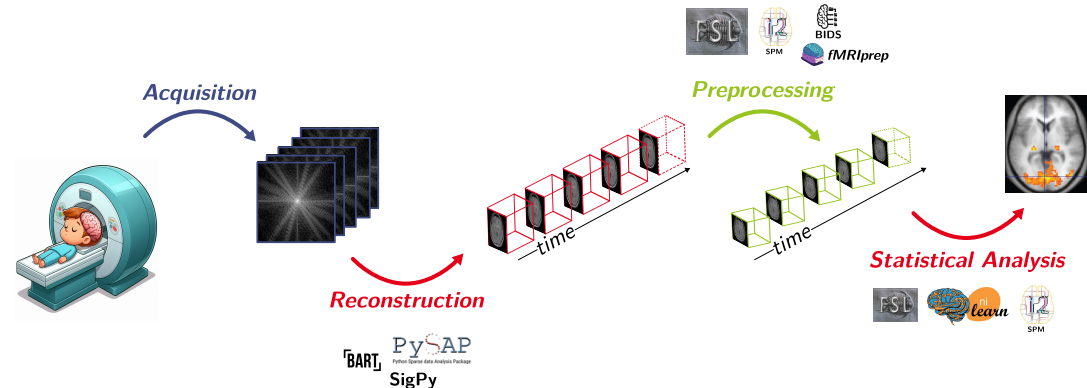
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9.5/6 A journey between physics & applied mathematics

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A journey between physics & applied mathematics



9.6/6 A journey between physics & applied mathematics

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5. However the data needs to be further PREPROCESSED
6. Before it can finally undergo proper statistical ANALYSIS to extract the relevant EVOKED BRAIN ACTIVITY.

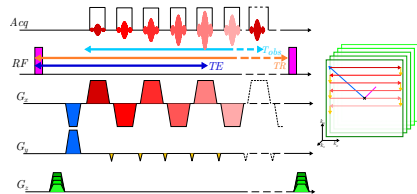
Now let's see how each step in this journey is used to tackle the Challenges of fMRI.



10.1/6 Acquisition

1. The first step of fMRI data processing is the acquisition of the raw data.

Acquisition

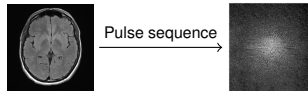
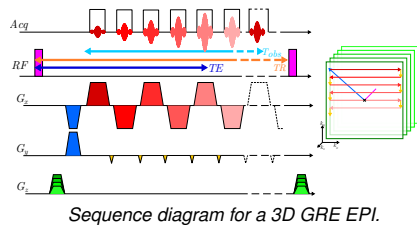


Sequence diagram for a 3D GRE EPI.

10.2/6 Acquisition

1. The first step of fMRI data processing is the acquisition of the raw data.
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For instance, here is the pulse sequence of the most common fMRI sequence: the EPI.
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However, the signal received is not directly the image we are looking for, but a set of complex numbers representing spatial frequencies, known as k-space.

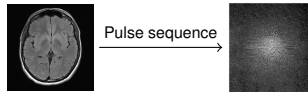
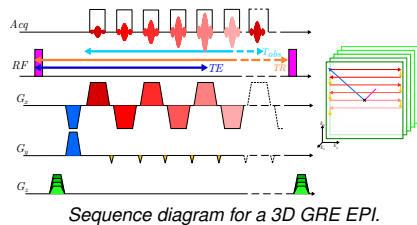
Acquisition



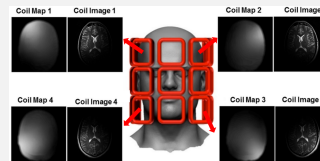
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Acquisition



Acceleration Strategies

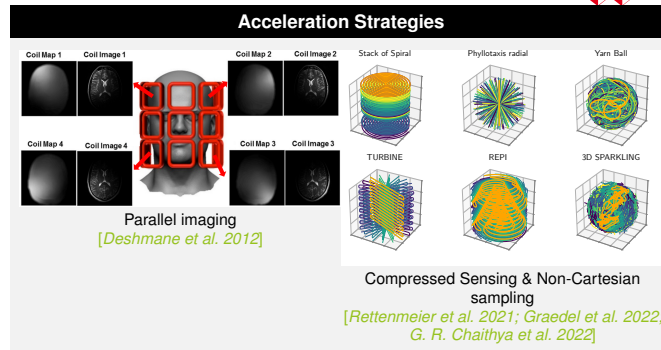
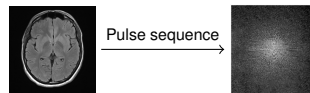
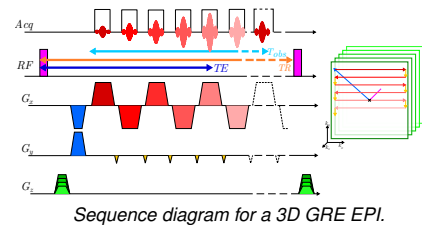


Parallel imaging
[Deshmane et al. 2012]

10.4/6 Acquisition

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However, the signal received is not directly the image we are looking for, but a set of complex numbers representing spatial frequencies, known as k-space.
3. Acquiring the signal fully is slow, and limits the temporal and spatial resolution.
To accelerate the acquisition, two major method exists: PARALLEL IMAGING and NON-CARTESIAN SAMPLING.

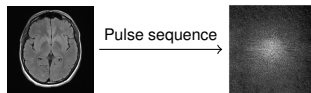
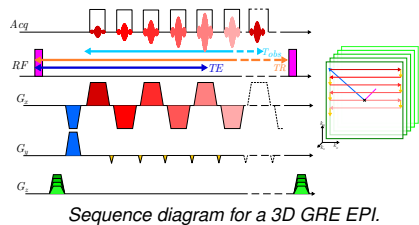
Acquisition



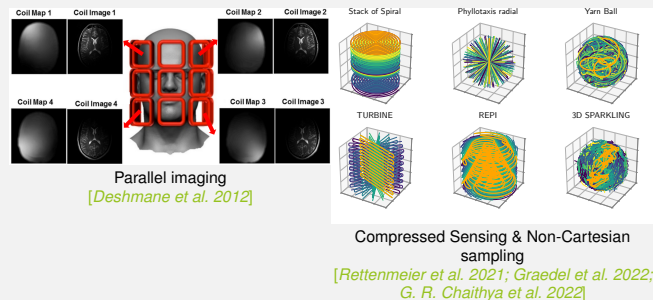
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4. NON CARTESIAN gives extra freedom in how the k-space is covered, but also requires more computations, with Compressed Sensing reconstruction

Acquisition



Acceleration Strategies



🎯 **Resolution:** T_2^* decay limits acquisition window

✗ Compromise on where to sample frequencies.

✓ *In this work:*

- Compressed sensing
- non-Cartesian sampling
- Parallel imaging

But ...

10.6/6 Acquisition

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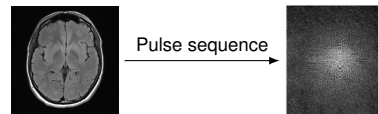
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4. NON CARTESIAN gives extra freedom in how the k-space is covered, but also requires more computations, with Compressed Sensing reconstruction
5. To aim for high resolution, we will use both PI and NC, but this has impact of on the reconstruction.

Reconstruction

- Raw data is encoded in spatial Fourier domain



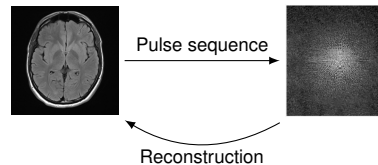
11.1/9 Reconstruction

1. The second step of fMRI data processing is the reconstruction of the raw data into a sequence of 3D images.

Reconstruction

- Raw data is encoded in spatial Fourier domain
- ✗ We want the image x_t :

$$y_{t,\ell} = \mathcal{F}_t \mathcal{S}_\ell x_t + n_{t,\ell}$$



11.2/9 Reconstruction

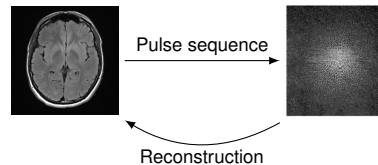
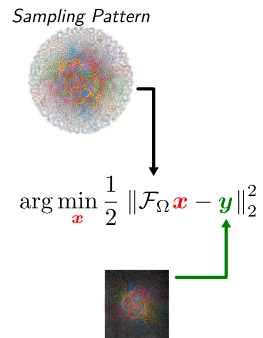
1. The second step of fMRI data processing is the reconstruction of the raw data into a sequence of 3D images.
2. The raw data is encoded in the spatial Fourier domain, and the image is retrieved by solving the inverse problem.

Reconstruction

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- ✗ We want the image x_t :

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- “Solving the Inverse Problem”
- Under-sampling ill-posed problem



11.3/9 Reconstruction

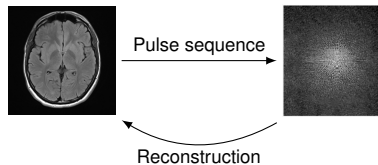
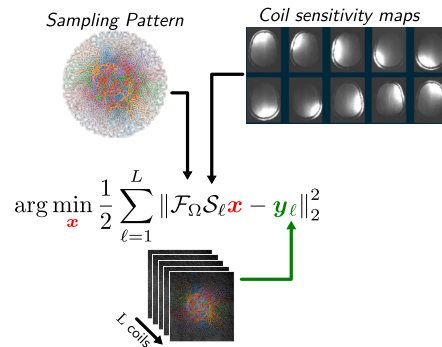
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Reconstruction

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- “Solving the Inverse Problem”
- Under-sampling ill-posed problem
 - Bring all informations



11.4/9 Reconstruction

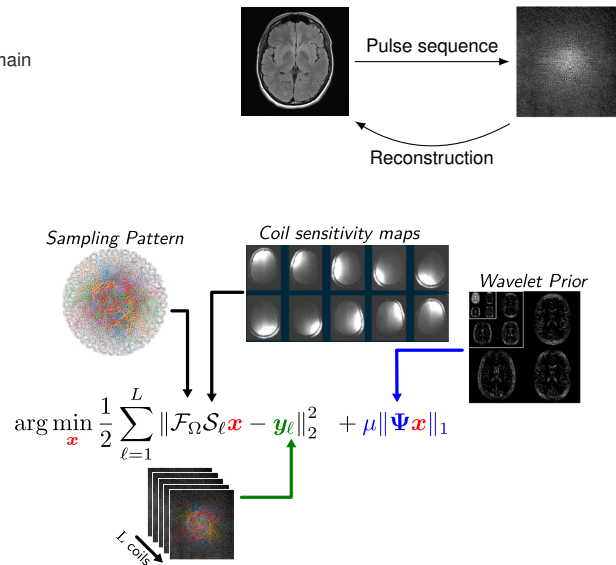
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4. To solve this, we need to bring all the information back, like parallel imaging

Reconstruction

- Raw data is encoded in spatial Fourier domain
- ✗ We want the image $\mathbf{x}_t$:

$$\mathbf{y}_{t,\ell} = \mathcal{F}_t \mathcal{S}_\ell \mathbf{x}_t + \mathbf{n}_{t,\ell}$$

- “Solving the Inverse Problem”
- Under-sampling ill-posed problem
 - Bring all informations
 - Add regularization



11.5/9 Reconstruction

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5. But we can also add regularization to the problem, to make it more stable.
There is a wide variety of prior available, like wavelet, low-rank+sparse, etc.

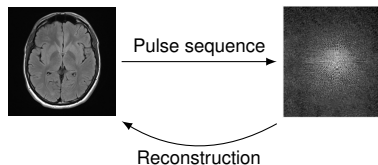
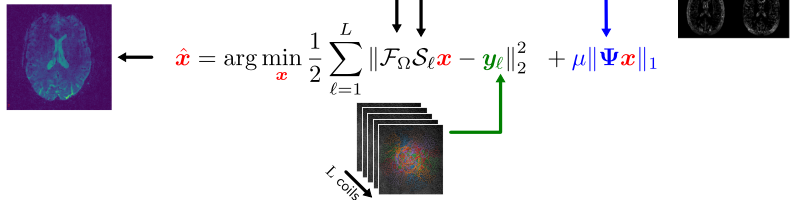
Reconstruction

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- "Solving the Inverse Problem"
- Under-sampling ill-posed problem
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[Lustig et al. 2008; Lin and Fessler 2019; Graedel et al. 2022]



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- Finally we can solve the inverse problem using an optimization algorithm to find the image.

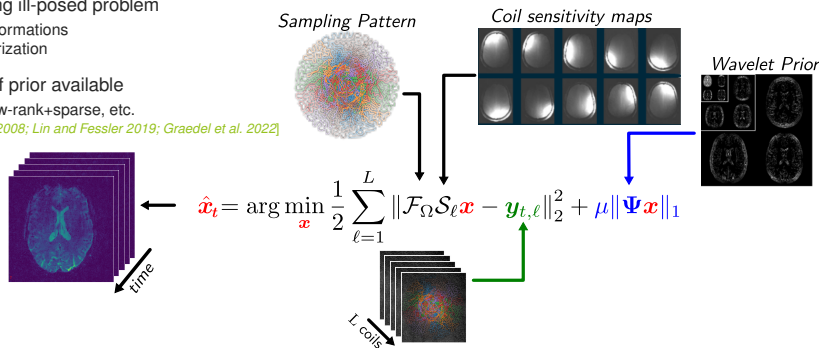
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[Lustig et al. 2008; Lin and Fessler 2019; Graedel et al. 2022]



11.7/9 Reconstruction

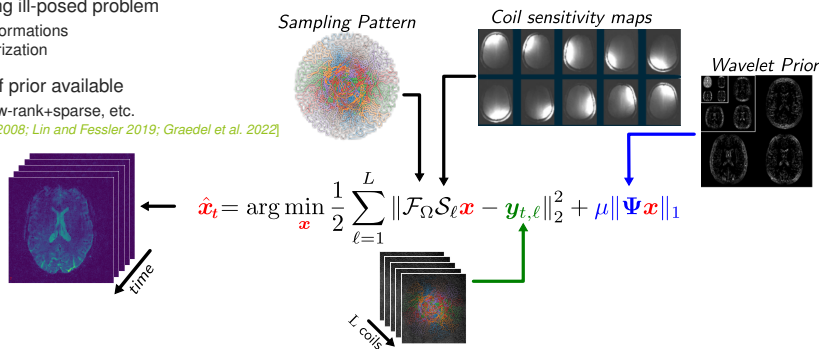
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- Finally we can solve the inverse problem using an optimization algorithm to find the image.
- This must be done for each time frame, to get the full sequence of images.

Reconstruction

- Raw data is encoded in spatial Fourier domain
- ✗ We want the image $\mathbf{x}_t$:

$$\mathbf{y}_{t,\ell} = \mathcal{F}_t \mathcal{S}_\ell \mathbf{x}_t + \mathbf{n}_{t,\ell}$$

- “Solving the Inverse Problem”
- Under-sampling ill-posed problem
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[Lustig et al. 2008; Lin and Fessler 2019; Graedel et al. 2022]



 **Resolution:** High dimension data

11.8/9 Reconstruction

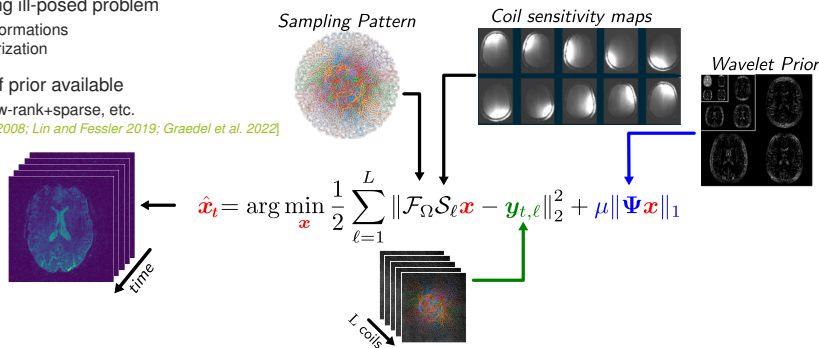
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7. This must be done for each time frame, to get the full sequence of images.
8. The reconstruction is crucial to get high resolution images, but challenging due to the high dimensionality of the data.

Reconstruction

- Raw data is encoded in spatial Fourier domain
- We want the image x_t :

$$y_{t,\ell} = \mathcal{F}_t \mathcal{S}_\ell x_t + n_{t,\ell}$$

- “Solving the Inverse Problem”
 - Under-sampling ill-posed problem
 - Bring all informations
 - Add regularization
 - Wide variety of prior available
 - Wavelet, low-rank+sparse, etc.
- [Lustig et al. 2008; Lin and Fessler 2019; Graedel et al. 2022]



Resolution: High dimension data

Quality: Regularization and prior

Does the reconstruction invent or forget brain activity?

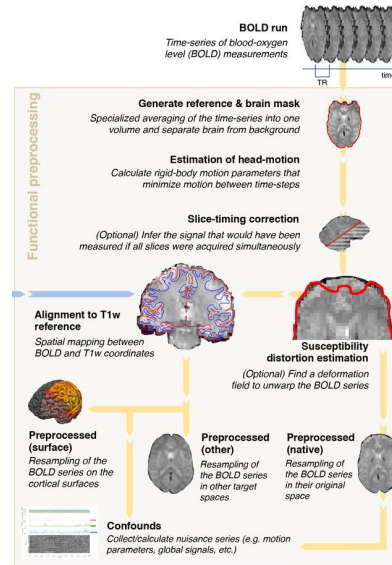
11.9/9 Reconstruction

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- Finally we can solve the inverse problem using an optimization algorithm to find the image.
- This must be done for each time frame, to get the full sequence of images.
- The reconstruction is crucial to get high resolution images, but challenging due to the high dimensionality of the data.
- The reconstruction can also affect the quality of the images, by introducing artifacts or removing brain activity.

