National Technical University of Athens
School of Electrical and Computer Engineering

Microprocessors Laboratory
MicroLAB

Functional Ultrasound Imaging: Study of the brain using the ICA modality

Diploma Thesis of Vaia I. Kontopoulou

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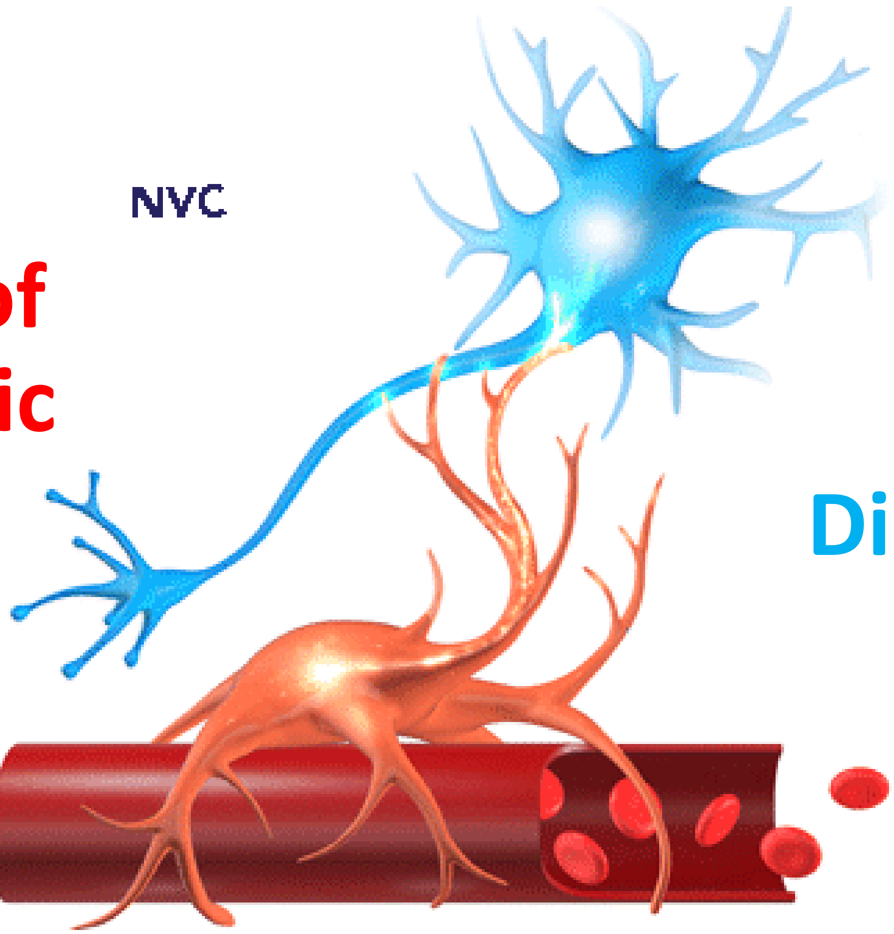
Division of Computer Science, NTUA

Erasmus MC
University Medical Center Rotterdam

Functional Imaging of the Brain

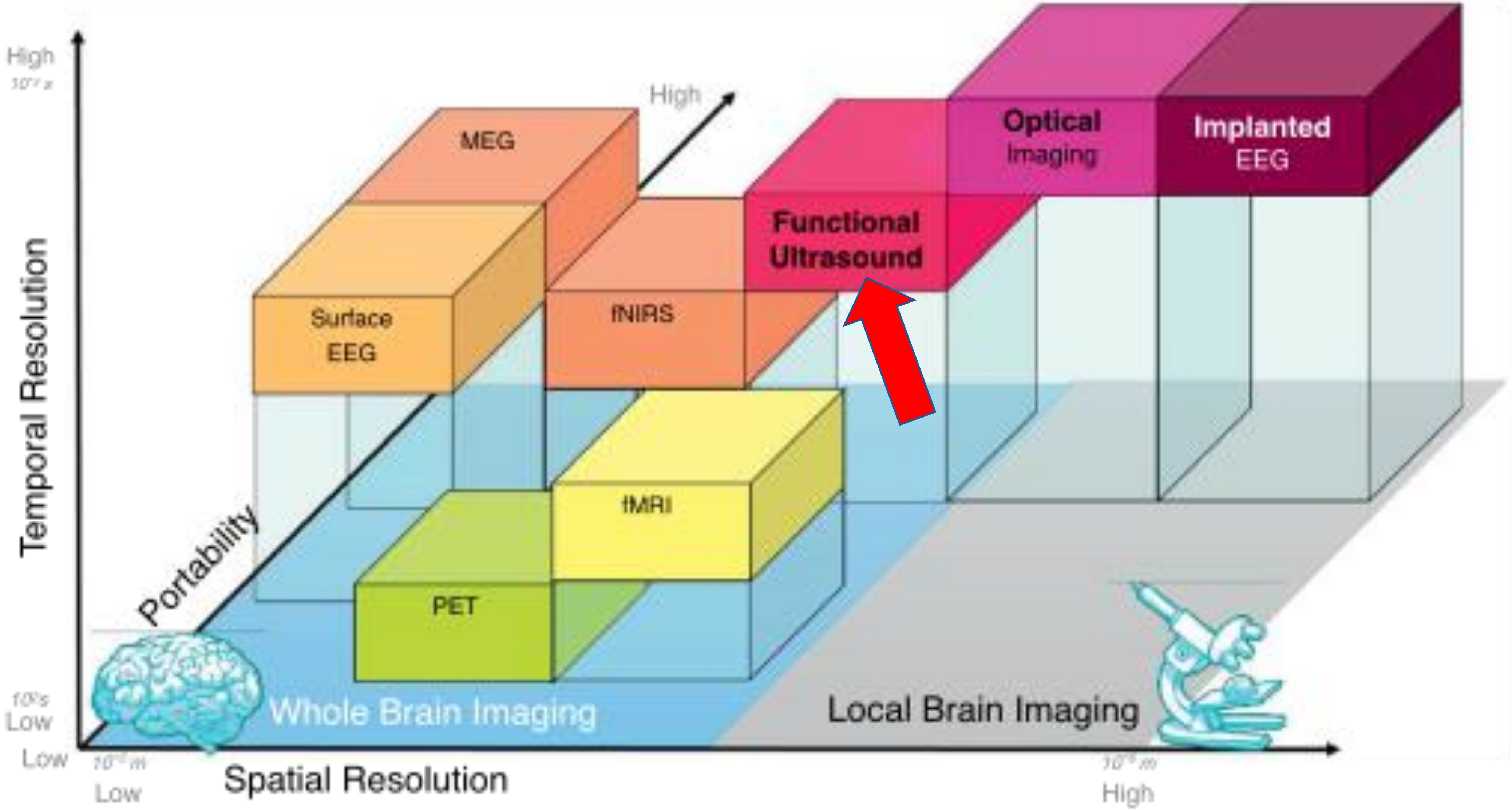
Indirect Imaging of the hemodynamic response



Direct Imaging of the Neuronal Signals

Neurovascular Coupling

Brain Imaging Techniques



Functional Magnetic Resonance Imaging

Based on the measurement of the **BOLD** signal

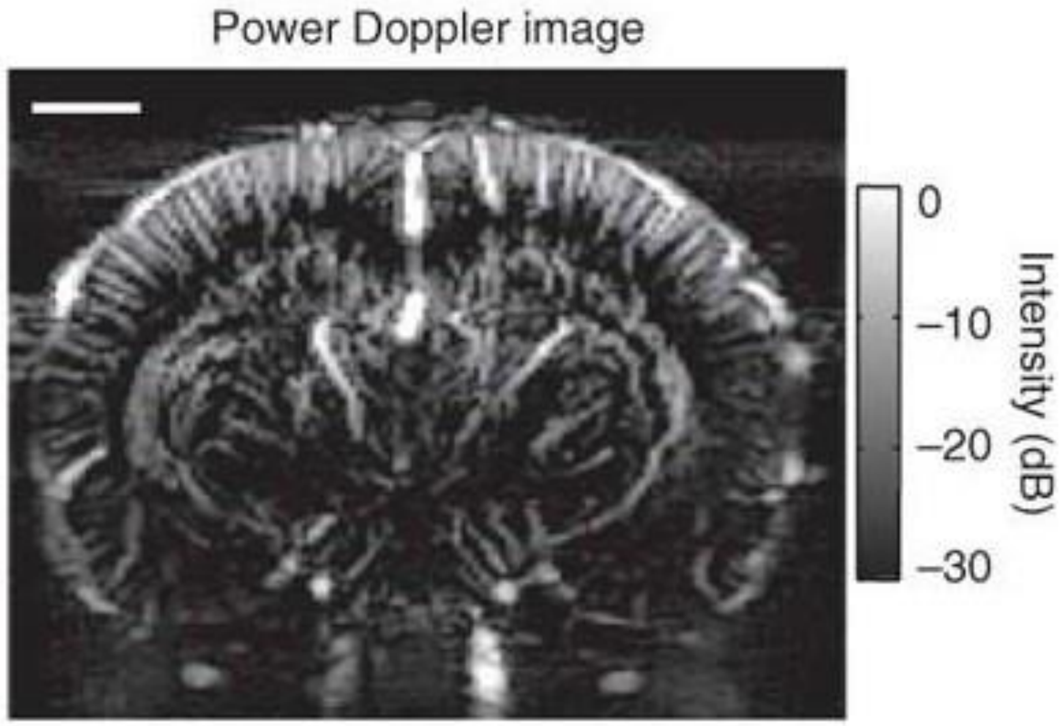
- Non-invasive
- Widely used in research and clinical applications

BUT:
- Very high values of magnetic field required for high spatial resolution
- Decrease in temporal resolution and SNR values in return
- Cannot be used during surgery due to the large size of MRI machines
- High cost

Functional Ultrasound

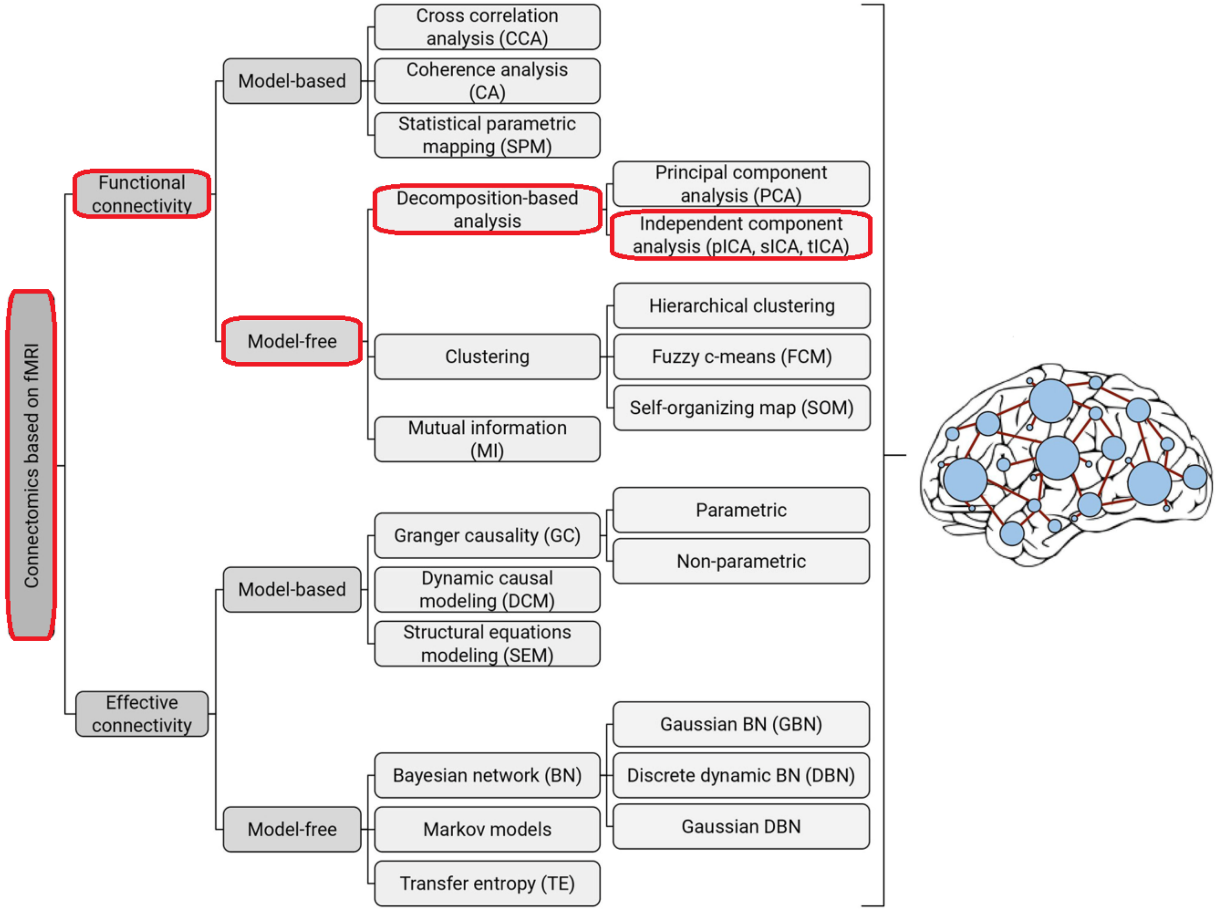
Introductory work: "Functional ultrasound imaging of the brain" (Macé et al. 2011)

- High spatio-temporal resolution
- Portability
- Low cost
- Novel approach to the functional imaging of the brain



FMRI analysis methods:

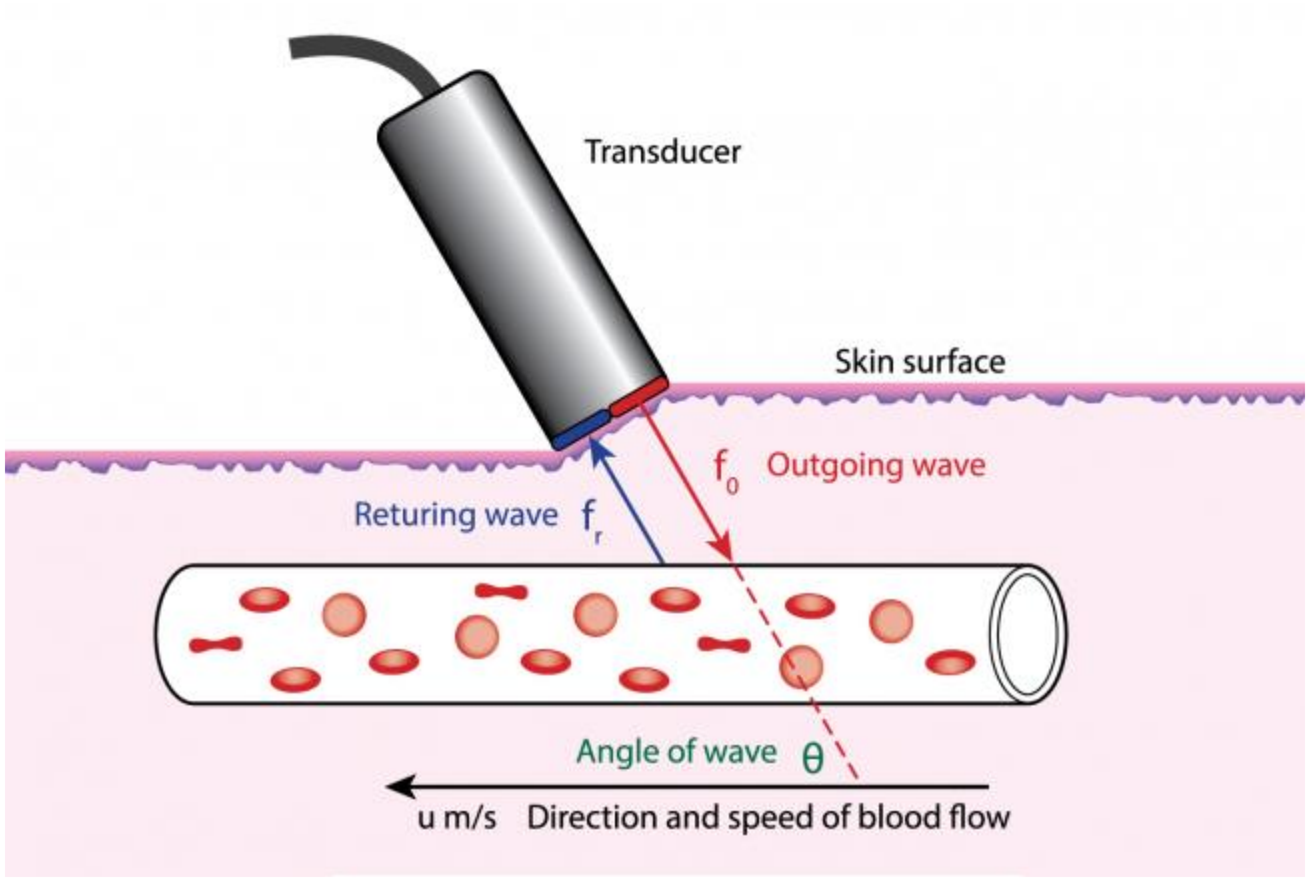
(Where does the ICA lie?)



