European Molecular Imaging Meeting | EMIM 2020

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Declaration of Financial Interests or Relationships

I have **no financial interests** or **relationships** to disclose with regard to the subject matter of this presentation.

Biomedical imaging as an inverse problem

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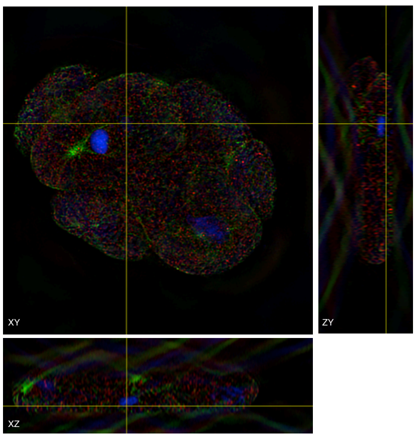
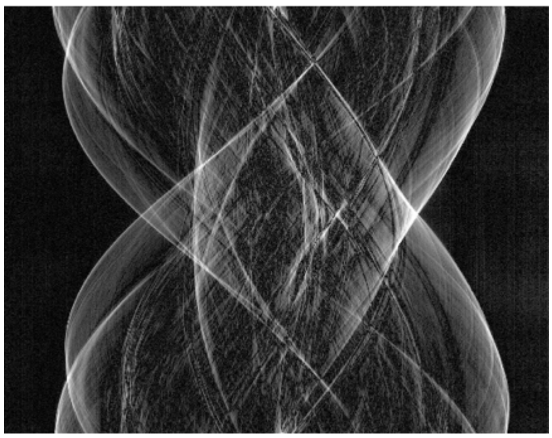




Slides mostly based on the work of Prof. Michaël Unser and the EPFL's Biomedical Imaging Group, in Lausanne, Switzerland.

Biomedical imaging as an inverse problem

$\mathbf{n}$ noise
statistical variability

Biomedically relevant quantity $s \mapsto \mathbf{s}$ $\longrightarrow$ Process and/or instrument physics $\mathbf{H}$ $\longrightarrow$ $\oplus$ $\longrightarrow$ $\mathbf{y} = \mathbf{H}(\mathbf{s}) + \mathbf{n}$

Measurements / data

- **1. Imaging as an inverse problem**
  - Basic imaging operators $\mathbf{H}$
  - Discretization of the inverse problem $s \mapsto \mathbf{s}$
- **2. A condensed history of image reconstruction**
  - Classical image reconstruction (1st gen.)
  - Sparsity-based image reconstruction (2nd gen.)
  - The learning revolution (3rd gen.)

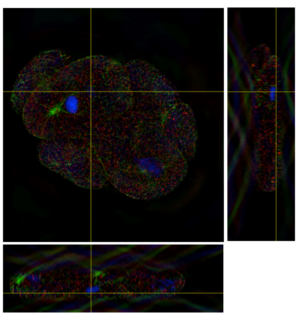
EXAMPLE I

3D widefield microscopy

$s(x_1, x_2, x_3, c)$ (3D + 3 fluorophores)

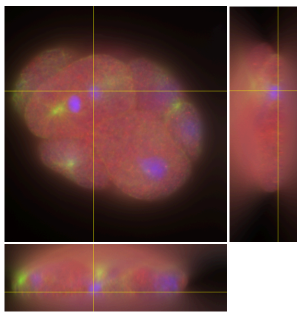
$\downarrow$

$\mathbf{s}$



noise
$\mathbf{n}$

$\mathbf{y} = \mathbf{H}(\mathbf{s}) + \mathbf{n}$



Download the data from: http://bigwww.epfl.ch/deconvolution/bio/ (C. Elegans embryo)

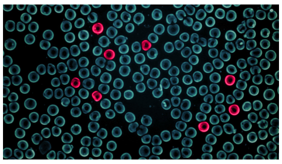
EXAMPLE II

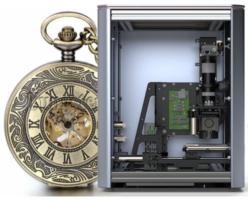
ELISpot and FluoroSpot immunoassays

$s(x_1, x_2, \sigma)$ (2D + time)

$\downarrow$

$\mathbf{s}$

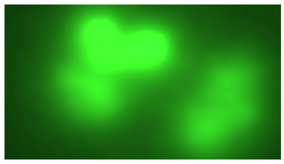




noise

$\mathbf{n}$

$$\mathbf{y} = \mathbf{H}(\mathbf{s}) + \mathbf{n}$$



- Vaccine development (very timely)
- 2D $\mathbf{y} \rightarrow$ 3D $\mathbf{s}$

See more at youtu.be/lUHr0nVJ_H0

[del Aguila Pla, Jaldén, 2018] - IEEE TSP, Parts I and II

Download from: https://poldap.github.io/#/pubs

Slide borrows material from: Prof. Joakim Jaldén, and Mabtech AB.

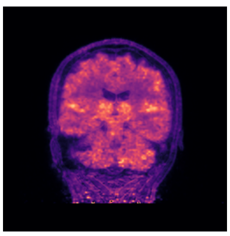
EXAMPLE III

Positron emission tomography (PET)

$s(\cdots)$ (2D/3D/+time)