Image Preprocessing

- Reconstruction does not compensate all issues
- 🎯 Quality

🎯 Reproducibility



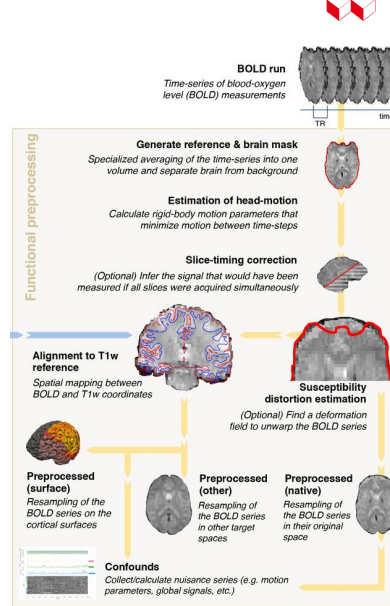
fMRIprep workflow [Esteban et al. 2019]

12.1/7 Image Preprocessing

1. The third step of fMRI data processing is the preprocessing of the images. The reconstruction does not compensate all issues, and the images need to be preprocessed before analysis.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion



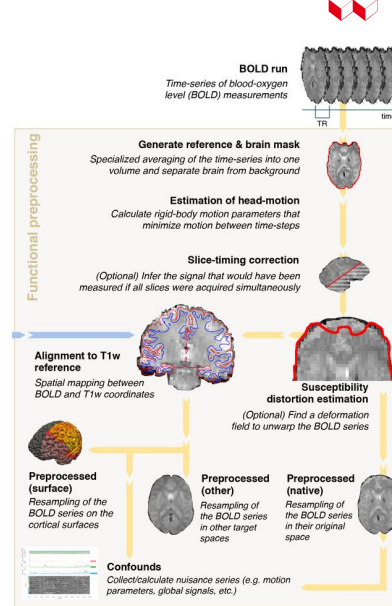
fMRIprep workflow [Esteban et al. 2019]

12.2/7 Image Preprocessing

1. The third step of fMRI data processing is the preprocessing of the images. The reconstruction does not compensate all issues, and the images need to be preprocessed before analysis.
2. The first issue is motion, which can create artifacts in the images.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion
- Field inhomogeneities



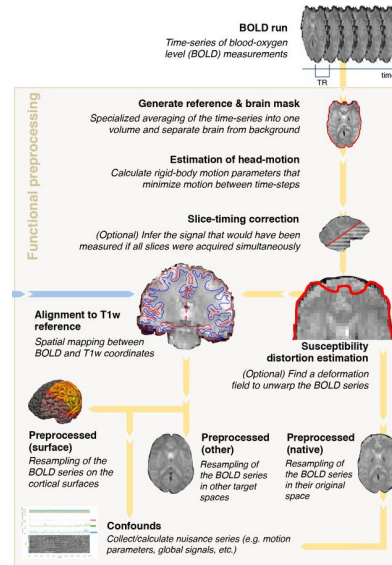
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12.3/7 Image Preprocessing

1. The third step of fMRI data processing is the preprocessing of the images. The reconstruction does not compensate all issues, and the images need to be preprocessed before analysis.
2. The first issue is motion, which can create artifacts in the images.
3. The second issue is field inhomogeneities, which can create geometric distortions in the images.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion
- Field inhomogeneities
- Variability between subjects



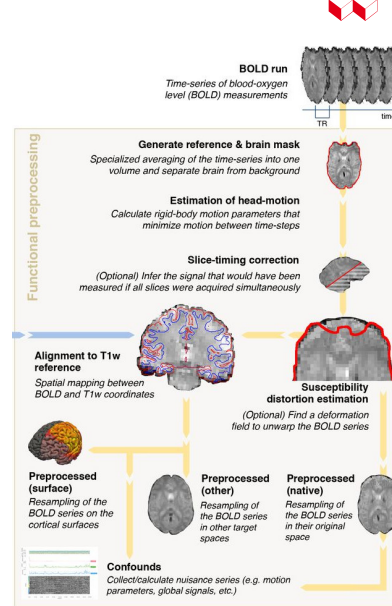
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4. The third issue is the variability between subjects, which can make it difficult to compare images.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion
→ Realign images in the series
- Field inhomogeneities
- Variability between subjects



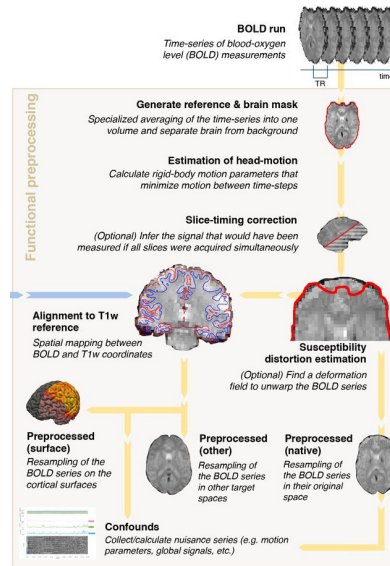
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4. The third issue is the variability between subjects, which can make it difficult to compare images.
5. To correct for motion, the images in the series are realigned.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion
→ Realign images in the series
- Field inhomogeneities
→ Geometric distortion (EPI, TOPUP)
- Variability between subjects



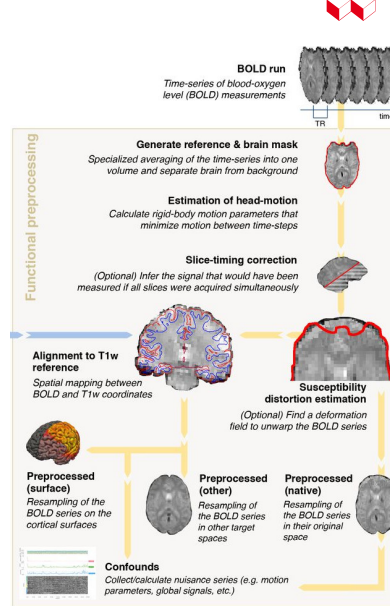
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4. The third issue is the variability between subjects, which can make it difficult to compare images.
5. To correct for motion, the images in the series are realigned.
6. To correct for field inhomogeneities, the images are corrected for geometric distortion.

Image Preprocessing

- Reconstruction does not compensate all issues  **Quality**  **Reproducibility**
- Motion
 - Realign images in the series
- Field inhomogeneities
 - Geometric distortion (EPI, TOPUP)
- Variability between subjects
 - Projection to a template (MNI)



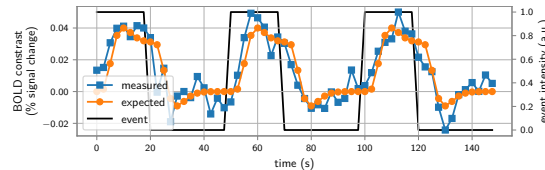
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4. The third issue is the variability between subjects, which can make it difficult to compare images.
5. To correct for motion, the images in the series are realigned.
6. To correct for field inhomogeneities, the images are corrected for geometric distortion.
7. To correct for variability between subjects, the images are projected to a template. This workflow is typically done using a standardized pipeline, like fMRIprep.

Statistical Analysis

- Task-based or resting-state analysis
 - brain mapping, decoding, functional connectivity.



13.1/4 Statistical Analysis

1. Once the data has been acquired, reconstructed, and preprocessed, it can finally be analysed using statistical procedures.

Statistical Analysis

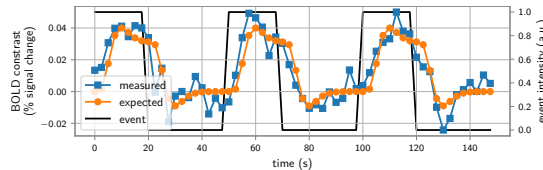
- Task-based or resting-state analysis
 - brain mapping, decoding, functional connectivity.

🎯 Statistical analysis
use a General Linear Model (GLM)

$$\mathbf{y} = \mathbf{X} \boldsymbol{\beta} + \boldsymbol{\epsilon}$$

Voxel time series (points to $\mathbf{y}$)
Design Matrix (points to $\mathbf{X}$)
Effect size (points to $\boldsymbol{\beta}$)
Noise (Gaussian) (points to $\boldsymbol{\epsilon}$)

Hypothesis testing $H_0 : \mathbf{c}^\top \boldsymbol{\beta} = 0$



13.2/4 Statistical Analysis

1. Once the data has been acquired, reconstructed, and preprocessed, it can finally be analysed using statistical procedures.
2. The most common method for analysing fMRI data is the General Linear Model (GLM), which is used to extract the effect of a stimulus on the brain. To validate the presence of an effect, we try to reject the null hypothesis.

Statistical Analysis

■ Task-based or resting-state analysis

■ brain mapping, decoding, functional connectivity.

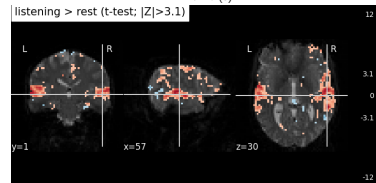
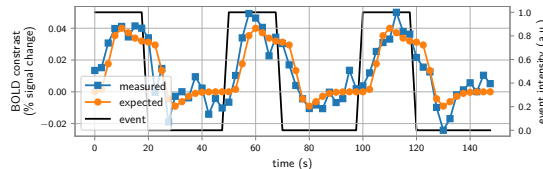
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🎯 p -values correction for multiple comparisons



[Pinho et al. 2020; Mensch et al. 2021]

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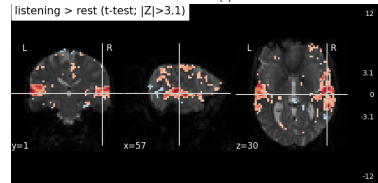
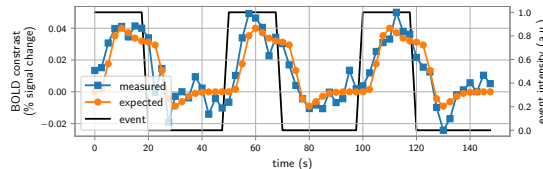
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🎯 Inter- and intra-subject variability

🎯 loss of specificities and individual characteristics



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4. The analysis can be affected by inter- and intra-subject variability, which can lead to a loss of specificity and individual characteristics.

Summary

- ✓ fMRI is the go-to modality to explore the brain in action.



14.1/7 Summary

1. In summary, fMRI is the go-to modality to explore the brain in action.

Summary

- ✓ fMRI is the go-to modality to explore the brain in action.
- ✗ The underlying physics and noise sources of fMRI create 3 challenges



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14.5/7 Summary

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5. The third challenge is about the quality, and reconstructing fMRI images should be the solid ground on which statistical analysis is performed.

Summary

✓ fMRI is the go-to modality to explore the brain in action.

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 **Resolution** limited by MR physics and acquisition noise

 **Reproducibility** Intra-, inter-subject variability, habituation, physiological noises

 **Quality** Reconstructing fMRI images should be the solid ground on which statistical analysis is performed.

Acquisition and **reconstruction** steps are intricate, difficult, and crucial in the fMRI workflow.

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Acquisition and **reconstruction** steps are intricate, difficult, and crucial in the fMRI workflow.

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14.7/7 Summary

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1



Image denoising to boost statistical performances

P.-A. Comby, Z. Amor, A. Vignaud, and P. Ciuciu (Apr. 18, 2023). "Denoising of FMRI Volumes Using Local Low Rank Methods". In: ISBI 2023 - International Symposium on Biomedical Imaging



Quality



Resolution



15.1/1

1. In this part we will look in how an extra step in the preprocessing after the reconstruction could help us getting good statistical score at despites a high spatial resolution

Context

- Denoising fMRI images is not novel
[Kay et al. 2013; Bernier et al. 2014; Bhushan et al. 2016; Zaroubi and Goelman 2000]
- At UHF and high spatial resolution noise is mostly thermal (Gaussian) *[Christina Triantafyllou et al. 2011; Bianciardi et al. 2009]*
- ✗ Smoothing incompatible with



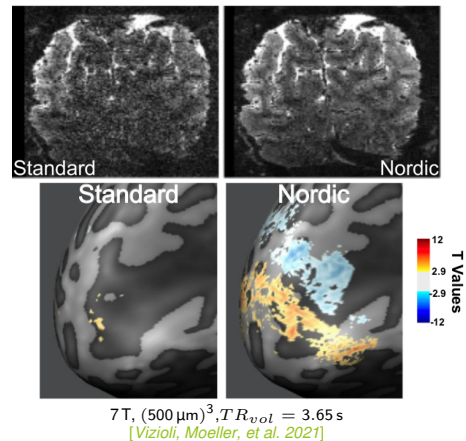
Resolution

16.1/2 Context

1. The denoising of fMRI images is not a new topic, and has been addressed in the past. However, at UHF, the noise is mostly thermal, and smoothing is not an option.

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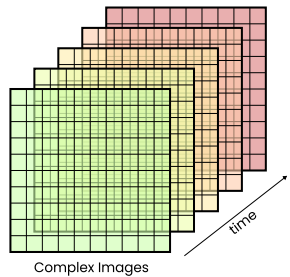
1. The denoising of fMRI images is not a new topic, and has been addressed in the past. However, at UHF, the noise is mostly thermal, and smoothing is not an option.
2. Here is an example of the seminal work of NORDIC, using a SO CALLED LLR prior, applied to 7 Tesla fMRI data. Now, we are going to see in greater details how this prior can be used to boost the statistical performances of fMRI data.

Local low rank denoising

$$\mathbf{Y} = \mathbf{X} + \mathbf{Z}$$

$\mathbf{Y}$: observed fMRI Images
 $\mathbf{X}$: Desired signal $\in \mathbb{C}^{N_{xyz} \times N_t}$
 $\mathbf{Z}$: Thermal noise $\sim \mathcal{N}(0, \Sigma)$

■ $N_t \sim 10^2, N_{xyz} \sim 10^7$



17.1/9 Local low rank denoising

1. If we consider the sequence of fMRI Images, at UHF, we can model the data as polluted by Gaussian Noise

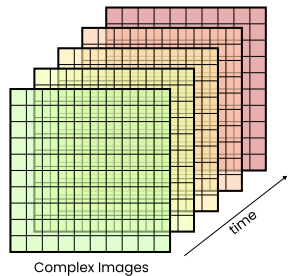
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$$\mathbf{Y} = \mathbf{X} + \mathbf{Z}$$

observed fMRI Images $\uparrow$ $\uparrow$ Thermal noise $\sim \mathcal{N}(0, \Sigma)$
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- $N_t \sim 10^2, N_{xyz} \sim 10^7$
- Low-rank prior (data does not change much over time)

$$\hat{\mathbf{X}} = \arg \min_{\mathbf{X}} \frac{1}{2} \|\mathbf{Y} - \mathbf{X}\|_2^2 + \mu \|\mathbf{X}\|_*$$



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Local low rank denoising

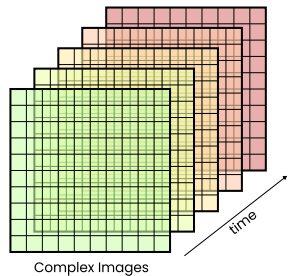
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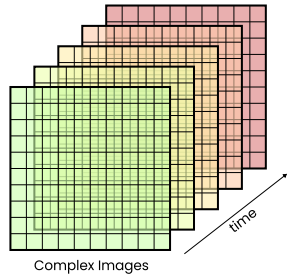
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- ✗ Degrees of freedom ($\frac{N_{xyz}}{N_t} \simeq 10^5$) & memory requirements



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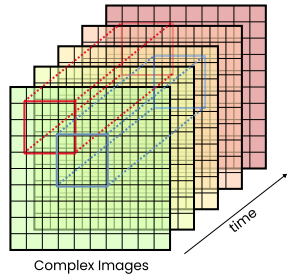
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- ✓ Use a local low-rank (LLR) approach

$$\mathbf{Y}_{[u]} = \mathbf{X}_{[u]} + \mathcal{N}(0, \sigma_{[u]})$$



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Local low rank denoising

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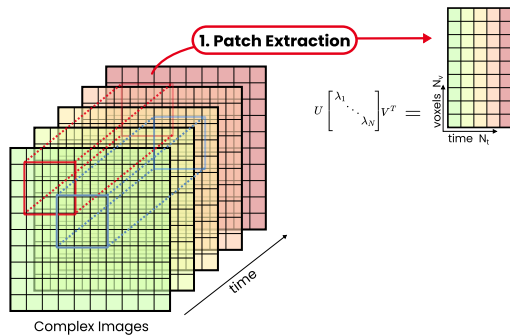
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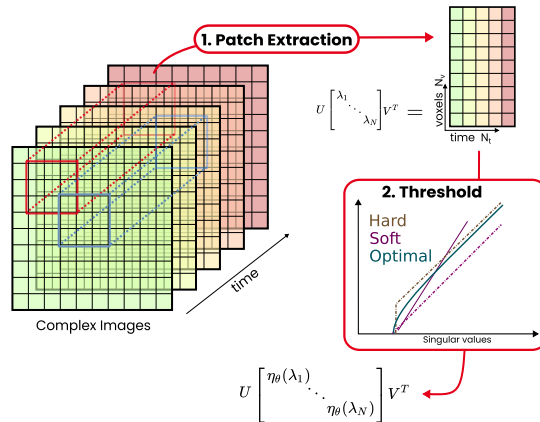
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6. First the patch are extracted and unravelled in the so call CASORATTI matrix
7. Then Patch are processed and denoised by thresholding their SV Decomposition