Purpose statement of the Thesis:

"Explorative study of the Independent Component Analysis method, with regards to the analysis of functional ultrasound data from the brain."

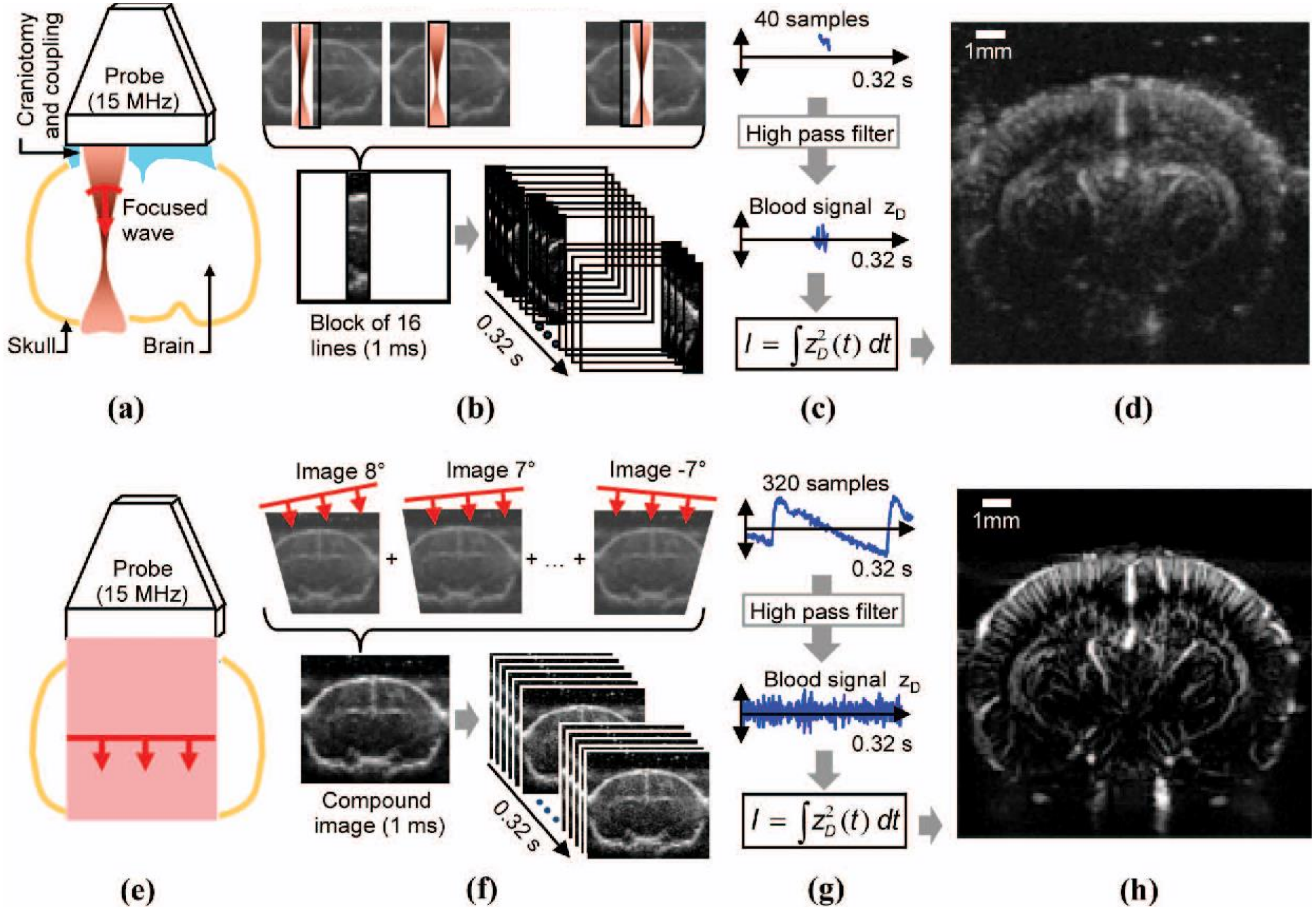
Functional Ultrasound Imaging



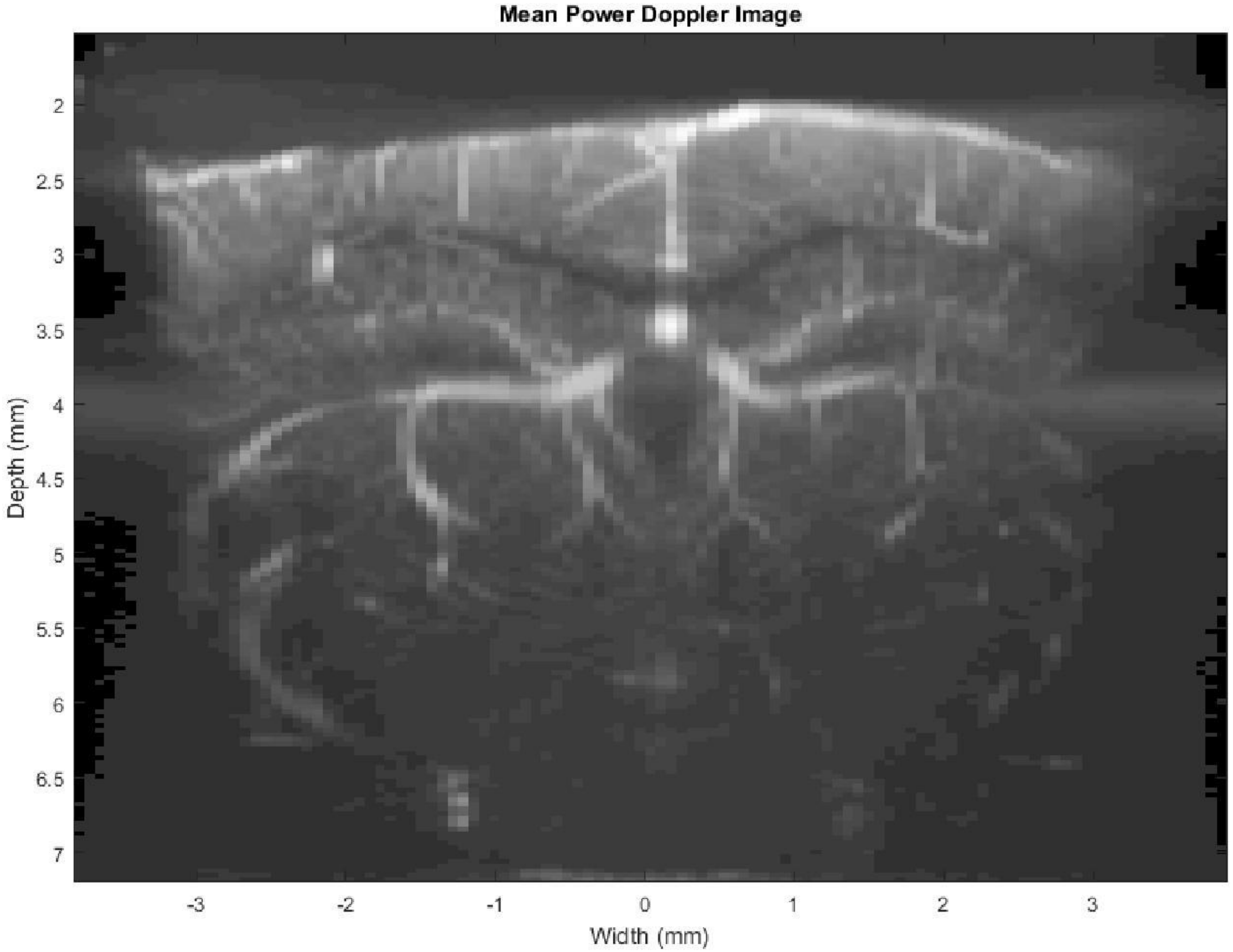
Cerebral Blood Volume
(measured signal)

Power Doppler Image
+
Ultrafast imaging
(µDoppler)

fUS: Conventional vs µDoppler imaging



fUS: Power Doppler Image



Each pixel (x, z) of the PDI has an intensity value I:

$$I(x, z) = \frac{1}{N} \sum_{i=1}^{N} s_F^2(x,\ z,\ t_i)$$

N, number of time samples

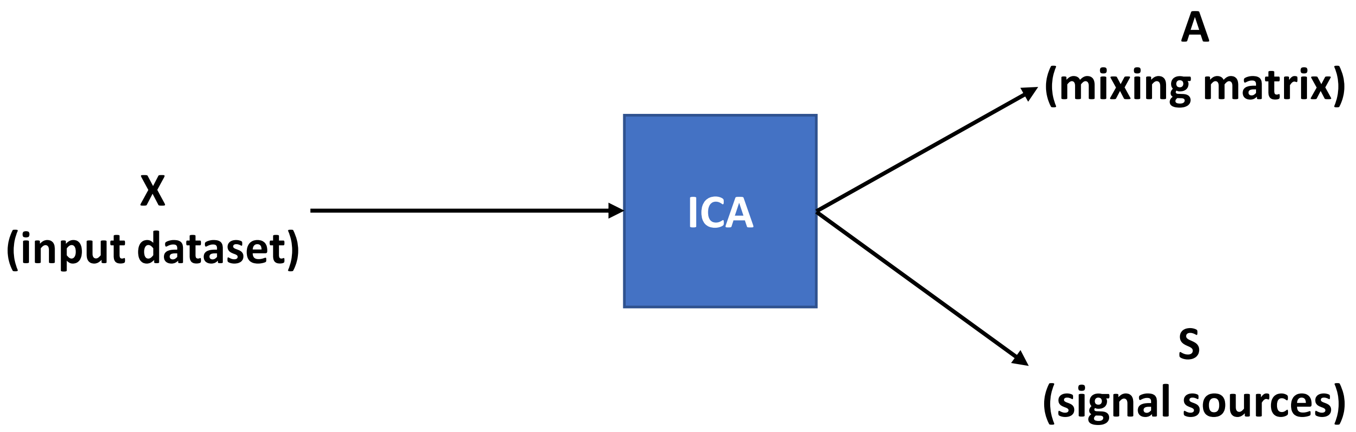
s, compound b-mode image amplitude

$$t_i = \frac{1}{f_{samp}}$$

f_{samp}, frame rate

Independent Component Analysis

- Statistical, model-free, computational technique
- Main goal: To reveal hidden signal sources inside the data



Additional limitations needed for convergence!

ICA ambiguities: Signal sources ordering, Model order, Results ranking

Solution: Icasso clustering software

Stability measurement using Iq index

ICA assumptions

- Statistical independence of signal sources (A and/or S matrix)
- Non gaussian signal sources
  - Algorithmic approach: Informax principle of least mutual information, contrast function maximization

In our work we used the tanh contrast function due to its low rise-time which results in more robust estimators.

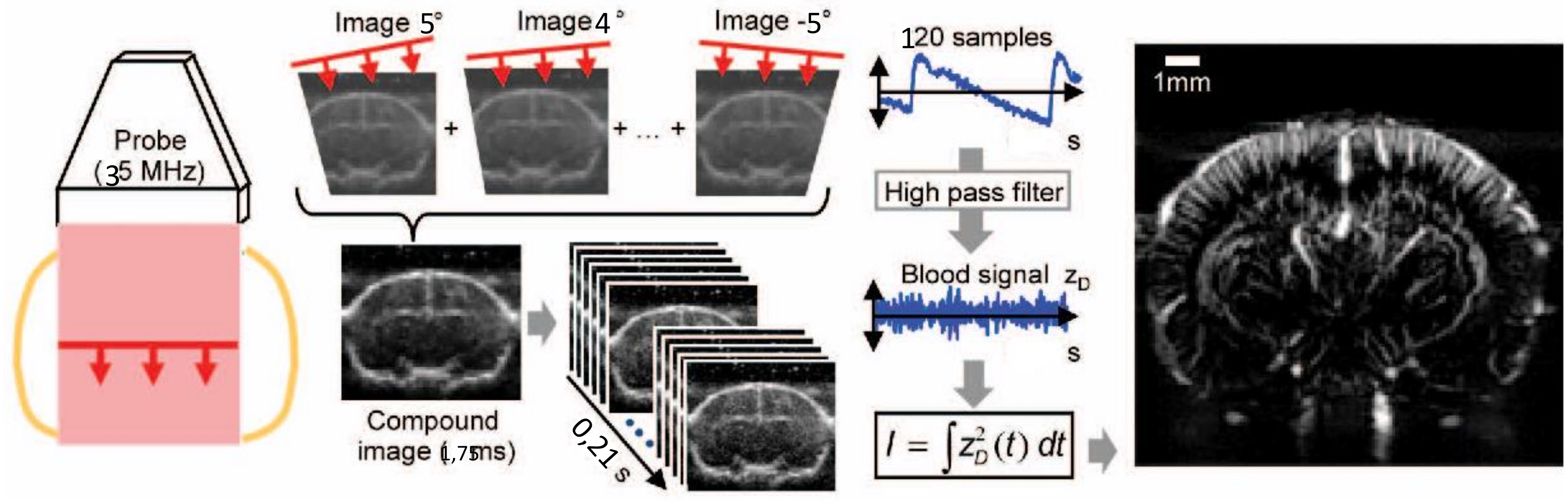
ICA ambiguities

- Signal sources ordering
- Model order (user defined)
- Results ranking: cannot compare between different runs of the ICA algorithm

Solution: Icasso clustering software

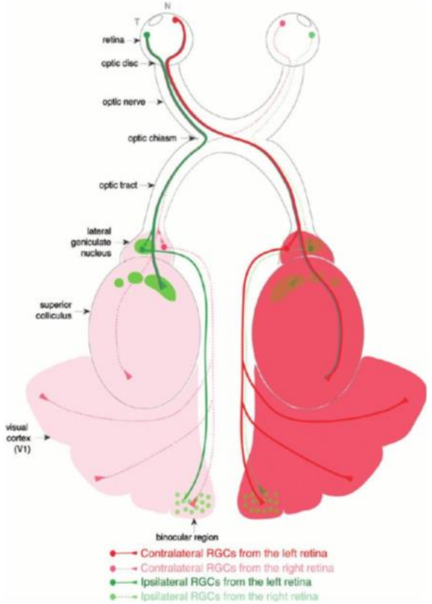
Experimental setup

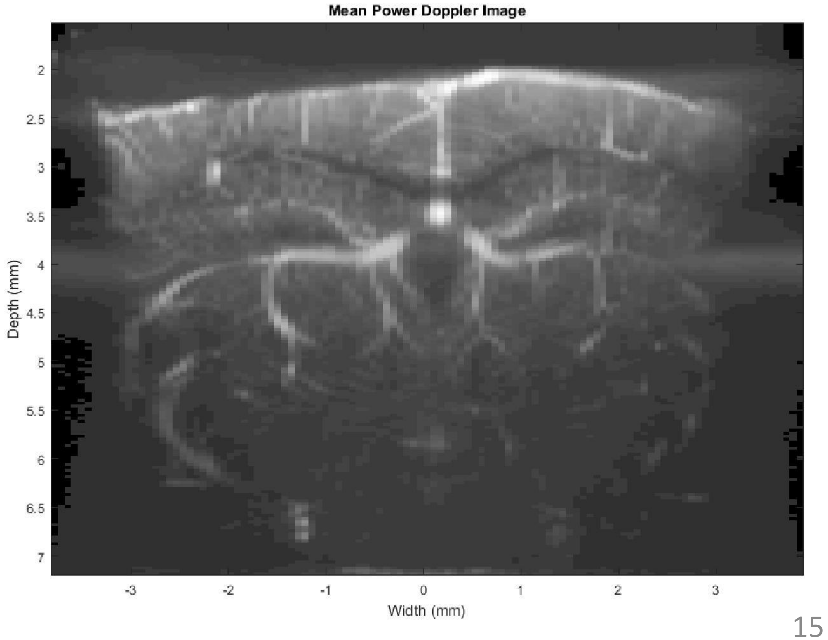
- task-based fUS
- Ultrafast imaging device: VANTAGE 64-LE
- -5 to +5 degrees, 14 pulses per cycle, 8kHz pulse frequency
- 120 images per PDI => 4.76Hz time resolution



Visual stimulation paradigm

- 5, 2D datasets from the same mouse
- 1143 PDI images in 240 sec
- Optical stimulation, on/off optical sequence





PDI dataset preprocessing

- Removal of PDI dataset spatial border
- Gaussian smoothing (3D gaussian kernel)
- Removal of time limit values from the 3D dataset (proportional to the gaussian kernel size)
- Data normalization

- PCA (research parameter)

FastICA algorithm

- Calculates independent signal sources, from multidimensional inputs.
- Goal: Maximization of the contrast function, which measures non-gaussianity.