$\downarrow$

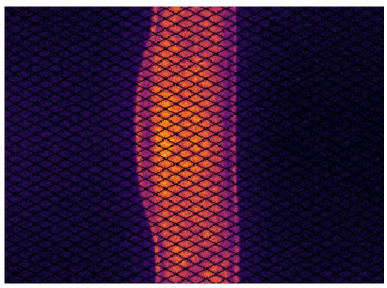
$\mathbf{s}$



noise

$\mathbf{n}$

$$\mathbf{y} = \mathbf{H}(\mathbf{s}) + \mathbf{n}$$

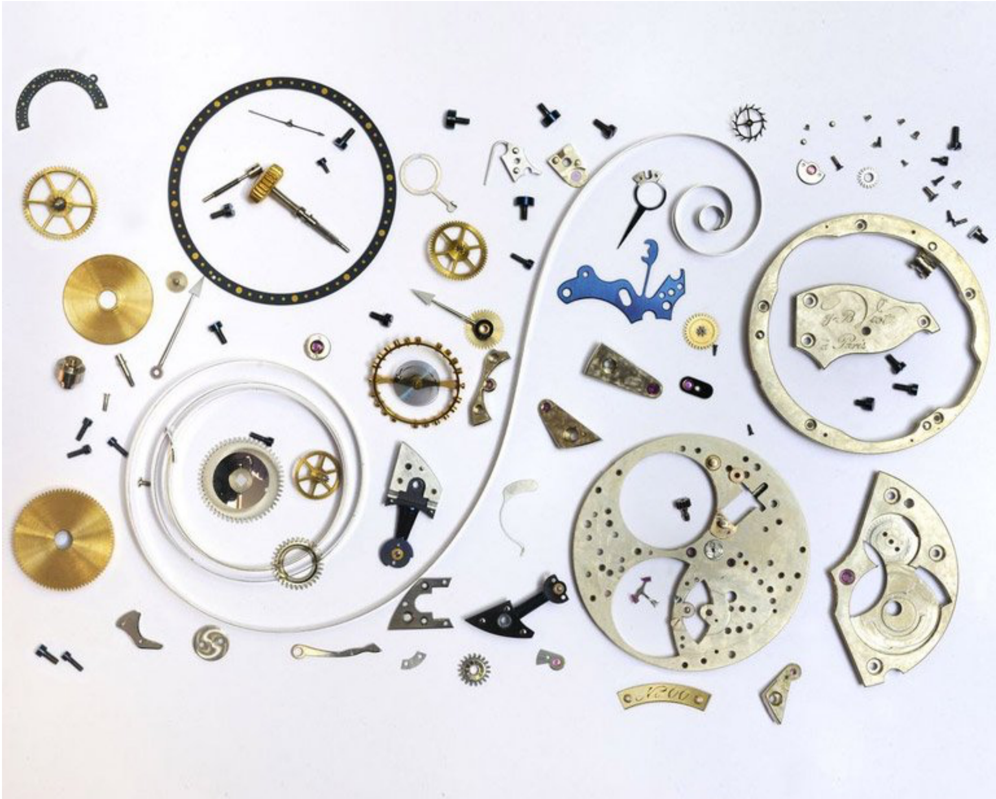


Slide borrows material from: NiftyPET (github.com/NiftyPET).

Part 1

Imaging as an inverse problem

Biomedical Imaging Group



Forward imaging model (noise-free)

Unknown molecular/anatomical map: $s(\boldsymbol{r}), \boldsymbol{r} = (x, y, z, t) \in \mathbb{R}^d$

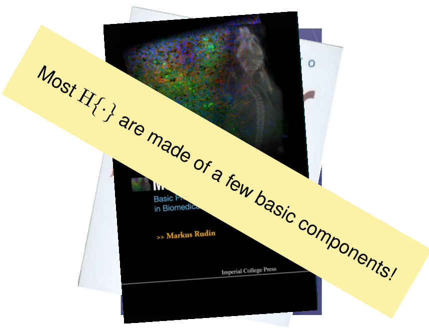
defined over a continuum in space-time

$s \in L_2(\mathbb{R}^d)$ (space of finite-energy functions)

Imaging operator $\mathrm{H} : s \mapsto \mathbf{y} = (y_1, \cdots, y_M) = \mathrm{H}\{s\}$

from continuum to discrete (finite dimensional)

$\mathrm{H} : L_2(\mathbb{R}^d) \rightarrow \mathbb{R}^M$



Linearity assumption: for all $s_1, s_2 \in L_2(\mathbb{R}^d)$, $\alpha_1, \alpha_2 \in \mathbb{R}$

$$\mathrm{H}\{\alpha_1 s_1 + \alpha_2 s_2\} = \alpha_1 \mathrm{H}\{s_1\} + \alpha_2 \mathrm{H}\{s_2\}$$

impulse response of the mth detector

$$\Rightarrow \quad [\mathbf{y}]_m = y_m = \langle \eta_m, s \rangle = \int_{\mathbb{R}^d} \eta_m(\boldsymbol{r}) s(\boldsymbol{r}) \mathrm{d}\boldsymbol{r}$$

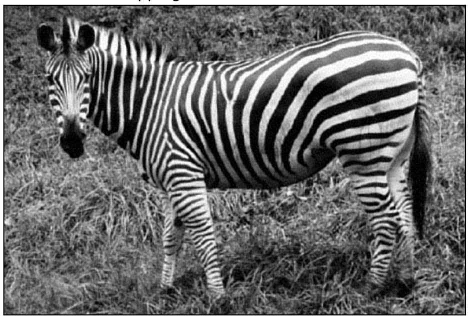
(by the Riesz representation theorem)

$\eta_m(\cdot)$: analysis function

Basic operators: Fourier transform

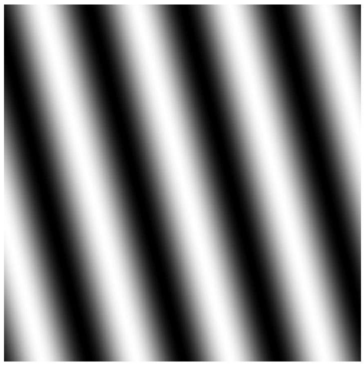
Images are obviously made of sine waves…

Clipping the Fourier transform



EPFL Biomedical Imaging Group

$\mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_0, \boldsymbol{x}\rangle}$



$$\mathcal{F} : L_2(\mathbb{R}^d) \to L_2(\mathbb{R}^d)$$

$$\hat{s}(\boldsymbol{\omega}) = \mathcal{F}\{s\}(\boldsymbol{\omega}) = \int_{\mathbb{R}^d} s(\boldsymbol{r})\mathrm{e}^{-\mathrm{j}\langle \boldsymbol{\omega}, \boldsymbol{r}\rangle} \mathrm{d}\boldsymbol{x}$$

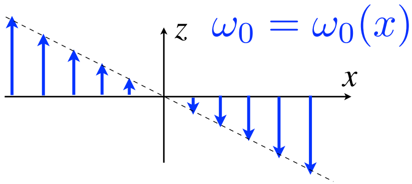
Reconstruction formula (inverse Fourier transform)

$$s(\boldsymbol{r}) = \mathcal{F}^{-1}\{s\}(\boldsymbol{r}) = \frac{1}{(2\pi)^d} \int_{\mathbb{R}^d} \hat{s}(\boldsymbol{\omega}) e^{j\langle \boldsymbol{\omega}, \boldsymbol{r}\rangle} \mathrm{d}\boldsymbol{\omega} \qquad \text{(a.e.)}$$

Ex.: Magnetic resonance imaging

- Magnetic resonance: $\omega_0 = \gamma B_0$

  Frequency encode:



- Linear forward model for MRI $\quad \boldsymbol{r} = (x, y, z)$

$$\hat{s}(\boldsymbol{\omega}_m) = \int_{\mathbb{R}^3} s(\boldsymbol{r})\mathrm{e}^{-\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle} \mathrm{d}\boldsymbol{r}$$

(sampling of Fourier transform)

Equivalent analysis functions: $\eta_m(\boldsymbol{r}) = \mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle}$ (complex sinusoids)

- Extended forward model with coil sensitivity

$$\hat{s}_w(\boldsymbol{\omega}_m) = \int_{\mathbb{R}^3} w(\boldsymbol{r}) s(\boldsymbol{r})\mathrm{e}^{-\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle} \mathrm{d}\boldsymbol{r} \qquad \eta_m(\boldsymbol{r}) = w(\boldsymbol{r})\mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle}$$

Basic operators: Multiplication

$$\mathrm{M}_w : L_2(\mathbb{R}^d) \to L_2(\mathbb{R}^d)$$

$$\mathrm{M}_w\{s\}(\boldsymbol{r}) = w(\boldsymbol{r})s(\boldsymbol{r})$$

Positive window function (cont. and bounded):
$w \in \mathbf{C}_{\mathrm{b}}(\mathbb{R}^d), w(\boldsymbol{r}) \geq 0$

