



# Deep Learning for Signal Processing and Medical Applications

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# Acknowledgements

The projects described in this presentation are funded by NIH and NSF

## Blind denoising of natural images

Bias-free CNNs

Wiener filtering

CNNs learn adaptive filters

CNNs learn unions of subspaces

## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

## Data-driven estimation of sinusoid frequencies

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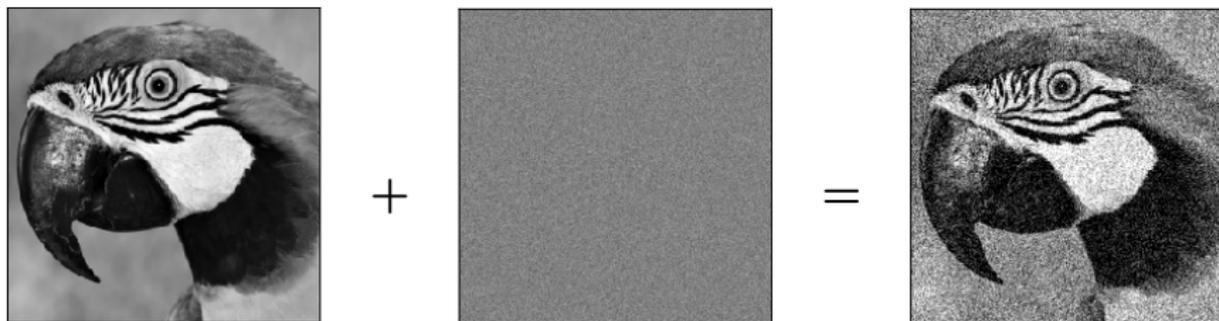
# Acknowledgements

Joint work with Zahra Kadkhodaie, Sreyas Mohan, and Eero Simoncelli

# Image denoising

**Goal:** Estimate image from noisy data

Popular model: Additive Gaussian noise

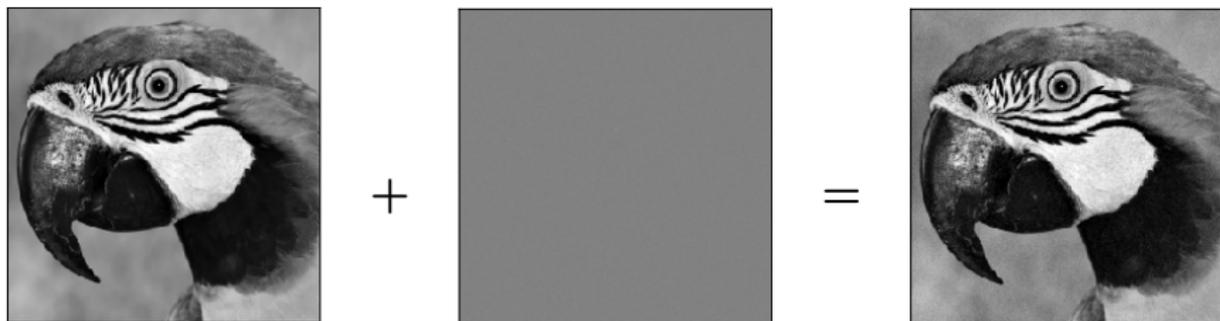


**Blind** denoising: Noise level is unknown

# Image denoising

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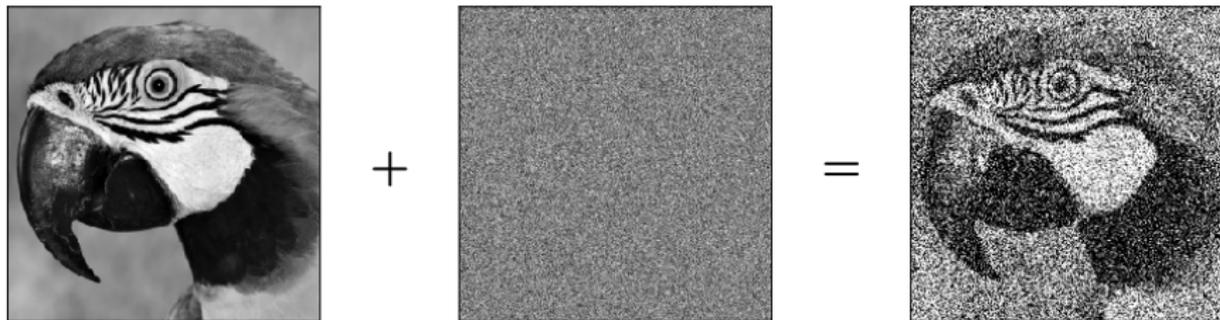


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**Blind** denoising: Noise level is unknown

# Deep learning for blind image denoising

- ▶ Gather dataset of natural images
- ▶ Add noise from a range of noise levels
- ▶ Train convolutional neural network (CNN) to estimate clean image minimizing mean squared error
- ▶ Works very well for additive Gaussian noise (state of the art)

## Generalization across noise levels

What if we test on noise level **not** seen during training?

Training data  
(low noise)



Test image  
(high noise)



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CNN



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## First-order Taylor expansion

Let  $f$  be the function learned by a CNN trained for denoising

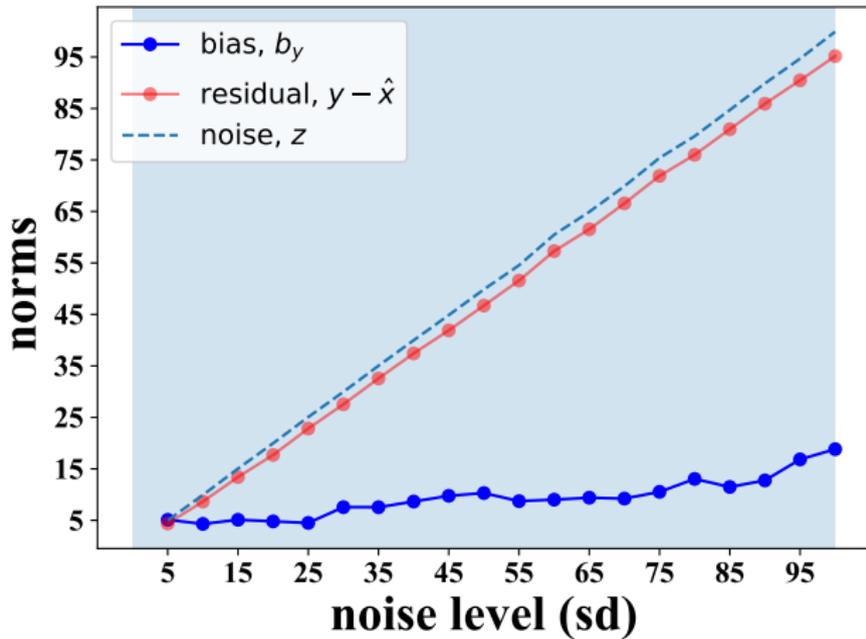
The first-order Taylor expansion for a fixed input  $y$  is exact

$$\begin{aligned}\hat{x} = f(y) &= W_L R(\dots W_2 R(W_1 y + b_1) + b_2 \dots) + b_L \\ &= A_y y + b_y\end{aligned}$$

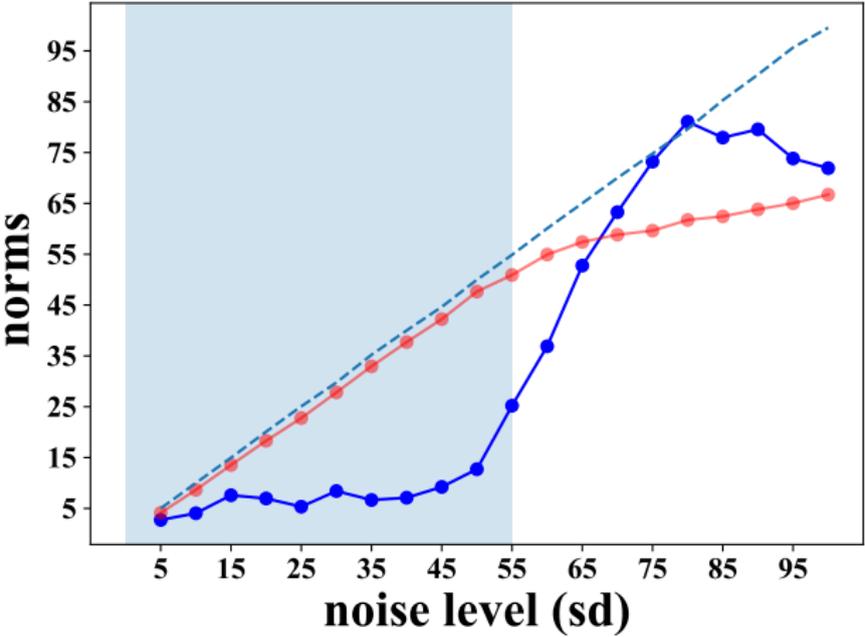
$W_1, W_2, \dots, W_L$  are weight matrices

$b_1, b_2, \dots, b_L$  are bias vectors

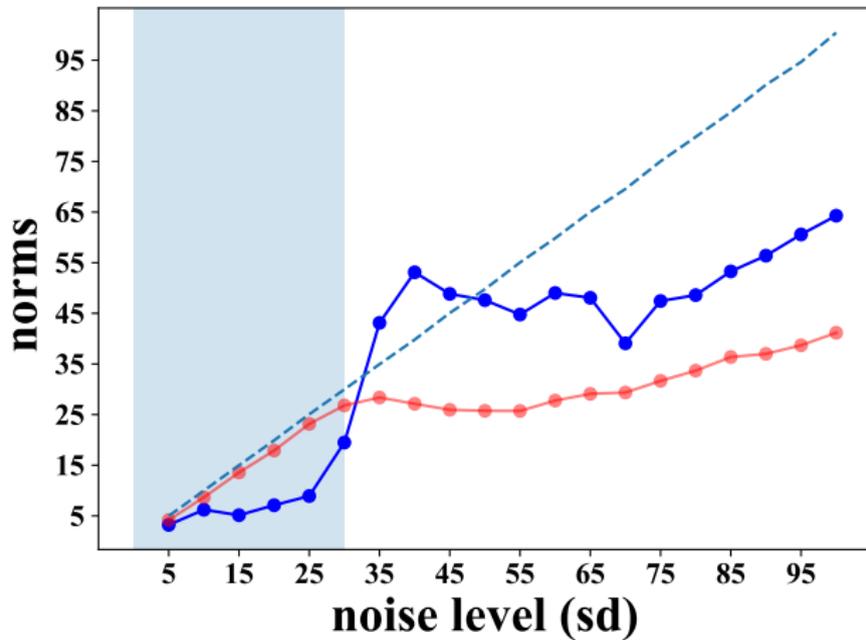
## Residual and net bias



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## Residual and net bias



## Bias-free networks

Within training range, learned net bias is small

Out of the range, it explodes, coinciding with dramatic performance loss

Net bias seems to **overfit** trained noise levels

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This motivates *removing all additive constants*

$$f(y) = W_L R(\dots W_2 R(W_1 y + b_1) + b_2 \dots) + b_L$$

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$$f(y) = W_L R(\dots W_2 R(W_1 y + \cancel{b_1}) + \cancel{b_2} \dots) + \cancel{b_L}$$