Local low rank denoising

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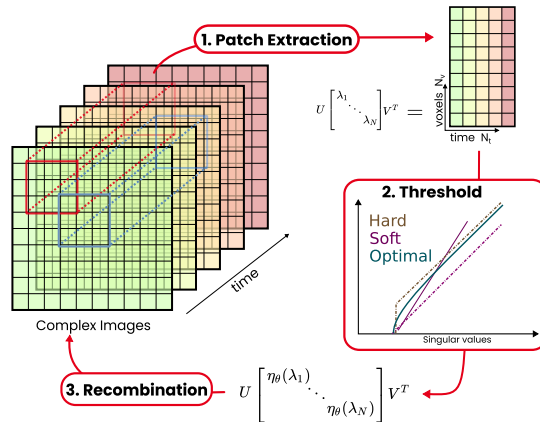
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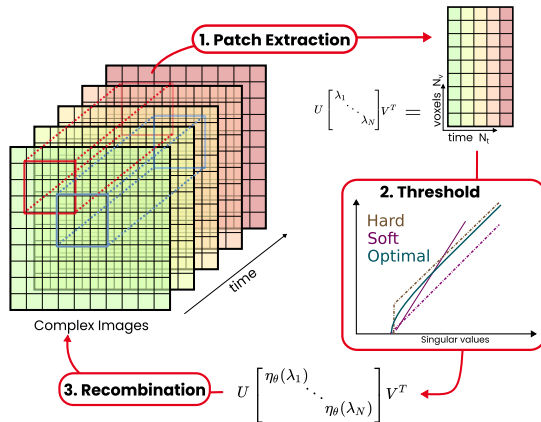
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$$\mathbf{Y}_{[u]} = \mathbf{X}_{[u]} + \mathcal{N}(0, \sigma_{[u]})$$

Challenges

- What is the best choice of the threshold / thresholding function?
- Order of operations may matter
- Efficient implementation for fMRI data



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8. Finally, The patches are recombined to produce the denoised Serie
9. However, there are some challenges to take upon:
 - What is the best choice for the threshold of the singular values
 - Where should the denoising step be perform in the Preprocessing
 - This is still very memory demanding

Threshold choice

Singular Value Thresholding

- Solution of $\hat{\mathbf{X}} = \arg \min_{\mathbf{X}} \frac{1}{2} \|\mathbf{Y} - \mathbf{X}\|_2^2 + \mu \|\mathbf{X}\|_*$
- SVD: $\mathbf{Y} = \mathbf{U} \mathbf{S} \mathbf{V}^\top = \sum_{i=1}^N \lambda_i \mathbf{u}_i \mathbf{v}_i$
- nuclear norm: $\|\mathbf{X}\|_* = \sum_{i=1}^N |\lambda_i|$
- $\hat{\mathbf{X}} = \sum_{i=1}^N \eta(\lambda_i) \mathbf{u}_i \mathbf{v}_i$

18.1/7 Threshold choice

1. The Low rank prior is enforced by solving the constrained nuclear norm problem.
In practice we use the SVD of the noisy data and threshold its singular values

Threshold choice

Singular Value Thresholding

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Marčenko-Pastur law

[Marčenko and Pastur 1967]

- For $\mathbf{X}_N \in \mathbb{C}^{N \times \beta N} \sim \mathcal{N}(0, \sigma)$
- $\beta_{\pm} = \sigma(1 \pm \sqrt{\beta})^2$ and $N \rightarrow \infty$

18.2/7 Threshold choice

1. The Low rank prior is enforced by solving the constrained nuclear norm problem. In practice we use the SVD of the noisy data and threshold its singular values
2. For RANDOM, we can get insights on the singular values distribution using the MP LAW

Threshold choice

Singular Value Thresholding

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[Marčenko and Pastur 1967]

- For $\mathbf{X}_N \in \mathbb{C}^{N \times \beta N} \sim \mathcal{N}(0, \sigma)$
- $\beta_{\pm} = \sigma(1 \pm \sqrt{\beta})^2$ and $N \rightarrow \infty$
- Eigenvalues $\lambda(\mathbf{Y}_N = \frac{1}{N} \mathbf{X}_N^\top \mathbf{X}_N)$ follow:

$$p(\lambda|\sigma, \beta) = \frac{\sqrt{(\beta_+ - \lambda)(\lambda - \beta_-)}}{2\pi\beta\lambda\sigma} \mathbf{1}_{\beta_- \leq \lambda \leq \beta_+}$$

- $\mathbb{E}(\lambda) = \sigma$

18.3/7 Threshold choice

1. The Low rank prior is enforced by solving the constrained nuclear norm problem. In practice we use the SVD of the noisy data and threshold its singular values
2. For RANDOM, we can get insights on the singular values distribution using the MP LAW
3. Which is an ASYMPTOTICAL Results

Threshold choice

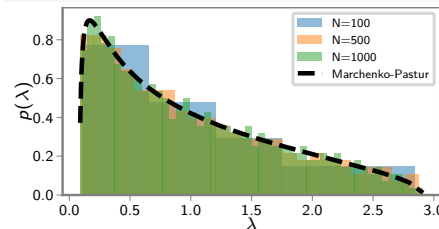
Singular Value Thresholding

- Solution of $\hat{\mathbf{X}} = \arg \min_{\mathbf{X}} \frac{1}{2} \|\mathbf{Y} - \mathbf{X}\|_2^2 + \mu \|\mathbf{X}\|_*$
- SVD: $\mathbf{Y} = \mathbf{U} \mathbf{S} \mathbf{V}^\top = \sum_{i=1}^N \lambda_i \mathbf{u}_i \mathbf{v}_i$
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Marčenko-Pastur law

[Marčenko and Pastur 1967]

- For $\mathbf{X}_N \in \mathbb{C}^{N \times \beta N} \sim \mathcal{N}(0, \sigma)$
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- $\mathbb{E}(\lambda) = \sigma$



18.4/7 Threshold choice

1. The Low rank prior is enforced by solving the constrained nuclear norm problem. In practice we use the SVD of the noisy data and threshold its singular values
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NORDIC (fMRI) [Vizioli, Moeller, et al. 2021]

- Normalization of variance
- Empirical threshold θ
Largest singular value of a noise-only patch
- $\eta(\lambda) = \lambda \mathbf{1}_{\lambda > \theta}$

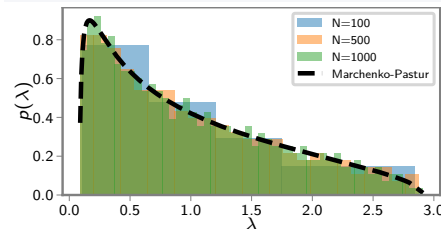
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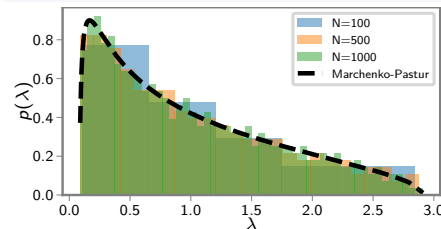
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Threshold choice

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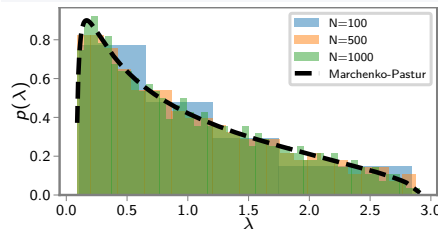
Hybrid PCA [Neto Henriques et al. 2022]

MP-PCA [Manjón et al. 2013]

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6. The SECOND is OPTIMAL THRESHOLD which leverages more RESULTS from MP Law and use a more COMPLICATED Threshold function
7. Let's ALSO mention TWO other methods used for fMRI Denoising with local lowrank Method. They mainly differ in how the noise variance is estimated or provided externally from the data, and were first proposed in the context of DIFFUSION MRI.

Application to fMRI

Methodology

- Apply denoising before or after motion correction (realignment)?



19.1/5 Application to fMRI

1. Now let's Consider the application of LLR in the FMRI PIPELINE
First, WHERE the DENOISING step should takeplace, typically before or AFTER motion correction.

Application to fMRI

Methodology

- Apply denoising before or after motion correction (realignment)?
- Consider complex-valued or magnitude images?



19.2/5 Application to fMRI

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2. Second, should we apply the denoising of the Complex Valued data, more close to the gaussian noise model hypothesis or does MAGNITUDE images, MORE AVAILABLE in practice SUFFICE.

Application to fMRI

Methodology

- Apply denoising before or after motion correction (realignment)?
- Consider complex-valued or magnitude images?
- Select the best denoising methods
 - NORDIC, Hybrid-PCA, MP-PCA, Optimal-Threshold (OT), Hybrid-OT



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- Consider complex-valued or magnitude images?
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Acquisition

- 7Tesla, 3D-EPI (1mm-iso, $TE=20$ ms, $TR_v = 2.4$ s, 120 reps)
- Retinotopy task (2 runs)
- 6 subjects

19.4/5 Application to fMRI

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4. In order to conduct this study we acquired 6 Volunteer undergoing a retinotopic task at 7 Tesla using a 3D-EPI Cartesian setting.

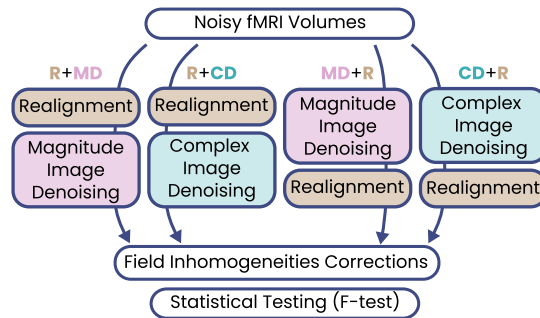
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Reproducibility

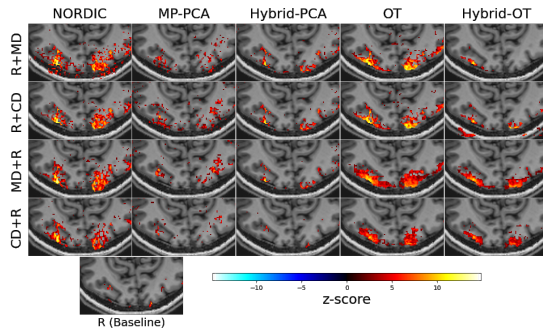
5 denoisers $\times$ 4 combinations $\times$ 6 subjects $\times$ 2 runs = 120 cases

- Open source python package: `patch-denoise`
- Bindings for standard fMRI preprocessing (Nipype)

19.5/5 Application to fMRI

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5. We tested 4 Scenarios for applying the Denoising, before correcting for field inhomogeneities and the statistical Analysis
Here we can see how to try to enforce REPRODUCIBILITY we had to conduct 120 differents experiments.

Results

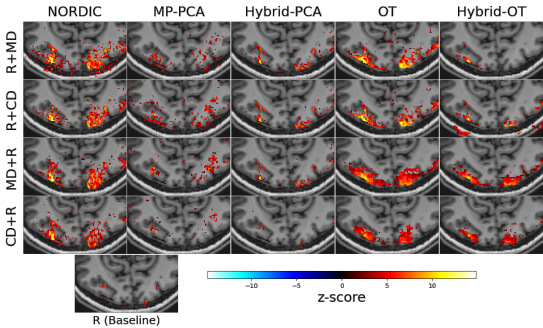


Volunteer # 3, FDR corrected $p < 10^{-3}$ (occipital cortex only)

20.1/3 Results

1. Here on the left we present the results for a single volunteer. Compared to the BASELINE, where only MOTION COMPENSATION is performed, all denoising methods improve the detection of activations, however they present different activations patterns

Results



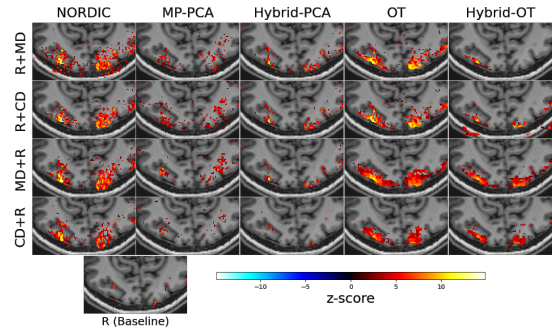
Denoiser	NORDIC	MP-PCA	Hybrid-PCA	OT	Hybrid-OT
R+MD	$\times 3.52$	$\times 6.02$	$\times \mathbf{6.09}$	$\times 3.73$	$\times 0.91$
	$\times 3.64$	$\times 4.92$	$\times \mathbf{4.93}$	$\times 4.33$	$\times 1.00$
R+CD	$\times 0.57$	$\times 2.98$	$\times 3.27$	$\times \mathbf{8.03}$	$\times 5.29$
	$\times 0.55$	$\times 2.70$	$\times 2.91$	$\times \mathbf{5.04}$	$\times 4.01$
MD+R	$\times 3.36$	$\times 6.32$	$\times \mathbf{7.55}$	$\times 3.10$	$\times 1.22$
	$\times 3.48$	$\times 4.77$	$\times \mathbf{6.10}$	$\times 3.19$	$\times 4.90$
CD+R	$\times 2.57$	$\times 5.53$	$\times 4.97$	$\times \mathbf{7.91}$	$\times 5.45$
	$\times 2.59$	$\times 4.39$	$\times 4.27$	$\times \mathbf{6.26}$	$\times 5.00$

Group-level results: Average gain in activation detection.
Whole brain (top) / Occipital cortex (bottom)

20.2/3 Results

1. Here on the left we present the results for a single volunteer. Compared to the BASELINE, where only MOTION COMPENSATION is performed, all denoising methods improve the detection of activations, however they present different activations patterns
2. On a more global picture, we report here the average boost of activation obtained by LLR Denoising.

Results



Denoiser	NORDIC	MP-PCA	Hybrid-PCA	OT	Hybrid-OT
R+MD	× 3.52	× 6.02	× 6.09	× 3.73	× 0.91
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2. On a more global picture, we report here the average boost of activation obtained by LLR Denoising.
3. The Takeaway: DENOISE your UHF Data to avoid compromise on Stats vs Resolution. BEST is OT on CD after Realign. STRONG VARIABILITY BETWEEN METHODS

Takeaway

- ✓ Denoise your UHF fMRI images
- ✓ Best: Optimal Thresholding (OT) on complex images, after motion correction.
- ✗ Variability between methods, getting reference data will is unfeasible.

Interim Summary

 **Resolution:** ✓ Local low-rank methods can remove thermal noise at UHF

21.1/3 Interim Summary

1. LLR Remove THERMAL noise at UHF

Interim Summary

 **Resolution:** ✓ Local low-rank methods can remove thermal noise at UHF

 **Reproducibility:** 🌀 Variability between LLR Methods

21.2/3 Interim Summary

1. LLR Remove THERMAL noise at UHF
2. However Reproducibility is a still a concern , we get strong DISCREPANCY in the results

Interim Summary

 **Resolution:** ✓ Local low-rank methods can remove thermal noise at UHF

 **Reproducibility:** 🌀 Variability between LLR Methods

 **Quality:** ✗ We cannot use denoised data as a ground truth

- Limited to given spatial and temporal resolution
- No flexibility / controlled variability
- No guarantees on activation locations.

21.3/3 Interim Summary

1. LLR Remove THERMAL noise at UHF
2. However Reproducibility is a still a concern , we get strong DISCREPANCY in the results
3. Cannot use DENOISED DATA as REFERENCE, as it brings to much constrains on the experimental setup and no guarantees on true activations.

2. Building a ground truth for fMRI

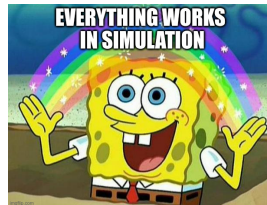
P.-A. Comby, A. Vignaud, and P. Ciuciu (2025). *SNAKE-fMRI: A Modular fMRI Data Simulator from the Space-Time Domain to k-Space and Back*. In revision to Imaging Neuroscience



Quality



Reproducibility



22.1/1

1. In order to get such HIGH QUALITY GROUND TRUTH DATA with REPRODUCIBILITY GUARANTEES , we turned to build a proper SIMULATION SETUP

The need for a ground-truth

- 🎯 It is impossible to get the same fMRI experiment results twice
- Noise, habituation effect [*Dehaene-Lambertz et al. 2006*], etc.



23.1/7 The need for a ground-truth

1. Impossible to get same fMRI twice due to inter and intra subject

The need for a ground-truth

- ✖ It is impossible to get the same fMRI experiment results twice
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- ✔ How can we compare two reconstruction results without reference?



23.2/7 The need for a ground-truth

1. Impossible to get same fMRI twice due to inter and intra subject
2. COMPARE Reconstruction without ground-truth ? Do the reconstruction HALLUCINATE cerebral activity ?