- Special case: modulation

$$w(\boldsymbol{r}) = \mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_0, \boldsymbol{r}\rangle}$$

$$\mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_0, \boldsymbol{r}\rangle} s(\boldsymbol{r}) \quad \stackrel{\mathcal{F}}{\longleftrightarrow} \quad \hat{s}(\boldsymbol{\omega} - \boldsymbol{\omega}_0)$$

Applications:

- MRI with coil sensitivity
- Structured illumination microscopy (SIM)

Convolution

$$\mathrm{C}_h : L_2(\mathbb{R}^d) \to L_2(\mathbb{R}^d)$$

$$\mathrm{C}_h\{s\}(\boldsymbol{r}) = (h * s)(\boldsymbol{r}) = \int_{\mathbb{R}^d} h(\boldsymbol{r} - \tilde{\boldsymbol{r}}) s(\tilde{\boldsymbol{r}}) \mathrm{d}\tilde{\boldsymbol{r}}$$

Equivalent analysis functions: $\eta_m(\boldsymbol{r}) = h(\boldsymbol{r}_m - \cdot)$

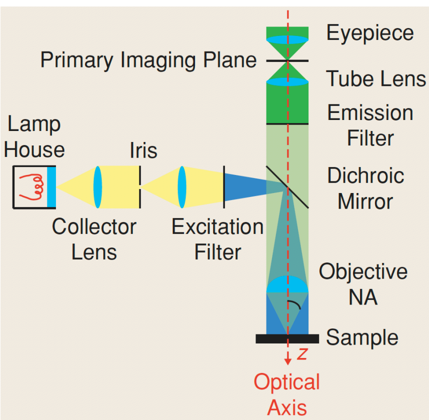
Frequency response: $\hat{h}(\boldsymbol{\omega}) = \mathcal{F}\{h\}(\boldsymbol{\omega})$

- Convolution as a frequency-domain product

$$(h * s)(\boldsymbol{r}) \quad \stackrel{\mathcal{F}}{\longleftrightarrow} \quad \hat{h}(\boldsymbol{\omega})\hat{s}(\boldsymbol{\omega})$$

$$\mathrm{C}_h = \mathcal{F}^{-1} \circ \mathrm{M}_{\hat{h}} \circ \mathcal{F}$$

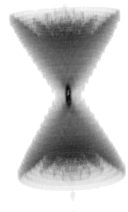
Ex.: 3D widefield microscopy

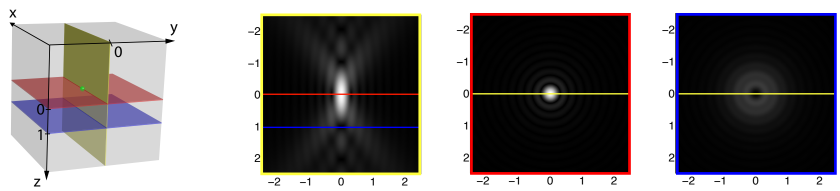


(Vonesch, Aguet, Vonesch, Unser, 2006)

- Diffraction-limited optics
  - Convolution / blur

$\mathbf{h}_{\mathrm{3D}}$





Generate PSFs for a specific microscope with: bigwww.epfl.ch/algorithms/psfgenerator/

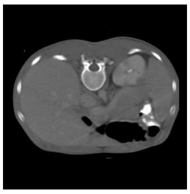
Basic operators: X-ray / Radon transform

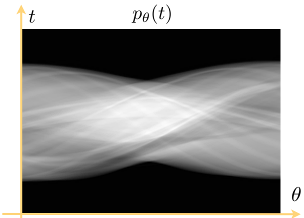
Projection geometry: $\boldsymbol{r} = t\boldsymbol{\theta} + q\boldsymbol{\theta}^{\perp}$ with $\boldsymbol{\theta} = [\cos\theta, \sin\theta]^{\mathrm{T}}$

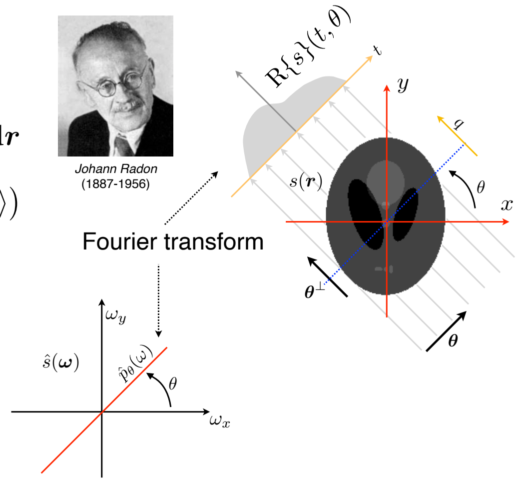
- Radon transform (line integrals) $\mathrm{R} : \mathcal{S}(\mathbb{R}^2) \to \mathcal{S}(\mathbb{R} \times S^1)$

$$p_\theta(t) = \mathrm{R}\{s\}(t,\theta) = \int_{\mathbb{R}} s(t\boldsymbol{\theta} + q\boldsymbol{\theta}^{\perp})\mathrm{d}q = \int_{\mathbb{R}^2} s(\boldsymbol{r})\delta(t - \langle \boldsymbol{r}, \boldsymbol{\theta}\rangle)\mathrm{d}\boldsymbol{r}$$

Equivalent analysis functions (generalized): $\eta_m(\boldsymbol{r}) = \delta\big(t_m - \langle \boldsymbol{r}, \boldsymbol{\theta}_m\rangle\big)$







- Central-slice theorem

$$\hat{p}_\theta(\omega) = (\mathcal{F}_t \circ \mathrm{R})\{s\}(\omega,\theta) = \mathcal{F}_{\boldsymbol{r}}\{s\}(\omega\boldsymbol{\theta}) = \hat{s}_{\mathrm{pol}}(\omega,\theta)$$

$\hat{s}_{\mathrm{pol}}$: 2D Fourier transform of s in polar coordinates.
$\mathcal{F}_t$ or $\mathcal{F}_{\boldsymbol{r}}$: Fourier transform along t or $\boldsymbol{r}$ (resp.)

What we have learned in the perspective of some common biomedical imaging modalities

$$[\mathrm{H}s]_m = y_m = \langle \eta_m, s\rangle = \int_{\mathbb{R}^d} \eta_m(\boldsymbol{r})s(\boldsymbol{r})\mathrm{d}\boldsymbol{r}$$

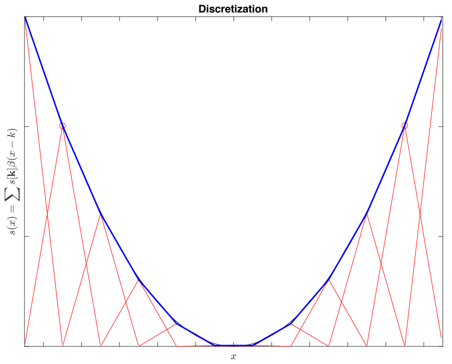
But how do we represent $s \in L_2(\mathbb{R}^d)$?