It works

Training data  
(low noise)



Test image  
(high noise)



CNN



# It works

Training data  
(low noise)



Test image  
(high noise)



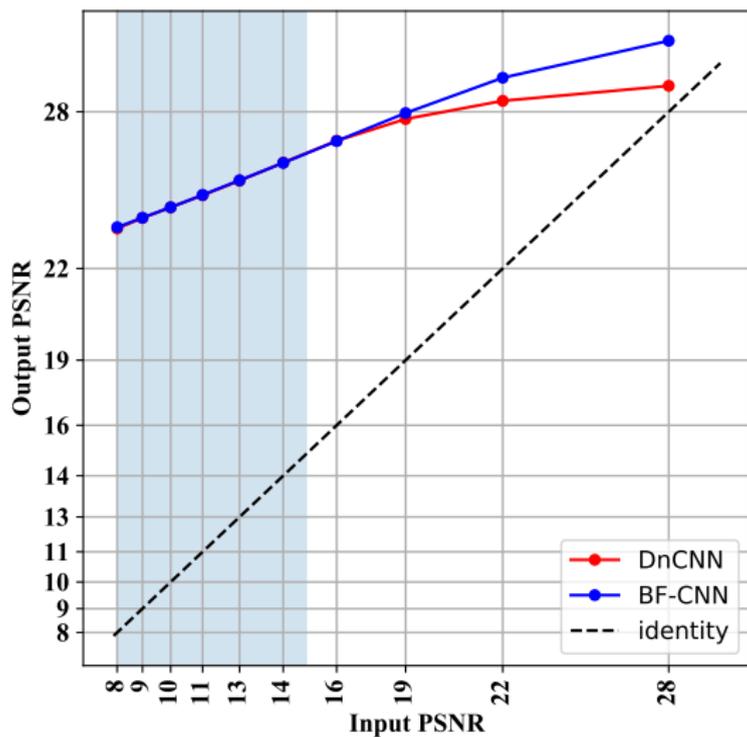
CNN



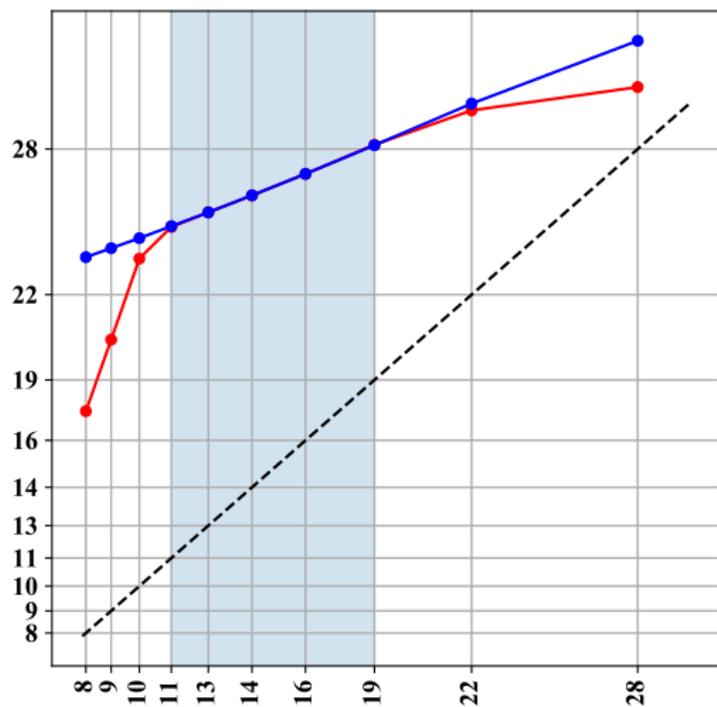
Bias-free CNN



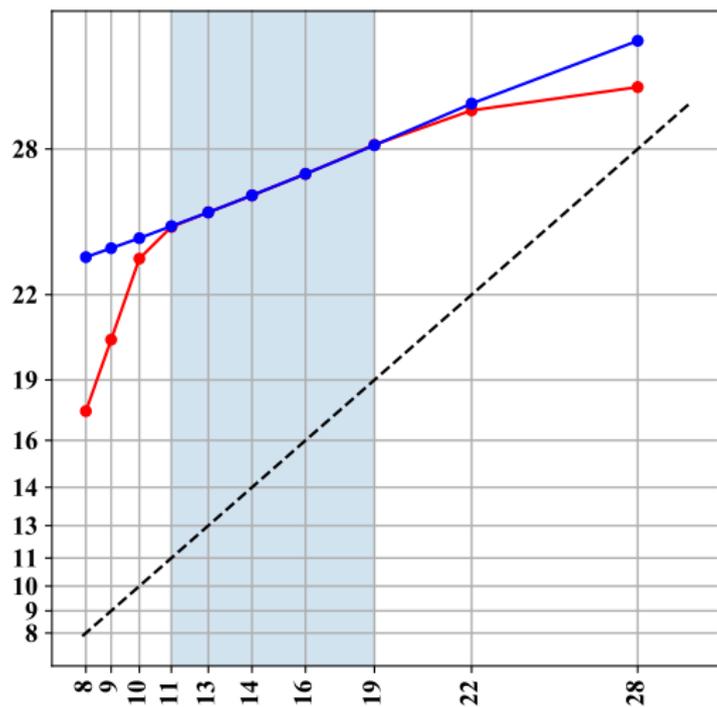
# DnCNN [Zhang *et al* 2016] vs bias-free DnCNN