Characteristics:

- Cubic (or quadratic) speed of convergence
- Easy to use
- Capability of calculating the independent sources in a specific order
- Optimizable and Scalable

FastICA parameters

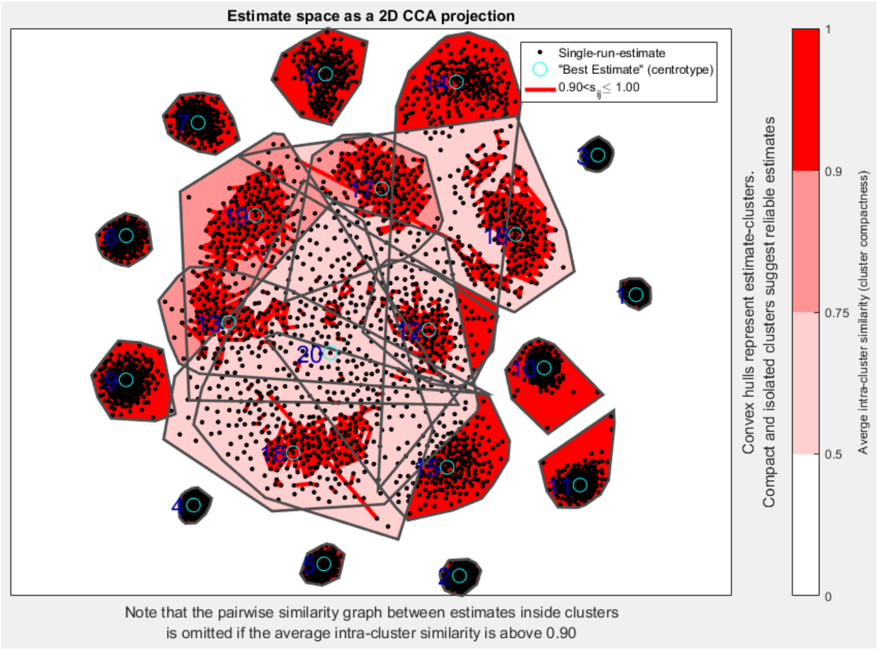
- Approach: **Symmetric** or Deflatory
- Number of independent components to be defined (numOfIC): user defined
- Non-linear contrast function: **tanh**
- PCA dimension (lastEig): user defined

Icasso parameters

- Resampling strategy: Average Linkage Criterion
- Number of resampling cycles: user defined
- Maximum allowed number of iterations: user defined

Output:

- Independent components matrix
- mixing matrix A
- demixing matrix W
- Iq component stability index

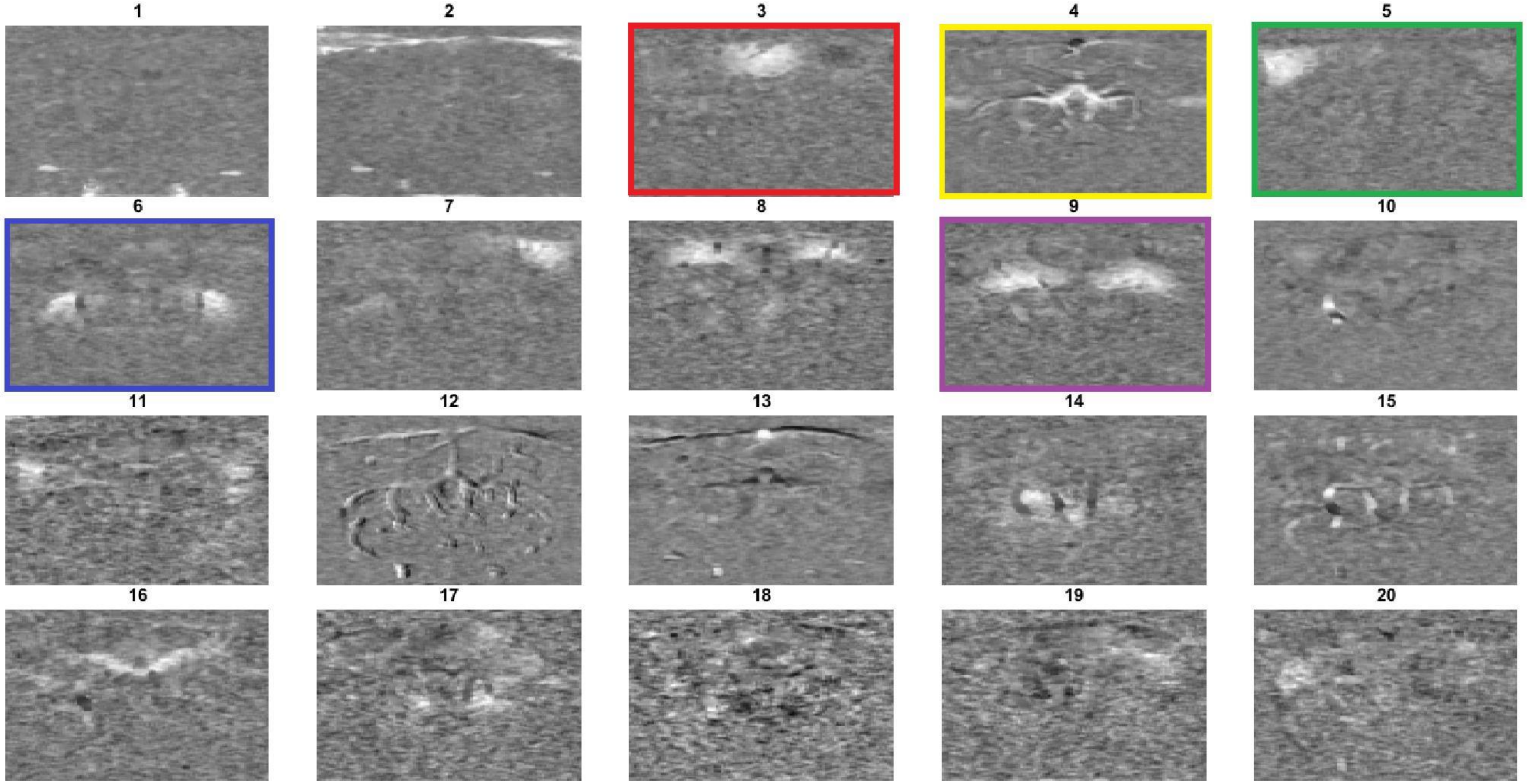


Reference datasets

For each of the five fUS datasets we generated:

- A reference set of 20 independent components
  - PCA dimension 20
  - 100 Icasso resampling cycles
- A reference set of 100 independent components
  - PCA dimension 100
  - 100 Icasso resampling cycles

Reference dataset example



ICA research directions

- Effect of the input PCA dimension to the ICA output, with fixed # of ICs
  - Icasso parameters: 20 Independent Components, PCA 20-200 (step 20), 100 resampling cycles, upper limit of iterations 300
- Noise tolerance: input with increasing added noise level
  - Icasso parameters: 20 Independent Components, PCA 20, snr 5-30 (step 5), 100 resampling cycles, upper limit of iterations 1000
- Dynamic analysis
  - Icasso parameters: 20 Independent Components, PCA 20, window length 200 samples (approx. 42sec), 30 resampling cycles

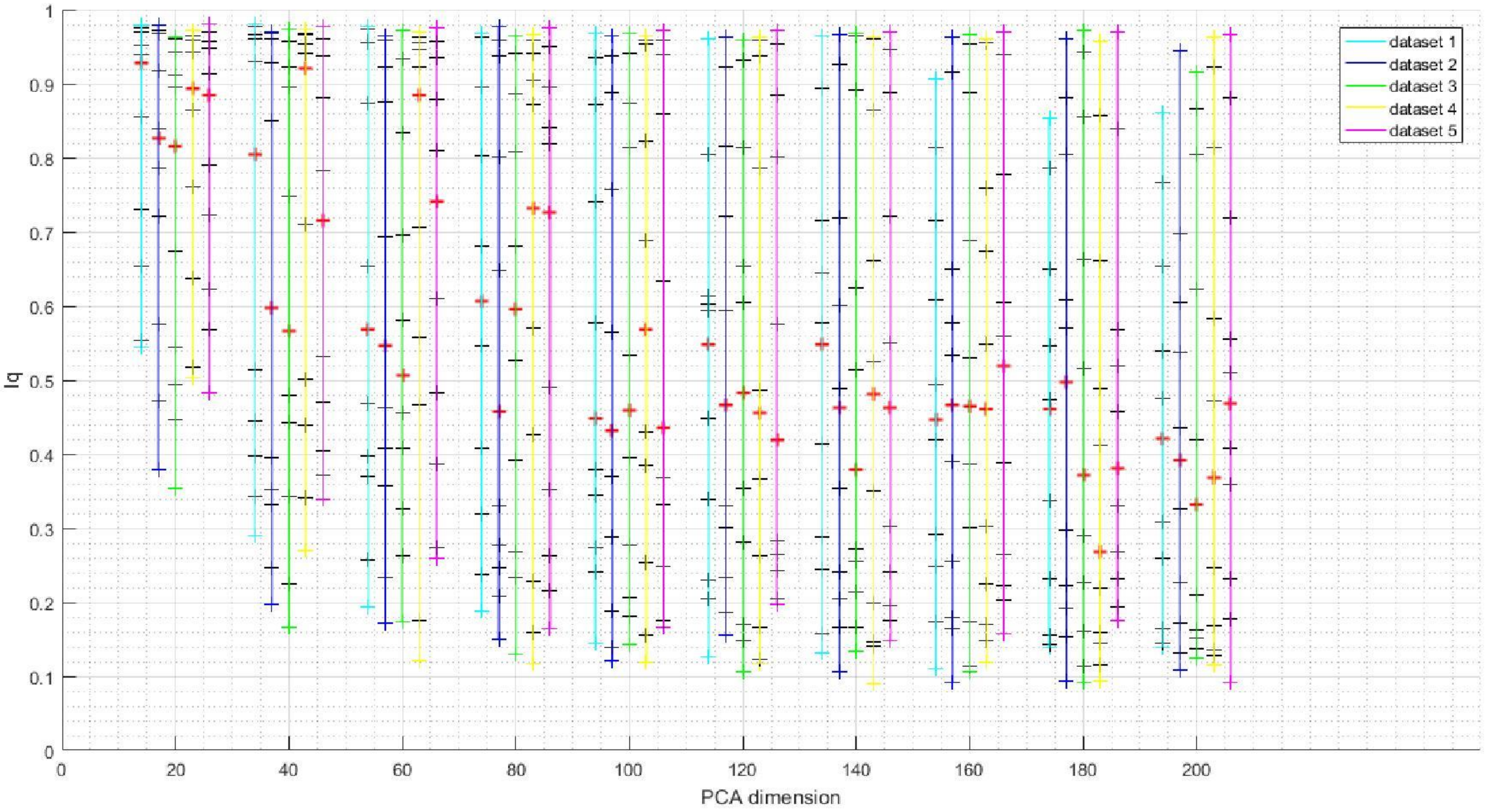
Analysis tools

- The analysis of the 5 fUS dataset was performed in the Matlab coding environment (R2016b).
- The open-source software package Icasso 1.21 was used, for investigating the reliability of ICA estimates by clustering and visualization.
- The FastICA algorithm was used for the implementation of the ICA.
- The analysis was performed using an Intel Core i5-4210U CPU, 1.70GHz to 2.40GHz processor frequency, 4GB RAM laptop.

Analysis performance

- Varying PCA dimension: approx. 2,5h/dataset for 300 iterations max per Icasso resampling cycle (100 resampling cycles)
- Noise tolerance: approx. 3,5h/dataset for 1000 iterations max per Icasso resampling cycle (100 resampling cycles)
- Dynamic analysis: approx. 2,5h/dataset for 19 time steps (30 resampling cycles)
- Total input size: 717MB
- Data size for each analysis direction: 12GB(PCA), 6,55GB(snr)