Modality	Radiation	Analysis function η_m
2D or 3D tomography	coherent x-ray	$\delta(t_m - \langle \boldsymbol{r}, \boldsymbol{\theta}_m\rangle)$ $\boldsymbol{\theta}_m$: mth sampled direction
3D deconvolution microscopy	fluorescence	$h(\boldsymbol{r}_m - \boldsymbol{r})$ h: PSF of microscope
Structured illumination microscopy (SIM)	fluorescence	$h(\boldsymbol{r}_m - \boldsymbol{r})w_m(\boldsymbol{r})$ w_m: mth illumination pattern
Positron emission tomography (PET)	gamma rays	$\delta(t_m - \langle \boldsymbol{r}, \boldsymbol{\theta}_m\rangle)$ $(\boldsymbol{\theta}_m, t_m)$: mth LoR
Magnetic resonance imaging (MRI)	radio frequency	$\mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle}$
Cardiac MRI (parallel, non-uniform)	radio frequency	$w_m(\boldsymbol{r})\mathrm{e}^{\mathrm{j}\langle \boldsymbol{\omega}_m, \boldsymbol{r}\rangle}$ w_m: sensitivity of the mth coil

Discretization: Finite dimensional formalism

Represent the continuous signal on a finite combination of synthesis functions $\beta_{\boldsymbol{k}}(\boldsymbol{r})$

$s(\boldsymbol{r}) = \sum_{\boldsymbol{k}\in\Omega} s[\boldsymbol{k}]\beta_{\boldsymbol{k}}(\boldsymbol{r})$ with the signal vector (of coefficients): $\boldsymbol{s} = \left[s[\boldsymbol{k}]\right]_{\boldsymbol{k}\in\Omega}$ of dimension $K = |\Omega|$.



- Applying the forward imaging model to such a signal

$$\begin{aligned} y_m &= \int_{\mathbb{R}^d} s(\boldsymbol{r})\eta_m(\boldsymbol{r})\mathrm{d}\boldsymbol{r} + n[m] = \langle s, \eta_m\rangle + n[m], \quad (m = 1, \ldots, M) \\ &= \sum_{\boldsymbol{k}\in\Omega} \langle \beta_{\boldsymbol{k}}, \eta_m\rangle s[\boldsymbol{k}] + n[m] \end{aligned}$$

η_m: analysis function, $\beta_{\boldsymbol{k}}$: synthesis function
$n[\cdot]$: additive noise

$$\Rightarrow \mathbf{y} = \mathbf{H}\mathbf{s} + \mathbf{n} \qquad (M \times K) \text{ system matrix : } \qquad [\mathbf{H}]_{m,\boldsymbol{k}} = \langle \eta_m, \beta_{\boldsymbol{k}}\rangle = \int_{\mathbb{R}^d} \eta_m(\boldsymbol{r})\beta_{\boldsymbol{k}}(\boldsymbol{r})\mathrm{d}\boldsymbol{r}$$

Example of basis functions

Shift-invariant representation: $\beta_{\boldsymbol{k}}(\boldsymbol{r}) = \beta(\boldsymbol{r} - \boldsymbol{k})$

Separable generator: $\beta(\boldsymbol{r}) = \prod_{n=1}^{d} \beta(\boldsymbol{r}[n])$

- Pixelated model

$$\beta(x) = \mathrm{rect}(x)$$

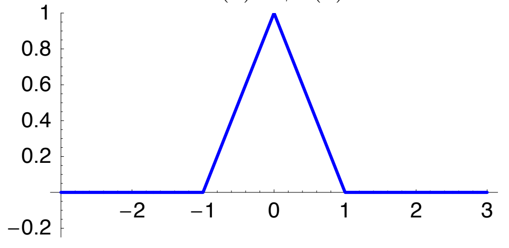
- Bilinear model

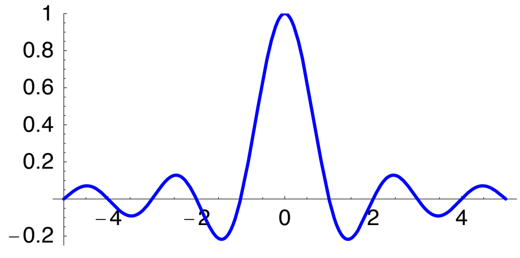
$$\beta(x) = (\mathrm{rect} * \mathrm{rect})(x) = \mathrm{tri}(x)$$

- Bandlimited representation

$$\beta(x) = \mathrm{sinc}(x)$$

$\mathrm{tri}(x) = \beta^1(x)$





Part 2: A condensed history of image reconstruction

Classical image reconstruction (1st gen., 20th century)

Sparsity-based image reconstruction (2nd gen., 21st century)

The learning revolution (3rd gen.)

ICASSP2020 Barcelona


See more (2h 30min) at youtu.be/J6_5rPYnr_s

Classical image reconstruction (1st gen., 20th century)

- Easy scenario, well posedness:

$C_1\|\mathbf{s}\|_2 \le \|\mathbf{Hs}\|_2 \le C_2\|\mathbf{s}\|_2$ for all $\mathbf{s} \in \mathcal{X}$

$\Rightarrow \quad \mathbf{s} \approx \mathbf{H}^{-1}\mathbf{y}$

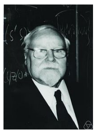
Backprojection: $\mathbf{s} \approx \mathbf{H}^{\mathrm{T}}\mathbf{y}$

Least-squares: $\min_{\tilde{\mathbf{s}} \in \mathbb{R}_+^M} \left\{ \|\mathbf{y} - \mathbf{H}\tilde{\mathbf{s}}\|^2 \right\}$

$\Rightarrow \boldsymbol{s} = (\mathbf{H}^{\mathrm{T}}\mathbf{H})^{-1}\mathbf{H}^{\mathrm{T}}\boldsymbol{y}$

- **Limitations:**
  - Amplification of the noise
  - Interesting problems are ill-posed
  - Computationally expensive matrix inversions

$\mathbf{L} = \mathbf{C}_s^{-1/2}, \lambda = 1$



Andrey N. Tikhonov
(1906-1993)

$\mathbf{L}$ to promote smoothness

- Tikhonov / Wiener theory

$$\min_{\tilde{\mathbf{s}} \in \mathbb{R}_+^K} \underbrace{\|\mathbf{y} - \mathbf{H}\tilde{\mathbf{s}}\|_2^2}_{\text{data consistency}} + \underbrace{\lambda\|\mathbf{L}\tilde{\mathbf{s}}\|_2^2}_{\text{regularization or Gaussian prior}}$$

Norbert Wiener
(1894-1964)

$s \sim \mathcal{N}(\mathbf{0}, \mathbf{C}_s)$

"Filtered" backprojection

$\Rightarrow \mathbf{s} = (\mathbf{H}^T\mathbf{H} + \lambda\mathbf{L}^T\mathbf{L})^{-1}\mathbf{H}^T\mathbf{y}$

- **Limitations:**
  - Computationally expensive matrix inversions

- Efficient iterative algorithms $\min_{\tilde{\mathbf{s}} \in \mathbb{R}_+^K} J(\tilde{\mathbf{s}}, \boldsymbol{y})$

