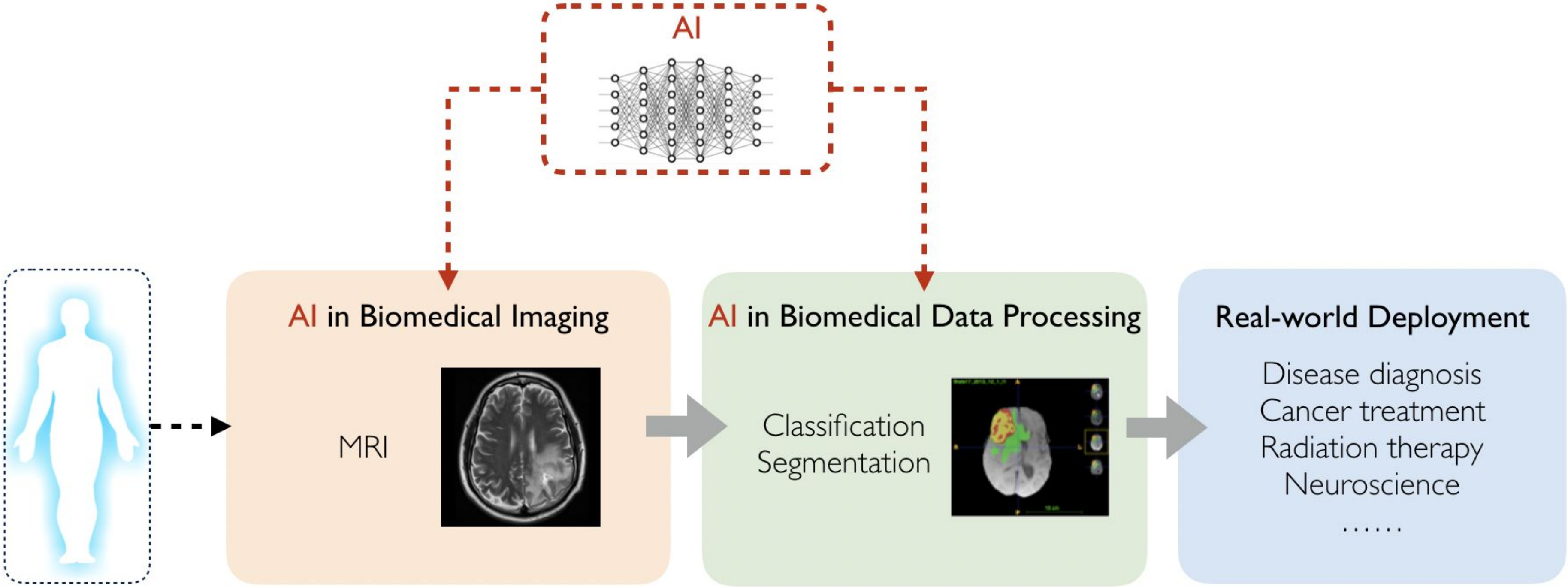
Lecture 2:
Biomedical Imaging with Deep Learning

Announcements

- Waiting list students:
  - Send email to jiayx@umich.edu to request a enrollment permission
- Go through the paper reading list
- Paper bidding:
  - Complete google form by 11:59 pm EDT on September 8
- Sign up Piazza through sign-up link

In this class:

- Part I: AI in biomedical imaging
- Part II: AI in biomedical data processing



Today’s agenda

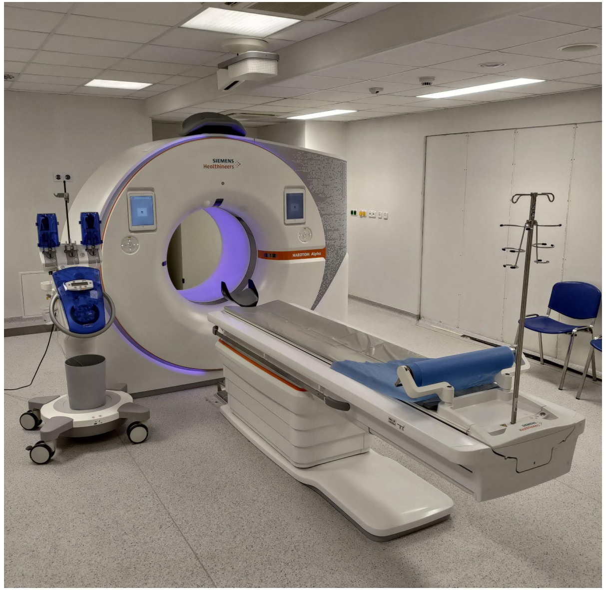
- Motivation and physics background
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