Constant # of ICs, Varying PCA dimension



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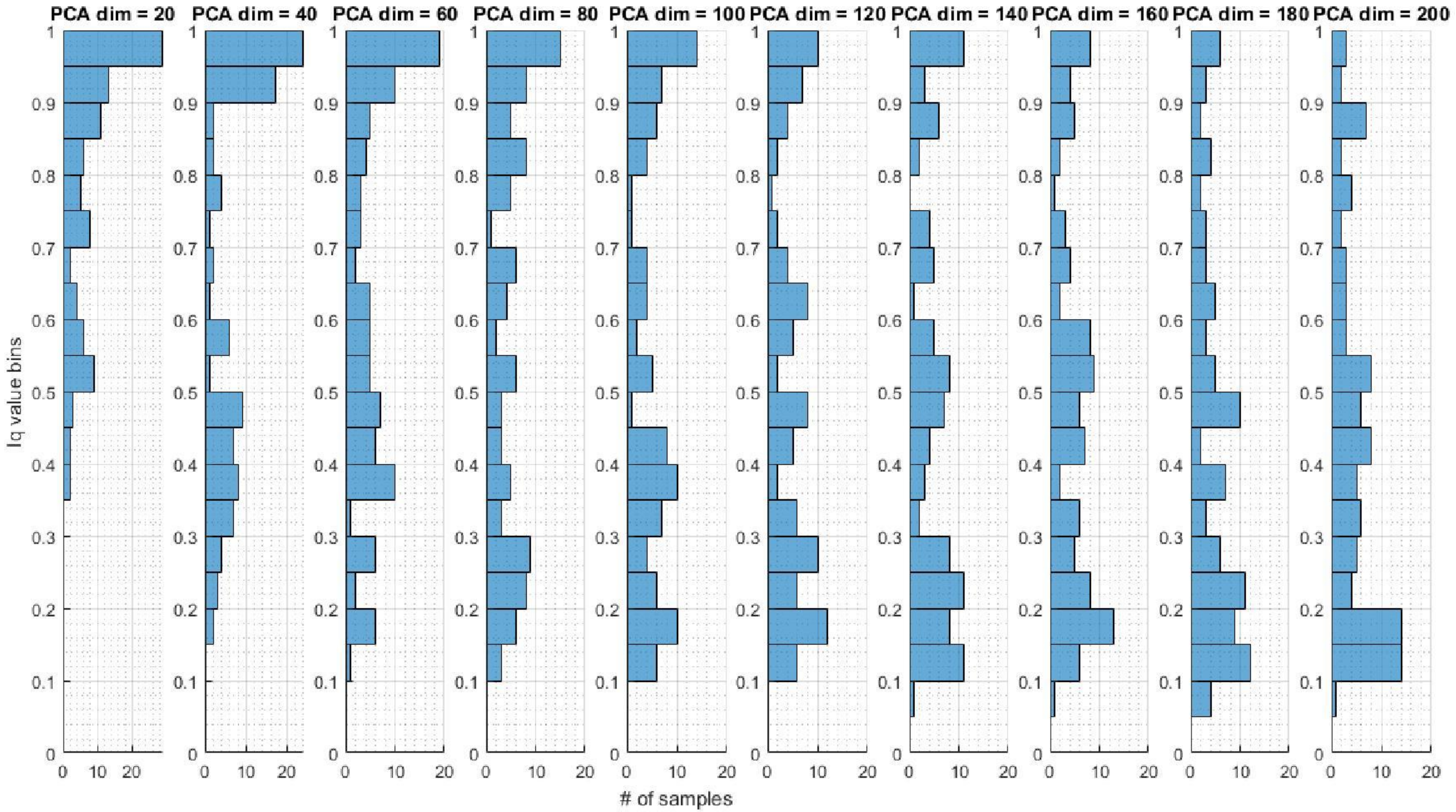
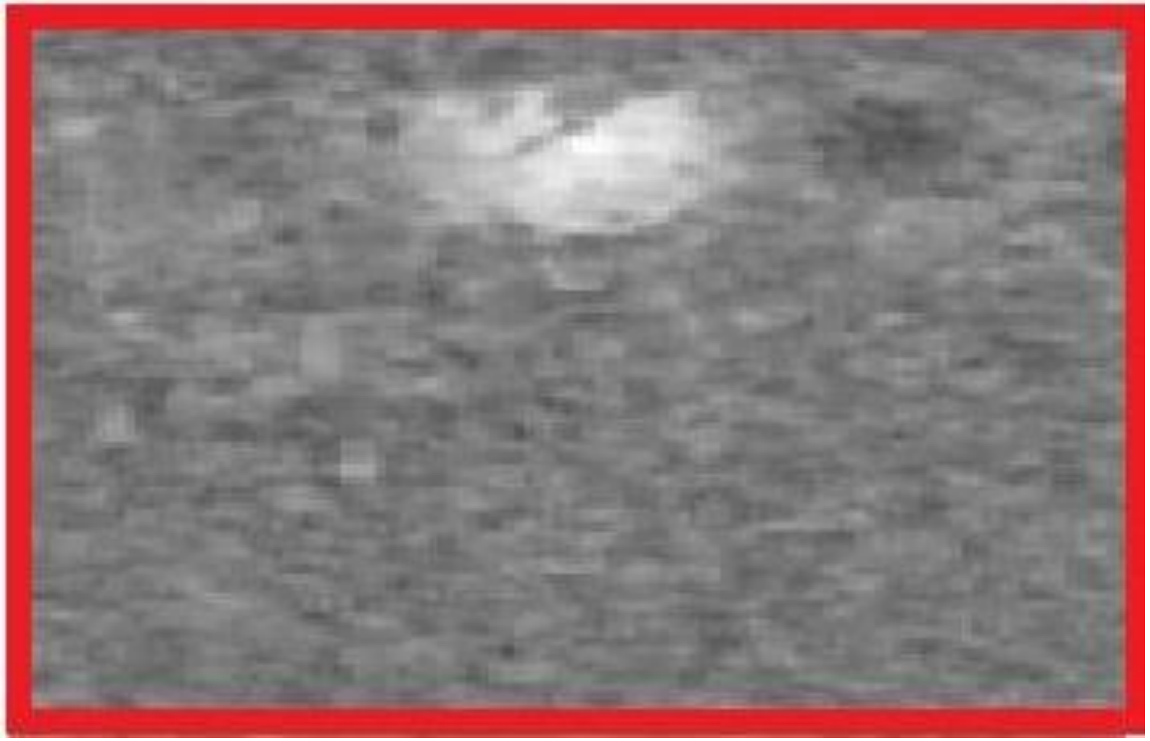
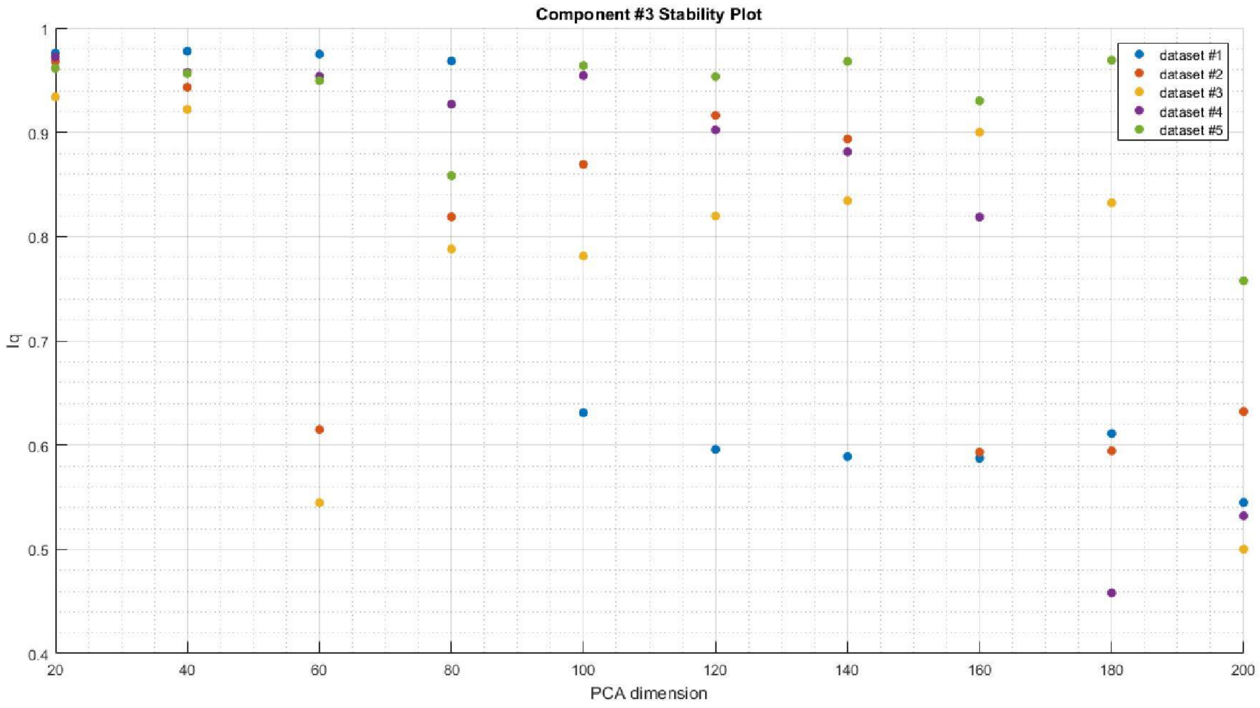


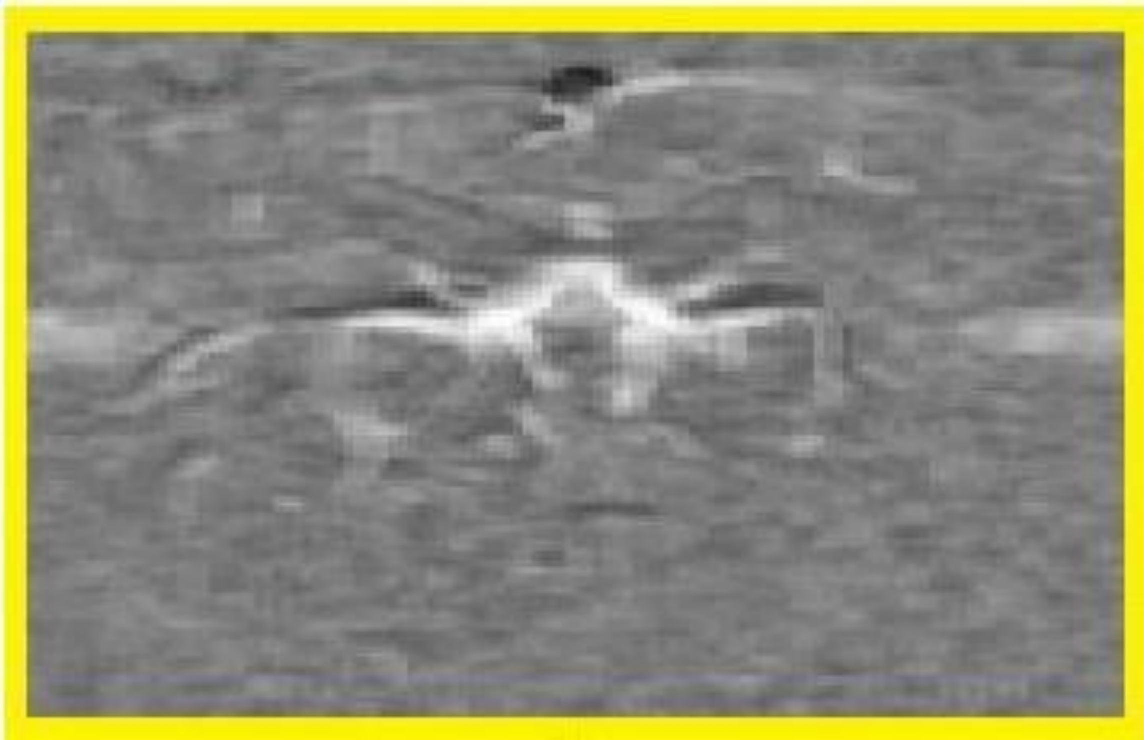
Constant # of ICs, Varying PCA dimension

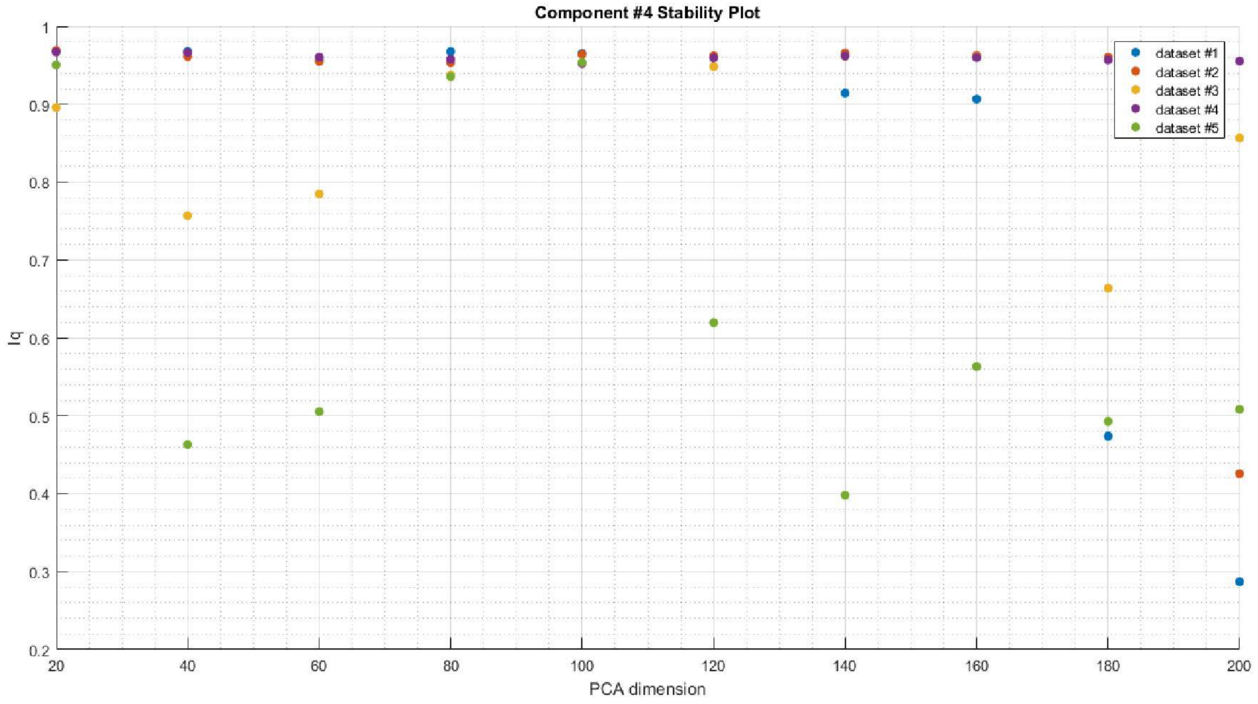




Retrosplenial Cortex (RSP v, d)

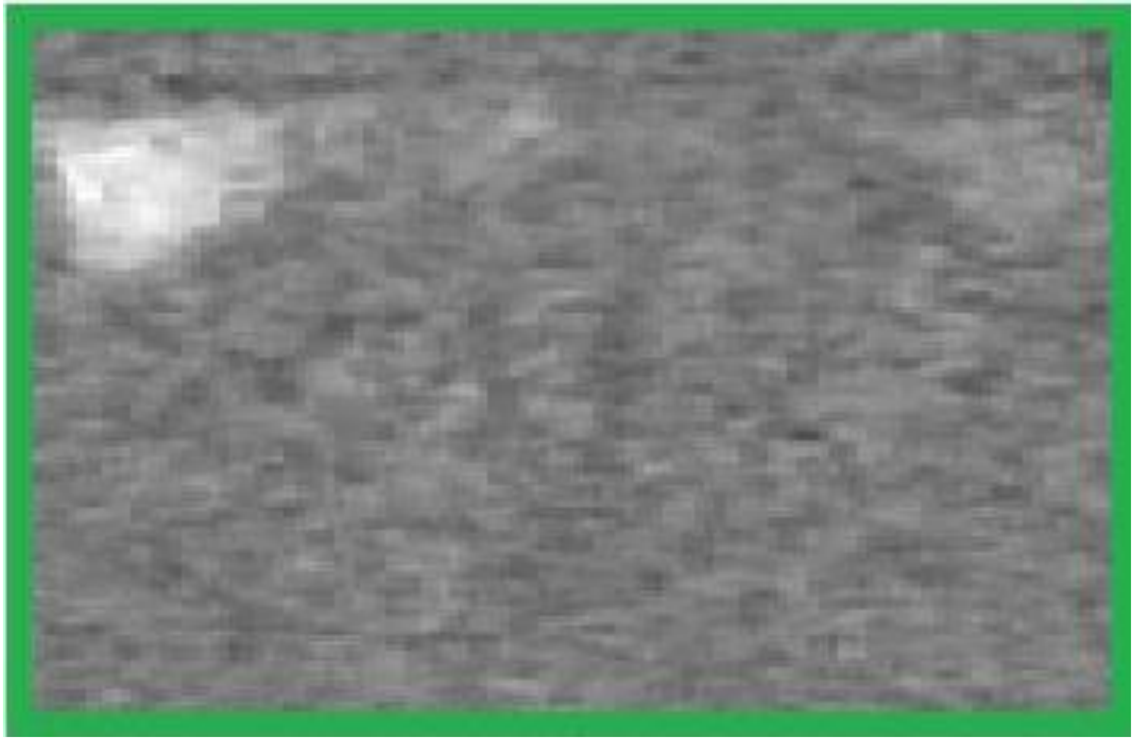
Constant # of ICs, Varying PCA dimension



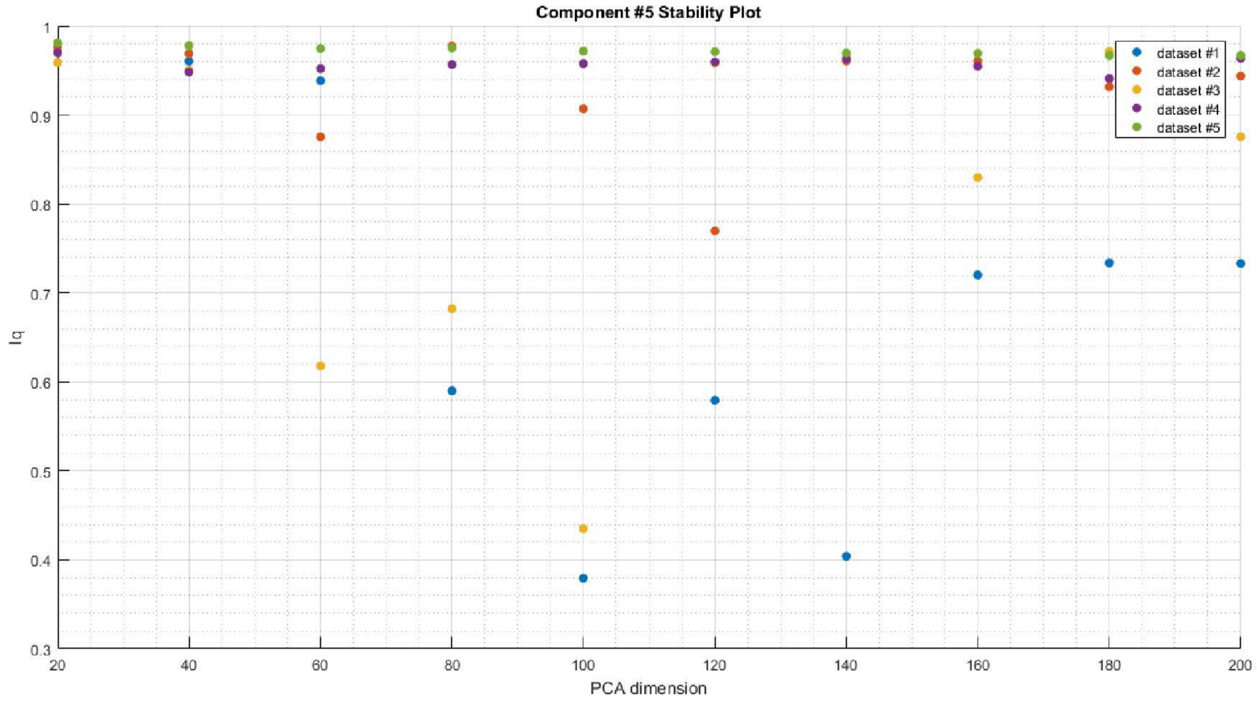


Main Blood Supply (MBS)