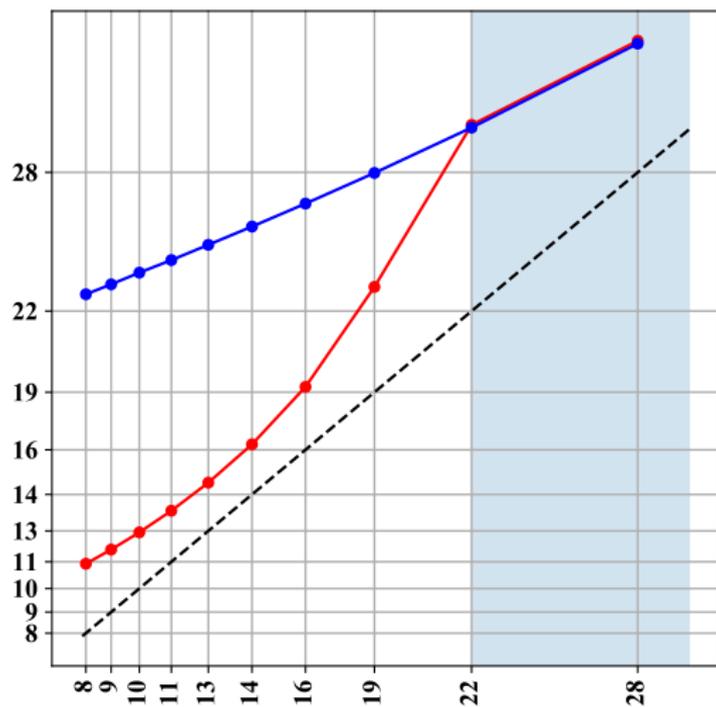
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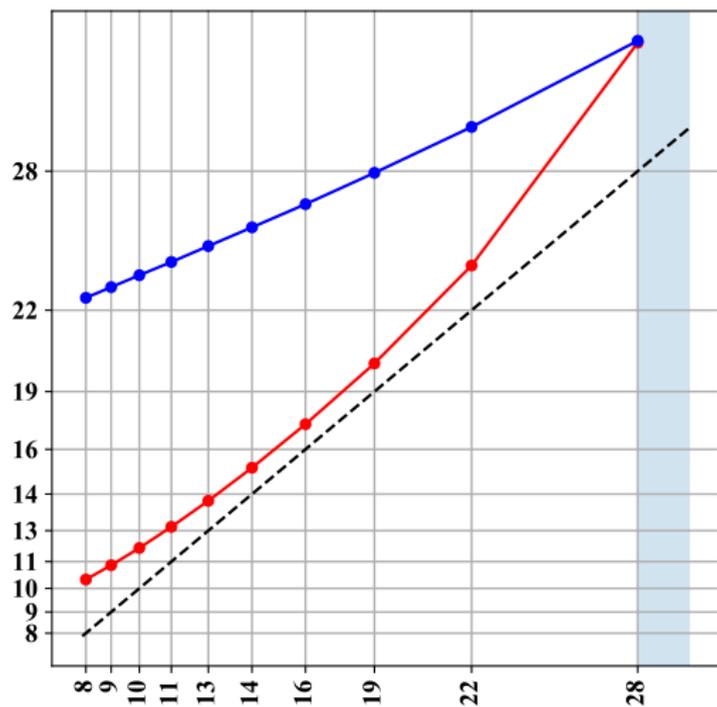
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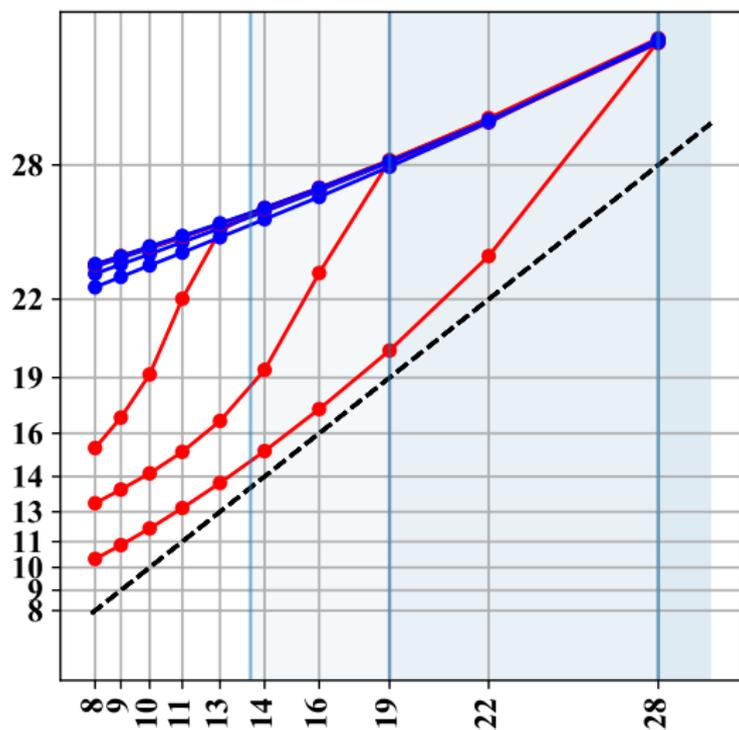
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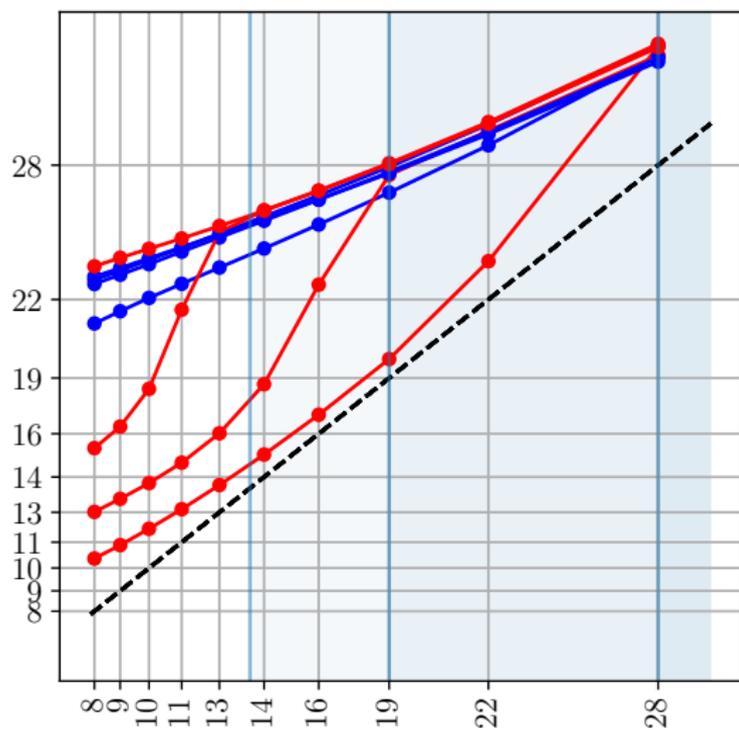
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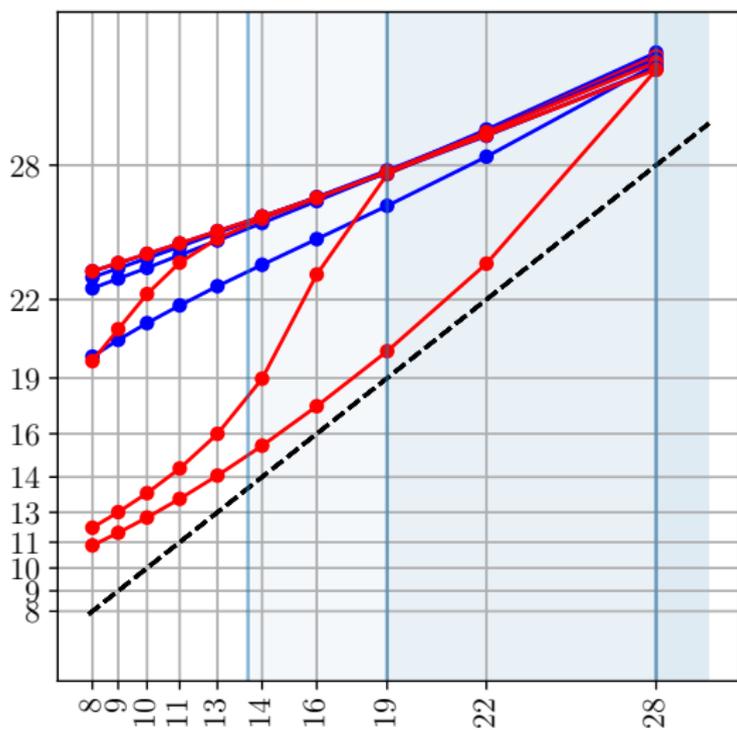
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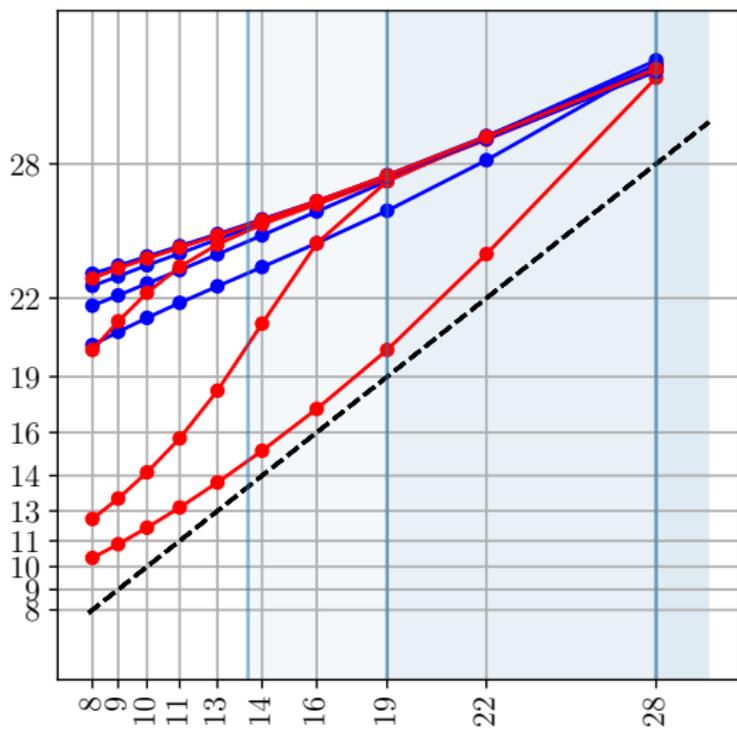
# DenseNet [Huang et al/ 2017] vs bias-free DenseNet



# UNet [Ronneberger et al 2015] vs bias-free UNet



# Recurrent CNN [Zhang et al/ 2018] vs bias-free recurrent CNN



## Blind denoising of natural images

Bias-free CNNs

Wiener filtering

CNNs learn adaptive filters

CNNs learn unions of subspaces

Quantitative magnetic-resonance imaging

Early diagnostics of Alzheimer's disease

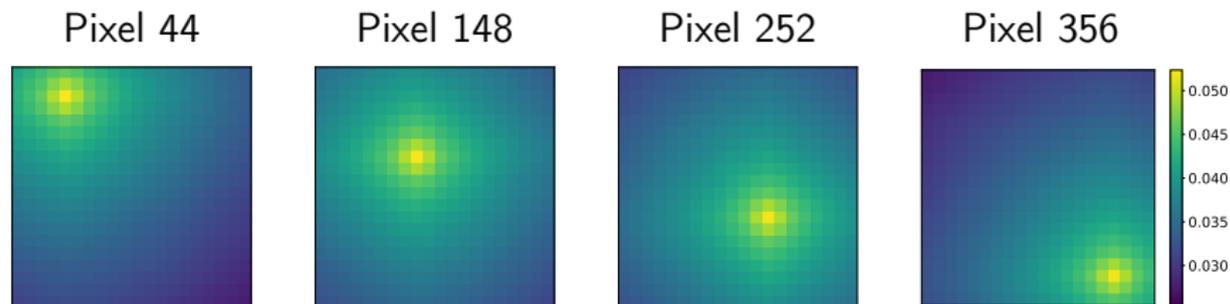
Quantitative rehabilitation of stroke patients

Data-driven estimation of sinusoid frequencies

## Linear estimation

Linear regression from pixels to pixels is intractable ( $10^4 \times 10^4$  matrix!)

No need: covariance between pixels is **translation invariant**



Linear estimator can be parameterized by a convolutional filter

## Wiener filter [Wiener 1950]

Filter  $w$  that achieves optimal mean squared error

Random vectors:  $x$  (image),  $z$  (noise),  $y := x + z$  (data)

Fourier transform is an orthogonal transformation so

$$\mathbb{E} \left( \|x - w * y\|_2^2 \right) = \mathbb{E} \left( \|\hat{x} - \hat{w} \circ \hat{y}\|_2^2 \right)$$

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$$\begin{aligned} \mathbb{E} \left( \|x - w * y\|_2^2 \right) &= \mathbb{E} \left( \|\hat{x} - \hat{w} \circ \hat{y}\|_2^2 \right) \\ &= \sum_k \mathbb{E} \left( (\hat{x}_k - \hat{w}_k \hat{y}_k)^2 \right) \end{aligned}$$

We can estimate each Fourier coefficient separately

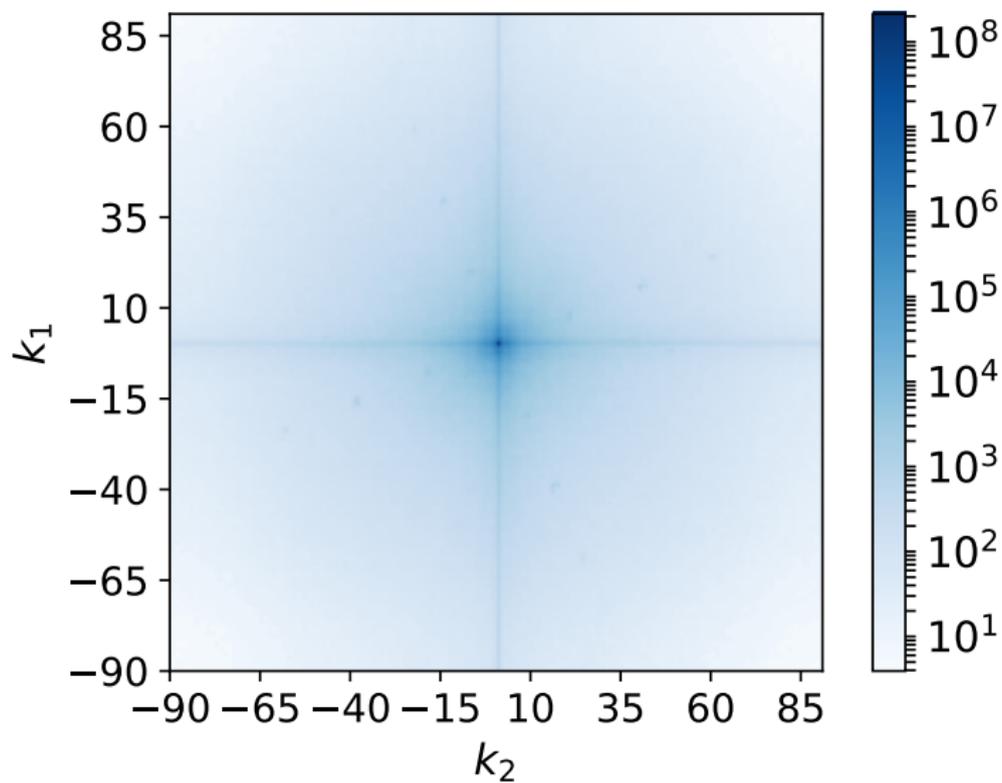
## Wiener filter

If  $x$  and  $z$  are independent, and  $z$  is i.i.d. with variance  $\sigma^2$

$$\begin{aligned}\hat{w}_k^{\text{opt}} &:= \arg \min_{\hat{w}} \mathbb{E} \left( (\hat{x}_k - \hat{w}_k \hat{y}_k)^2 \right) \\ &= \frac{\mathbb{E} \left( |\hat{x}_k|^2 \right)}{\mathbb{E} \left( |\hat{x}_k|^2 \right) + n\sigma^2}\end{aligned}$$