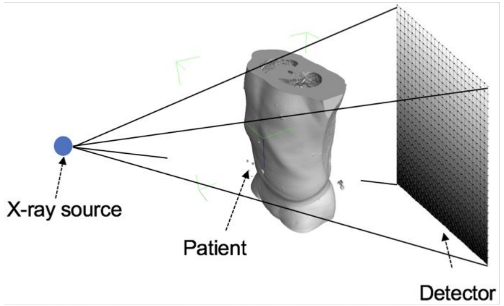
Today's agenda

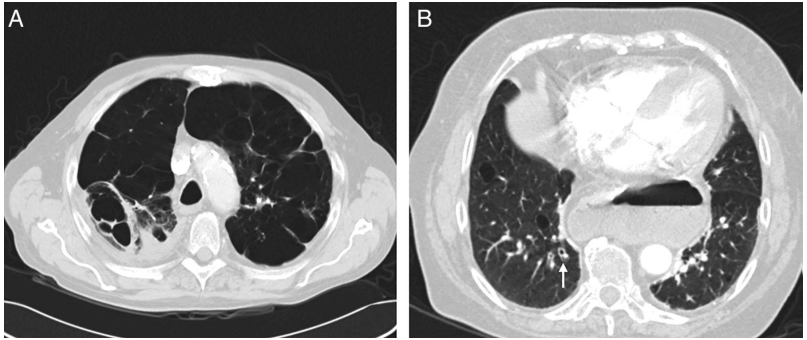
- Motivation and physics background
  - Computed Tomography (CT) imaging
  - Magnetic Resonance Imaging (MRI)
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

Biomedical imaging

- X-ray Computed Tomography (CT) imaging
    - Reconstruct cross-sectional images of internal structures from X-ray projections at different angles