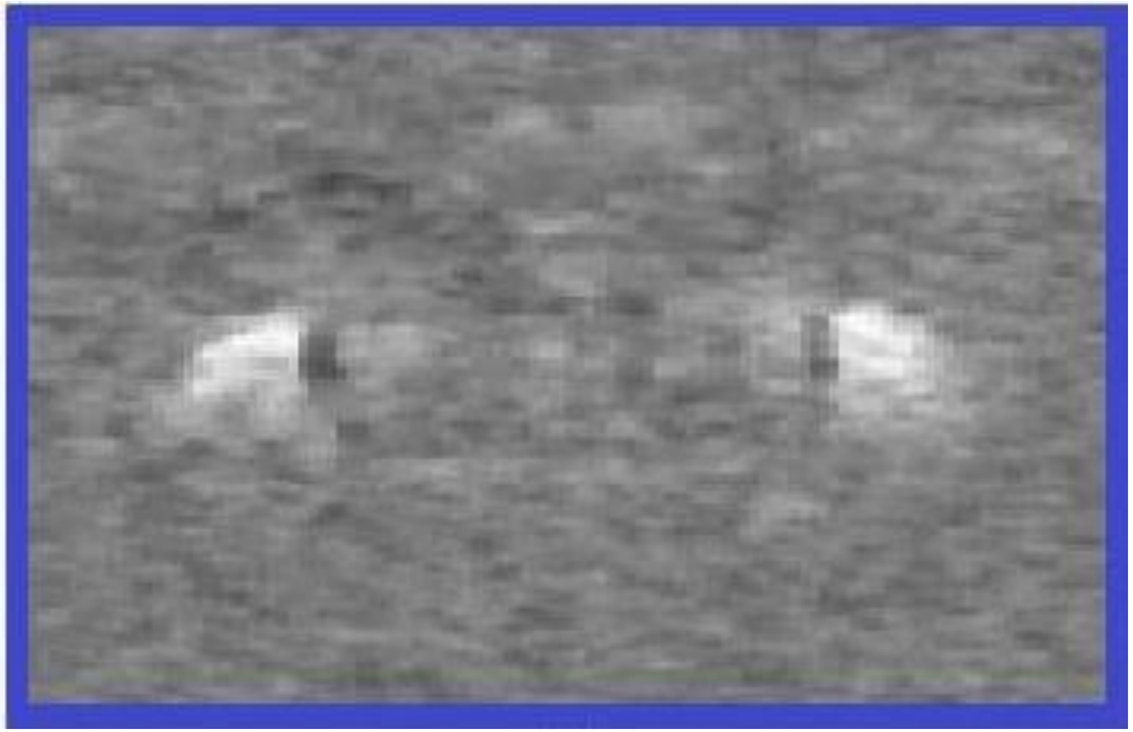
Constant # of ICs, Varying PCA dimension

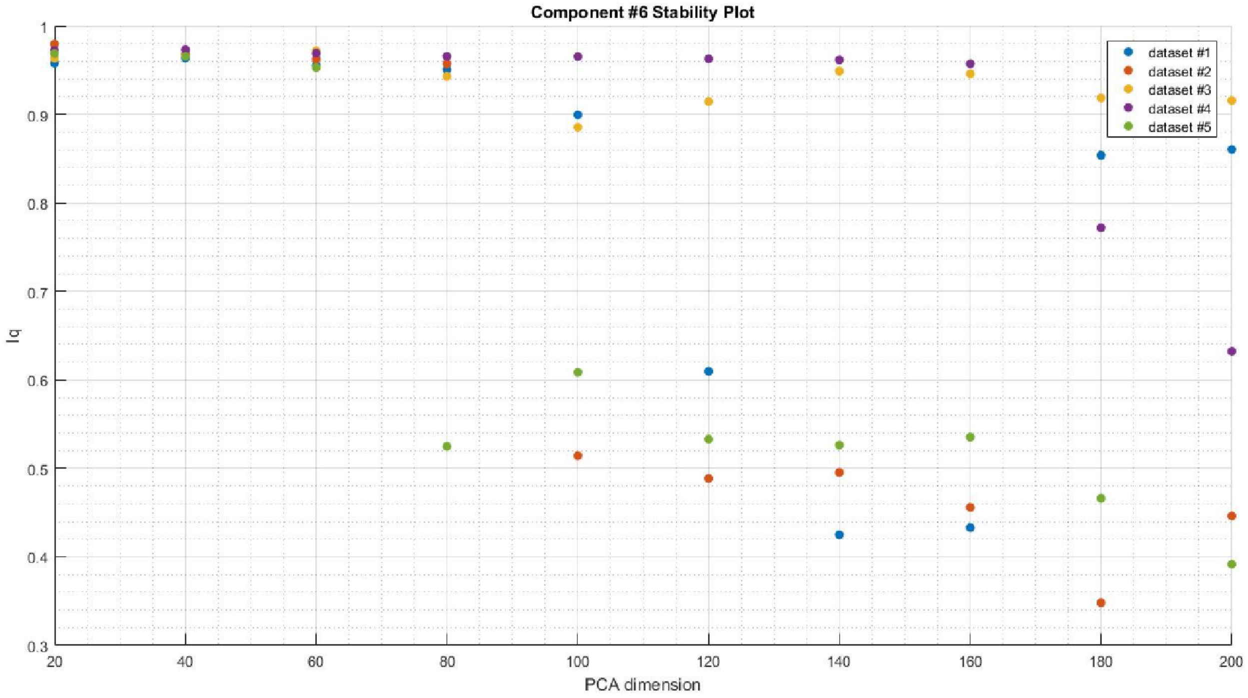


primary Somatosensory area (SSp)



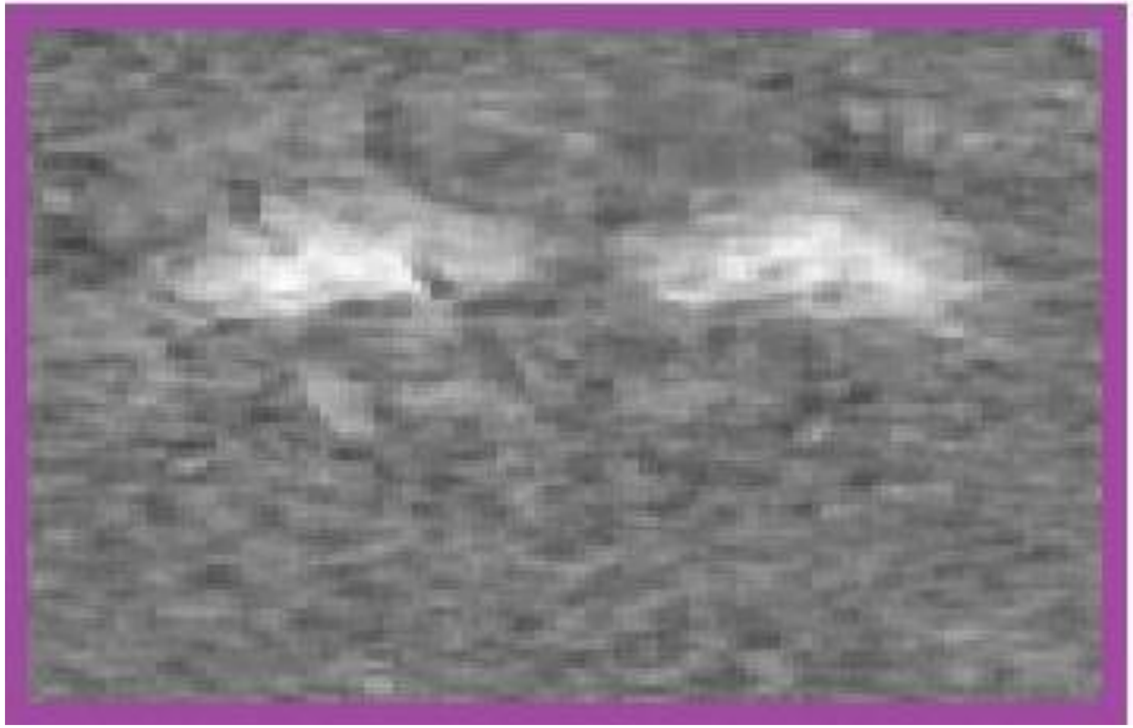
Constant # of ICs, Varying PCA dimension



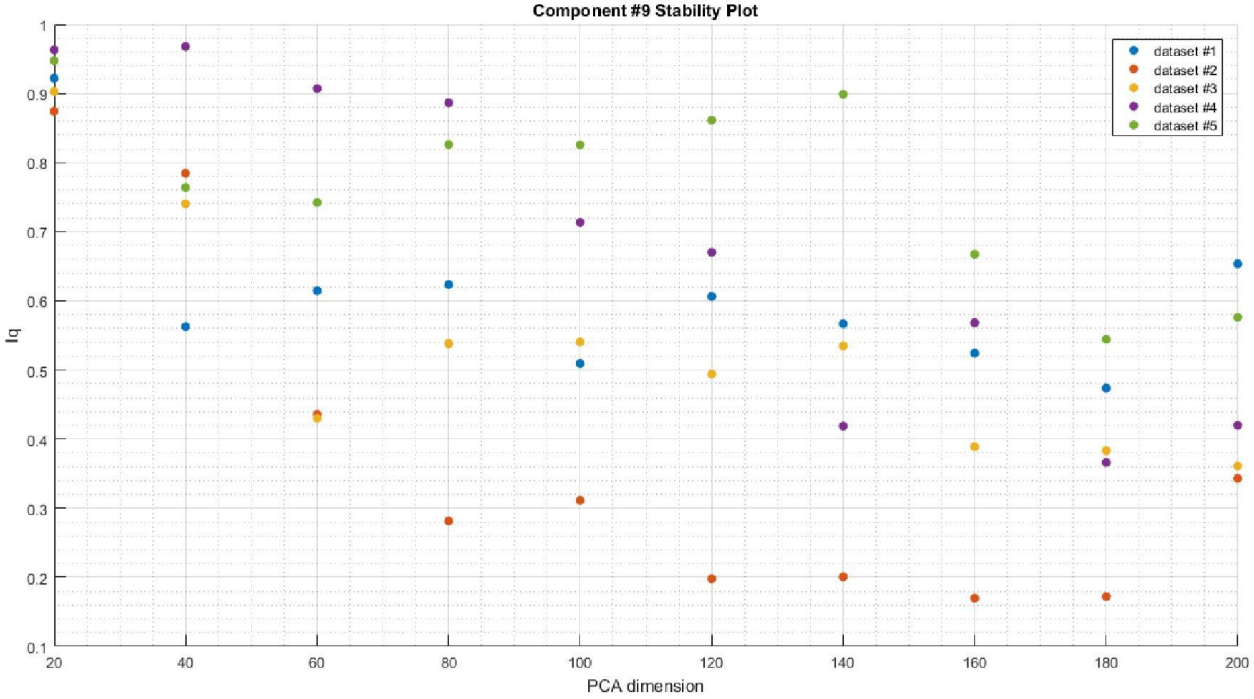


LGN (Lateral Geniculate Nucleus)

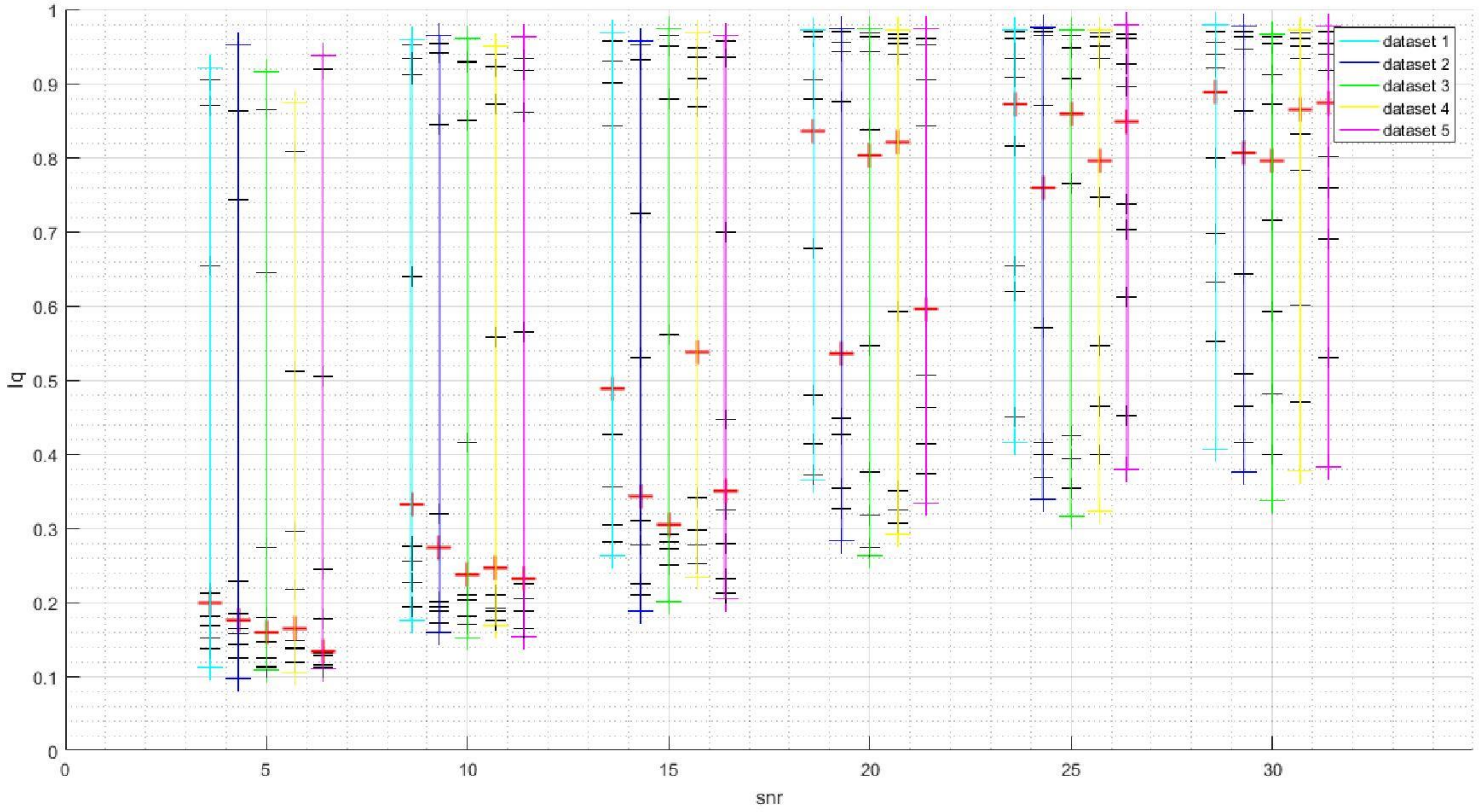
Constant # of ICs, Varying PCA dimension



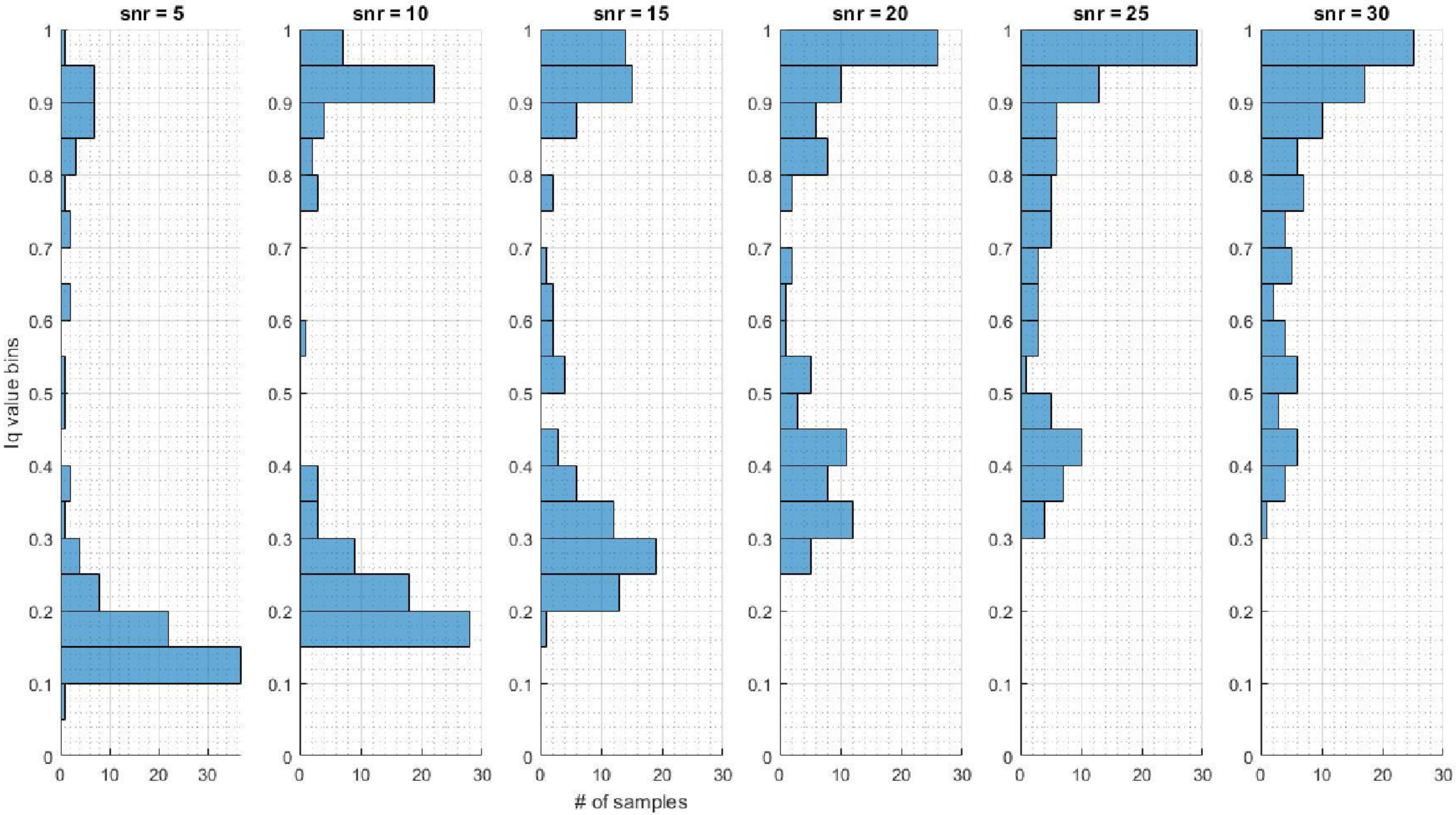
Hippocampus (Hip)