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4. Furthermore, acquisition and reconstruction could be optimized together

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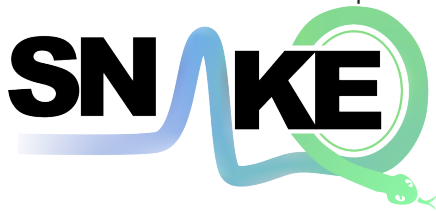
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5. To try to answer these questions, we proposed to use a controlled simulation environment, name SNAKE

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 - Our proposal:

Simulator from **Neuro-Activation** to **K-space Evaluation**



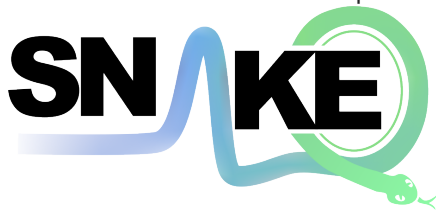
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 - Our proposal:
- ✓ Tackle intra-subject variability ✓ Support for non-Cartesian sampling

Simulator from **Neuro-Activation** to **K-space** **E**valuation



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Existing simulators

MRI Simulator	Simulator Name	Source	API	Sim. Domain	Required External Data	Interface	Reconstr.	Ecosystem
	The Virtual Brain [<i>Sanz Leon et al. 2013</i>]	GPL-3.0		Image		GUI/script	N/A	N/A
	Jemris [<i>Stöcker et al. 2010</i>]	GPL-2.0		Bloch		GUI	ISMRMD raw data	N/A
	ODIN [<i>Jochimsen et al. 2006</i>]	GPL-2.0		Bloch	Tissue Maps, Sequence	c++/GUI	FFT	OdinReco
	MRILab [<i>Liu et al. 2017</i>]	BSD-2		Bloch	Preset Macros	GUI	FFT Non-Cartesian	GUI Gadgetron
	Bloch-Solver [<i>R. Kose and K. Kose 2017</i>]	Proprietary		Bloch	Tissue Maps,	script	FFT	N/A
	Fabian [<i>Lajous et al. 2022</i>]	BSD-3		Bloch (EPG)	Tissue Maps, Sequence	script	FFT	N/A
	KomaMRI [<i>Castillo-Passi et al. 2023</i>]	MIT		Bloch	Pulseq	GUI	FFT	Pulseq

24.1/3 Existing simulators

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	MRILab [<i>Liu et al. 2017</i>]	BSD-2		Bloch	Pseudo-Magnetic	GUI	FFT Non-Cartesian	GUI Gadgetron
	Bloch-Solver [<i>R. Kose and K. Kose 2017</i>]	Proprietary		Bloch	Tissue Maps,	script	FFT	N/A
	Fabian [<i>Lajous et al. 2022</i>]	GPL-3		Bloch (EPG)	Tissue Maps, Sequence	script	FFT	N/A
fMRI Simulator	KomaMRI [<i>Castillo-Passi et al. 2023</i>]	MIT		Bloch	Pulseq	GUI	FFT	Pulseq
	POSSUM [<i>Drobnjak et al. 2006</i>]	FSL		Bloch	Tissue Maps Sequence, Events	CLI	FFT	FSL
	Neurolib [<i>Cakan et al. 2023</i>]	MIT		Image	Connectivity Matrices	script	N/A	Jupyter
	SimTB [<i>Erhardt et al. 2012</i>]	Open Source		Image	Spatial Maps, Events	GUI	N/A	MATLAB
	NeuRoSim [<i>Welvaert et al. 2011</i>]	GPL-2.0		Image		script	N/A	N/A
	fmriSim [<i>Ellis et al. 2020</i>]	Apache-2.0		Image		script	N/A	Brainiak

Expensive single k-space

24.2/3 Existing simulators

Existing simulators

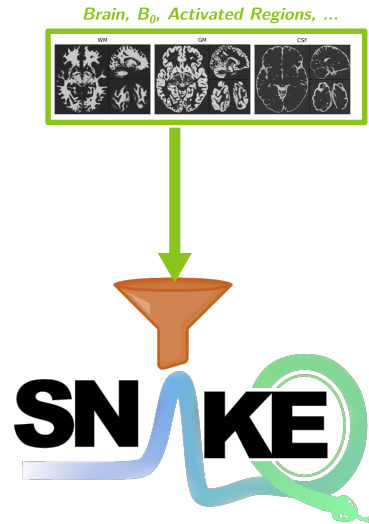
	Simulator Name	Source	API	Sim. Domain	Required External Data	Interface	Reconstr.	Ecosystem
MRI Simulator	The Virtual Brain [<i>Sanz Leon et al. 2013</i>]	GPL-3.0		Image		GUI/script	N/A	N/A
	Jemris [<i>Stöcker et al. 2010</i>]	GPL-2.0		Bloch		GUI	ISMRMD raw data	N/A
	ODIN [<i>Jochimsen et al. 2006</i>]	GPL-2.0		Bloch	Tissue Maps, Sequence	GUI	FFT	OdinReco
	MRILab [<i>Liu et al. 2017</i>]	BSD-2		Bloch	Preset Macros	GUI	FFT Non-Cartesian	GUI Gadgetron
	Bloch-Solver [<i>R. Kose and K. Kose 2017</i>]	Proprietary		Bloch	Tissue Maps,	script	FFT	N/A
	Fabian [<i>Lajous et al. 2022</i>]	GPL-3		Bloch (EPG)	Tissue Maps, Sequence	script	FFT	N/A
fMRI Simulator	KomaMRI [<i>Castillo-Passi et al. 2023</i>]	MIT		Bloch	Pulseq	GUI	FFT	Pulseq
	POSSUM [<i>Drobnjak et al. 2006</i>]	FSL		Bloch	Tissue Maps Sequence, Events	CLI	FFT	FSL
	Neurolib [<i>Cakan et al. 2023</i>]	MIT		Image	Connectivity Matrices	script	N/A	Jupyter
	SimTB [<i>Erhardt et al. 2012</i>]	Open Source		Image	Spatial Maps, Events	GUI	N/A	MATLAB
	NeuRoSim [<i>Welvaert et al. 2011</i>]	GPL-2.0		Image		script	N/A	N/A
	fmriSim [<i>Ellis et al. 2020</i>]	Apache-2.0		Image		script	N/A	Brainiak
	SNAKE-fMRI	MIT		Kspace & Image	Configuration files	script/CLI	Any (4D methods)	Any

Expensive single k-space

Image Only

24.3/3 Existing simulators

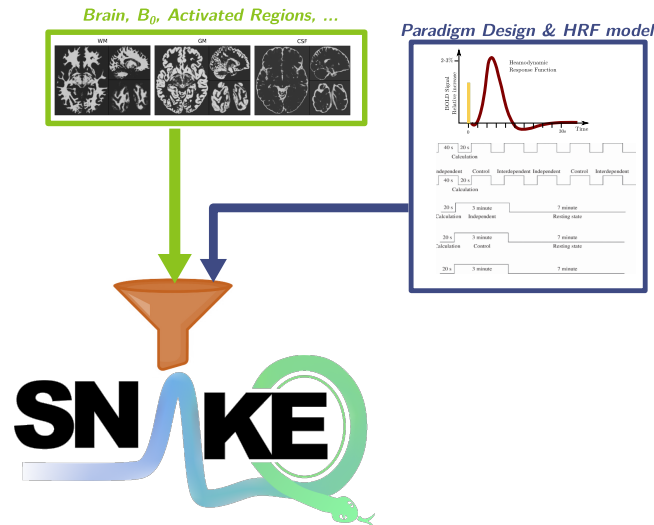
SNAKE: the Big Picture



25.1/6 SNAKE: the Big Picture

1. Here is an overview of the controllable inputs and outputs of SNAKE
Notably, since we fully know how the cerebral activity is added in the simulation, we can validate from end-to-end the fMRI pipeline.

SNAKE: the Big Picture



25.2/6 SNAKE: the Big Picture

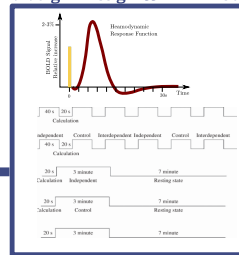
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SNAKE: the Big Picture

Acquisition Setting

Brain, B_0 , Activated Regions, ...

Paradigm Design & HRF model



25.3/6 SNAKE: the Big Picture

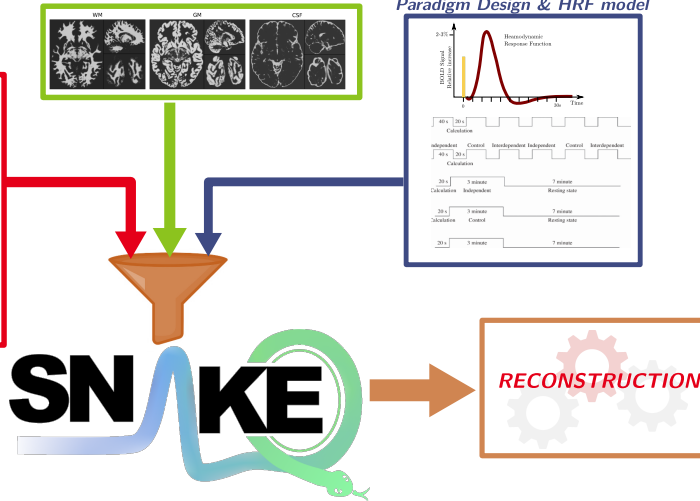
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SNAKE: the Big Picture

Acquisition Setting

Brain, B_0 , Activated Regions, ...

Paradigm Design & HRF model



25.4/6 SNAKE: the Big Picture

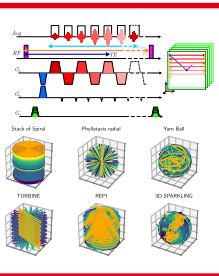
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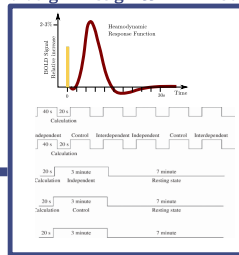
Brain, B_0 , Activated Regions, ...



Acquisition Setting



Paradigm Design & HRF model



SNKE

RECONSTRUCTION

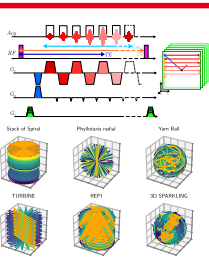
STATISTICAL
ANALYSIS
VALIDATION

25.5/6 SNAKE: the Big Picture

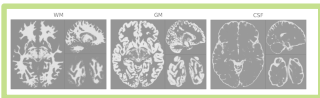
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SNAKE: the Big Picture

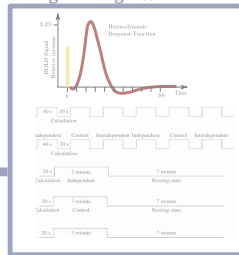
Acquisition Setting



Brain, B_0 , Activated Regions, ...



Paradigm Design & HRF model



SNKE

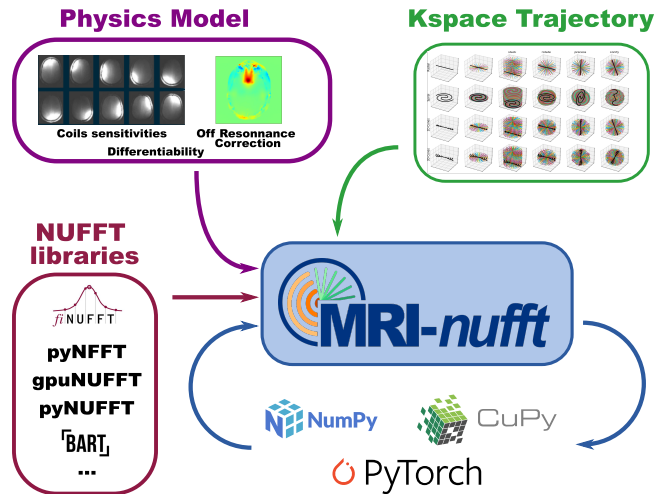
RECONSTRUCTION

STATISTICAL
ANALYSIS
VALIDATION

25.6/6 SNAKE: the Big Picture

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Notably, since we fully know how the cerebral activity is added in the simulation, we can validate from end-to-end the fMRI pipeline.
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MRI-NUFFT: Efficient non-Cartesian Sampling



26.1/1 MRI-NUFFT: Efficient non-Cartesian Sampling

1. Indeed, along the development of SNAKE, I was at the initiative of the development of MRI-NUFFT, to address the **COMPUTATIONAL BOTTLENECK** of Non-Cartesian Sampling of MRI data, done with a Non **UNIFORM** FFT. Wrapped around existing NUFFT library, MRI-NUFFT MRI-NUFFT is now a **CORNER-STONE** on which SNAKE, but also other tool in our team are dependent, Notably it will also be used in the last part of this presentation in a reconstruction setting.

SNAKE modeling choices

MRI Signal Equation

Acquiring a single shot s with the sampling trajectory $\mathbf{k}_s$ in the ℓ -th receiver coil:

$$y_{\ell,s}(t) = \int_{FOV} m(\mathbf{r}, \varphi, \theta) \mathcal{S}_{\ell}(\mathbf{r}) e^{(TE - t)/T_2^*(\mathbf{r})} e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}} d\mathbf{r}$$

27.1/5 SNAKE modeling choices

SNAKE modeling choices

MRI Signal Equation

Acquiring a single shot s with the sampling trajectory $\mathbf{k}_s$ in the ℓ -th receiver coil:

$$y_{\ell,s}(t) = \int_{FOV} m(\mathbf{r}, \varphi, \theta) \mathcal{S}_{\ell}(\mathbf{r}) e^{(TE - t)/T_2^*(\mathbf{r})} e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}} d\mathbf{r}$$

magnetization
contrast

Contrast: Result of the GRE sequence excitation

Dependent on the acquisition parametrization $\theta = (TE, TR, \alpha)$, and the tissue properties $\varphi = (T_1, T_2^*, \rho)$.

$$m(\mathbf{r}, \phi, \theta) = \rho(\mathbf{r}) \sin \alpha \frac{1 - e^{-TR/T_1(\mathbf{r})}}{1 - \cos \alpha e^{-TR/T_1(\mathbf{r})}} e^{-TE/T_2^*(\mathbf{r})}$$

Quantitative values available T_1, T_2^*, ρ for 1.5 T, 3 T and 7 T [Aubert-Broche et al. 2006; Bojorquez et al. 2017]

SNAKE modeling choices

27.3/5 SNAKE modeling choices

MRI Signal Equation

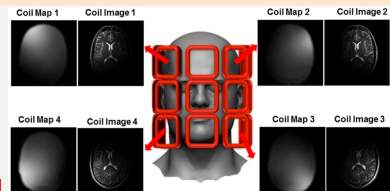
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magnetization contrast

Coil sensitivity maps

Sensitivity Maps: Encode field of view of each coil



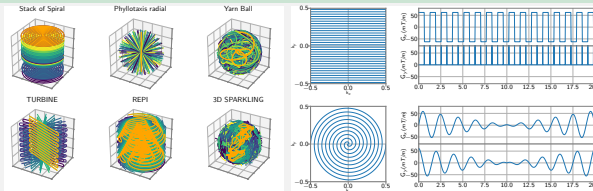
SNAKE modeling choices

MRI Signal Equation

Acquiring a single shot s with the sampling trajectory k_s in the ℓ -th receiver coil:

$$y_{\ell,s}(t) = \int_{FOV} \underbrace{m(\mathbf{r}, \varphi, \theta)}_{\text{magnetization contrast}} \underbrace{S_{\ell}(\mathbf{r})}_{\text{Coil sensitivity maps}} e^{(TE - t)/T_2^*(\mathbf{r})} \underbrace{e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}}}_{\text{Fourier encoding}} d\mathbf{r}$$

Fourier Encoding: Where is the information collected in k-space



SNAKE modeling choices

MRI Signal Equation

Acquiring a single shot s with the sampling trajectory $\mathbf{k}_s$ in the ℓ -th receiver coil:

$$y_{\ell,s}(t) = \int_{FOV} \underbrace{m(\mathbf{r}, \varphi, \theta)}_{\text{magnetization contrast}} \underbrace{\mathcal{S}_{\ell}(\mathbf{r})}_{\text{Coil sensitivity maps}} \underbrace{e^{(TE-t)/T_2^*(\mathbf{r})}}_{Ts \text{ relaxation}} \underbrace{e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}}}_{\text{Fourier encoding}} d\mathbf{r}$$

T_2^* relaxation: Signal decay

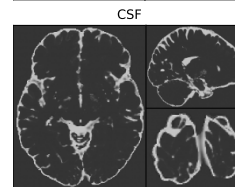
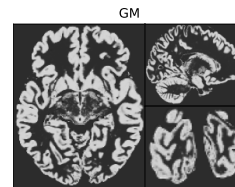
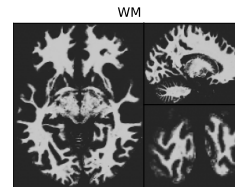
Due to local interaction of the magnetization

27.5/5 SNAKE modeling choices

SNAKE modeling choices

Tissue compartmentation

$$m(\mathbf{r}, \varphi, \theta) e^{(TE - t)/T_2^*} \triangleq \sum_{i=1}^{N_{tis}} w_i(\mathbf{r}) m(\varphi_i, \theta) e^{(TE - t)/T_{2,i}^*}$$



28.1/3 SNAKE modeling choices

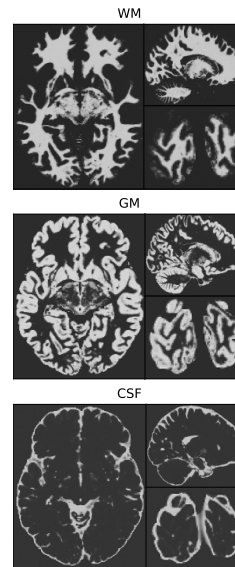
SNAKE modeling choices

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Extended vs basic Fourier model

$$\begin{aligned} y_{\ell,s}(t) &= \int_{FOV} \sum_{i=1}^{N_{tis}} w_i(\mathbf{r}) m(\varphi_i, \theta) e^{-t/T_{2,i}^*} \mathcal{S}_{\ell}(\mathbf{r}) e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}} d\mathbf{r} \\ &= \sum_{i=1}^{N_{tis}} m(\varphi_i, \theta) e^{(TE - t)/T_{2,i}^*} \int_{FOV} w_i(\mathbf{r}) \mathcal{S}_{\ell}(\mathbf{r}) e^{-2i\pi \mathbf{k}_s(t) \cdot \mathbf{r}} d\mathbf{r}. \end{aligned}$$



28.2/3 SNAKE modeling choices

SNAKE modeling choices

Tissue compartmentation

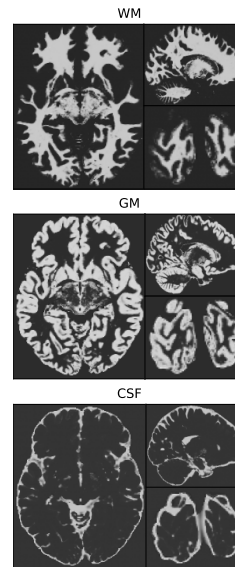
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Noise

- Thermal noise added to each shot: $\tilde{y}_{\ell,s}(t) = y_{\ell,s}(t) + n_{\ell}(t)$
- Noise level in k-space determined from real *in vivo* acquisition at 7T.



28.3/3 SNAKE modeling choices

And what about BOLD?



29.1/2 And what about BOLD?