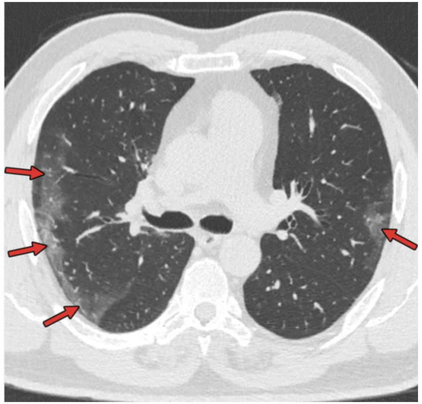


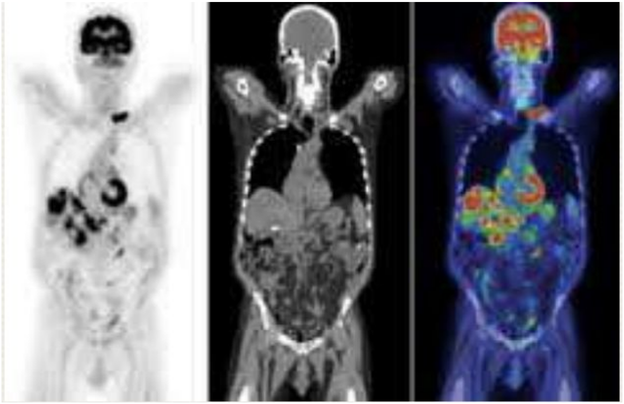




CT imaging

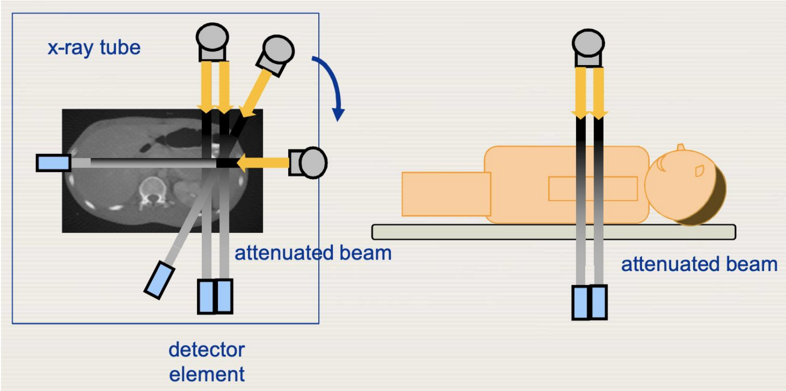
- Computed Tomography (CT) can be used for
  - Diagnosis and follow-up studies of patients
  - Planning of radiotherapy treatment
  - Screening of healthy subpopulations with specific risk factors
- Examples:
  - Covid-19 screening diagnosis
  - Radiotherapy planning
  - Integration of CT scanners in multi-modality imaging applications, for example, PET-CT scanner

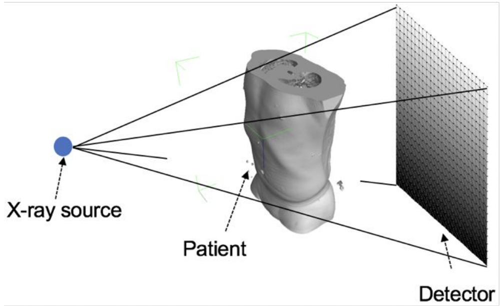




CT imaging: X-ray projection, attenuation and acquisition

- CT imaging acquisition:
  - Measure X-ray transmission through a patient for a large number of views
  - Different views are achieved by rotation of X-ray tube around patient for ~1000 angular measurements



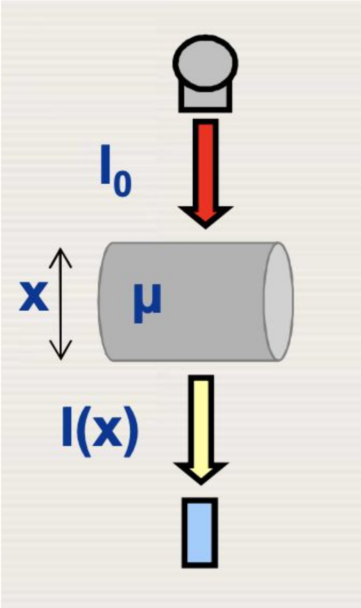


CT imaging: X-ray projection, attenuation and acquisition

- Attenuation:
  - The values that are assigned to the pixels in a CT image are associated with the average linear attenuation coefficient μ (m^{-1}) of the tissue represented within that pixel
  - Linear attenuation coefficient (μ) depends on the composition of the material, the density of the material, and the photon energy as seen in Beer's law:

$$I(x) = I_0 e^{-\mu x}$$

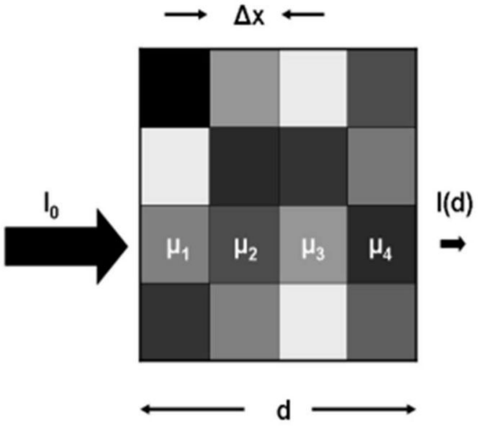
    - $I(x)$: intensity of the attenuated X-ray beam
    - I_0: unattenuated X-ray beam
    - x: thickness of the material