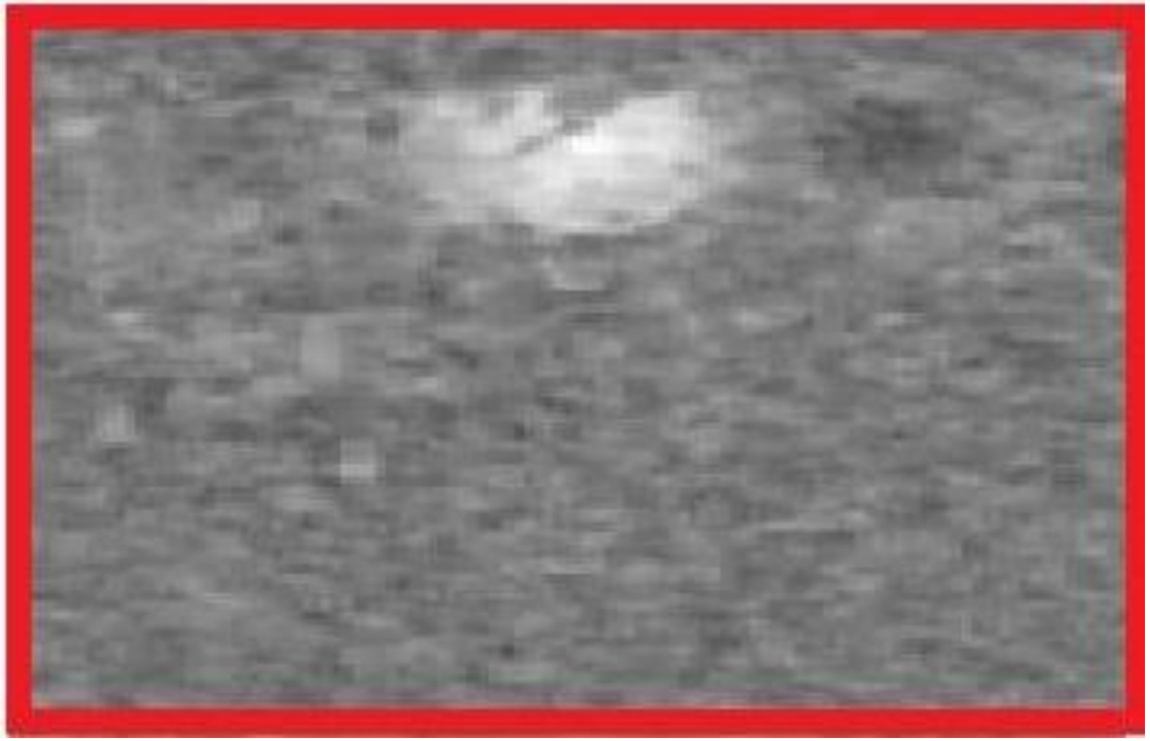
Noise tolerance

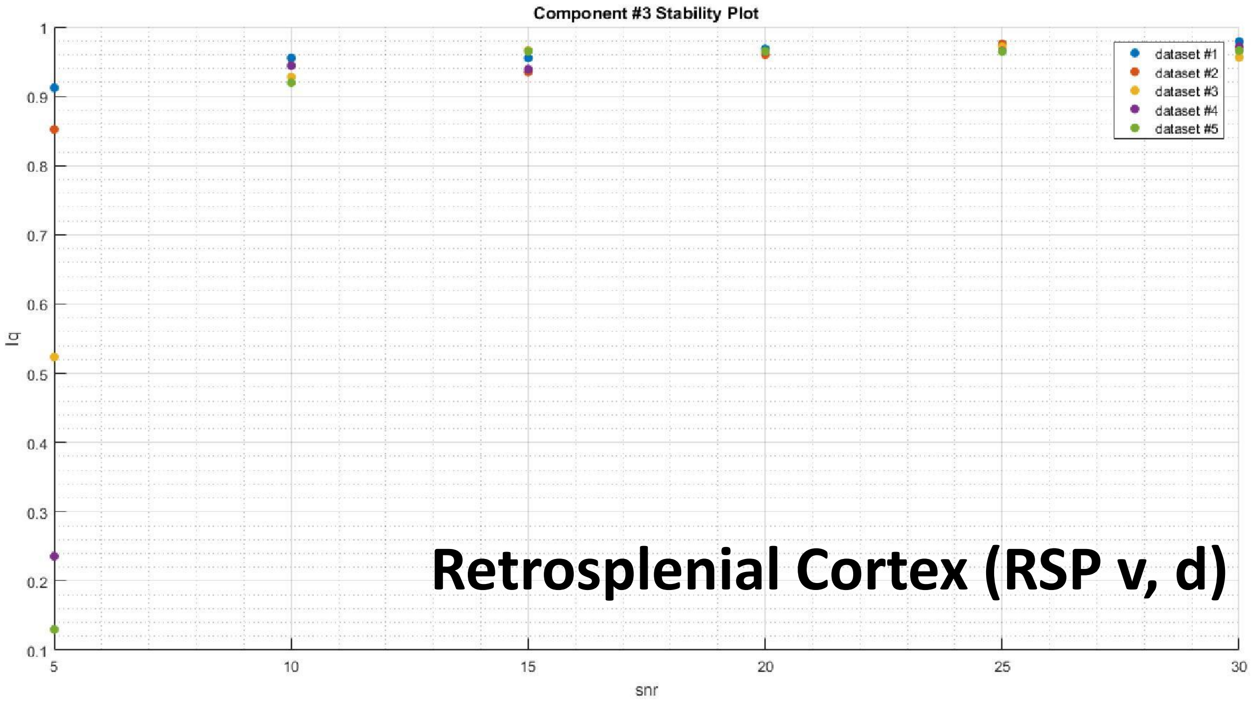


Noise tolerance

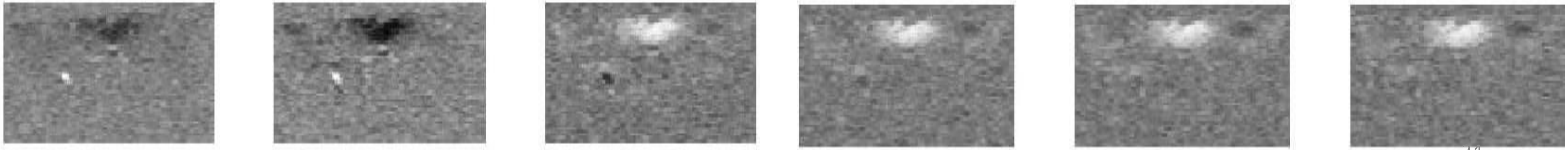


Noise tolerance

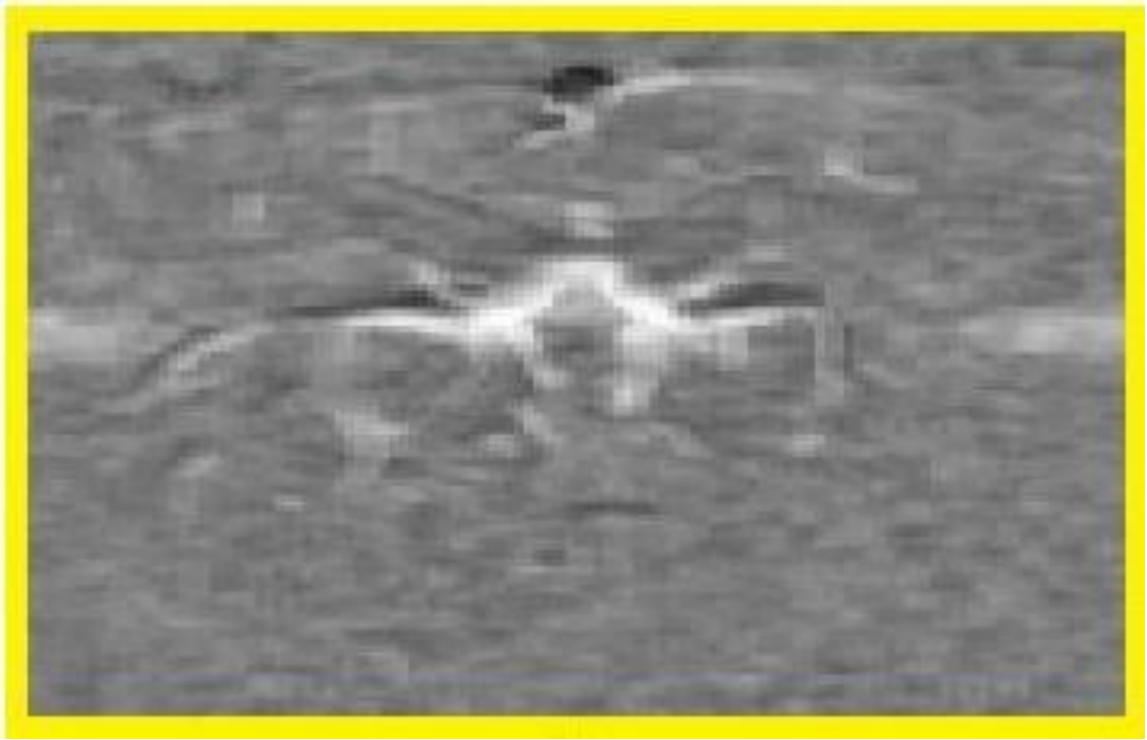


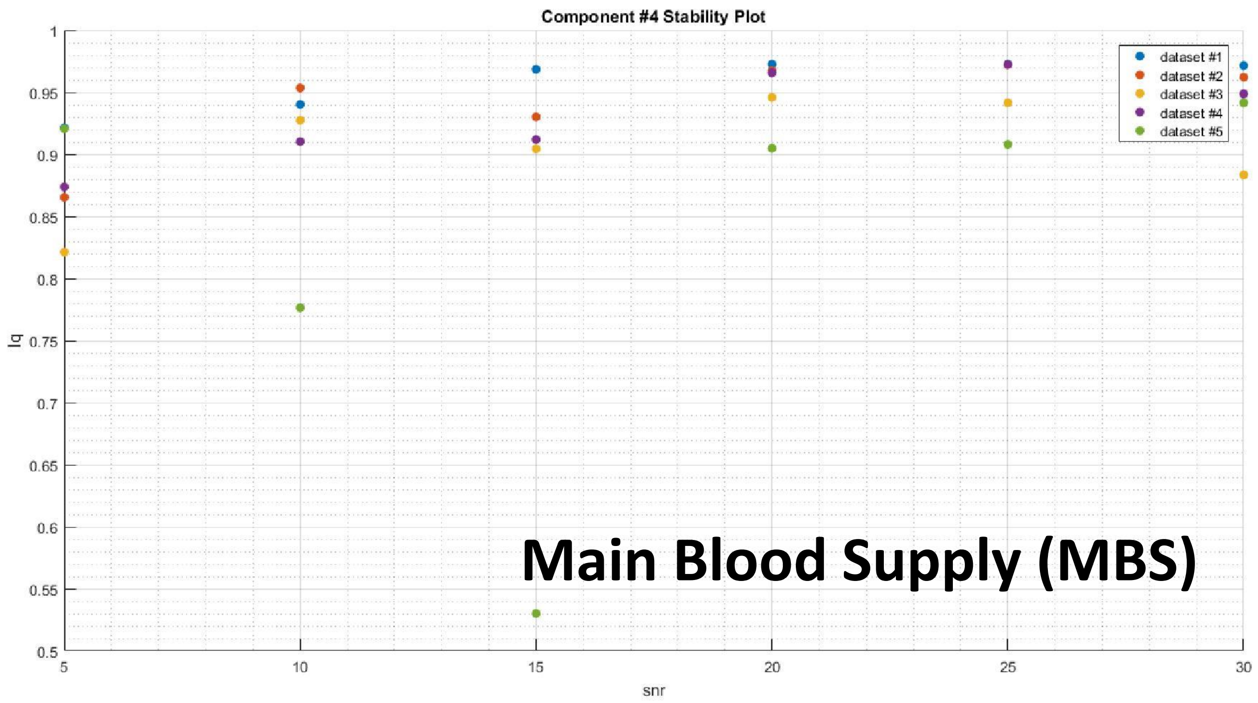


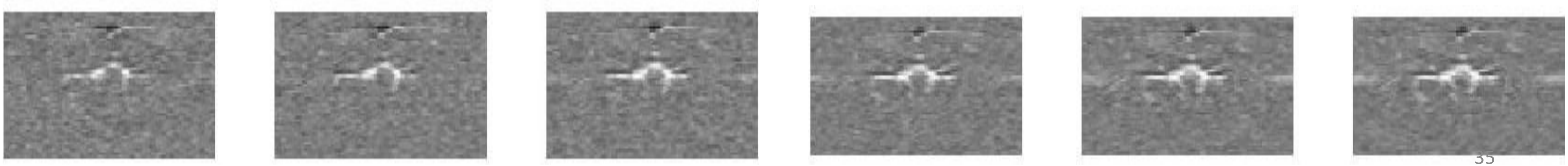
Retrosplenial Cortex (RSP v, d)