$\|\mathbf{y} - \mathbf{Hs}\|^2 = \boldsymbol{y}^{\mathrm{T}}\boldsymbol{y} - 2\boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\boldsymbol{y} + \boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\mathbf{H}\boldsymbol{s}$

Steepest-descent type: $\mathbf{s}^{(i+1)} \leftarrow \mathbf{s}^{(i)} - \gamma\nabla_{\mathbf{s}}\{J(\mathbf{s}, \mathbf{y})\}(\mathbf{s}^{(i)})$

ex.: projected gradient descent, followed by $\mathbf{s}^{(i+1)} \leftarrow [\mathbf{s}^{(i+1)}]_+$

Classical image reconstruction (1st gen., 20th century)

- **Easy scenario, well posedness:**

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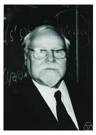

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$$\|\mathbf{y} - \mathbf{H}\mathbf{s}\|^2 = \boldsymbol{y}^{\mathrm{T}}\boldsymbol{y} - 2\boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\boldsymbol{y} + \boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\mathbf{H}\boldsymbol{s}$$

Least squares:
$\mathbf{s}^{(i+1)} \leftarrow \mathbf{s}^{(i)} + \tilde{\gamma}\big(\mathbf{s}_0 - (\mathbf{H}^T\mathbf{H})\mathbf{s}^{(i)}\big)$ with $\mathbf{s}_0 = \mathbf{H}^T\mathbf{y}$

Ground truth

Gaussian blur + additive noise

van Cittert animation

19

Classical image reconstruction (1st gen., 20th century)

- **Easy scenario, well posedness:**

$C_1\|\mathbf{s}\|_2 \leq \|\mathbf{H}\mathbf{s}\|_2 \leq C_2\|\mathbf{s}\|_2$ for all $\mathbf{s} \in \mathcal{X}$

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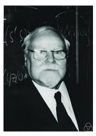

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$\mathbf{L}$ to promote smoothness

- **Tikhonov / Wiener theory**

$$\min_{\tilde{\mathbf{s}} \in \mathbb{R}_+^K} \underbrace{\|\mathbf{y} - \mathbf{H}\tilde{\mathbf{s}}\|_2^2}_{\text{data consistency}} + \underbrace{\lambda\|\mathbf{L}\tilde{\mathbf{s}}\|_2^2}_{\text{regularization or Gaussian prior}}$$

Norbert Wiener
(1894-1964)

$s \sim \mathcal{N}(\mathbf{0}, \mathbf{C}_s)$

"Filtered" backprojection

$$\Rightarrow \mathbf{s} = (\mathbf{H}^T\mathbf{H} + \lambda\mathbf{L}^T\mathbf{L})^{-1}\mathbf{H}^T\mathbf{y}$$

- **Limitations:**
  - Computationally expensive matrix inversions

- **Efficient iterative algorithms** $\min_{\tilde{\mathbf{s}} \in \mathbb{R}_+^K} J(\tilde{\mathbf{s}}, \boldsymbol{y})$

Steepest-descent type: $\mathbf{s}^{(i+1)} \leftarrow \mathbf{s}^{(i)} - \gamma\nabla_{\mathbf{s}}\{J(\mathbf{s}, \mathbf{y})\}(\mathbf{s}^{(i)})$

ex.: projected gradient descent, followed by $\mathbf{s}^{(i+1)} \leftarrow [\mathbf{s}^{(i+1)}]_+$

$$\|\mathbf{y} - \mathbf{H}\mathbf{s}\|^2 = \boldsymbol{y}^{\mathrm{T}}\boldsymbol{y} - 2\boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\boldsymbol{y} + \boldsymbol{s}^{\mathrm{T}}\mathbf{H}^{\mathrm{T}}\mathbf{H}\boldsymbol{s}$$

Tikhonov:
$\mathbf{s}^{(i+1)} \leftarrow \mathbf{s}^{(i)} + \tilde{\gamma}\big(\mathbf{s}_0 - (\mathbf{H}^T\mathbf{H} + \lambda\mathbf{L}^T\mathbf{L})\mathbf{s}^{(i)}\big)$

Ground truth

Gaussian blur + additive noise

Not enough: λ=0.2

Optimal: λ=2

Too much: λ=20

20

Classical image reconstruction (1st gen., 20th century)

- Easy scenario, well posedness:

$C_1\|\mathbf{s}\|_2 \le \|\mathbf{Hs}\|_2 \le C_2\|\mathbf{s}\|_2$ for all $\mathbf{s} \in \mathcal{X}$

$\Rightarrow \quad \mathbf{s} \approx \mathbf{H}^{-1}\mathbf{y}$

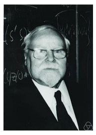
Backprojection: $\mathbf{s} \approx \mathbf{H}^{\mathrm{T}}\mathbf{y}$

Least-squares: $\min_{\tilde{\mathbf{s}}\in\mathbb{R}_+^M} \{\|\mathbf{y} - \mathbf{H}\tilde{\mathbf{s}}\|^2\}$

$\Rightarrow \boldsymbol{s} = (\mathbf{H}^{\mathrm{T}}\mathbf{H})^{-1}\mathbf{H}^{\mathrm{T}}\boldsymbol{y}$

- **Limitations:**
  - Amplification of the noise
  - Interesting problems are ill-posed
  - Computationally expensive matrix inversions

$\mathbf{L} = \mathbf{C}_s^{-1/2}, \lambda = 1$



Andrey N. Tikhonov
(1906-1993)

$\mathbf{L}$ to promote smoothness

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- Fast implementation
  - Diagonalization of convolution matrices $\Rightarrow$ FFT-based implementation
  - Applicable to:
    1. deconvolution microscopy (Wiener filter) $\rightarrow$ if $\mathbf{H}$ is a convolution matrix, so is $\mathbf{H}^{\mathrm{T}}\mathbf{H}$.
    2. parallel-ray computed tomography (FBP) $\rightarrow$ $\mathbf{H}^{\mathrm{T}}\mathbf{H}$ is a convolution matrix.
    3. MRI

Sparsity-based image reconstruction (2nd gen., 21st century)

- Non-quadratic regularization

$$\min_{\mathbf{s}\in\mathbb{R}_+^K} \|\mathbf{y} - \mathbf{Hs}\|_2^2 + \lambda\mathcal{R}(\mathbf{s})$$

$\mathcal{R}(\mathbf{s}) = \|\mathbf{Ls}\|_2^2 \quad \longrightarrow \|\mathbf{Ls}\|_p^p \quad \longrightarrow \mathcal{R}(\mathbf{s}) = \|\mathbf{Ls}\|_1$