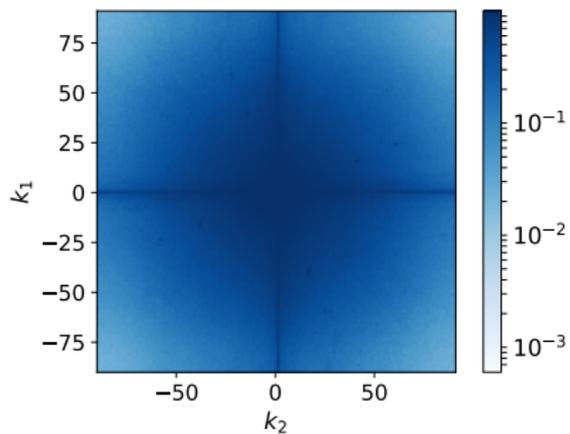
Depends on spectral statistics of natural images and on noise level  $\sigma^2$   
( $n$  is the number of pixels)

# Image data: Mean square of Fourier coefficients

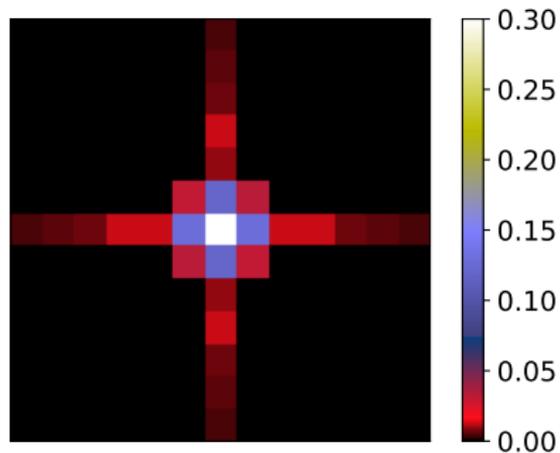


Wiener filter:  $\sigma = 0.04$

Frequency

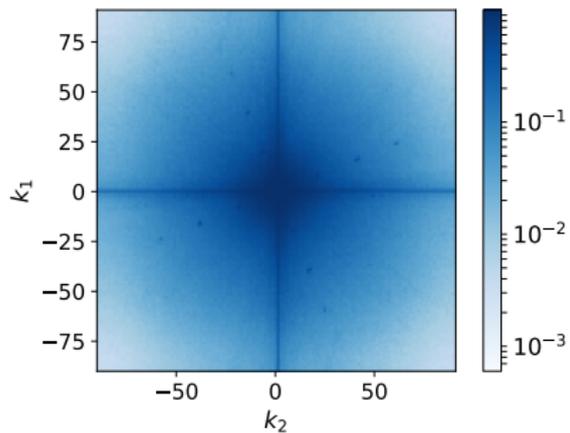


Space

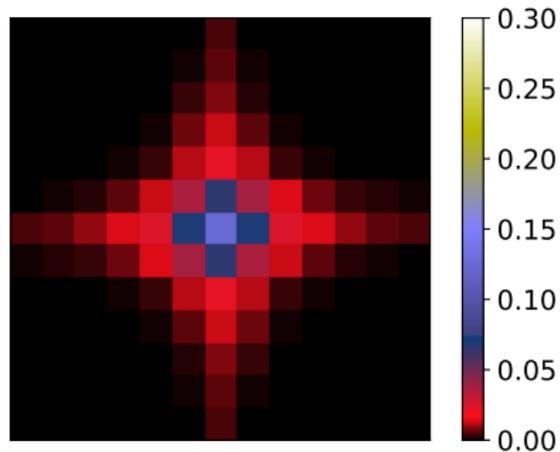


Wiener filter:  $\sigma = 0.1$

Frequency

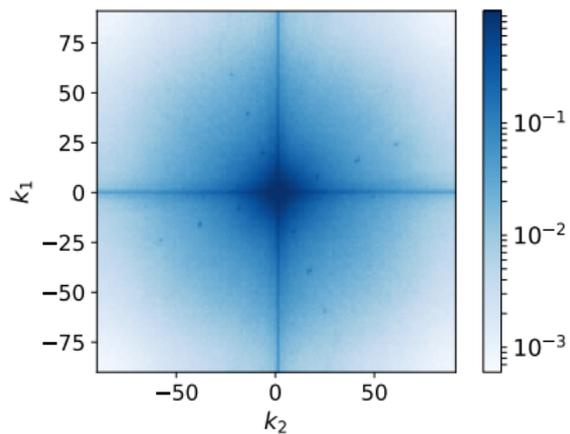


Space

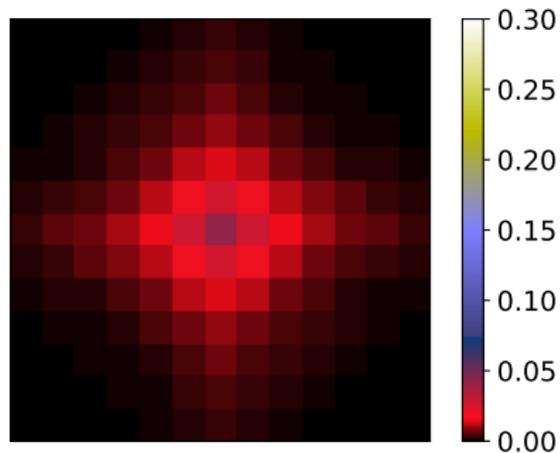


Wiener filter:  $\sigma = 0.2$

Frequency



Space



# Wiener filter

Two perspectives:

1. *Image domain*: Weighted **average** of nearby pixels
2. *Frequency domain*: Weighted **projection** onto low-pass 2D sinusoids

## Blind denoising of natural images

Bias-free CNNs

Wiener filtering

CNNs learn adaptive filters

CNNs learn unions of subspaces

## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

## Data-driven estimation of sinusoid frequencies

# Wiener filter

*Image domain:* Weighted **average** of nearby pixels

**Problem:** Same average for each pixel

Blurs edges and other features

Previous solution:

Adapt filter locally (e.g. bilateral filter [Tomasi and Manduchi 1998])

Bias-free CNN is locally linear

$$f(y) = W_L R W_{L-1} \dots R W_1 y = A_y y$$

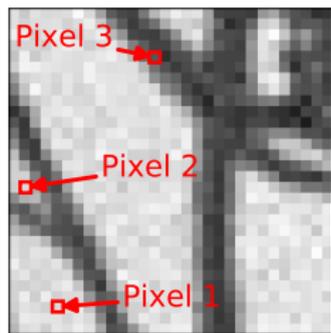
## Rows interpreted as filters

Estimate at pixel  $i$ :

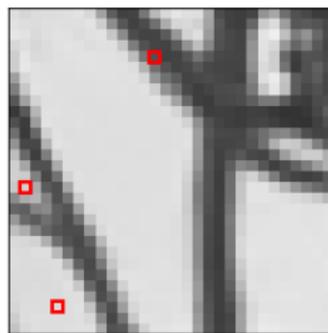
$$f_{\text{BF}}(y)(i) = (A_y y)(i) = \langle \text{ith row of } A_y, y \rangle$$

## Low noise

Noisy image



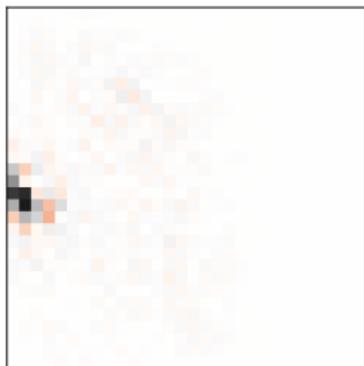
Denoised



Pixel 1



Pixel 2

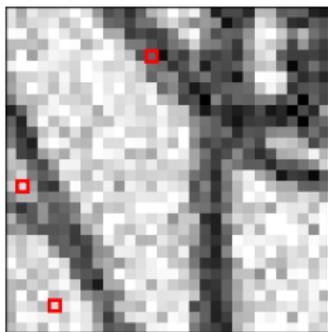


Pixel 3

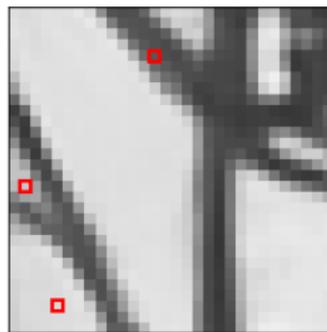


## Medium noise

Noisy image



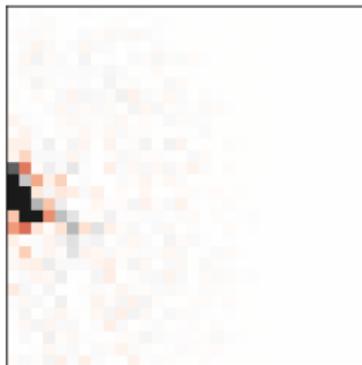
Denoised



Pixel 1



Pixel 2

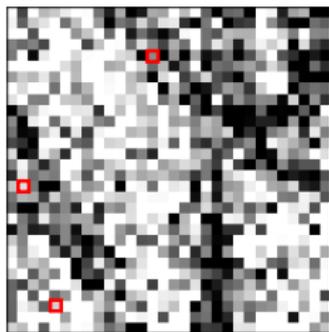


Pixel 3

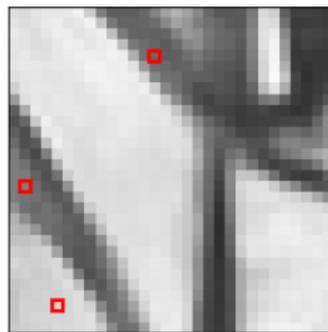


# High noise

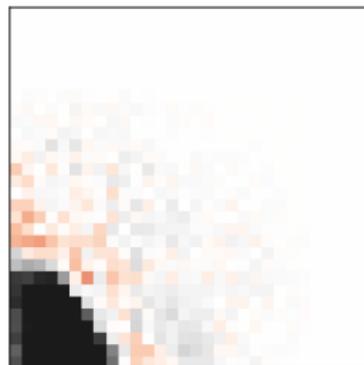
Noisy image



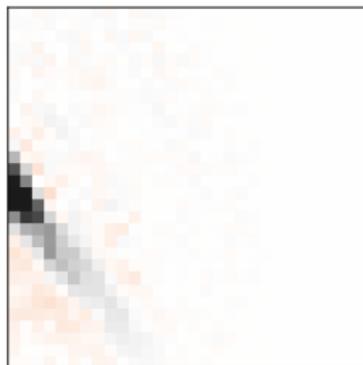
Denoised



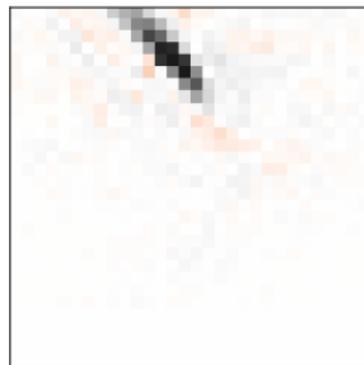
Pixel 1



Pixel 2



Pixel 3



## Conclusion

BF-CNN implicitly learns **filters** *adapted to image structure and noise!*

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Bias-free CNNs

Wiener filtering

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CNNs learn unions of subspaces

## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

## Data-driven estimation of sinusoid frequencies

# Wiener filter

*Frequency domain:* Approximate **projection** onto low-pass 2D sinusoids

**Problem:** Same projection for each image

Blurs edges and other features

# Projection onto union of subspaces

Previous methodology:

1. Learn/design overcomplete dictionary of basis functions
2. Select sparse subset for each image/patch through thresholding/optimization
3. Project on span of sparse subset

Projection onto **union of low-dimensional subspaces**

Bias-free CNN is locally linear

$$f(y) = W_L R W_{L-1} \dots R W_1 y = A_y y$$

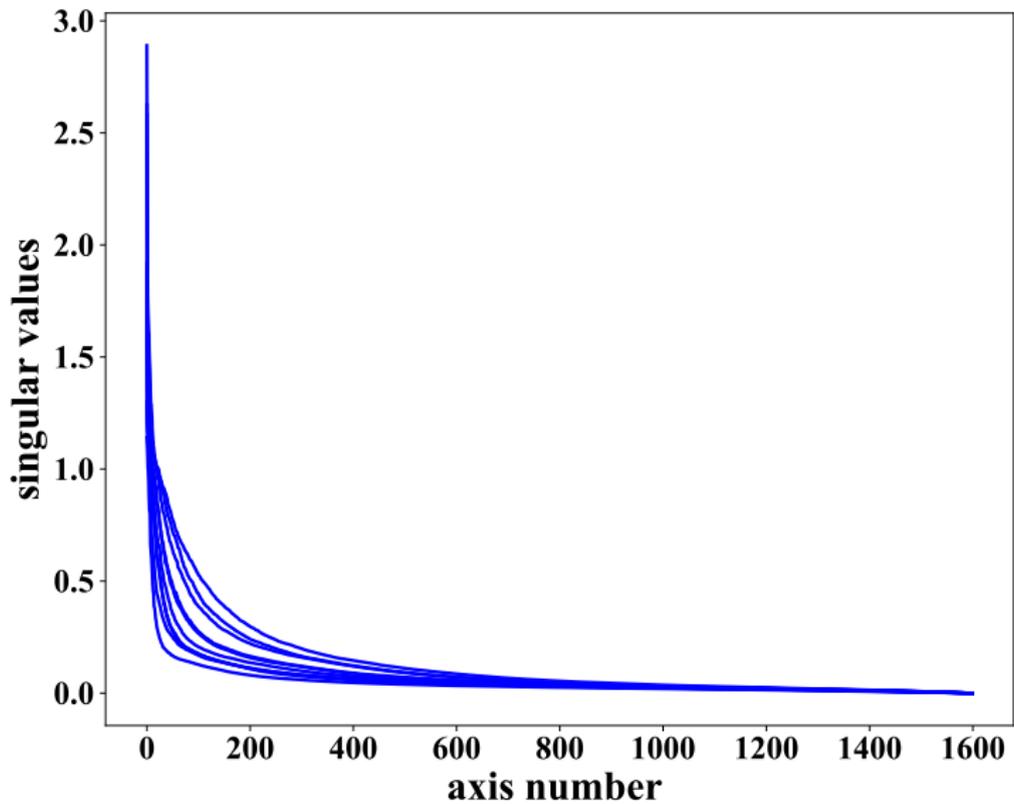
## SVD analysis

$$A_y = U S V^T$$

Empirical observations:

- ▶ Matrix is approximately symmetric  $U \approx V$
- ▶ Matrix is approximately low-rank

# Singular values

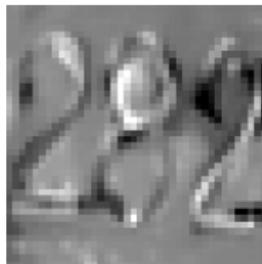


# Singular vectors computed from noisy image

Clean image



Large singular values

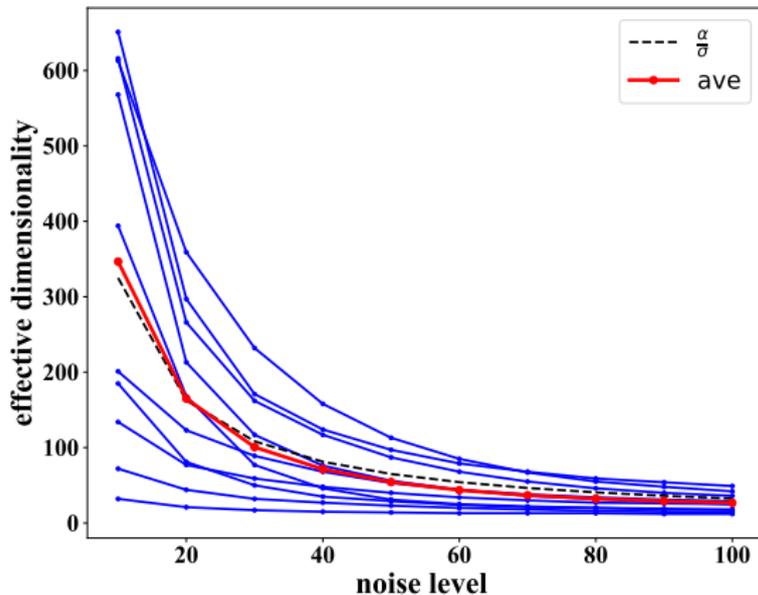


Small singular values



# Dimensionality of learned subspace

Approximate dimensionality = sum of squared singular values



Subspaces are approximately nested

## Conclusion

BF-CNN implicitly learns to project onto **union of subspaces** adapted to image features and noise!

For more information

**Robust and interpretable blind image denoising via bias-free convolutional neural networks**

S. Mohan, Z. Kadkhodaie, E. Simoncelli, C. Fernandez-Granda

## Directions for future research

Properties of the learned representation in frequency estimation

Why does bias hinder generalization across noise levels?

Linear-algebraic analysis is completely empirical and very local

How are these adaptive filters / unions of subspaces learned?

How do the learned mechanisms vary as we change the input?

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# Quantitative magnetic-resonance imaging

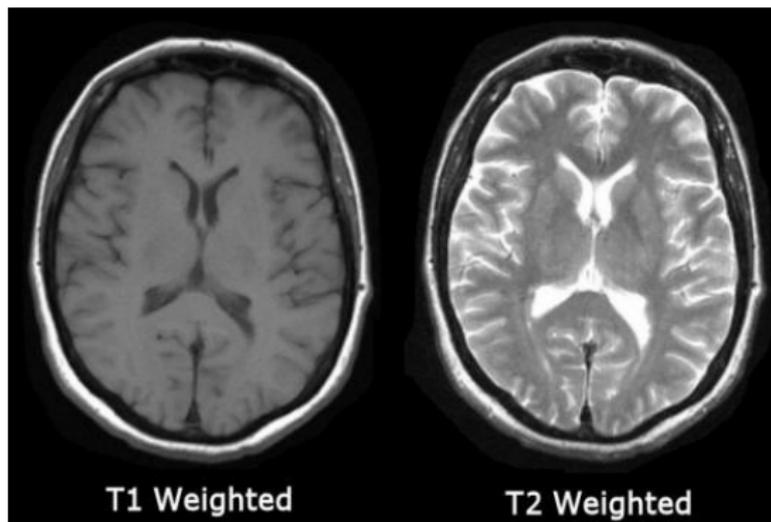
Collaboration with the Department of Radiology of the NYU School of Medicine

Joint work with Jakob Assländer, Brett Bernstein, Quentin Duchemin, Cem Gutelkin, Vlad Kobzar, Sylvain Lannuzel, and Sunli Tang

# Magnetic-resonance imaging (MRI)

- ▶ Hydrogen nuclei absorb/emit radio-frequency energy when placed in magnetic field
- ▶ Measured signal depends on **relaxation parameters**  $T_1$  and  $T_2$  of biological tissues