Model

- BOLD effect locally modifies the properties of the gray matter
 - $\simeq$ adding a new tissue to the simulation, with dynamic T_2^* [*Jin et al. 2006; Uludağ and Kasper 2023*]
 - $T_{2,BOLD}^* = \frac{1}{R_{2,GM}^* + \Delta R_2^*(t_s)}$
- Define a Region of Interest (ROI) and a given paradigm
- Here $\Delta R_2^* = -1\text{Hz}$ (following the value used by [*Jin et al. 2006*])

And what about BOLD?



29.2/2 And what about BOLD?

Model

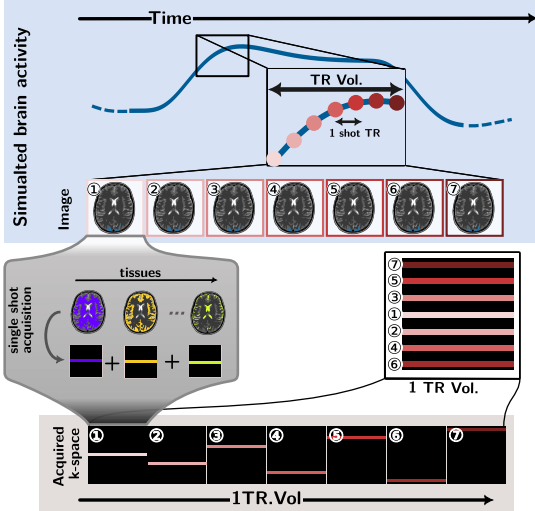
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- Define a Region of Interest (ROI) and a given paradigm
- Here $\Delta R_2^* = -1\text{Hz}$ (following the value used by [Jin et al. 2006])

For every shot s :

$$\frac{\mu_{BOLD}(t_s) - \mu_{GM}(t_s)}{\mu_{GM}(t_s)} = -TE \cdot \Delta R_2^* \tilde{h}(t_s) \lesssim 2.5\%$$

- $\tilde{h}(t)$ is the normalized hemodynamic response such that $\max\{\tilde{h}(t)\} = 1$.

Complete single frame simulation



Numerical Experiments



31.1/2 Numerical Experiments

Methodology

- Validate the capability of SNAKE to simulate whole fMRI experiment.
- Could we neglect the T_2^* relaxation?
- Low-spatial & high-temporal vs high-spatial & low-temporal
- SNR calibrated from real acquisition at 7T.

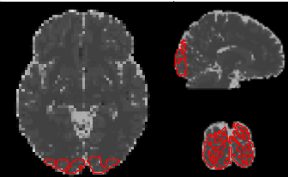


Methodology

- Validate the capability of SNAKE to simulate whole fMRI experiment.
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- SNR calibrated from real acquisition at 7T.

Setup	Res.	Readout	L	N_s	T_{obs}	TR_{vol}	n_{jobs}	Simulation time	
								No T_2^*	With T_2^*
Scenario 1	3mm	EPI	1	44	25ms	2.2s	6	3min54sec	3min55sec
Scenario 2	3mm	SoS	8	14	30ms	0.7s	6	1min31sec	5min10sec
Scenario 3	1mm	SPARKLING	32	48	25ms	2.4s	3	1h34min20sec	3h58min40sec

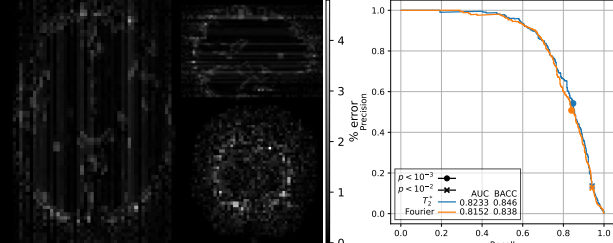
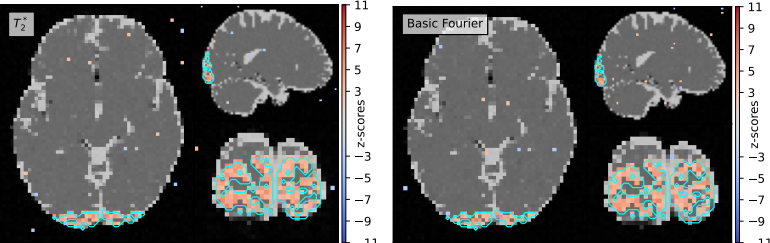
Hardware: CPU: Intel i9-13900H, RAM: 32Go, GPU: NVIDIA RTX 2000 Ada.
Common sequences parameters $TR_{shot} = 50\text{ms}$, $TE = 25\text{ms}$, $FA = 12^\circ$.
Paradigm design: Block ON/OFF (20s/20s), 5 minute run.



Ideal contrast and ROI
for activations.

Scenario 1 - Cartesian Validation

T_2^* model vs Basic Fourier



Takeaway

- Check specificity & sensitivity using ground truth ROI.
- in Cartesian, little differences between models.

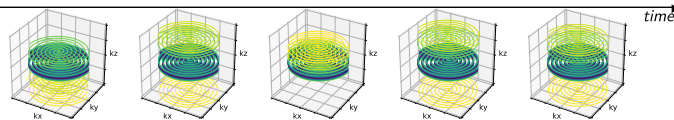
32.1/1 Scenario 1 - Cartesian Validation

Scenario 2 - Stack of Spirals

Acquisition and reconstruction strategies

Acquisition Setup

- $TR/TE/FA = 50\text{ms}/22\text{ms}/15^\circ$
- 3mm-iso, $TR_{\text{vol}} = 0.7\text{ s}$
- Stack of spirals
- Static or dynamic sampling [*Petrov et al. 2017*]



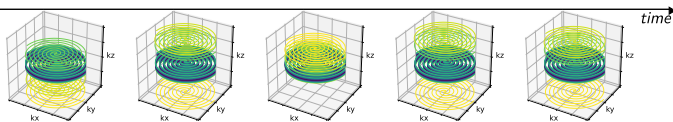
33.1/4 Scenario 2 - Stack of Spirals

Scenario 2 - Stack of Spirals

Acquisition and reconstruction strategies

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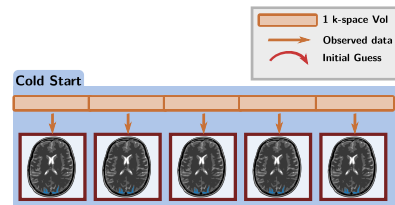
Reconstruction

- Compressed Sensing wavelet-based reconstruction

$$\hat{\mathbf{x}}_t = \arg \min_{\mathbf{x} \in \mathbb{C}^M} \frac{1}{2} \sum_{\ell=1}^L \|\mathcal{F}_t \mathcal{S}_\ell \mathbf{x} - \mathbf{y}_{t,\ell}\|_2^2 + \mu_t g(\Psi \mathbf{x})$$

- Warm start strategies (COLD, WARM, REFINE)
- Regularisation parameter auto-selected using SURE estimator.

33.2/4 Scenario 2 - Stack of Spirals

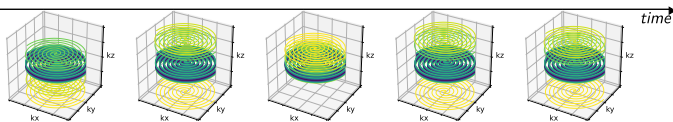


Scenario 2 - Stack of Spirals

Acquisition and reconstruction strategies

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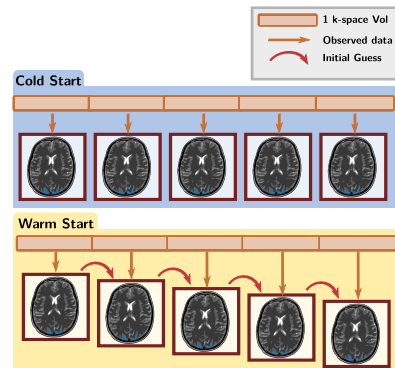
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33.3/4 Scenario 2 - Stack of Spirals

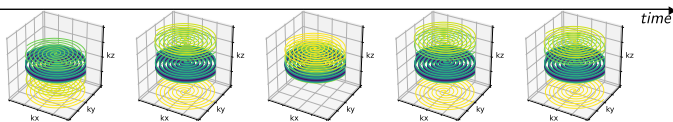


Scenario 2 - Stack of Spirals

Acquisition and reconstruction strategies

Acquisition Setup

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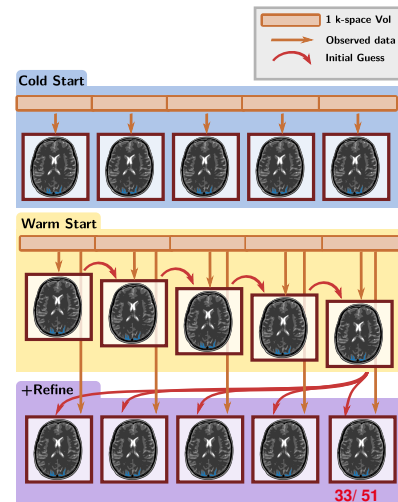


Reconstruction

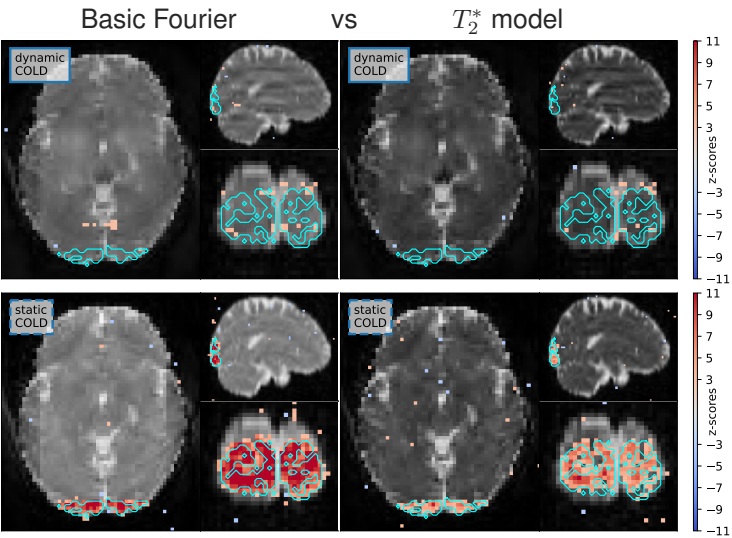
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Scenario 2 - Stack of Spirals

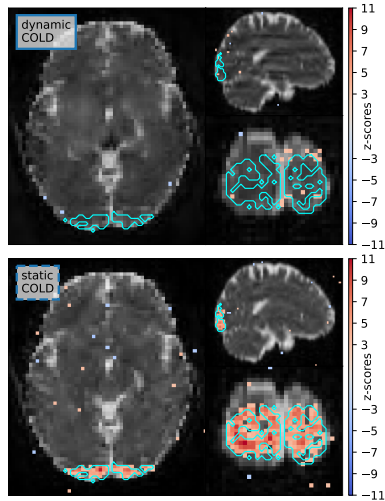


Impact of T_2^*

- T_2^* impact on contrast and statistics
- Unlike Scenario 1
- We cannot neglect it

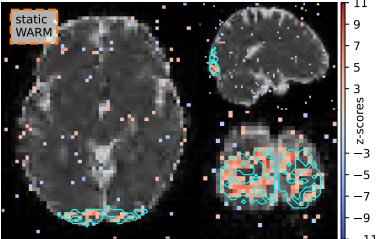
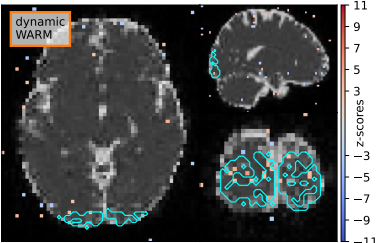
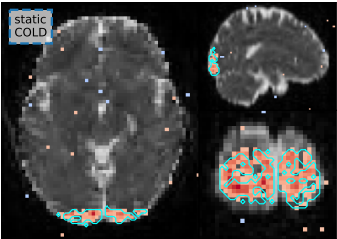
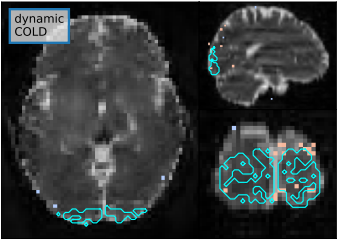
Scenario 2 - Stack of Spirals

T_2^* model



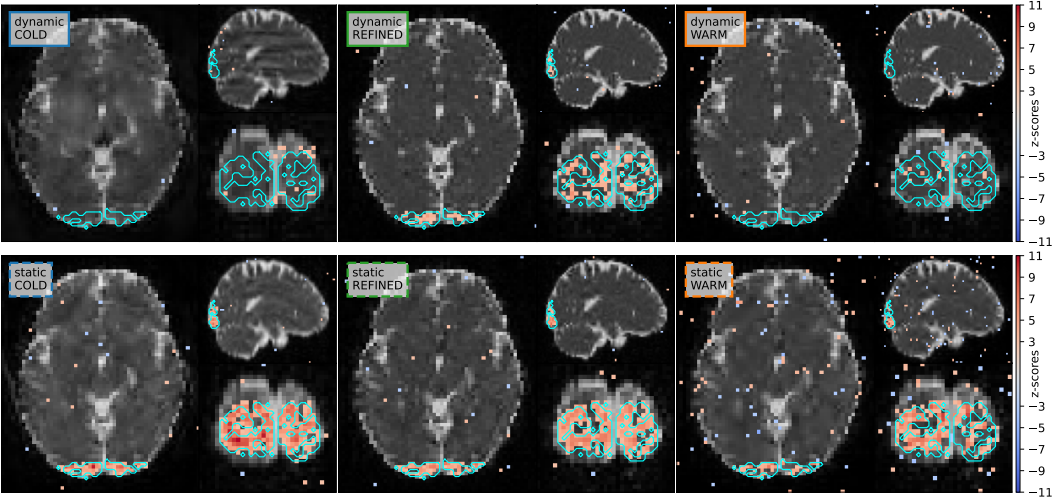
Scenario 2 - Stack of Spirals

T_2^* model

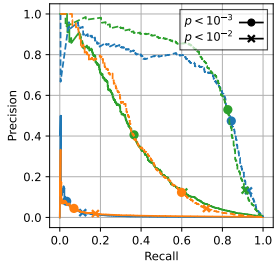


Scenario 2 - Stack of Spirals

T_2^* model



Scenario 2 - Quantitative results (T_2^* model)



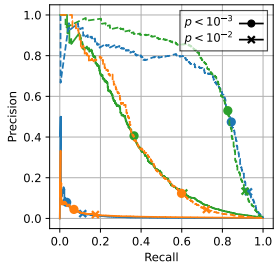
T_2^* model

Setup			SSIM		PSNR		tSNR	AUC	BACC
Label	Acq.	Recon.	First	Last	First	Last			
	dynamic	COLD	0.64	0.51	19.94	19.80	6.21	0.01	0.55
	dynamic	REFINED	0.67	0.69	21.08	<u>21.03</u>	23.64	0.34	0.80
	dynamic	WARM	0.64	0.79	19.94	21.06	12.95	0.01	0.58
	static	COLD	0.64	0.64	19.91	19.91	43.08	<u>0.70</u>	0.96
	static	REFINED	0.60	0.60	<u>20.46</u>	20.46	<u>37.99</u>	0.75	<u>0.95</u>
	static	WARM	<u>0.64</u>	<u>0.74</u>	19.91	20.26	20.18	0.35	0.84

35.1/2 Scenario 2 - Quantitative results (T_2^* model)

- Dynamic refined brings the best image quality and good statistical performances
- Static acquisitions get best statistical performance, but poor image quality.
- warm start (and refined) works best with dynamic acquisition (new information at each frame)
- Cold Start works best with static acquisition

Scenario 2 - Quantitative results (T_2^* model)



T_2^* model

Setup			SSIM		PSNR		tSNR	AUC	BACC
Label	Acq.	Recon.	First	Last	First	Last			
	dynamic	COLD	0.64	0.51	19.94	19.80	6.21	0.01	0.55
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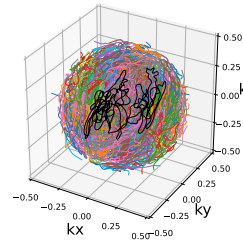
Takeaway

- Image quality $\nRightarrow$ statistical performances
- Static $\rightarrow$ cold start
- Dynamic $\rightarrow$ refined strategy
- Use T_2^* model for fidelity to real fMRI data

35.2/2 Scenario 2 - Quantitative results (T_2^* model)

- Dynamic refined brings the best image quality and good statistical performances
- Static acquisitions get best statistical performance, but poor image quality.
- warm start (and refined) works best with dynamic acquisition (new information at each frame)
- Cold Start works best with static acquisition

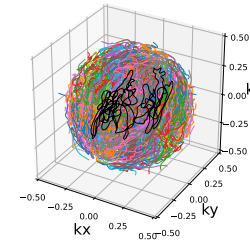
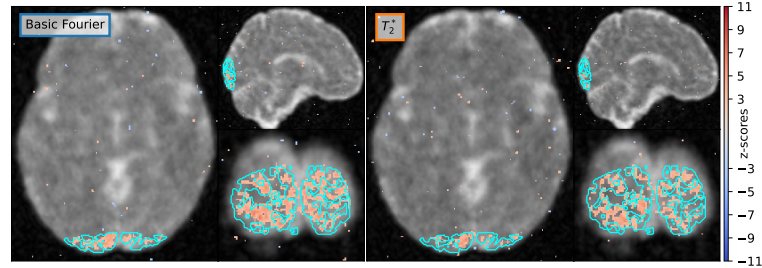
Scenario 3



48-shot SPARKLING
(1mm-iso, $TR_{vol} = 2.4$ s)
[G. R. Chaithya et al. 2022]