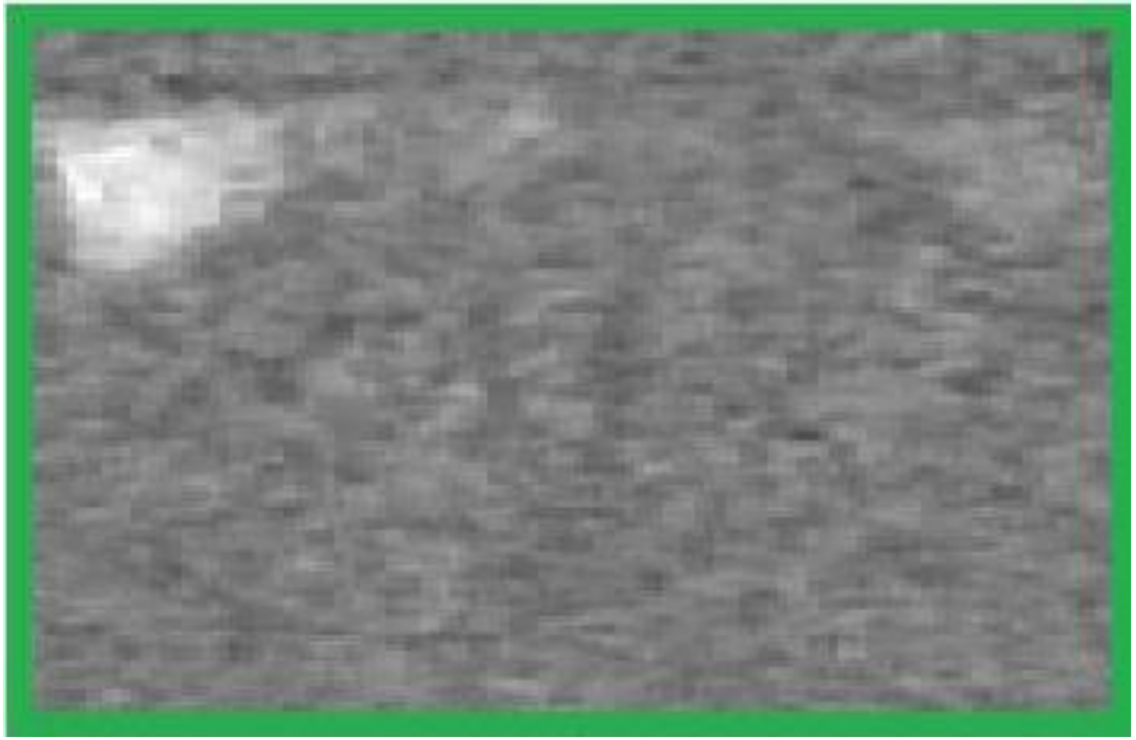
Noise tolerance

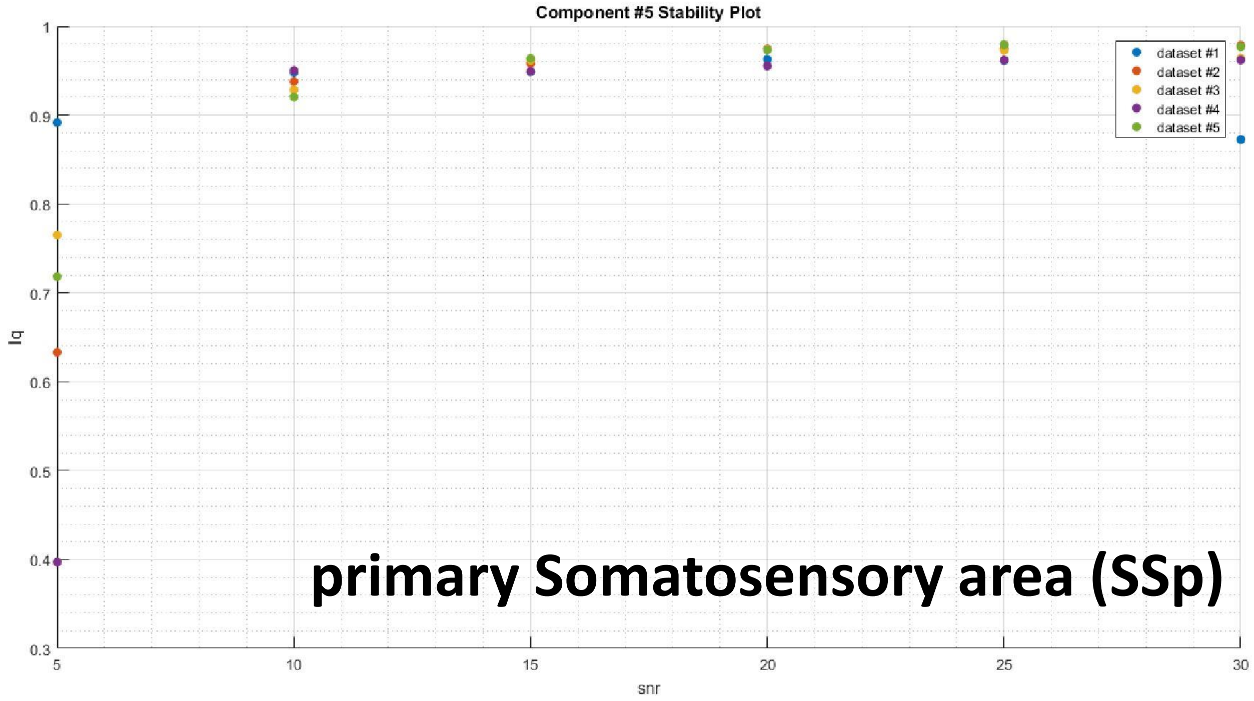


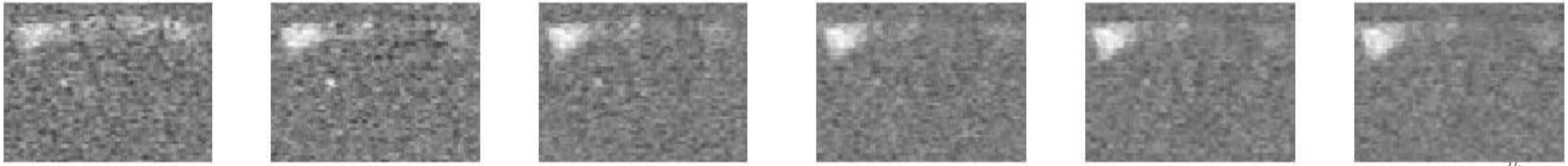




Noise tolerance







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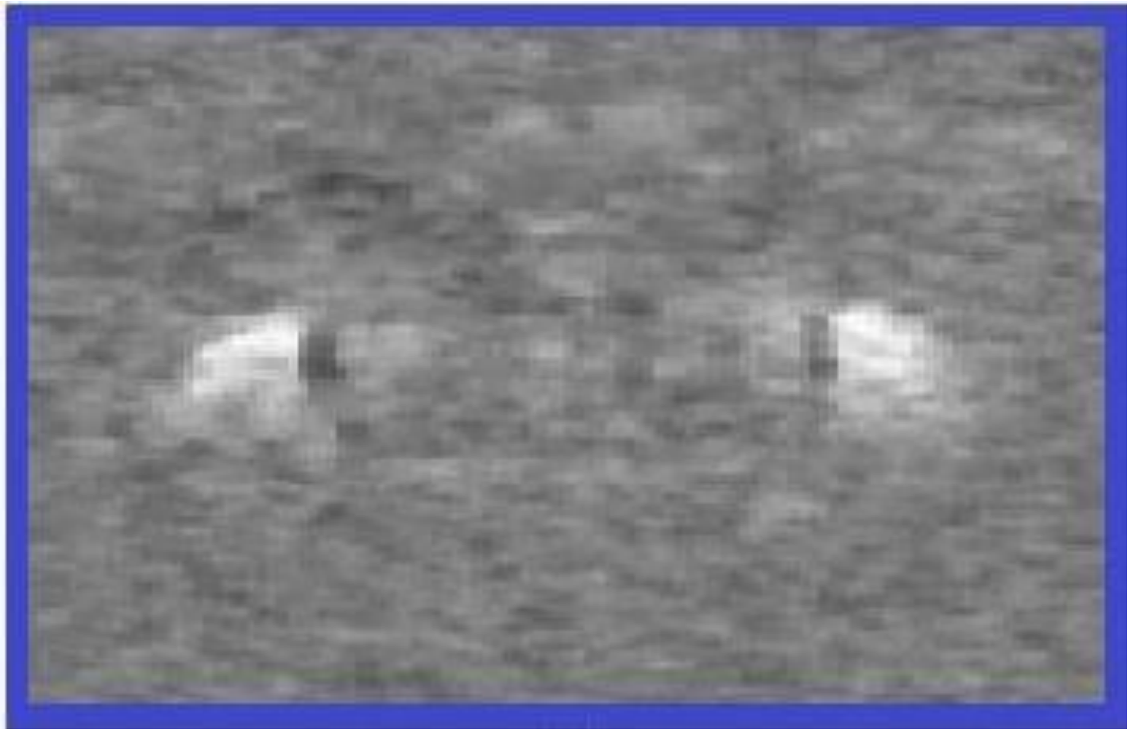
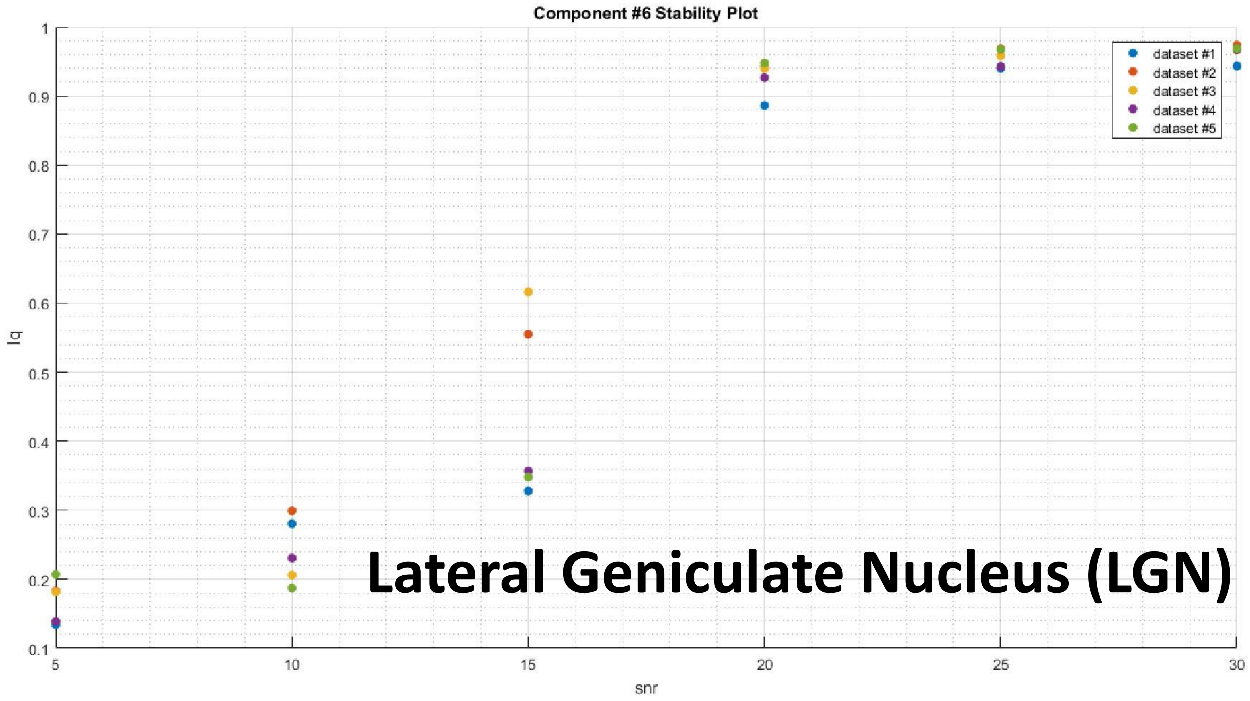
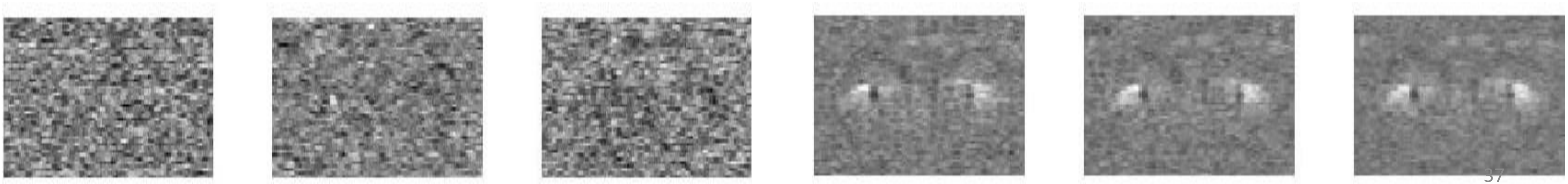




Lateral Geniculate Nucleus (LGN)



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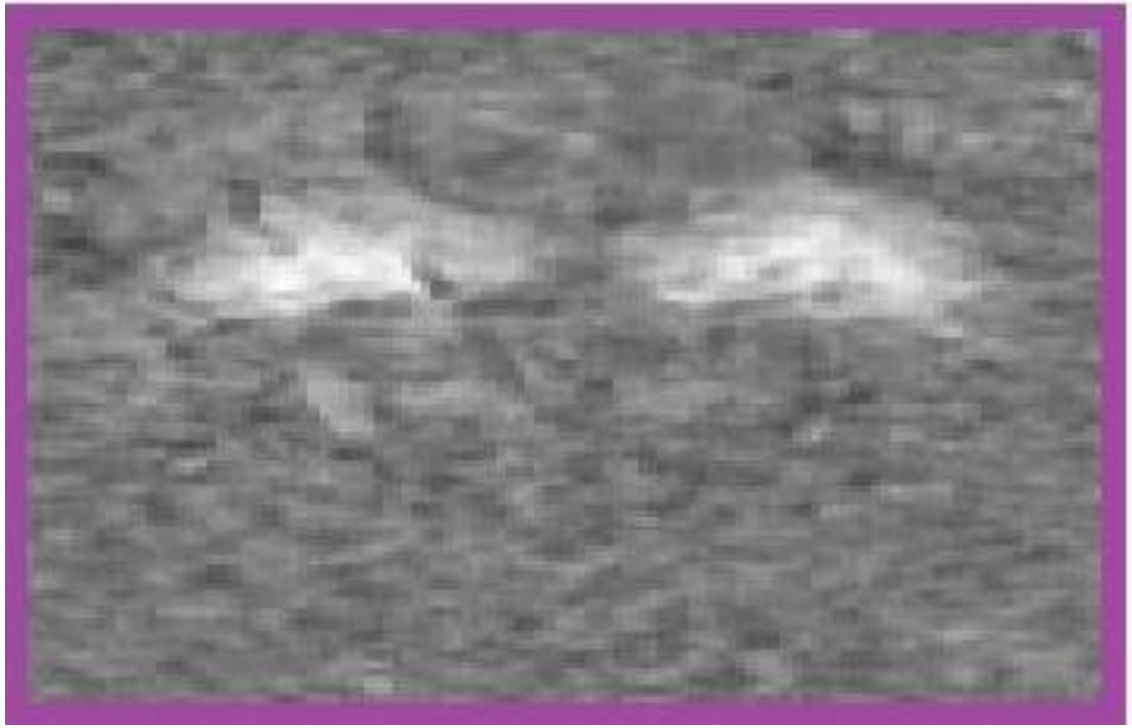
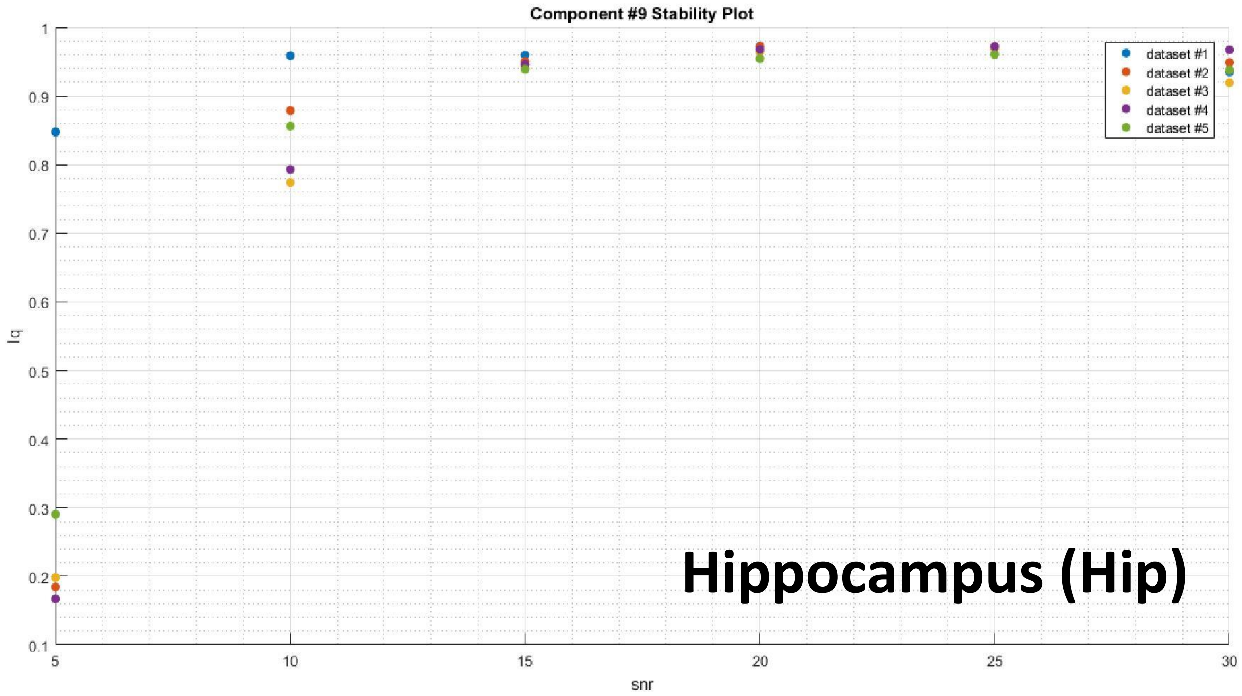
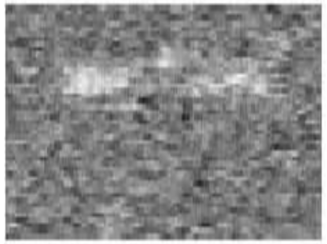
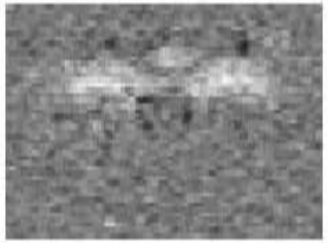
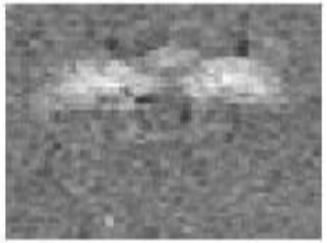
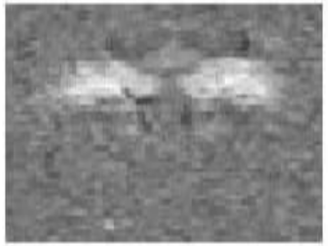