## Traditional contrast-based MRI

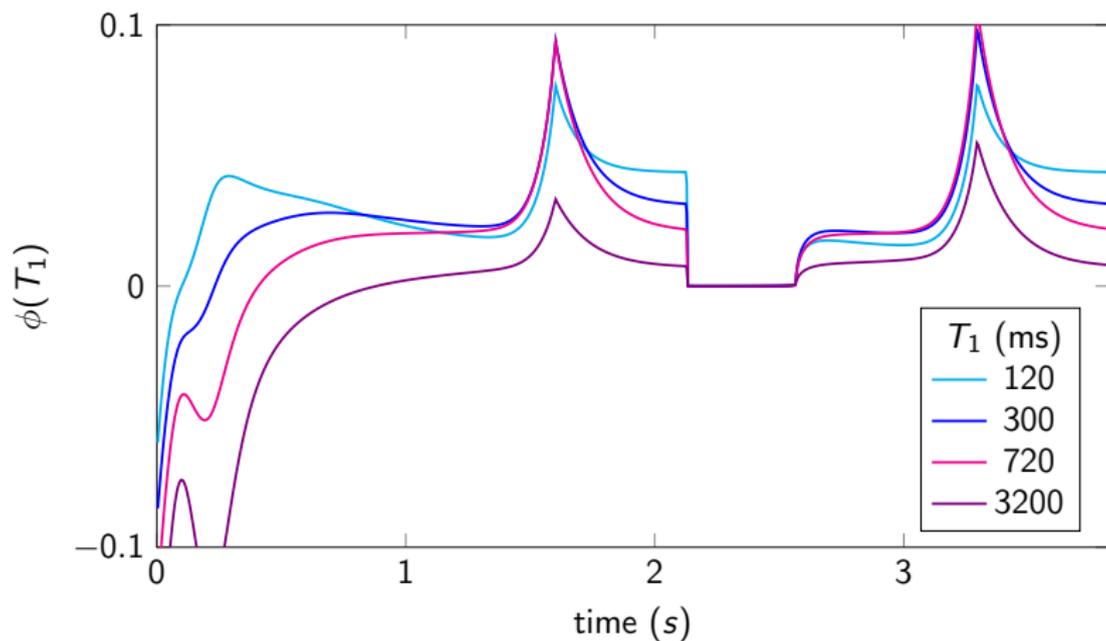


**Not** quantitative!

Difficult to reproduce/compare

## Quantitative MRI via fingerprinting

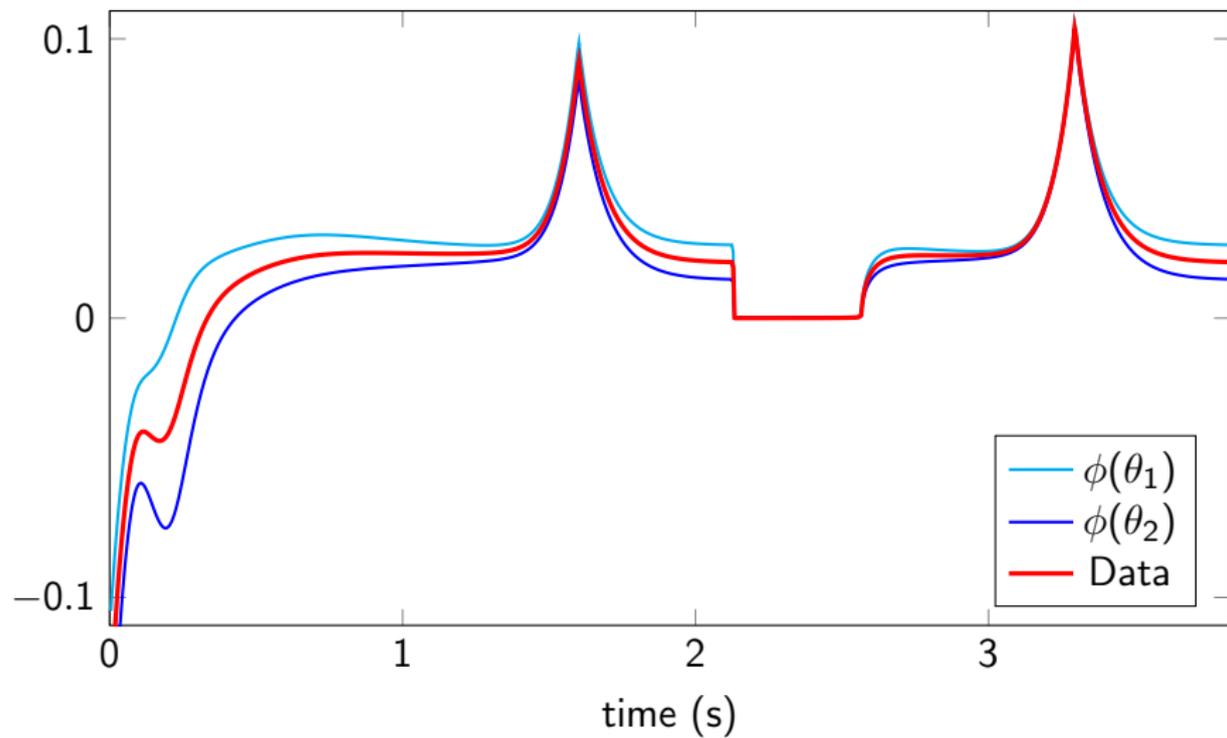
Radio-frequency pulses are designed to produce irregular magnetization signals (**fingerprints**) encoding relaxation parameters



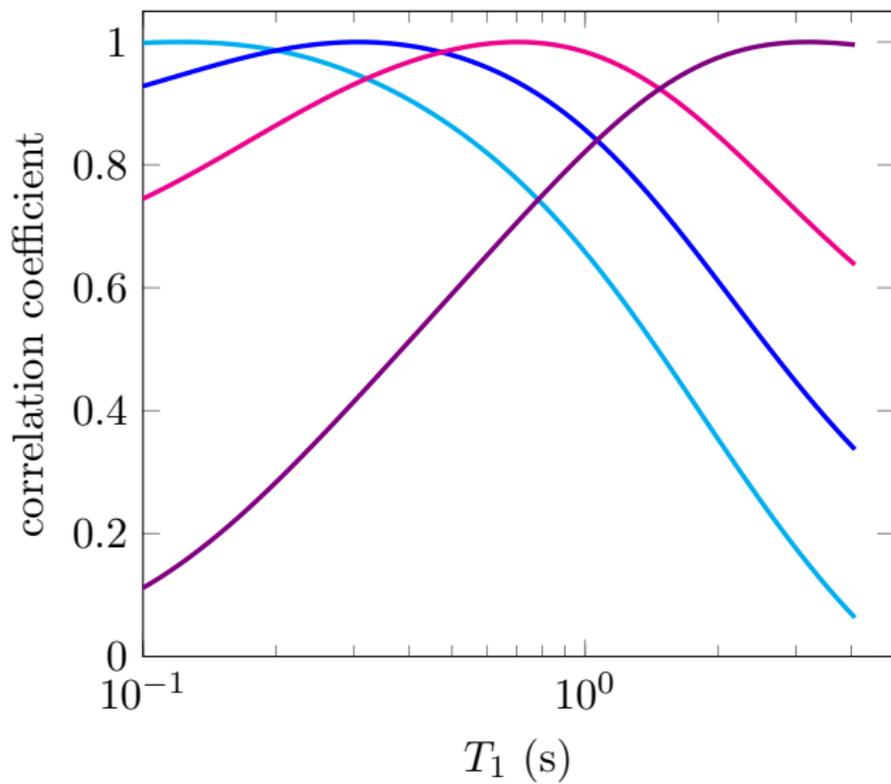
# Multicompartment magnetic resonance fingerprinting

- ▶ Assumption in MRF: One tissue per voxel
- ▶ Problematic at tissue boundaries
- ▶ Ignores sub-voxel structure

## Additive model



## Correlation structure

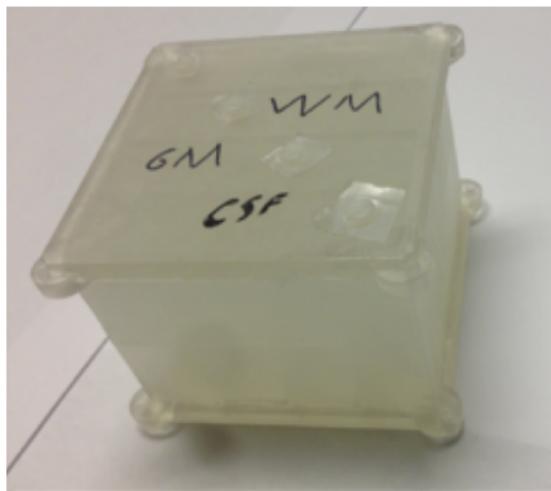
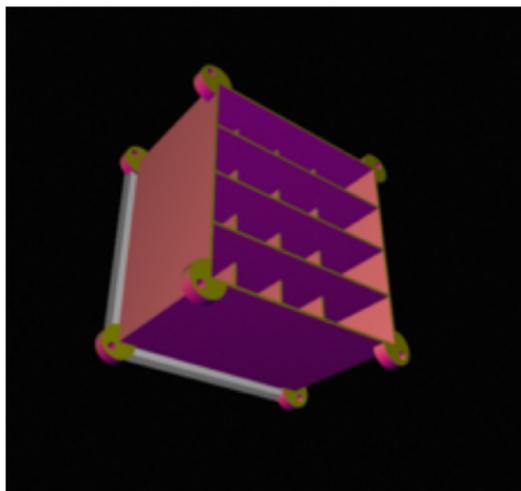


## Multicompartment MRF via $\ell_1$ -norm regularization

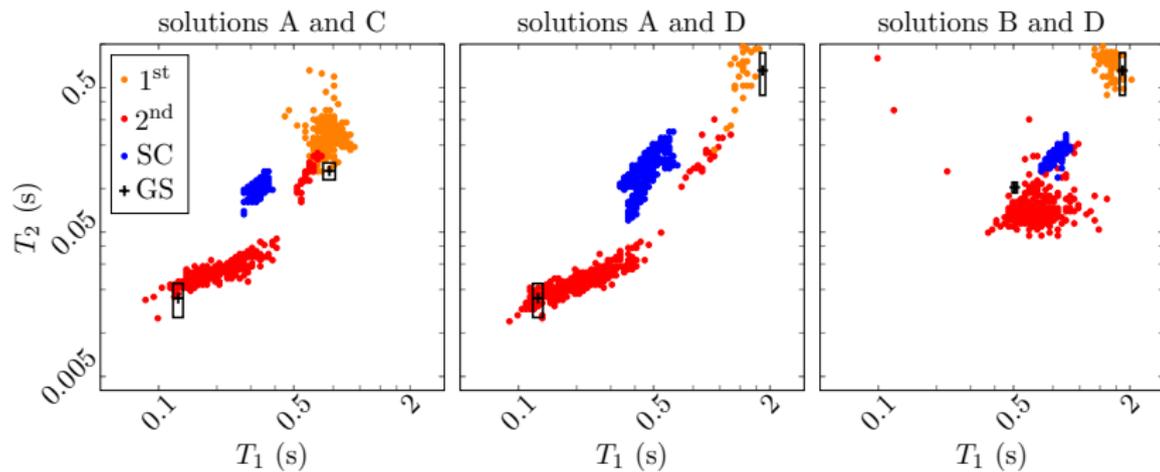
- ▶ Fast-thresholding methods don't work
- ▶ We use an efficient interior-point solver
- ▶ Solving sequence of reweighted problems improves the solution

Drawback: Very slow

# Validation with phantom



# Validation with phantom



## Current research

**Goal:** Fast multicompartment MRF for non-additive model

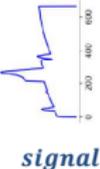
- ▶ Measurement design via ODE-constrained optimization
- ▶ Parameter estimation using a feedforward deep neural network trained on simulated data

# Current research

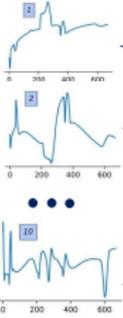
TRAINING

Sampling  
 $m_0^S$   
 $T_1$   
 $T_2^f$   
 $R$   
 $T_2^S$   
 $PD$

Hybrid-state simulation

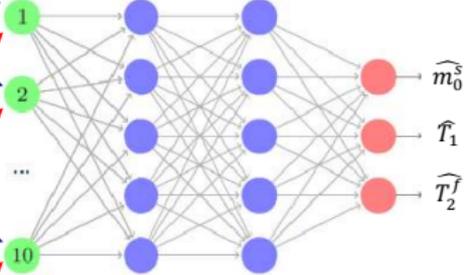


$\times$   
basis



14 hidden layers with skip connections

Output layer



RECONSTRUCTION

Undersampled k-space data at  $n$  time points

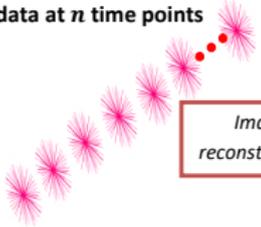
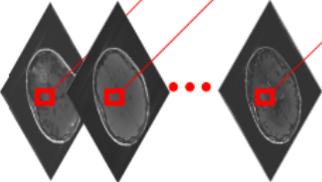