36.1/4 Scenario 3

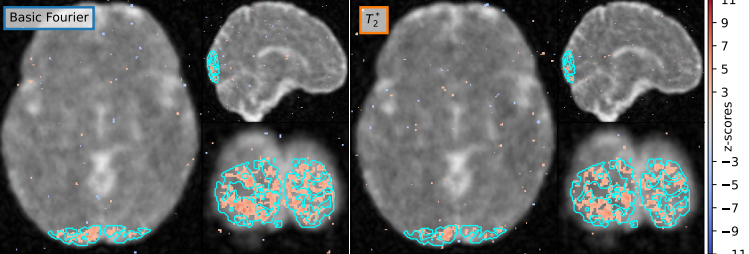
Scenario 3



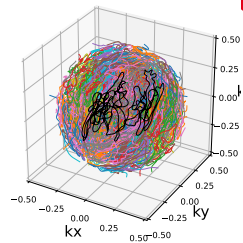
48-shot SPARKLING
(1mm-iso, $TR_{vol} = 2.4$ s)
[G. R. Chaithya et al. 2022]

36.2/4 Scenario 3

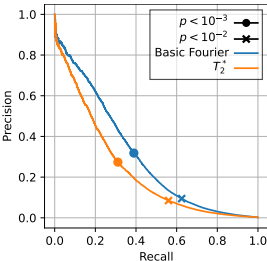
Scenario 3



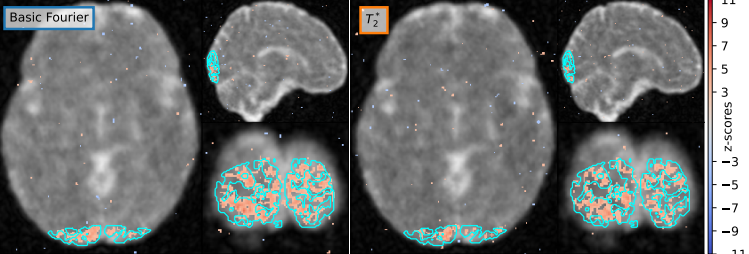
Setup		SSIM		PSNR		tSNR	AUC	BACC
Label	Acq.	First	Last	First	Last			
Basic Fourier		0.306	0.309	22.204	22.220	36.224	0.298	0.806
T_2^*		<u>0.305</u>	<u>0.307</u>	<u>22.100</u>	<u>22.115</u>	<u>34.894</u>	<u>0.229</u>	<u>0.774</u>



48-shot SPARKLING
(1mm-iso, $TR_{vol} = 2.4$ s)
[G. R. Chaithya et al. 2022]



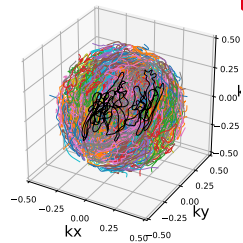
Scenario 3



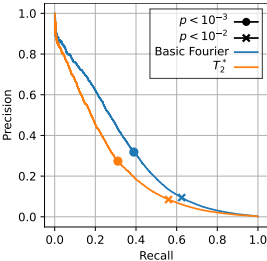
Setup		SSIM		PSNR		tSNR	AUC	BACC
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Basic Fourier		0.306	0.309	22.204	22.220	36.224	0.298	0.806
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Takeaway

- Quality comparable with *in vivo* results [Z. Amor, G. Chaithya, et al. 2022]
- T_2^* degrades everything, but has to be taken into account



48-shot SPARKLING
(1mm-iso, $TR_{vol} = 2.4$ s)
[G. R. Chaithya et al. 2022]



Interim summary



Reproducibility: ✓ SNAKE provides a reproducible setup for fMRI



37.1/6 Interim summary

Interim summary

 **Reproducibility:** ✓ SNAKE provides a reproducible setup for fMRI

 **Reproducibility:** ✓ Full control on all inputs



37.2/6 Interim summary

Interim summary

 **Reproducibility:** ✓ SNAKE provides a reproducible setup for fMRI

 **Reproducibility:** ✓ Full control on all inputs

 **Quality:**  The basic Fourier model can lead to misleading results



37.3/6 Interim summary

Interim summary

 **Reproducibility:** ✓ SNAKE provides a reproducible setup for fMRI

 **Reproducibility:** ✓ Full control on all inputs

 **Quality:**  The basic Fourier model can lead to misleading results

 **Quality:** ✓ T_2^* model brings us closer to reality.



37.4/6 Interim summary

Interim summary

 **Reproducibility:** ✓ SNAKE provides a reproducible setup for fMRI

 **Reproducibility:** ✓ Full control on all inputs

 **Quality:**  The basic Fourier model can lead to misleading results

 **Quality:** ✓ T_2^* model brings us closer to reality.

 **Quality:**  Image quality $\nRightarrow$ statistical performances

37.5/6 Interim summary

Interim summary

 **Reproducibility:** ✓ SNAKE provides a reproducible setup for fMRI

 **Reproducibility:** ✓ Full control on all inputs

 **Quality:**  The basic Fourier model can lead to misleading results

 **Quality:** ✓ T_2^* model brings us closer to reality.

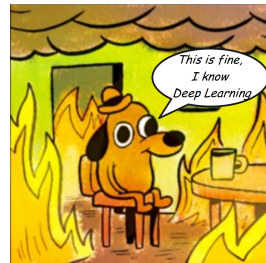
 **Quality:**  Image quality $\nRightarrow$ statistical performances

✓ Modular, open-source, extensible, fast.

37.6/6 Interim summary

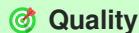
3

Deep Learning to the rescue of fMRI reconstruction?



P.-A. Comby, B. Lapostolle, M. Terris, and P. Ciuciu (Oct. 2024). *Robust Plug-and-Play Methods for Highly Accelerated Non-Cartesian MRI Reconstruction*. Accepted to ISBI 2025

P.-A. Comby, M. Terris, A. Vignaud, and P. Ciuciu (Mar. 2025). *Plug-and-Play Reconstruction for 3D Non-Cartesian fMRI Data*. Submitted to EUSIPCO 2025



Quality



Resolution



Reproducibility

38.1/1 With SNAKE we saw how the CS could perform, and nowadays a natural endeavour is to try if deep-learning could help. THE work of the second paper outlined here was realized after the first submission of the manuscript, and has been submitted two weeks ago.

Deep learning for Inverse problems

$$\mathbf{y} = \mathbf{A}\mathbf{x} + \epsilon$$
$$\hat{\mathbf{x}} = \arg \min_{\mathbf{x}} \underbrace{\frac{1}{2} \|\mathbf{A}\mathbf{x} - \mathbf{y}\|_2^2}_{f(\mathbf{x})} + \underbrace{\mu g(\mathbf{x})}_{\text{prior}}$$

The diagram illustrates the optimization problem for inverse problems. It shows the equation $\mathbf{y} = \mathbf{A}\mathbf{x} + \epsilon$ and the minimization problem for $\hat{\mathbf{x}}$. The term $\frac{1}{2} \|\mathbf{A}\mathbf{x} - \mathbf{y}\|_2^2$ is highlighted in an orange box and labeled "Data-Consistency" with an orange arrow. The term $\mu g(\mathbf{x})$ is highlighted in a green box and labeled "prior" with a green arrow. A bracket under the orange box indicates it is $f(\mathbf{x})$.

39.1/4 Deep learning for Inverse problems

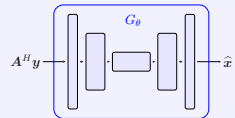
1. At the beginning of this presentation, we saw how the inverse problem could be solved by minimizing an objective function that combines a data-consistency term and a regularization term.

Deep learning for Inverse problems

$$y = Ax + \epsilon$$
$$\hat{x} = \arg \min_x \underbrace{\frac{1}{2} \|Ax - y\|_2^2}_{f(x)} + \underbrace{\mu g(x)}_{\text{prior}}$$

Data-Consistency prior

Single domain



- + simple
- no physics knowledge
- expensive

[Nataraj and Otazo 2020;
Akçakaya et al. 2019]

39.2/4 Deep learning for Inverse problems

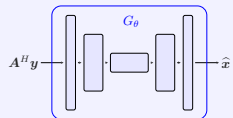
1. At the beginning of this presentation, we saw how the inverse problem could be solved by minimizing an objective function that combines a data-consistency term and a regularization term.
2. In the context of deep learning, one can decide to ignore this objective, and try to use a single-domain network to solve the problem.

Deep learning for Inverse problems

$$y = Ax + \epsilon \quad \hat{x} = \arg \min_x \underbrace{\frac{1}{2} \|Ax - y\|_2^2}_{f(x)} + \underbrace{\mu g(x)}_{\text{prior}}$$

Data-Consistency

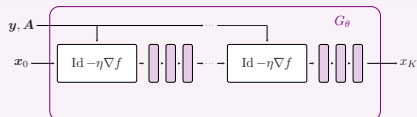
Single domain



- + simple
- no physics knowledge
- expensive

[Nataraj and Otazo 2020;
Akçakaya et al. 2019]

Unfolded



- + learned prior
- ± differentiable physics
- - - very expensive
- fails out-of distribution

[Hammernik, Klatzer, et al. 2018;
Aggarwal et al. 2019; Adler and
Öktem 2017; Ramzi et al. 2022;
Demirel et al. 2021]

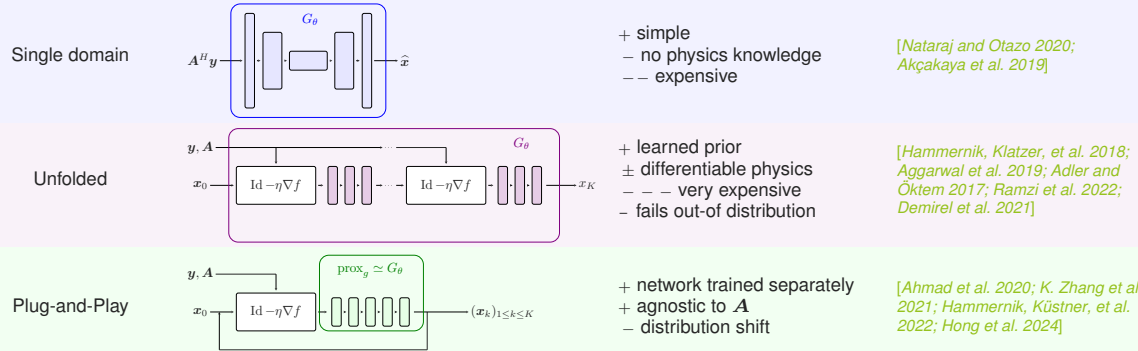
39.3/4 Deep learning for Inverse problems

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3. Another popular approach is to use a physics-informed network, where the network is trained to solve the inverse problem, by unrolling or unfolding an existing algorithm, with the physics of the problem embedded in the network.

Deep learning for Inverse problems

$$y = Ax + \epsilon \quad \hat{x} = \arg \min_x \underbrace{\frac{1}{2} \|Ax - y\|_2^2}_{f(x)} + \underbrace{\mu g(x)}_{\text{prior}}$$

Data-Consistency



39.4/4 Deep learning for Inverse problems

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2. In the context of deep learning, one can decide to ignore this objective, and try to use a single-domain network to solve the problem.
3. Another popular approach is to use a physics-informed network, where the network is trained to solve the inverse problem, by unrolling or unfolding an existing algorithm, with the physics of the problem embedded in the network.
4. The last approach is to use a plug-and-play method, where the network is used as a denoiser in an iterative algorithm.

(f)MRI & deep learning challenges

- Overfitting and hallucinations [*Antun et al. 2020; Gottschling et al. 2025*]



40.1/5 (f)MRI & deep learning challenges

(f)MRI & deep learning challenges

- Overfitting and hallucinations [*Antun et al. 2020; Gottschling et al. 2025*]
- Dimensionality of the dataset
 - fMRI: 10^2 frames, 10^7 $\mathbb{C}$ -valued voxels $\implies$ more problems



40.2/5 (f)MRI & deep learning challenges

(f)MRI & deep learning challenges

- Overfitting and hallucinations [*Antun et al. 2020; Gottschling et al. 2025*]
- Dimensionality of the dataset
 - fMRI: 10^2 frames, 10^7 $\mathbb{C}$ -valued voxels $\implies$ more problems
- Large raw k-space dataset availability
 - FastMRI (2D) [*Zbontar et al. 2019*]
 - Calgary-Campaninas (3D) [*Souza et al. 2018*]
 - ✗ NONE for functional MRI reconstruction



40.3/5 (f)MRI & deep learning challenges

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40.4/5 (f)MRI & deep learning challenges

(f)MRI & deep learning challenges

- Overfitting and hallucinations [*Antun et al. 2020; Gottschling et al. 2025*]
- Dimensionality of the dataset
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 - FastMRI (2D) [*Zbontar et al. 2019*]
 - Calgary-Campaninas (3D) [*Souza et al. 2018*]
 - ✗ NONE for functional MRI reconstruction
- Data crimes [*Shimron et al. 2022*]
- Generalization to other datasets and sampling patterns
 - ✓ Good candidate: PnP



40.5/5 (f)MRI & deep learning challenges

Plug-and-Play (PnP) methods

- Solve the inverse problem $\mathbf{y} = \mathbf{A}\mathbf{x} + \mathbf{n}$

$$\mathbf{x} = \arg \min_{\mathbf{x}} \underbrace{\frac{1}{2} \|\mathbf{A}\mathbf{x} - \mathbf{y}\|_2^2}_{f(\mathbf{x})} + g(\mathbf{x})$$



41.1/7 Plug-and-Play (PnP) methods

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- Forward-Backward Splitting

$$\forall k = 0, \dots, N \quad \begin{cases} \mathbf{z}_k = \mathbf{x}_k - \eta_k \nabla f(\mathbf{x}_k) \\ \mathbf{x}_{k+1} = \mathbf{x}_k + \lambda_k (\text{prox}_{\eta_k g}(\mathbf{z}_k) - \mathbf{x}_k) \end{cases}$$



Plug-and-Play (PnP) methods

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Half-Quadratic Splitting (HQS) [K. Zhang et al. 2021]

$$\begin{array}{l} \forall k = 0, \dots, N \\ \left[\begin{array}{l} \mathbf{z}_k = \mathbf{x}_k - \text{prox}_{\eta_k f}(\mathbf{x}_k) \\ \mathbf{x}_{k+1} = \mathbf{x}_k + \lambda_k (\text{prox}_{\eta_k g}(\mathbf{z}_k) - \mathbf{x}_k) \end{array} \right] \end{array}$$

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Preconditioning [Hong et al. 2024]

- Reweight data-consistency with $\mathbf{P}$

Plug-and-Play (PnP) methods

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Preconditioning [Hong et al. 2024]

- Reweight data-consistency with $\mathbf{P}$
- $\min_P = \rho(I - \mathbf{P}\mathbf{A}^H\mathbf{A})$
- “F-1” $\mathbf{P} = 2 - \alpha\mathbf{A}^H\mathbf{A}$

Plug-and-Play (PnP) methods

- Solve the inverse problem $\mathbf{y} = \mathbf{A}\mathbf{x} + \mathbf{n}$

$$\mathbf{x} = \arg \min_{\mathbf{x}} \underbrace{\frac{1}{2} \|\mathbf{A}\mathbf{x} - \mathbf{y}\|_{2,P}^2}_{f(\mathbf{x})} + g(\mathbf{x})$$

- Forward-Backward Splitting

$$\begin{array}{l} \forall k = 0, \dots, N \\ \left[\begin{array}{l} \mathbf{z}_k = \mathbf{x}_k - \eta_k \mathbf{P} \nabla f(\mathbf{x}_k) \\ \mathbf{x}_{k+1} = \mathbf{x}_k + \lambda_k (\text{prox}_{\eta_k g}(\mathbf{z}_k) - \mathbf{x}_k) \end{array} \right] \xrightarrow{PnP} \forall k = 0, \dots, N \\ \left[\begin{array}{l} \mathbf{z}_k = \mathbf{x}_k - \eta_k \mathbf{P} \nabla f(\mathbf{x}_k) \\ \mathbf{x}_{k+1} = G_{\theta}(\mathbf{z}_k) \end{array} \right] \end{array}$$

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Preconditioning [Hong et al. 2024]

- Reweight data-consistency with $\mathbf{P}$
- $\min_P = \rho(I - \mathbf{P}\mathbf{A}^H\mathbf{A})$
- “F-1” $\mathbf{P} = 2 - \alpha\mathbf{A}^H\mathbf{A}$
- ✓ Stabilize PnP methods

MRI

- Validation of preconditioning PnP for MRI [*Hong et al. 2024*]



MRI

- Validation of preconditioning PnP for MRI [*Hong et al. 2024*]
- Denoiser (DRUNET) [*Z. Zhang et al. 2018*] trained on fastMRI dataset (2D T_2 Images)



Material and methods

MRI

- Validation of preconditioning PnP for MRI [*Hong et al. 2024*]
- Denoiser (DRUNET) [*Z. Zhang et al. 2018*] trained on fastMRI dataset (2D T_2 Images)
- Spiral undersampling at AF=4, and AF=16



42.3/7 Material and methods

Material and methods

MRI

- Validation of preconditioning PnP for MRI [*Hong et al. 2024*]
- Denoiser (DRUNET) [*Z. Zhang et al. 2018*] trained on fastMRI dataset (2D T_2 Images)
- Spiral undersampling at AF=4, and AF=16
- Goal: Choose the best method before moving to fMRI



42.4/7 Material and methods

MRI

- Validation of preconditioning PnP for MRI [*Hong et al. 2024*]
- Denoiser (DRUNET) [*Z. Zhang et al. 2018*] trained on fastMRI dataset (2D T_2 Images)
- Spiral undersampling at AF=4, and AF=16
- Goal: Choose the best method before moving to fMRI
- Baseline:
 - Compressed sensing
 - unrolled network (NCPDNET [*Ramzi et al. 2022*]) trained at AF=4





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fMRI 3D

- Use scenario 2 of SNAKE



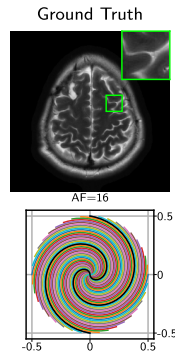
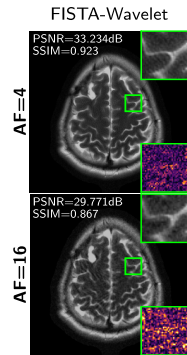
MRI