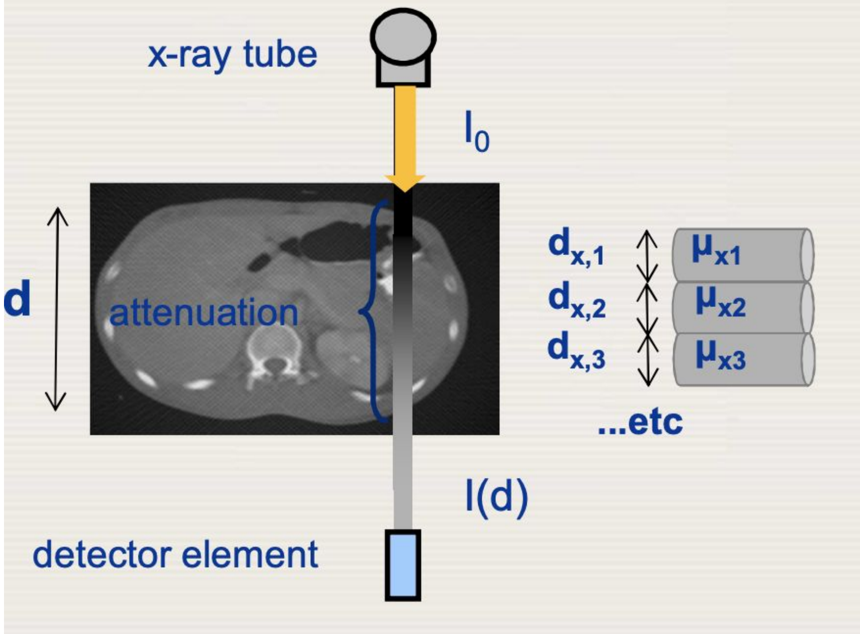


CT imaging: X-ray projection, attenuation and acquisition

- Attenuation:
  - As an X-ray beam is transmitted through the patient, different tissues are encountered with different linear attenuation coefficients.
  - The intensity of the attenuated X ray beam, transmitted a distance d, can be expressed as:

$$I(d) = I_0 e^{-\int_0^d \mu(x)dx}$$





CT imaging: Hounsfield units

- In CT the matrix of reconstructed linear attenuation coefficients ($\mu_{material}$) is transformed into a corresponding matrix of Hounsfield units ($HU_{material}$)
- HU scale is expressed relative to the linear attenuation coefficient of water at room temperature (μ_{water})

$$HU_{material} = \frac{\mu_{material} - \mu_{water}}{\mu_{water}} \times 1000$$

  - HU_{water} = ?
  - HU_{air} = ?

CT imaging: Hounsfield units

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$$HU_{material} = \frac{\mu_{material} - \mu_{water}}{\mu_{water}} \times 1000$$

  - $HU_{water} = 0$ as ($\mu_{material} = \mu_{water}$)
  - $HU_{air} = -1000$ as ($\mu_{material} = 0$)
  - HU = 1 is associated with 0.1% of the linear attenuation coefficient of water

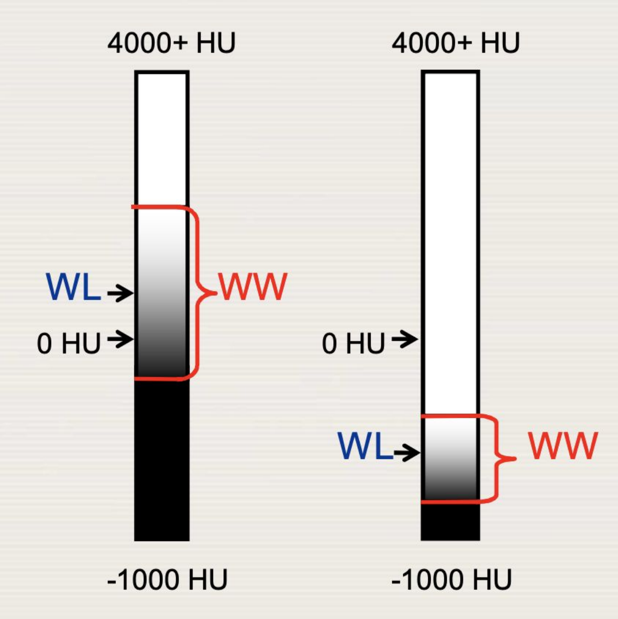
CT imaging: Hounsfield units

- Typical values for body tissues
  - The actual value of the Hounsfield unit depends on the composition of the tissue or material, the tube voltage, and the temperature

Substance	Hounsfield unit (HU)
Compact bone	+1000 (+300 to +2500)
Liver	+ 60 (+50 to +70)
Blood	+ 55 (+50 to +60)
Kidneys	+ 30 (+20 to +40)
Muscle	+ 25 (+10 to +40)
Brain, grey matter	+ 35 (+30 to +40)
Brain, white matter	+ 25 (+20 to +30)
Water	0
Fat	- 90 (-100 to -80)
Lung	- 750 (-950 to -600)
Air	- 1000