- Total variation, $\mathbf{L}$: gradient [Rudin, Osher et al., 1992]
- Wavelet-domain regularization, $\boldsymbol{s} = \mathbf{W}\boldsymbol{x}$, $\mathcal{R}(\boldsymbol{x}) = \|\boldsymbol{x}\|_1$
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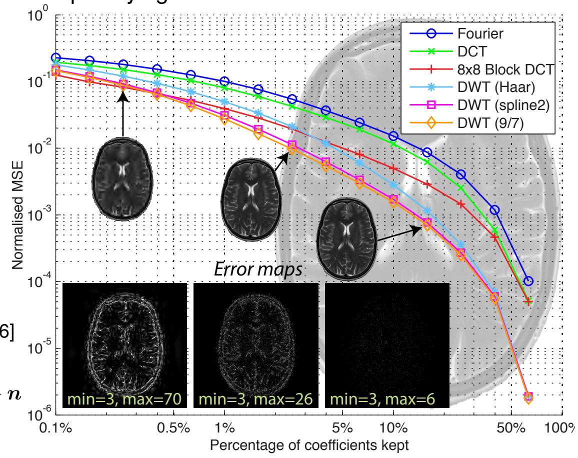
- Sparsifying transforms $\mathbf{W}^{-1}$



[Guerquin-Kern et al., 2011] - IEEE TMI

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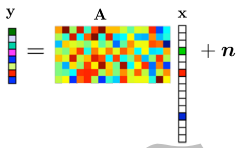

$$\min_{\boldsymbol{x}:\|\boldsymbol{x}\|_0\le K} \|\boldsymbol{y} - \mathbf{A}\boldsymbol{x}\|_2^2 \quad \Leftrightarrow \quad \min_{\boldsymbol{x}:\|\boldsymbol{x}\|_1\le C} \|\boldsymbol{y} - \mathbf{A}\boldsymbol{x}\|_2^2$$

(nonconvex) (convex)

w. some conditions on $\mathbf{A}$

- A representer-theorem view [Unser, Fageot, Gupta, 2016] - IEEE TIT

$\min_{\mathbf{x}} \{\|\mathbf{y} - \mathbf{Ax}\|_2^2 + \lambda\|\mathbf{x}\|_2^2\} \Leftrightarrow \min_{\mathbf{x}} \|\mathbf{x}\|_2$ subject to $\|\mathbf{y} - \mathbf{Ax}\|_2^2 \le \sigma^2$

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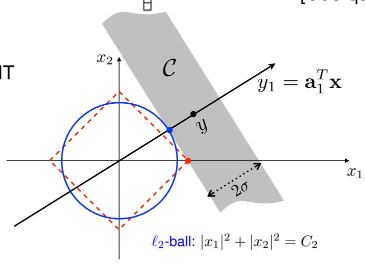

ℓ_2-ball: $|x_1|^2 + |x_2|^2 = C_2$
ℓ_1-ball: $|x_1| + |x_2| = C_1$

Sparsity-based image reconstruction (2nd gen., 21st century)

Non-quadratic regularization

$$\min_{\mathbf{s}\in\mathbb{R}_+^K} \|\mathbf{y}-\mathbf{H}\mathbf{s}\|_2^2 + \lambda\mathcal{R}(\mathbf{s})$$

$\mathcal{R}(\mathbf{s}) = \|\mathbf{L}\mathbf{s}\|_2^2 \quad \longrightarrow \|\mathbf{L}\mathbf{s}\|_p^p \quad \longrightarrow \mathcal{R}(\mathbf{s}) = \|\mathbf{L}\mathbf{s}\|_1$

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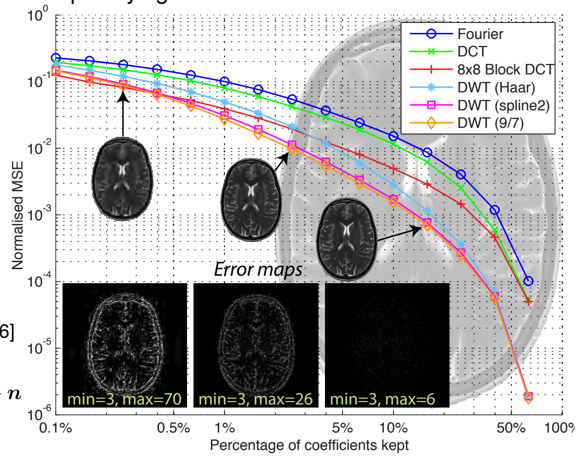

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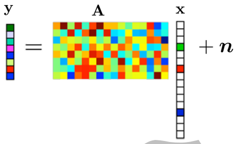

$$\min_{\boldsymbol{x}:\|\boldsymbol{x}\|_0 \le K} \|\boldsymbol{y}-\mathbf{A}\boldsymbol{x}\|_2^2 \quad \Leftrightarrow \quad \min_{\boldsymbol{x}:\|\boldsymbol{x}\|_1 \le C} \|\boldsymbol{y}-\mathbf{A}\boldsymbol{x}\|_2^2$$

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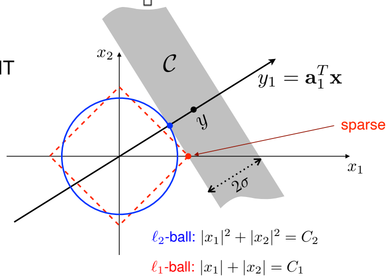

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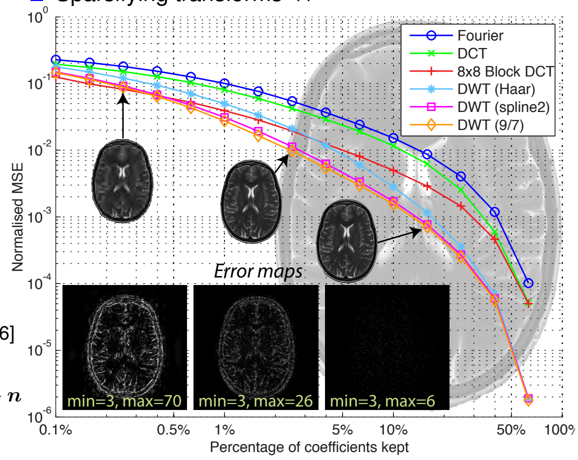

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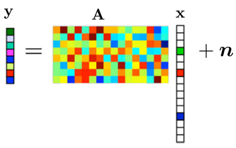

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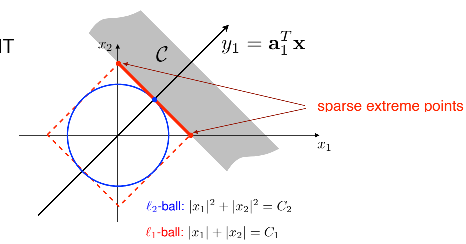

Sparsity-based image reconstruction (2nd gen., 21st century)

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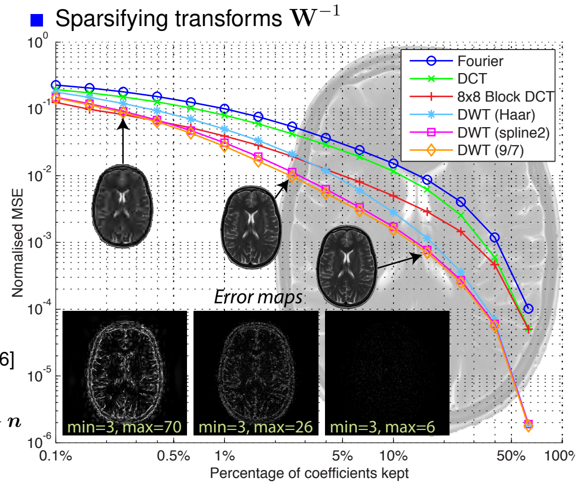