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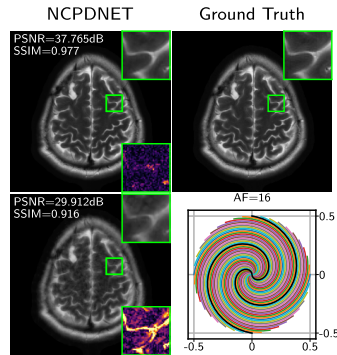
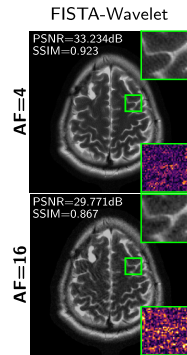
fMRI 3D

- Use scenario 2 of SNAKE
- 3D DRUNET trained on Calgary dataset (T1w, 1mm) [*Souza et al. 2018*]

Starting with anatomical results

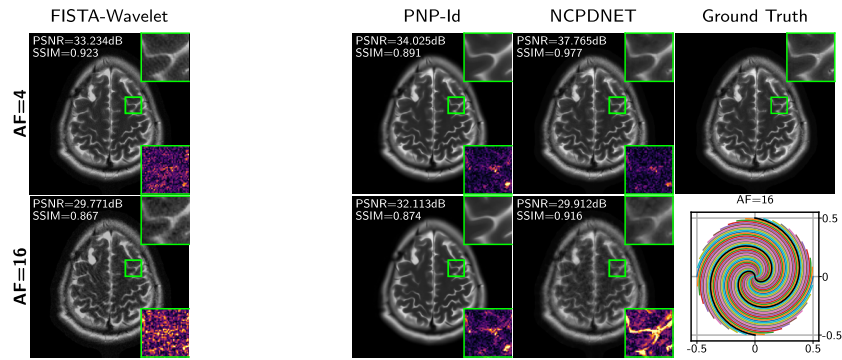


Starting with anatomical results

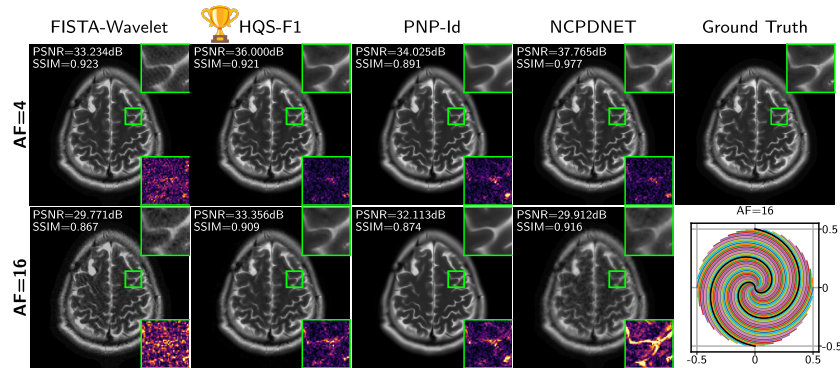


43.2/8 Starting with anatomical results

Starting with anatomical results

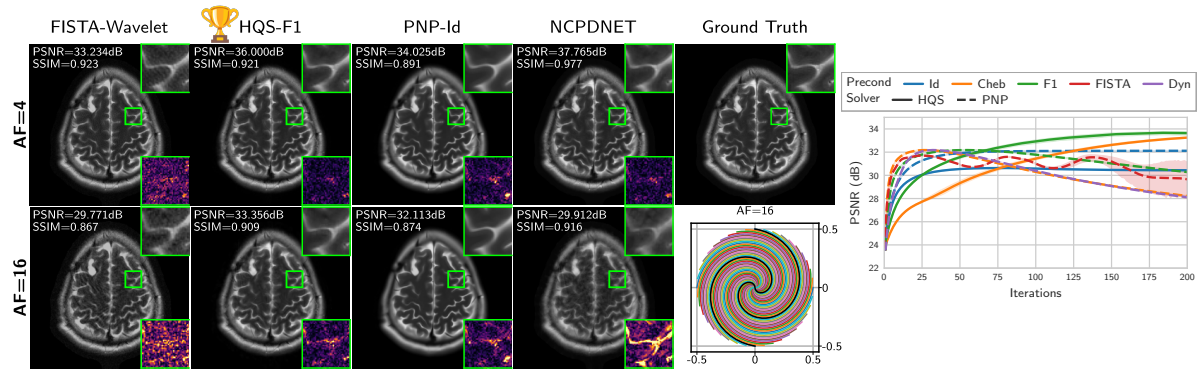


Starting with anatomical results



43.4/8 Starting with anatomical results

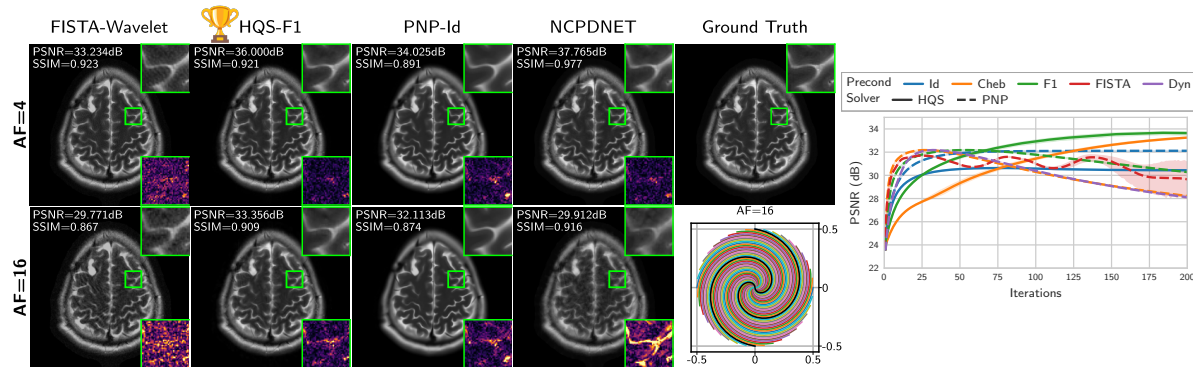
Starting with anatomical results



43.5/8 Starting with anatomical results

Starting with anatomical results

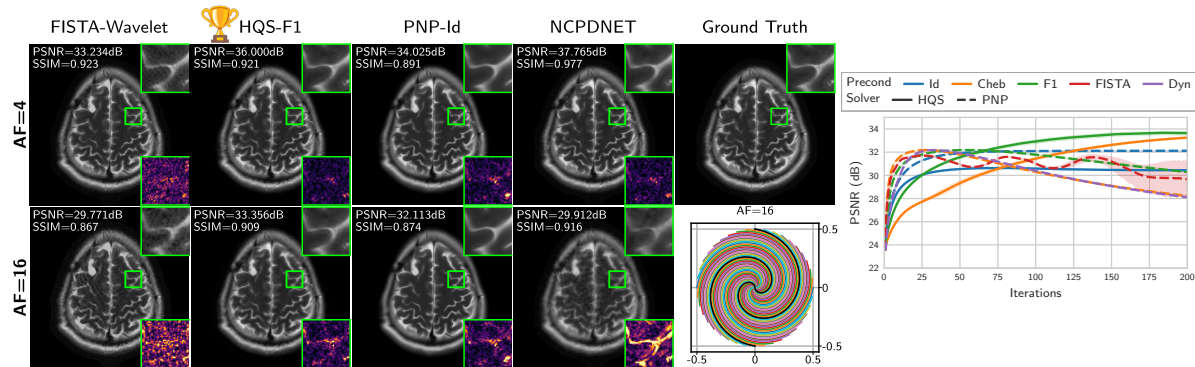
43.6/8 Starting with anatomical results



Takeaway

✓ HQS-F1 performs best

Starting with anatomical results

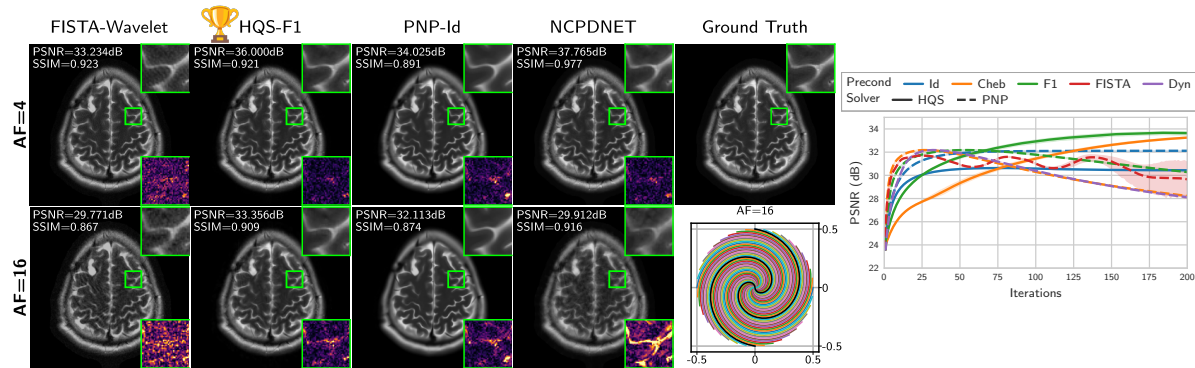


Takeaway

- ✓ HQS-F1 performs best
- ✗ NCPDNET collapses on out of distribution data

43.7/8 Starting with anatomical results

Starting with anatomical results



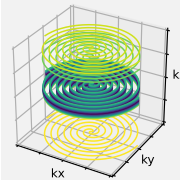
Takeaway

- ✓ HQS-F1 performs best
- ✗ NCPDNET collapses on out of distribution data
- 🎯 PnP method robust to acceleration (*no fine-tuning!*)

43.8/8 Starting with anatomical results



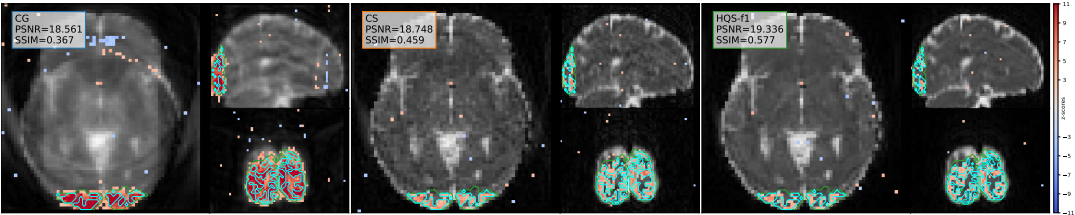
Scenario 2 of SNAKE



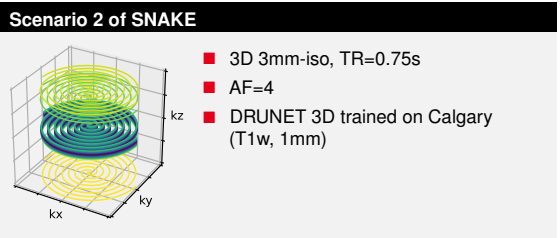
- 3D 3mm-iso, TR=0.75s
- AF=4
- DRUNET 3D trained on Calgary (T1w, 1mm)

Application of PnP to fMRI using SNAKE

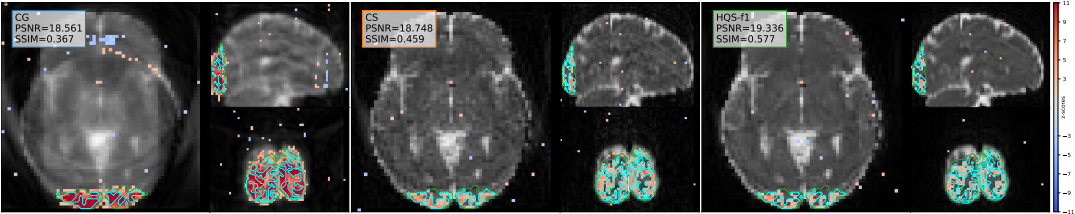
44.2/5 Application of PnP to fMRI using SNAKE



	Name	PSNR	SSIM	tSNR	AUC	BACC
—	CG	18.560	0.367	nan	0.782	0.754
—	CS	18.748	0.459	6.706	0.758	0.948
—	HQS-F1	19.338	0.577	6.286	0.574	0.891



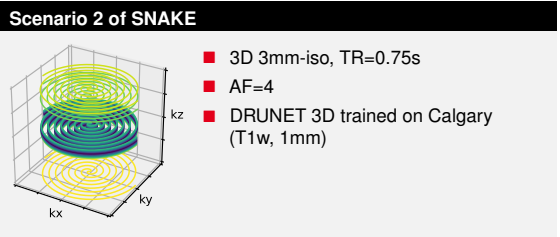
Application of PnP to fMRI using SNAKE



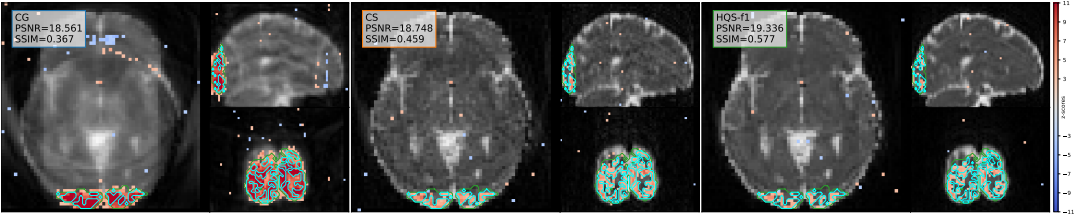
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Takeaway

- ✓ First use of SNAKE + PnP method (3D)



Application of PnP to fMRI using SNAKE



	Name	PSNR	SSIM	tSNR	AUC	BACC
—	CG	18.560	0.367	nan	0.782	0.754
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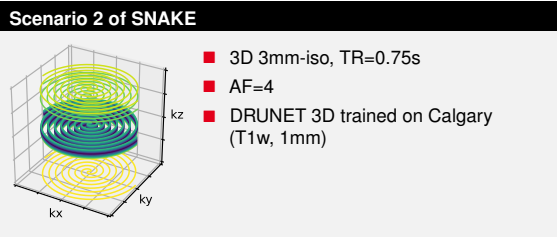
Takeaway

✓

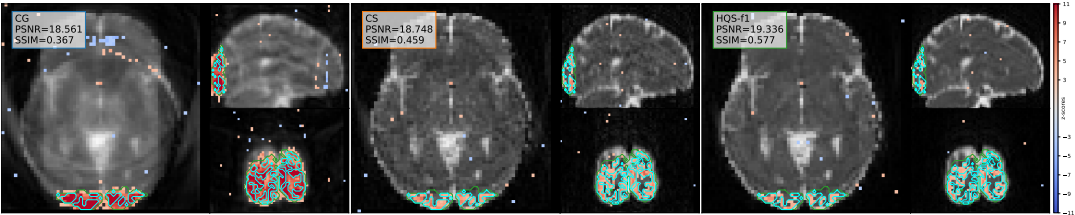
First use of SNAKE + PnP method (3D)

🎯

HQS-F1: Image quality ↗, stats ↘



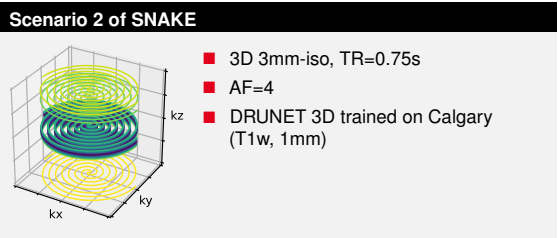
Application of PnP to fMRI using SNAKE



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	HQS-F1	19.338	0.577	6.286	0.574	0.891

Takeaway

- ✓ First use of SNAKE + PnP method (3D)
- 🎯 HQS-F1: Image quality ↗, stats ↘
- 🧠 Denoiser trained with OOD data (T1w, 1mm)





- Deep learning-based methods are usable for inverse problem and (f)MRI, but consider them carefully.



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- ✓ PnP method provides great flexibility for MRI and fMRI reconstruction
 - Agnostic to sampling and acquisition setup (🎯🎯🎯)



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- 🎯✓ SNAKE provides a controlled environment to evaluate deep learning based reconstruction, up to the statistical analysis



- Deep learning-based methods are usable for inverse problem and (f)MRI, but consider them carefully.
- ✓ PnP method provides great flexibility for MRI and fMRI reconstruction
 - Agnostic to sampling and acquisition setup (🎯🎯🎯)
- 🎯✓ SNAKE provides a controlled environment to evaluate deep learning based reconstruction, up to the statistical analysis
- 🧠 More work required to leverage PnP along temporal dimension.



5. Conclusion & Perspectives

46.1/1 After this journey, I would like to conclude this presentation by summarizing the contributions I made during my PhD, and discuss the perspectives that I see for the future.