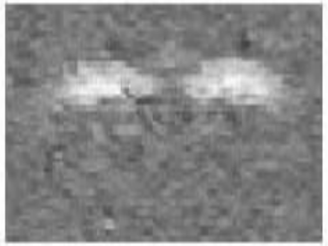


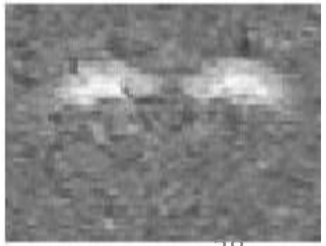




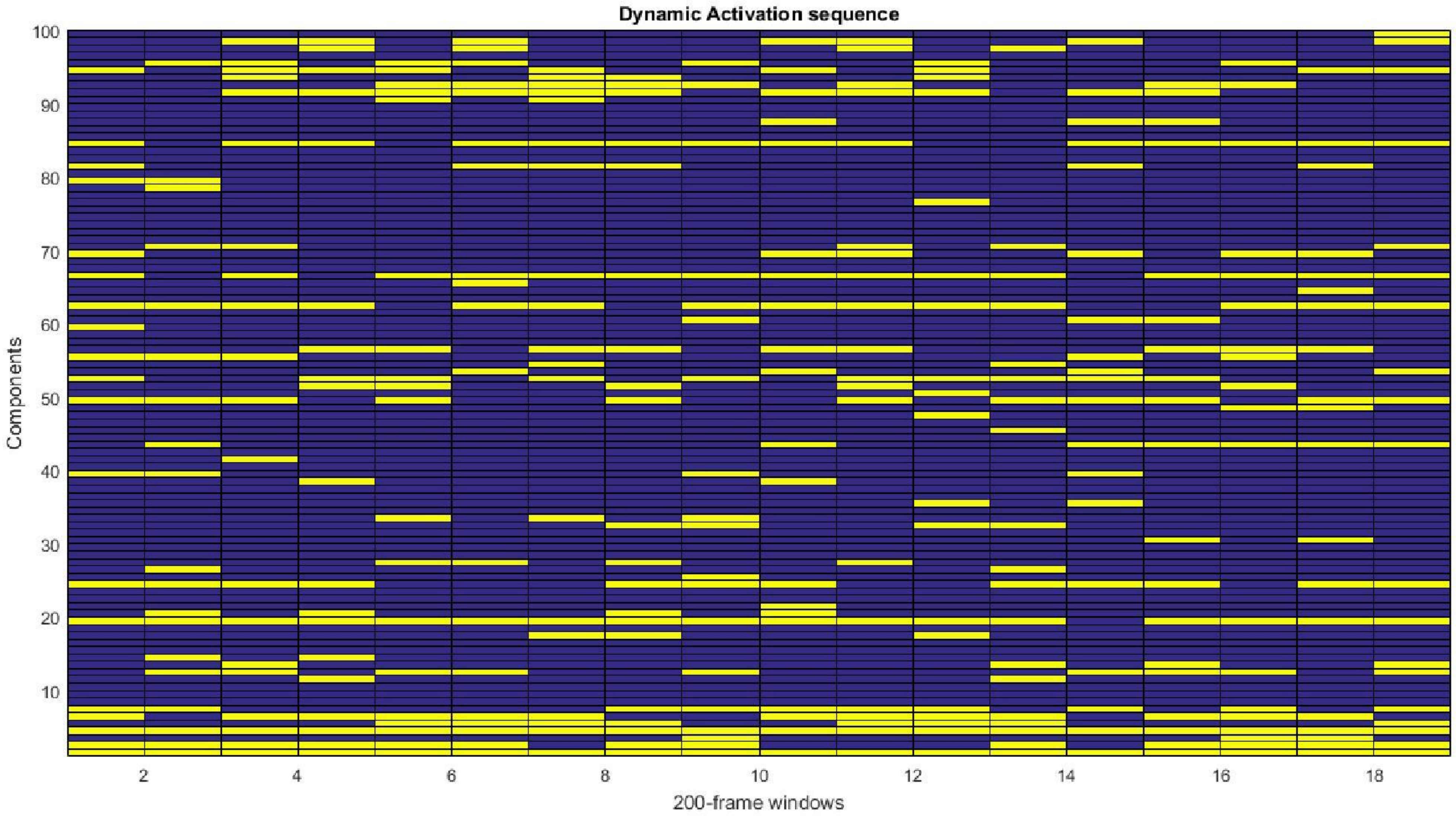




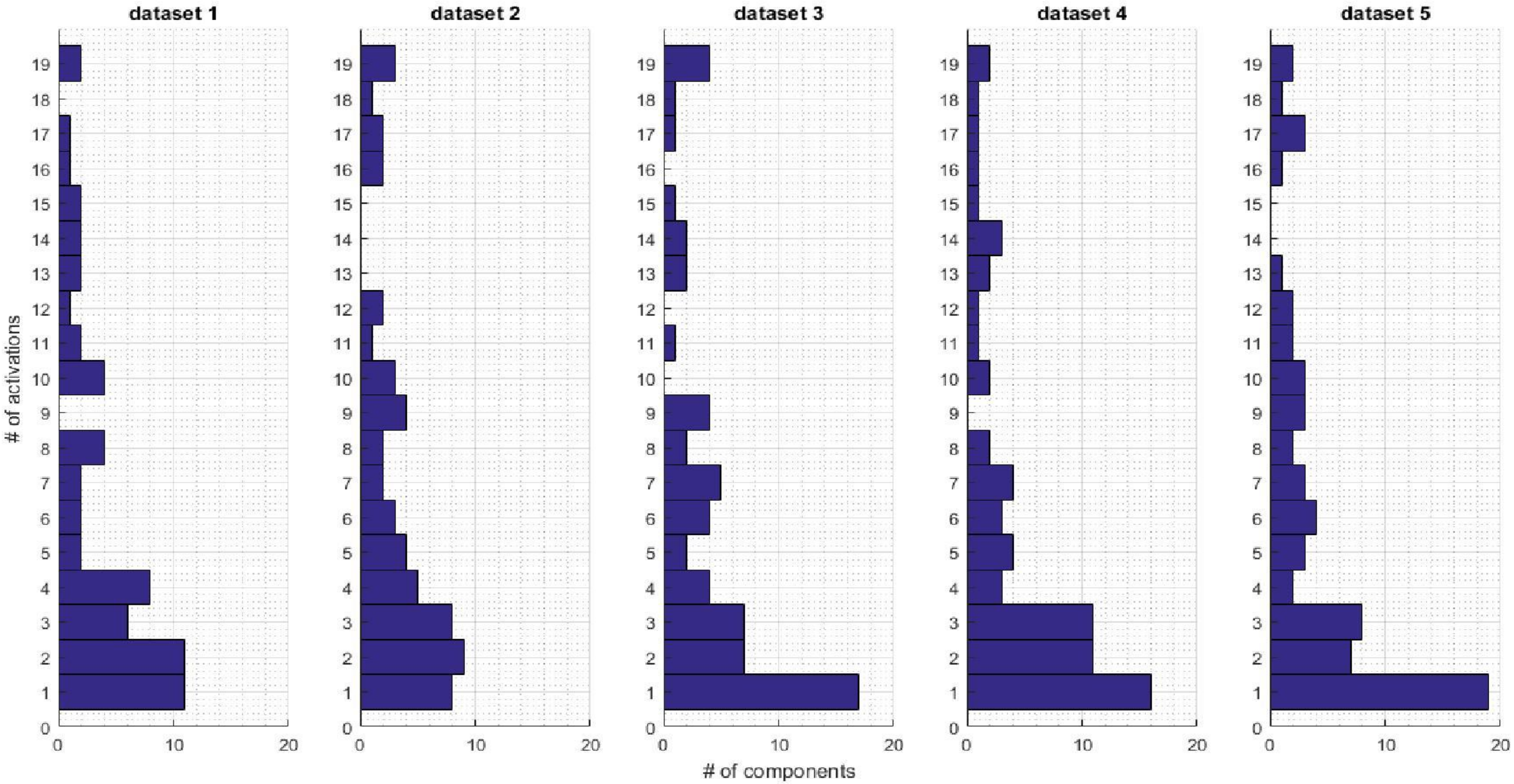




Dynamic analysis



Dynamic analysis



# of non-active components: 30-40 out of 100

Dynamic analysis

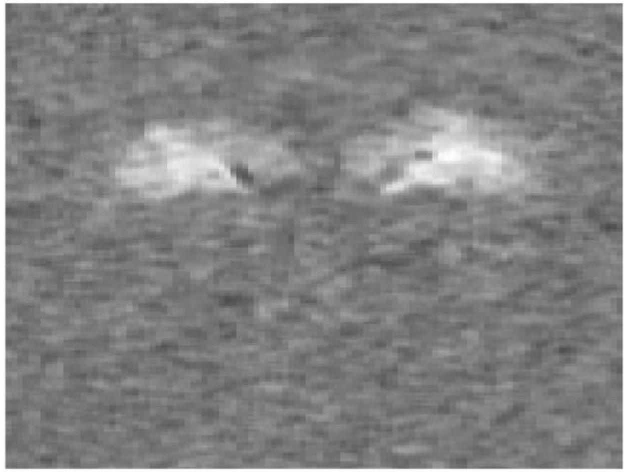
Total $\#frames = 19$	19 frames on	18 frames on	17 frames on	16 frames on
Dataset 14_14_53	1, 4	-	19	66
Dataset 14_30_03	1, 4, 43	19	5, 56	2, 62
Dataset 14_39_20	1, 4, 28, 91	62	19	-
Dataset 14_43_46	4, 5	62	19	1
Dataset 14_48_15	12, 19	4	1, 2, 6	66

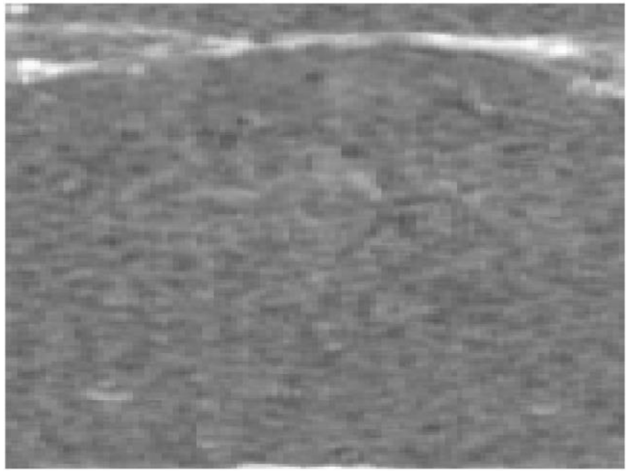
Most activated signal sources during the dynamic analysis experiment.

The numbering of the ICs follows the reference set of 100 ICs for the dataset 14_30_03.

Dynamic analysis

Hippocampus (Hip)





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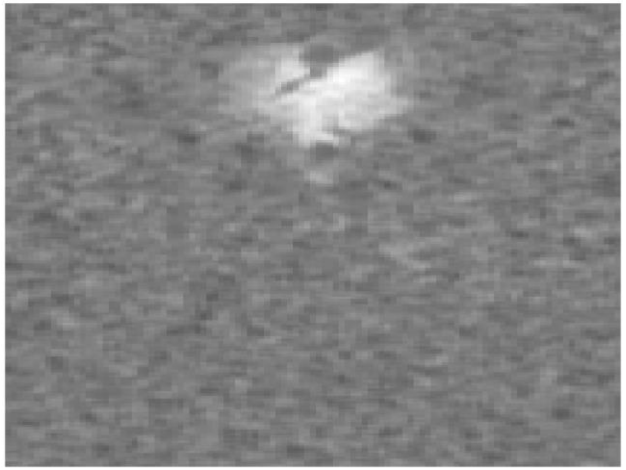
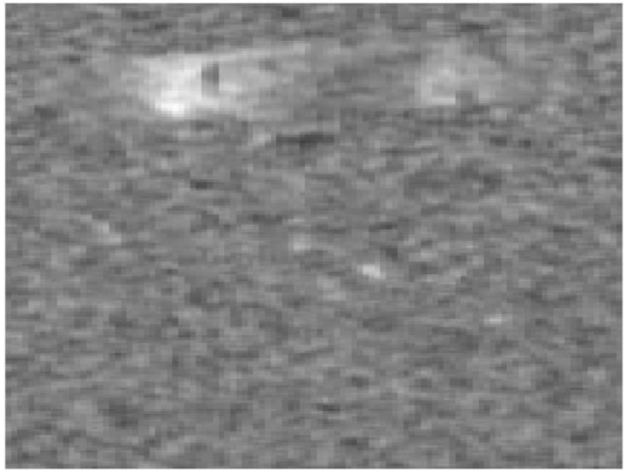
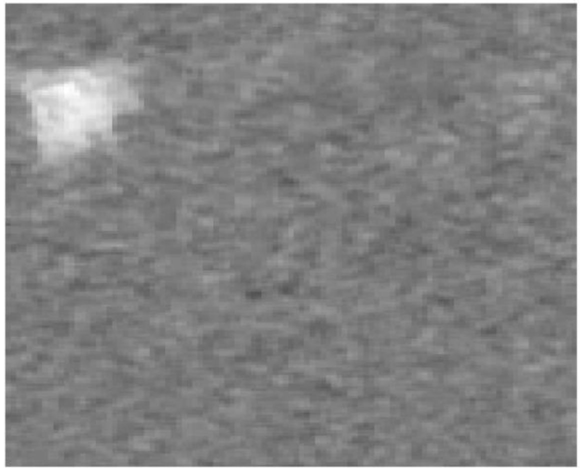
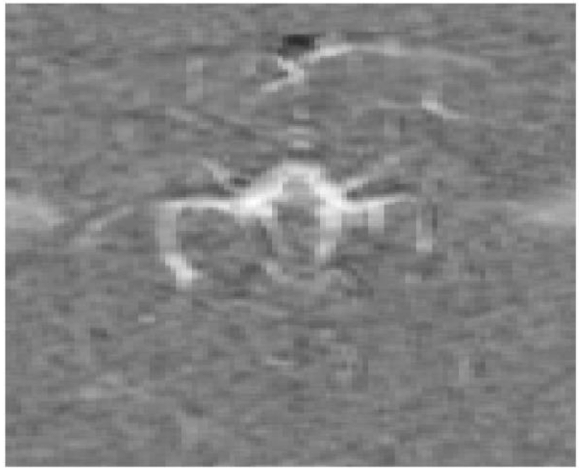




primary Somatosensory area (SSp)





Main Blood Supply (MBS)

Observations and Conclusions

- Reduction of the PCA dimension of the input simplifies the ICA analysis (time and resource-wise) **BUT** it can result in the loss of briefly activated signal sources.
- A decrease of the snr of the input results in a decrease of the stability of the Icasso results, as expected.
- Snr=5 appears to be a limit value for the convergence of the Icasso results.
- Each of the estimated signal sources, appears to have an individual "stability profile".
- The dynamic analysis appears to have great potential in discovering hidden relations and activation patterns in the dataset.
- The ICA can be used for profiling each of the spatial components in depth, using specific knowledge of the experimental fUS setup.

Future directions

General directions:

- Expansion of the fUS dataset.
- Expansion of the processing resources.
- Dataset and analysis focus on specific analysis tasks (eg. tracking of specific brain anomalies).

Targeted approach:

- Increase of the ICA iterations using Icasso and explore its potential.
- Further analysis of all the ICs.
- Explore different kinds of added noise in the data.
- Further explore the dynamic analysis parameters (window size, step, # of iterations).
- Explore the activation sequences using a neuronal computational approach.
- Distinguish ICs based on the physiological system they belong to, and develop different analysis paths.

Acknowledgements

- Dr. Harry Sidiropoulos, Postdoctoral Fellow, Erasmus MC
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- Dimitrios Soudris, Professor, Division of Computer Science, NTUA

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