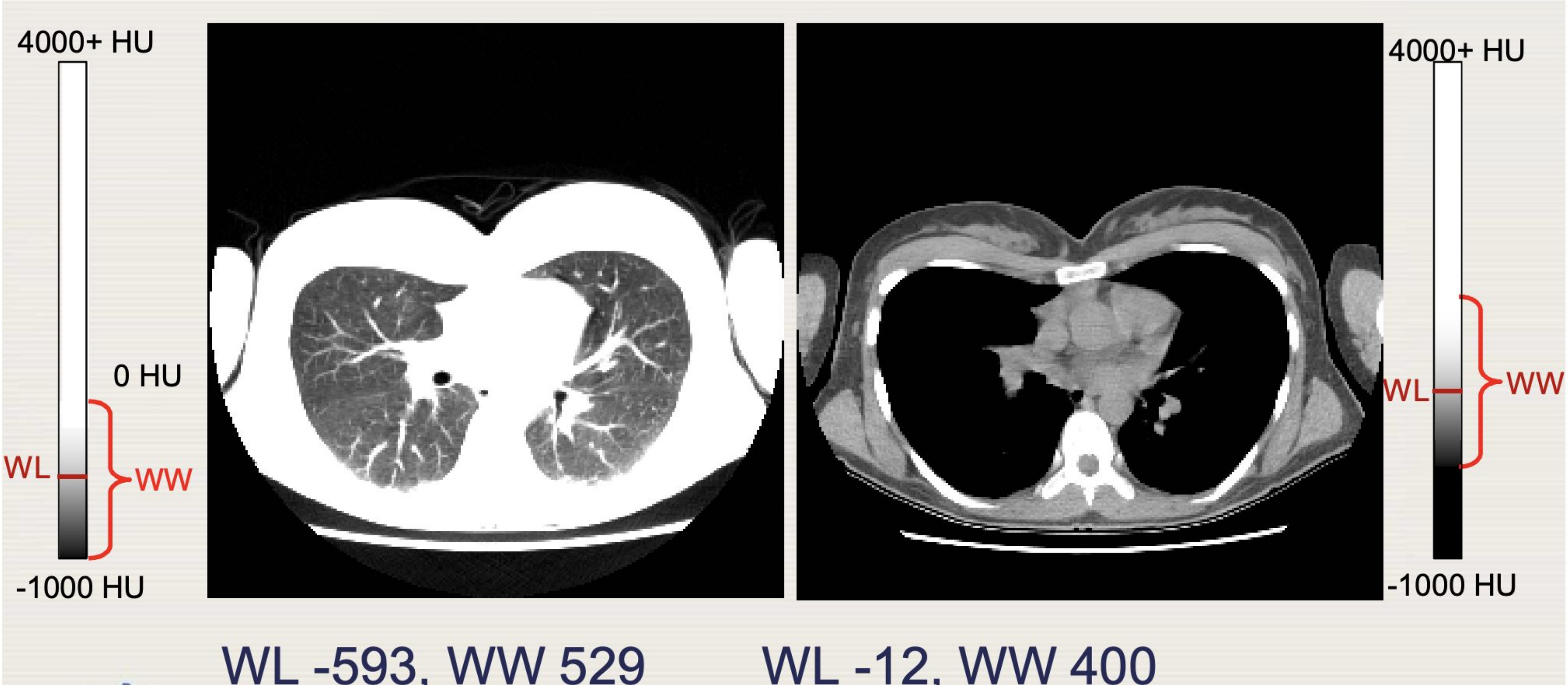
CT imaging: Hounsfield units

- CT image display window:
  - Window level (WL): midpoint of HU intensity range mapped to the middle of the grayscale display
  - Window width (WW): range of HU intensity values
- The choice of WW and WL is dictated by clinical need
- Optimal visualization of the tissues of interest in the CT image can only be achieved by selecting the most appropriate window width and window level
- Different settings of the WW and WL are used to visualize for example soft tissue, lung tissue or bone