Conclusion & Next Actions

Reproducibility & Quality

- ✓ SNAKE simulator to generate ground-truth data
- ✓ Evaluate fMRI pipeline end to end



47.1/3 Conclusion & Next Actions

Conclusion & Next Actions

Reproducibility & Quality

- ✓ SNAKE simulator to generate ground-truth data
- ✓ Evaluate fMRI pipeline end to end

Resolution & Reproducibility

- ✓ SNAKE can generate high-resolution data
- ☐ Validate LLR Denoising with SNAKE, and explore more methods



47.2/3 Conclusion & Next Actions

Conclusion & Next Actions

Reproducibility & Quality

- ✓ SNAKE simulator to generate ground-truth data
- ✓ Evaluate fMRI pipeline end to end

Resolution & Reproducibility

- ✓ SNAKE can generate high-resolution data
- Validate LLR Denoising with SNAKE, and explore more methods

Resolution & Quality

- ✓ LLR denoising with optimal threshold to get  quality without sacrificing  resolution
- ✓ High image quality reconstruction with PnP methods
- Use PnP at higher resolution for fMRI
- Use SNAKE to generate high-resolution supervised dataset



47.3/3 Conclusion & Next Actions

Perspectives

- Denoising
 - ☐ LLR denoising on GPU and at the Scanner console.
 - ☐ LLR denoising for brain decoding

48.1/4 Perspectives

1. I am happy to see that the work I have done during my PhD is now the cornerstone of several projects that are planned or on going

Perspectives

- Denoising
 - ☐ LLR denoising on GPU and at the Scanner console.
 - ☐ LLR denoising for brain decoding
- SNAKE
 - ☐ SNAKE as a deep learning tool: create a high-resolution dataset
 - ☐ Extend SNAKE modeling (resting-state, field inhomogeneities)
 - ☐ Comparison of SNAKE with *in vivo* acquisition (PhD thesis of **Caini Pan**, 2024-)
 - ☐ Optimization of 3D+T sampling (PhD thesis of **Caini Pan**, 2024-)

48.2/4 Perspectives

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Perspectives

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- fMRI Reconstruction
 - ☐ Unrolling of fMRI reconstruction (M2 internship of **Albane Dourdet-Lavie** summer 2025)
 - ☐ Explore temporal regularization prior (**Qiaoxin Li**, PhD thesis June 2025-)

48.3/4 Perspectives

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Perspectives

- Denoising
 - ☐ LLR denoising on GPU and at the Scanner console.
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 - ☐ Unrolling of fMRI reconstruction (M2 internship of **Albane Dourdet-Lavie** summer 2025)
 - ☐ Explore temporal regularization prior (**Qiaoxin Li**, PhD thesis June 2025-)
- Plug-and-Play and beyond
 - ☐ Explore temporal prior with energy-based models.
 - ☐ More use of PnP methods (**Chaithya GR**, **Matthieu Terris**)
 - ☐ Equivariant PnP for MP2RAGE at 7T (**Chaithya GR**, **Alexandre Vignaud**)

48.4/4 Perspectives

1. I am happy to see that the work I have done during my PhD is now the cornerstone of several projects that are planned or on going

Summary of Contributions

Software contributions	
Logo & Name	Description
 MRI-NUFFT	A unified interface for efficient forward model computations of non-Cartesian MRI.
 SNAKE	A simulator for fMRI data in k-space.
 PySAP-fMRI	Variational methods for reconstructing fMRI time-series.
patch-denoise	Denoising of fMRI images data using patch-based methods.
hydra-callbacks	A collection of callbacks for the hydra framework.
brainweb-dl	A download interface for the BrainWeb Dataset
benchmark-mri-pnp	A reproducible benchmark of Plug-and-Play methods for MRI reconstruction.

Students supervision	
■ Benjamin Lapostolle (M2, Summer 2024): PnP for anatomical MRI	
■ Marie Dogo (L2, Summer 2023): Local Low-rank denoising on IBC dataset.	

49.1/2 Summary of Contributions

1. Now, I would like to highlight some of the contributions I made during my PhD. Notably, major outcomes of this thesis are the software I have developed, to foster reproducibility and open-science. I also had the pleasure to supervised TWO student as summer interns, and our collaboration shined through this work.

Summary of Contributions

Under revisions for publication in peer-reviewed journals

- **P.-A. Comby**, A. Vignaud, and P. Ciuciu (2025). *SNAKE-fMRI: A Modular fMRI Data Simulator from the Space-Time Domain to k-Space and Back*. In revision to Imaging Neuroscience
- **P.-A. Comby**, G. Daval-Fr erot, C. Pan, A. Tanabene, L. Oudjman, M. Cencini, P. Ciuciu, and GR. Chaithya (Nov. 2024). *MRI-NUFFT: Doing Non-Cartesian MRI Has Never Been Easier*. in revision to Journal of Open Source Software.

Publications in peer-reviewed conferences

- **P.-A. Comby**, M. Terris, A. Vignaud, and P. Ciuciu (Mar. 2025). *Plug-and-Play Reconstruction for 3D Non-Cartesian fMRI Data*. Submitted to EUSIPCO 2025
- **P.-A. Comby**, B. Lapostolle, M. Terris, and P. Ciuciu (Oct. 2024). *Robust Plug-and-Play Methods for Highly Accelerated Non-Cartesian MRI Reconstruction*. Accepted to ISBI 2025
- Z. Amor, **P.-A. Comby**, C. Le Ster, A. Vignaud, and P. Ciuciu (n.d.). *“Non-Cartesian Non-Fourier FMRI Imaging for High-Resolution Retinotopic Mapping at 7 Tesla”*. In: CAMSAP 2023 - International Workshop on Computational Advances in Multi-Sensor Adaptive Processing
- **P.-A. Comby**, Z. Amor, A. Vignaud, and P. Ciuciu (Apr. 18, 2023). *“Denoising of FMRI Volumes Using Local Low Rank Methods”*. In: ISBI 2023 - International Symposium on Biomedical Imaging

+ 6 ISMRM abstracts (2023, 2024, 2025)

49.2/2 Summary of Contributions

1. Now, I would like to highlight some of the contributions I made during my PhD. Notably, major outcomes of this thesis are the software I have developed, to foster reproducibility and open-science. I also had the pleasure to supervised TWO student as summer interns, and our collaboration shined through this work.
2. In term of scientific publication, I have submitted two papers for peer-reviewed journals, and I have presented my work in several conferences.

Acknowledgments

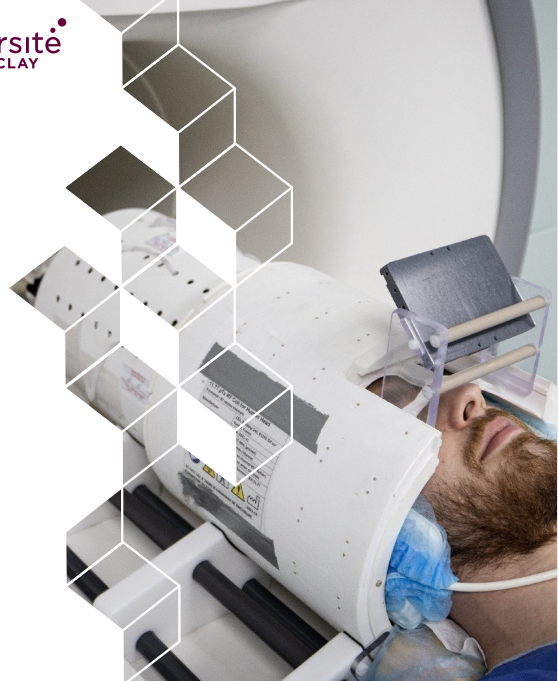


50.1/1 Acknowledgments As a final note, I would like to thank all the people who have contributed to this work, and notably my supervisors and colleagues at Neurospin and Inria.



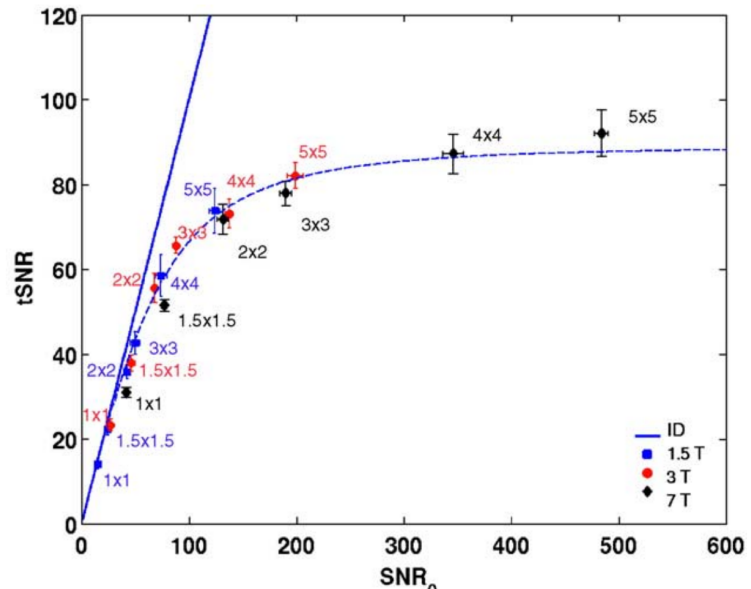
and many more...

Thank you
for your attention

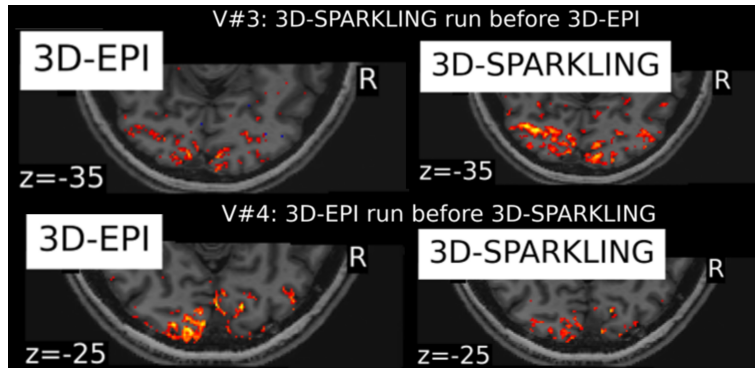




6. Backup Slides !



Acquisition and Habituation



[Zaineb Amor, Ciuciu, et al. 2024]

3.1/1 Acquisition and Habituation

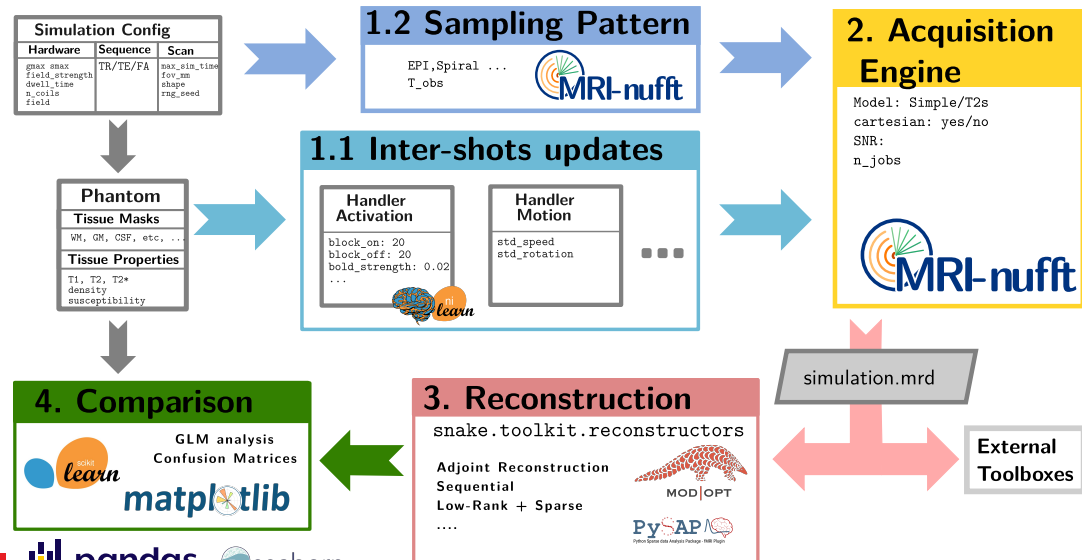


- Reduce Computations
 - Use a Mask to reduce the number of mask to compute
 - Tune Overlap of patches
- Recombination:
 - Average
 - Weighted average to promote lower rank patches

$$X_i = \frac{\sum_{j=1}^P w_j X[u_j]}{\sum_{j=1}^P w_j} \quad w_j = \frac{1}{1 + \|S^*[u_j]\|_0}$$

- Convolution style (maximum overlap)

SNAKE internals



5.1/1 SNAKE internals

Why we did not take B0 into account

- Very Expensive to compute

$$y_{\ell,s}(t) = \int_{FOV} m(\mathbf{r}, TR, TE, \alpha) \mathcal{S}_{\ell}(\mathbf{r}) e^{(TE-t)/T_2^*(\mathbf{r})} e^{-2i\pi\Delta f_r(\mathbf{r})t} e^{-2i\pi\mathbf{k}_s(t)\cdot\mathbf{r}} d\mathbf{r}$$

Diagram illustrating the components of the signal equation:

- magnetization** (blue arrow) points to $m(\mathbf{r}, TR, TE, \alpha)$.
- Coil Sensitivity maps** (orange arrow) points to $\mathcal{S}_{\ell}(\mathbf{r})$.
- T_2^* relaxation** (red arrow) points to $e^{(TE-t)/T_2^*(\mathbf{r})}$.
- Field inhomogeneities** (red arrow) points to $e^{-2i\pi\Delta f_r(\mathbf{r})t}$.
- Fourier Encoding** (green arrow) points to $e^{-2i\pi\mathbf{k}_s(t)\cdot\mathbf{r}}$.

- Bilinearization $\sum_{p=1}^P c_p(t) b_p(r) \simeq e^{-2i\pi\Delta f_r(\mathbf{r})t}$

$$y_{\ell,s}(t_n) = \sum_{i=1}^{N_{tis}} \mu_i e^{-t_n/T_{2,i}^*} \sum_{p=1}^P c_p[t_n] \sum_{m=1}^M w_i[\mathbf{r}_m] \mathcal{S}_{\ell}[\mathbf{r}_m] b_p[\mathbf{r}_m] e^{-2i\pi\mathbf{k}_s[t_n]\cdot\mathbf{r}_m}$$

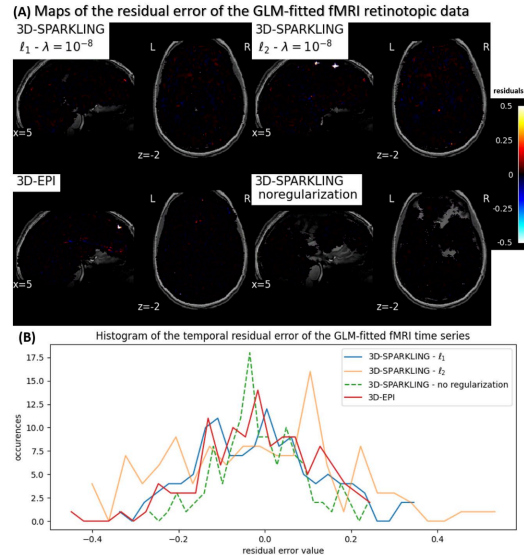
- SNAKE is a “best-case” scenario simulator
- Experimental data can be transformed in this best-case scenario
 - Field monitoring and correction [Zaineb Amor, Radhakrishna, et al. 2022; Z. Amor, Comby, et al. n.d.]
 - Good MR Hardware (no eddy current artifacts)

6.1/1 Why we did not take B0 into account

Compressed Sensing and residuals gaussianity

7.1/1 Compressed Sensing and residuals gaussianity

- Supplementary of [Zaineb Amor, Ciuciu, *et al.* 2024]
- Residual are Gaussian (at least for SPARKLING)





$$\hat{\mathbf{x}}_t = \arg \min_{\mathbf{x} \in \mathbb{C}^M} \frac{1}{2} \sum_{\ell=1}^L \|\mathcal{F}_t \mathcal{S}_\ell \mathbf{x} - \mathbf{y}_{t,\ell}\|_2^2 + \mu_t g(\Psi \mathbf{x})$$

Estimation of μ_t

Data: $\mathbf{x}_t, \Psi$

Result: μ_t

```
 $\alpha_H \leftarrow P^{HHH}(\Psi(\mathbf{x}_t))$  // Extract high-details wavelet coeffs
```

```
 $n \leftarrow \text{size}(\alpha_H)$ 
```

```
 $\sigma \leftarrow \text{MAD}(\alpha_H) * 0.675$  // Estimate variance using Median Absolute Deviation
```

```
 $\alpha_H \leftarrow \alpha_H / \sigma$ 
```

```
if  $\frac{1}{n} \alpha_H^T \alpha_H < \log_2(n)^{3/2} / \sqrt{n}$  then
```

```
     $\mu_t \leftarrow \sqrt{2 \log_2(n)}$ 
```

```
else
```

```
     $\hat{\mu}_t \leftarrow \arg \min_{w \in \alpha_H} \sum_{i=1}^n \min(\alpha_{H,i}^2, w^2) - 2 * I\{\alpha_{H,i}^2 < w^2\}$  // minimizes the SURE
```

```
    estimator
```

```
     $\mu_t \leftarrow \min(\hat{\mu}_t, \sqrt{2 \log_2(n)})$ 
```

```
end
```

- Preconditioned Proximal operator

$$\begin{aligned}\text{prox}_f^P(\mathbf{x}) &= \arg \min_{\mathbf{u}} f(\mathbf{u}) + \frac{1}{2} \|\mathbf{x} - \mathbf{u}\|_P \\ &= \arg \min_{\mathbf{u}} f(\mathbf{u}) + (\mathbf{x} - \mathbf{u})^\top \mathbf{P}(\mathbf{x} - \mathbf{u})\end{aligned}$$

- [Hong et al. 2024] uses polynomial preconditioners $P = \sum_k p_k (\mathbf{A}^\mathcal{H} \mathbf{A})^k$
- Minimize the spectral radius of Data-Consistency $\text{Id} - \alpha \mathbf{P} \mathbf{A}^\mathcal{H} \mathbf{A}$
- F-1: $p_0 = 2, p_1 = 1$
- Chebychev: $p_0 = 4, p_1 = \frac{10}{3} \alpha$
- also dynamic preconditioning
- HQS stabilize a lot but converges to $f + {}^1g$, not $f + g$.



$$L, S = \arg \min_{L, S} \|\mathcal{F}(L + S) - y\|_2^2 + \lambda_L \|L\|_* + \lambda_S \|\mathcal{T}S\|_1$$

- Two parameters to tune
- BOLD effect is very small
- Choice of the temporal sparsity basis
- Heavy memory workload (whole 4D data loaded)
- Conditioning issues (non-aCartesian)
- Indenpendency of voxels (DOF) for GLM analysis ?
- *[Graedel et al. 2022; Petrov et al. 2017; Lin and Fessler 2019; Otazo et al. 2015]*