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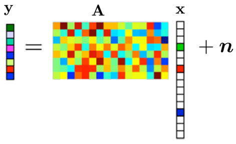

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Representer theorem for constrained ℓ_1 minimization

(P1) $\mathcal{V} = \arg\min_{x\in\ell_1(\mathbb{Z})} \|x\|_{\ell_1}$ s.t. $\mathrm{H}\{x\}\in\mathcal{C}$

is convex, weak*-compact with extreme points of the form

$$x_{\text{sparse}}[\cdot] = \sum_{k=1}^{S} a_k\delta[\cdot - n_k] \quad \text{with} \quad S = \|x_{\text{sparse}}\|_0 \le M.$$

■ Sparse stochastic processes

Unser and Tafti | An Introduction to Sparse Stochastic Processes | CAMBRIDGE

There is an operator L that "whitens" the continuous signal, i.e., $w = \mathrm{L}\{s\}$

$\Rightarrow \mathbf{u} = \mathbf{L}\mathbf{s}$ where $\mathbf{L}$ discretizes L, and $p_U(\boldsymbol{u})$ is inifinitely divisible

$$p_{S|Y}(\mathbf{s}|\mathbf{y}) \propto \exp\left(-\frac{\|\mathbf{y}-\mathbf{H}\mathbf{s}\|^2}{2\sigma^2}\right)\prod_{\boldsymbol{k}\in\Omega} p_U\left([\mathbf{L}\mathbf{s}]_{\boldsymbol{k}}\right) \qquad \|\cdot\|_1 \Leftrightarrow U \text{ is Laplace}$$

Sparsity-based image reconstruction (2nd gen., 21st century)

■ Proximal optimization algorithms: The workhorse of 2nd generation methods

- Ex: Altenating direction method of multipliers (ADMM), [Boyd et al., 2011]

$$\min_{\boldsymbol{s},\mathbf{u}:\mathbf{u}=\mathbf{L}\mathbf{s}} \frac{1}{2}\|\mathbf{y}-\mathbf{H}\mathbf{s}\|_2^2 + \lambda\mathcal{R}(\mathbf{u}) \qquad \mathcal{L}_{\mathcal{A}}(\mathbf{s},\mathbf{u},\boldsymbol{\alpha}) = \frac{1}{2}\|\mathbf{y}-\mathbf{H}\mathbf{s}\|_2^2 + \lambda\mathcal{R}(\mathbf{u}) + \boldsymbol{\alpha}^T(\mathbf{L}\mathbf{s}-\mathbf{u}) + \frac{\mu}{2}\|\mathbf{L}\mathbf{s}-\mathbf{u}\|_2^2$$

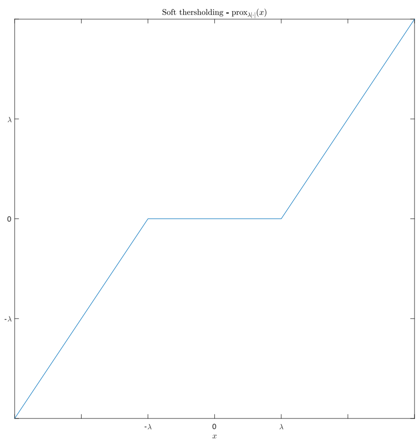
Linear inverse problem: $\mathbf{s}^{k+1} \leftarrow \left(\mathbf{H}^T\mathbf{H} + \mu\mathbf{L}^T\mathbf{L}\right)^{-1}\left(\mathbf{H}^T\mathbf{y} + \mathbf{z}^{k+1}\right)$ with $\mathbf{z}^{k+1} \leftarrow \mathbf{L}^T\left(\mu\mathbf{u}^k - \boldsymbol{\alpha}^k\right)$

$$\boldsymbol{\alpha}^{k+1} \leftarrow \boldsymbol{\alpha}^k + \mu\left(\mathbf{L}\mathbf{s}^{k+1} - \mathbf{u}^k\right)$$

Nonlinear denoising: $\mathbf{u}^{k+1} \leftarrow \operatorname{prox}_{\frac{\lambda}{\mu}\mathcal{R}}\left(\mathbf{L}\mathbf{s}^{k+1} + \frac{1}{\mu}\boldsymbol{\alpha}^{k+1}\right)$

$\operatorname{prox}_{\lambda\mathcal{R}}(\mathbf{y}) = \arg\min_{\mathbf{u}} \frac{1}{2}\|\mathbf{y}-\mathbf{u}\|_2^2 + \lambda\mathcal{R}(\mathbf{u})$ (often separable)

- Example: $\mathbf{L}$ wavelet, $\mathcal{R}(\mathbf{u}) = \|\mathbf{u}\|_1$ (Laplace model) $\rightarrow$ wavelet thresholding denoiser
- Separation in linear step (problem specific) and statistical step (denoiser for prior distribution)



■ **Advantatges:**
- Higher reconstruction quality [Lustig et al., 2007]
- Low-dose, faster imaging (CS)
- Re-use of fast implementations for 1st gen. methods

■ **Limitations:**
- Increased complexity (despite efficient solutions)
- Challenging to implement efficiently

erc GlobalBioIm

Download from: github.com/Biomedical-Imaging-Group/GlobalBioIm

See more at bit.ly/GlobalBioIm-example

Explained with all detail at youtu.be/J6_5rPYnr_s?t=6240

The learning revolution (3rd gen.)

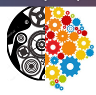
■ Overarching topic: How do we leverage what we already know?

Dimensionality of parameters learnt

Parameter tunning
- Learning λ
- Calibrate forward model

Dictionary learning
- An "optimal" $\mathbf{L}$

[Elad 2006]
[Ravishankar 2011]
[Mairal 2012]



Learning non-linear functions
- An "optimal" $\mathcal{R}$
- CNN parametrization
- Backpropagation

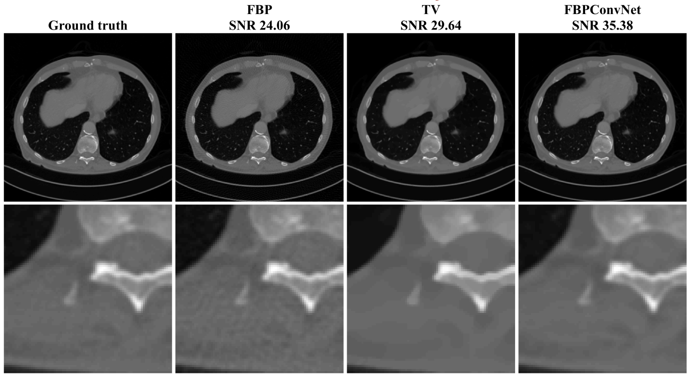
[Chen, Pock, 2015-2016]
[Kamilov 2016]

Task-specific learning (CNNs)
- Artifact removal for 1st gen. reconstructions
- Super-resolution in 3D imaging
- Speeding up well-performing 2nd gen. methods
- Low-dose / short-scan regime