Image reconstruction



For more information

**Multi-Compartment MR Fingerprinting via Reweighted- $l_1$ -norm Regularization.** S. Tang, J. Asslaender, L. Tanenbaum, R. Lattanzi, M. Cloos, F. Knoll, C. Fernandez-Granda. ISMRM 2017

**Multicompartment magnetic resonance fingerprinting.** S. Tang, C. Fernandez-Granda, S. Lannuzel, B. Bernstein, R. Lattanzi, M. Cloos, F. Knoll and J. Asslaender. Inverse Problems 34 (9) 4005. 2018

**Hybrid-State Free Precession for Measuring Magnetic Resonance Relaxation Times in the Presence of  $B_0$  Inhomogeneities.** V. Kobzar, C. Fernandez-Granda, J. Asslaender. ISMRM 2019

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## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

## Data-driven estimation of sinusoid frequencies

# Early diagnostics of Alzheimer's disease

Joint work with Sheng Liu, Narges Razavian, and Chhavi Yadav

# Early diagnostics of Alzheimer's disease

**Goal:** Distinguish between three classes

1. Normal
2. Mild cognitive impairment
3. Mild Alzheimer's

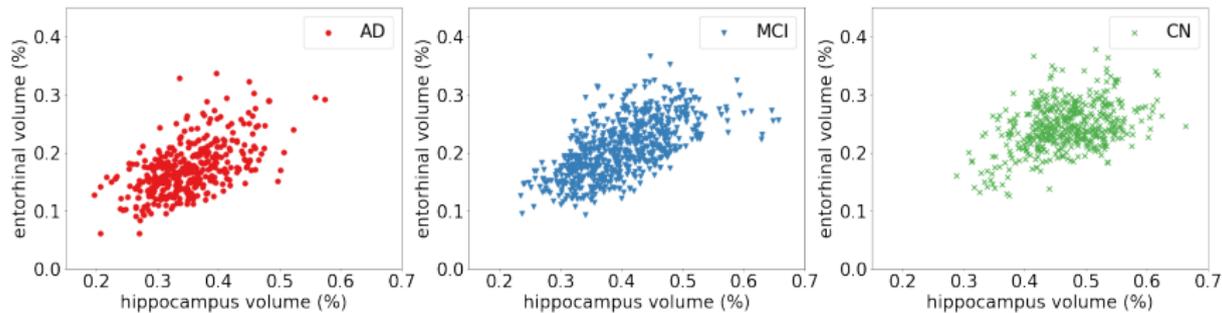
**Data:** Structural MRI (T1) from Alzheimer's Disease Neuroimaging Initiative

**Preprocessing:** Images are registered to a template

## Demographics

Split	Class	Num. subjects	Num. Scans	Mean Age (std)
Train	CN	140	567	77.0 (5.4)
	MCI	248	840	75.9 (7.3)
	AD	193	527	76.7 (7.4)
Val	CN	33	126	77.2 (5.6)
	MCI	39	138	73.3 (7.2)
	AD	41	124	76.1 (8.3)
Test	CN	24	105	79.0 (6.1)
	MCI	43	140	76.7 (6.5)
	AD	45	135	76.4 (5.1)

## Simple biomarker (normalized volumes)



Accuracy: around 50%

# Methodology

3D convolutional neural network

Main insights, performance is improved by:

- ▶ Using small (1x1) filter sizes in first layer
- ▶ Widening the network (as opposed to deepening)
- ▶ Using instance normalization instead of batch normalization
- ▶ Encoding age using a sinusoidal embedding

# Architecture

Block	Layer	Type	Output size
	Inputs		$96 \times 96 \times 96$
1	Conv3D	$k1-c4 \cdot f-p0-s1-d1$	$96 \times 96 \times 96$
	InstanceNorm3D		
	ReLU		
	MaxPool3D	$k3-s2$	$47 \times 47 \times 47$
2	Conv3D	$k3-c32 \cdot f-p0-s1-d2$	$43 \times 43 \times 43$
	InstanceNorm3D		
	ReLU		
	MaxPool3D	$k3-s2$	$21 \times 21 \times 21$
3	Conv3D	$k5-c64 \cdot f-p2-s1-d2$	$17 \times 17 \times 17$
	InstanceNorm3D		
	ReLU		
	MaxPool3D	$k3-s2$	$8 \times 8 \times 8$
4	Conv3D	$k3-c64 \cdot f-p1-s1-d2$	$6 \times 6 \times 6$
	InstanceNorm3D		
	ReLU		
	MaxPool3D	$k5-s2$	$5 \times 5 \times 5$
FC1		1024	
FC2		3	
Softmax		3	

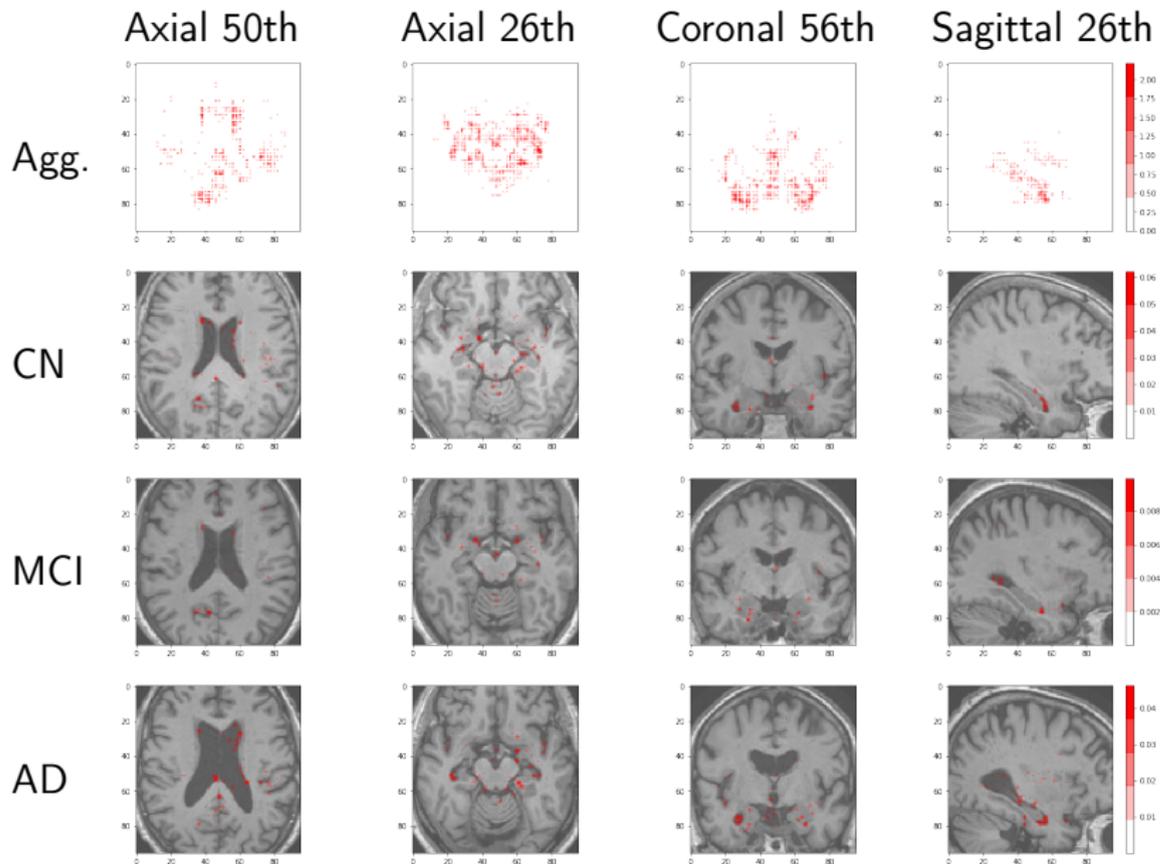
# Results

Method	Accuracy	Balanced Acc	Micro-AUC	Macro-AUC
ResNet-18	50.8%	-	-	-
ResNet-18 pretrained	56.8%	-	-	-
ResNet-18 3D	52.4 $\pm$ 1.8%	53.1%	-	-
ResNet-18 3D	50.1 $\pm$ 1.1%	51.3 $\pm$ 1.0%	71.2 $\pm$ 0.4%	72.4 $\pm$ 0.7%
AlexNet 3D	57.2 $\pm$ 0.5%	56.2 $\pm$ 0.8%	75.1 $\pm$ 0.4%	74.2 $\pm$ 0.5%
proposed	66.9 $\pm$ 1.2%	67.9 $\pm$ 1.1%	82.0 $\pm$ 0.7%	78.5 $\pm$ 0.7%
proposed + Age	<b>68.2 <math>\pm</math> 1.1%</b>	<b>70.0 <math>\pm</math> 0.8%</b>	<b>82.0 <math>\pm</math> 0.2%</b>	<b>80.0 <math>\pm</math> 0.5%</b>

## Australian Imaging, Biomarkers and Lifestyle dataset

Method	Accuracy	Balanced Acc	Micro-AUC	Macro-AUC
proposed on ADNI	$66.9 \pm 1.2\%$	$67.9 \pm 1.1\%$	$82.0 \pm 0.7\%$	$78.5 \pm 0.7\%$
proposed on AIBL	$63.6 \pm 0.7\%$	$65.7 \pm 1.1\%$	$90.0 \pm 0.6\%$	$82.1 \pm 0.7\%$

# Visualization of gradient with respect to input



## Blind denoising of natural images

Bias-free CNNs

Wiener filtering

CNNs learn adaptive filters

CNNs learn unions of subspaces

## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

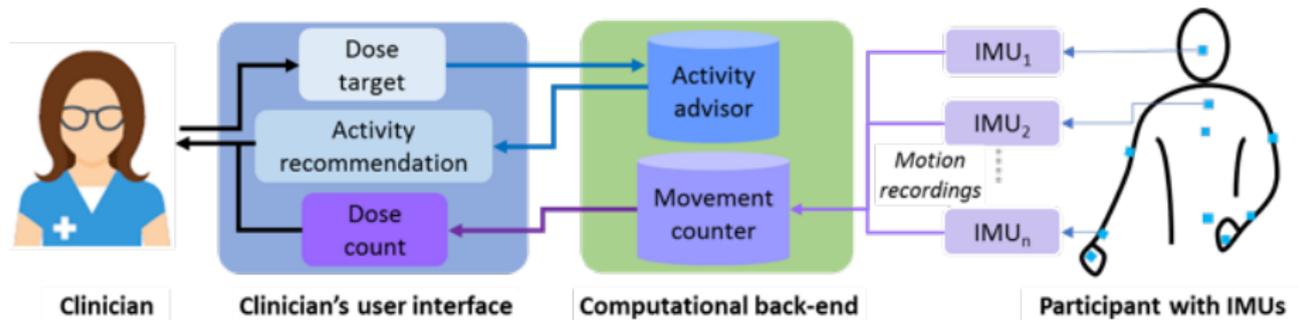
## Data-driven estimation of sinusoid frequencies

# Quantitative rehabilitation of stroke patients

Collaboration with the Mobilis lab at the Department of Neurology of the NYU School of Medicine

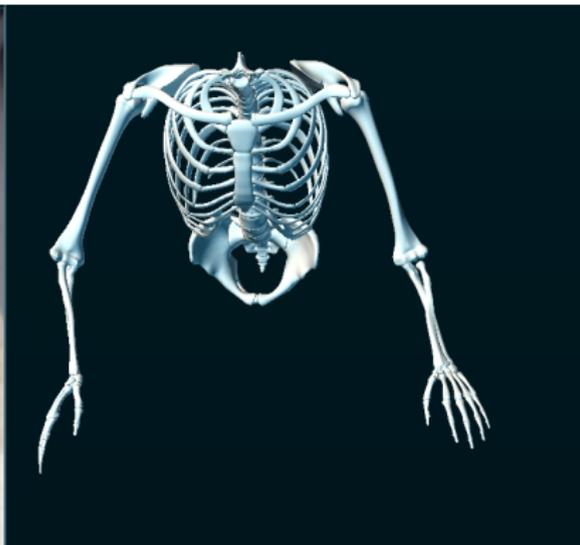
Joint work with Aakash Kaku, Avinash Parnandi, and Heidi Schambra

# Quantitative rehabilitation of stroke patients



**Goal:** Automatic identification/counting of basic upper body movements

Data: 100 dimensional time series (accelerations, rotations)



# Methodology

- ▶ Deep convolutional neural networks achieves great results for fixed group of patients
- ▶ To be clinically practical we need to generalize to **new** patients
- ▶ Promising results by normalizing features (*instance normalization*)

## Blind denoising of natural images

Bias-free CNNs

Wiener filtering

CNNs learn adaptive filters

CNNs learn unions of subspaces

## Quantitative magnetic-resonance imaging

## Early diagnostics of Alzheimer's disease

## Quantitative rehabilitation of stroke patients

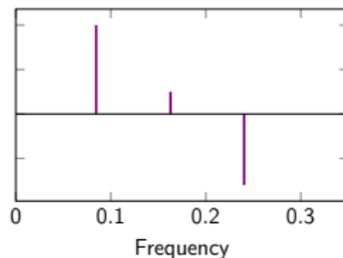
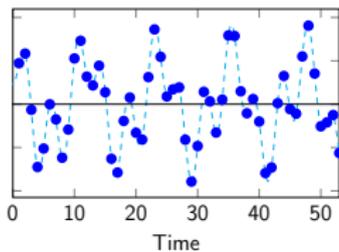
## Data-driven estimation of sinusoid frequencies

# Data-driven estimation of sinusoid frequencies

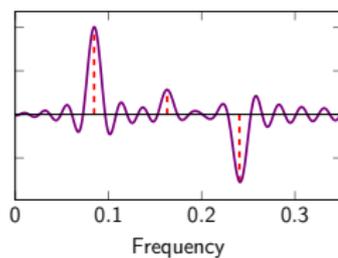
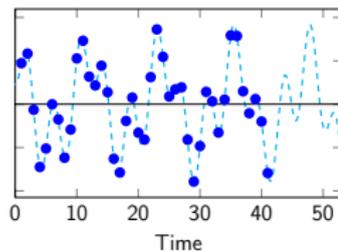
Joint work with Brett Bernstein, Gautier Izacard, and Sreyas Mohan

# Frequency estimation (aka super-resolution of line spectra)

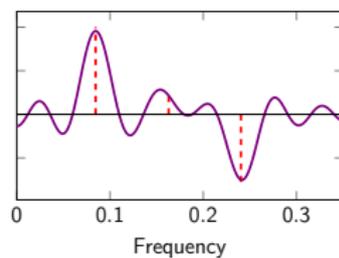
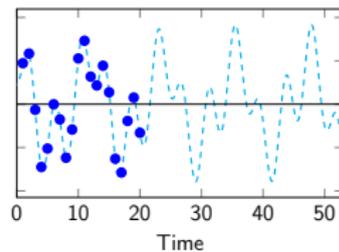
Infinite samples



$N = 40$



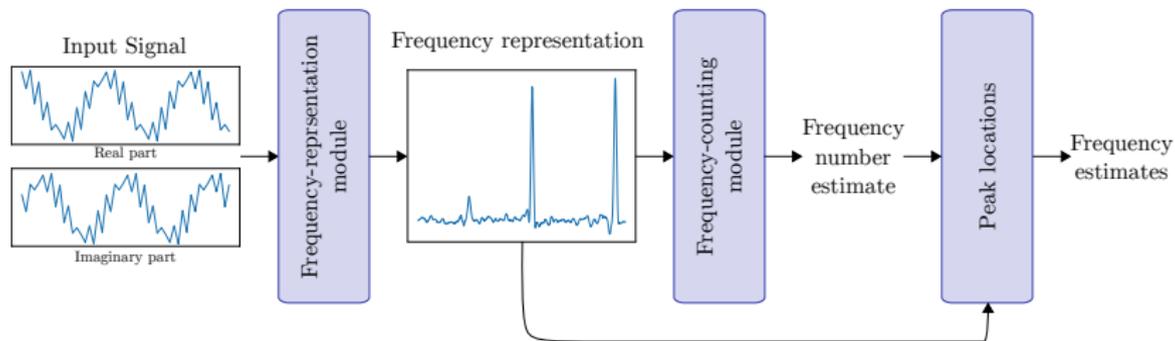
$N = 20$



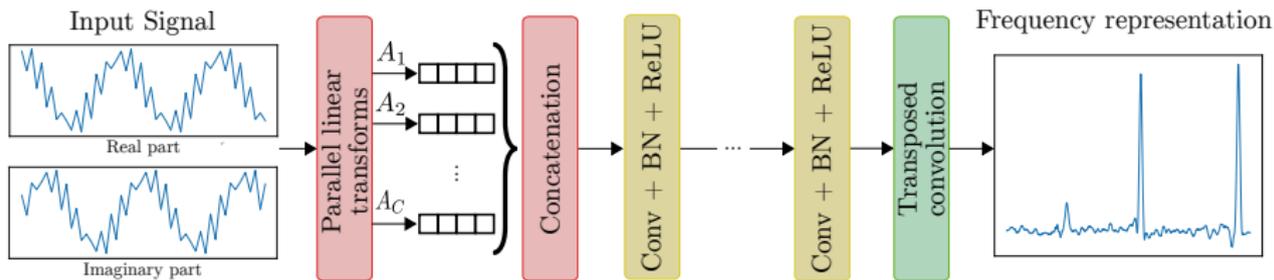
# Traditional methodology

- ▶ Linear estimation (periodogram)
- ▶ Parametric methods based on eigendecomposition of sample covariance matrix (MUSIC, ESPRIT, matrix pencil)
- ▶ Sparsity-based methods

# Learning-based approach

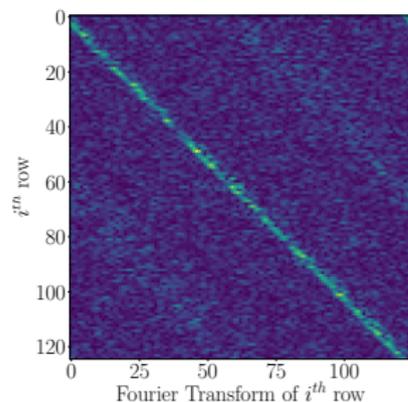


# Frequency-representation module

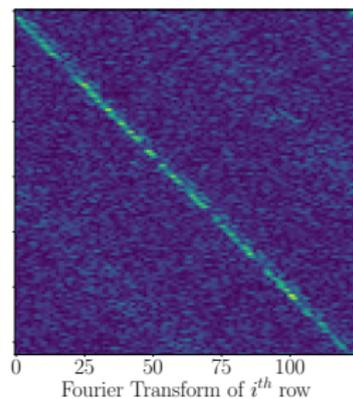


# Fourier transform of learned transformations

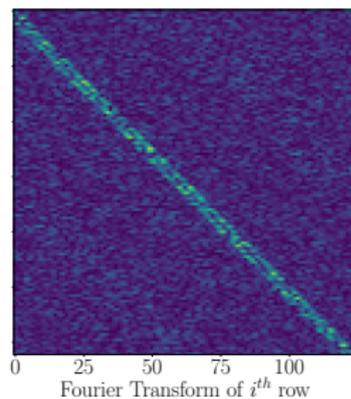
$A_1$



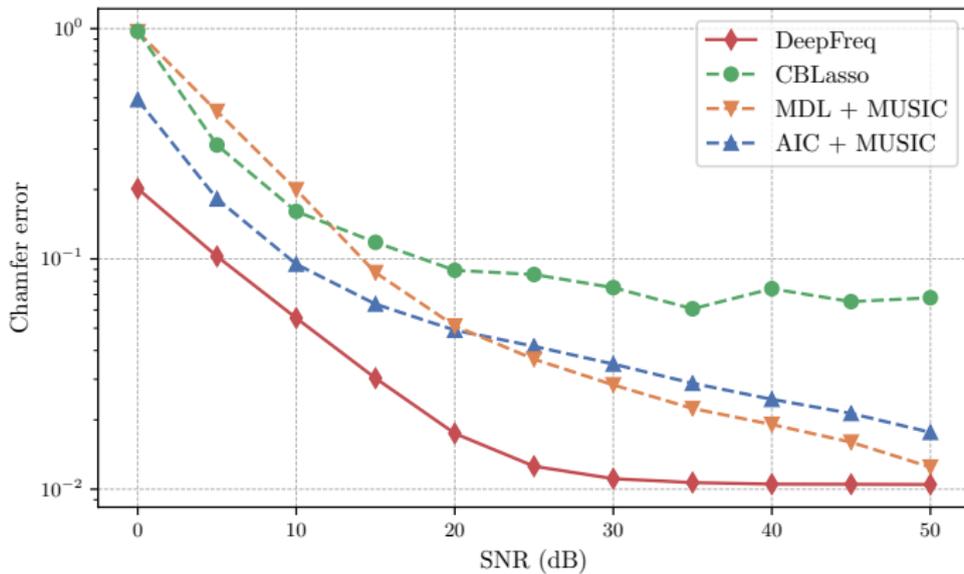
$A_2$



$A_3$



# Comparison to state of the art



For more information

**A Learning-Based Framework for Line-Spectra Super-resolution.**

G. Izacard, B. Bernstein, C. Fernandez-Granda. ICASSP 2019

**Data-driven Estimation of Sinusoid Frequencies.** G. Izacard,

S. Mohan, C. Fernandez-Granda. NeurIPS 2019