[Jin et al., 2016] → 2019 Best Paper Award IEEE Signal Processing Society
[Weigert et al., 2017]
[Hammernik et al., 2018]

Dose reduction by 7: 143 views

CT data



1000 views FBP

[Jin et al., 2016]

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■ Going too far to the right
- Ignoring the physics, learning them instead

[Zhu et al., 2018] - Nature

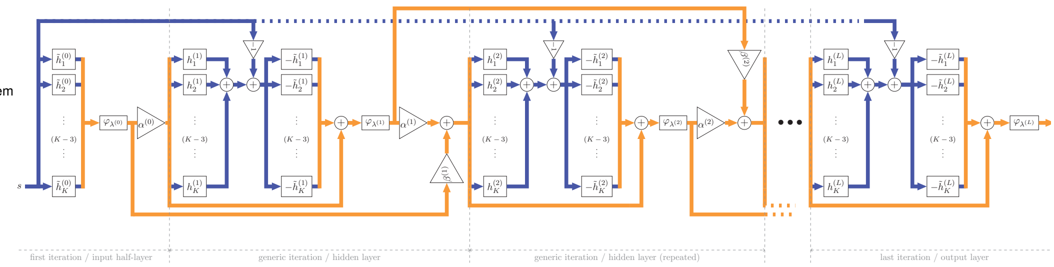
■ Guiding principles
- Learn image-to-image maps, either
  1. within the image (sparsified or not) domain, or
  2. within the measurement domain.
- Need for very large training datasets with gold-standard reconstructions. But exploit the problem structure.
- Data augmentation.

■ Unrolling as a motivation for deep architechtures

[Gregor, LeCun, 2010]

- Use 2nd generation methods as a starting point
- Motivate the architecture using optimization

■ **Ex:** Unrolled FISTA for inverse diffusion (immunoassays)



[del Aguila Pla, Saxena, Jaldén, 2019]

The learning revolution (3rd gen.)

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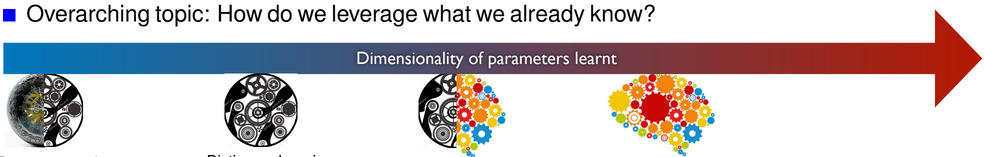

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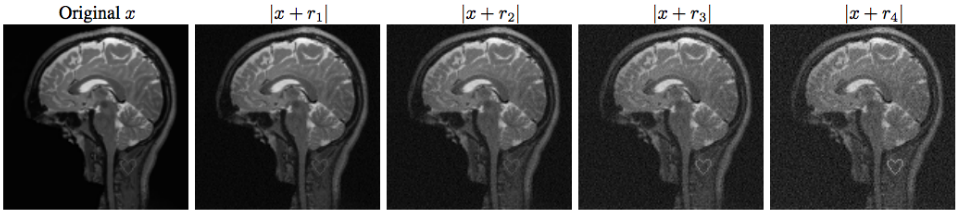
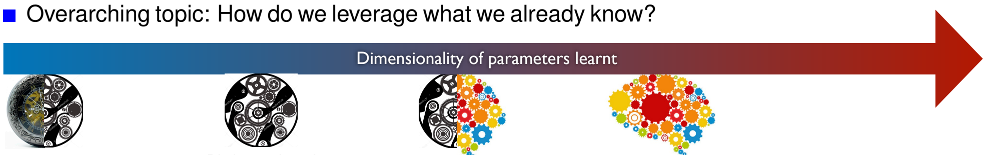
■ A word of warning: Instability in deep learning



[Antun et al., 2020] On instabilities of deep learning in image reconstruction - Does AI come at a cost?

The learning revolution (3rd gen.)

■ Overarching topic: How do we leverage what we already know?



Parameter tunning
- Learning λ
- Calibrate forward model

Dictionary learning
- An "optimal" $\mathbf{L}$

[Elad 2006]
[Ravishankar 2011]
[Mairal 2012]

Learning non-linear functions
- An "optimal" $\mathcal{R}$
- CNN parametrization
- Backpropagation

[Chen, Pock, 2015-2016]
[Kamilov 2016]

Task-specific learning (CNNs)
- Artifact removal for 1st gen. reconstructions
- Super-resolution in 3D imaging
- Speeding up well-performing 2nd gen. methods
- Low-dose / short-scan regime

[Jin et al., 2016] → 2019 Best Paper Award IEEE Signal Processing Society
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[Hammernik et al., 2018]

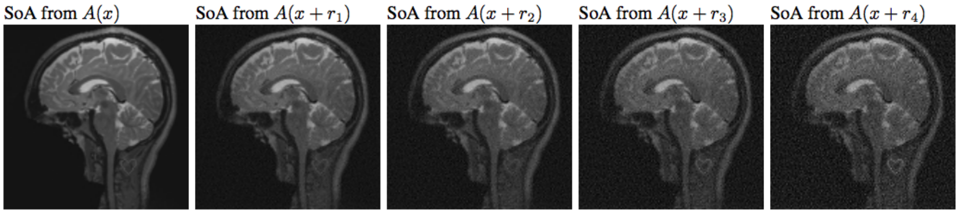
■ Going too far to the right
- Ignoring the physics, learning them instead

[Zhu et al., 2018] - Nature

■ Guiding principles
- Learn image-to-image maps, either
  1. within the image (sparsified or not) domain, or
  2. within the measurement domain.
- Need for very large training datasets with gold-standard reconstructions. But exploit the problem structure.
- Data augmentation.

■ Unrolling as a motivation for deep architechtures
[Gregor, LeCun, 2010]
- Use 2nd generation methods as a starting point
- Motivate the architecture using optimization

■ A word of warning: Instability in deep learning



[Antun et al., 2020] On instabilities of deep learning in image reconstruction - Does AI come at a cost?

The learning revolution (3rd gen.)

- Overarching topic: How do we leverage what we already know?

Dimensionality of parameters learnt

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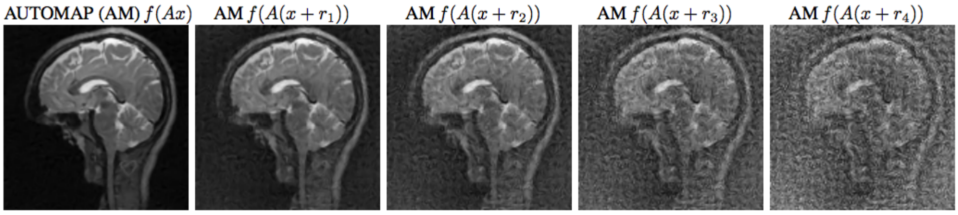
- A word of warning: Instability in deep learning Kernel (nullspace) awareness

AUTOMAP (AM) $f(Ax)$ AM $f(A(x+r_1))$ AM $f(A(x+r_2))$ AM $f(A(x+r_3))$ AM $f(A(x+r_4))$



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