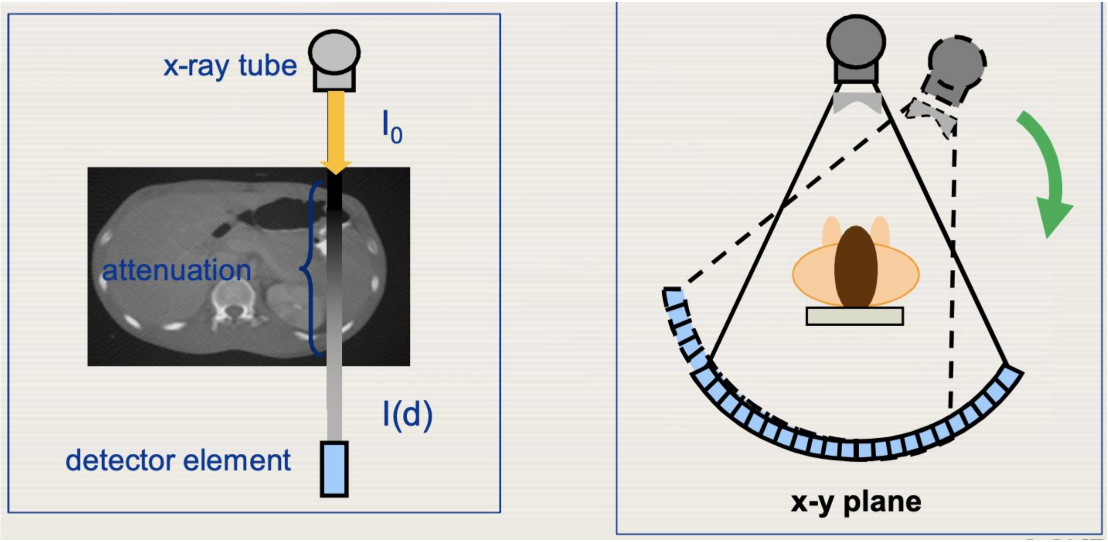
CT imaging: Hounsfield units

- Same image data at different WL and WW



CT imaging: Reconstruction

- Basis of CT image reconstruction:
    - During a CT scan, numerous measurements of the transmission of X-rays through a patient are acquired at many angles



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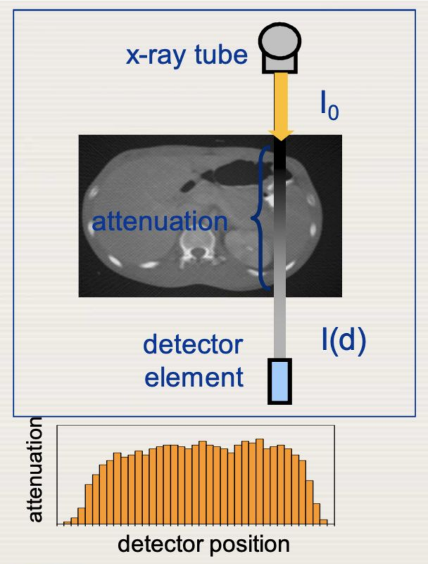
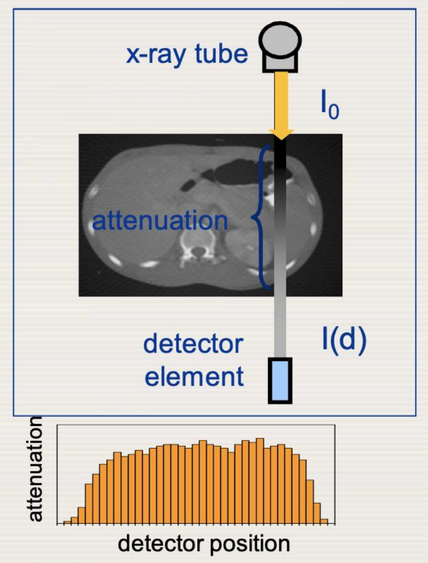


$$I(d) = I_0 e^{-\int_0^d \mu(x)dx}$$

CT imaging: Reconstruction

- Basis of CT image reconstruction:
  - During a CT scan, numerous measurements of the transmission of X-rays through a patient are acquired at many angles
  - The logarithm of the (inverse) measured normalized transmission yields a linear relationship with the products of $\mu_i \Delta x$



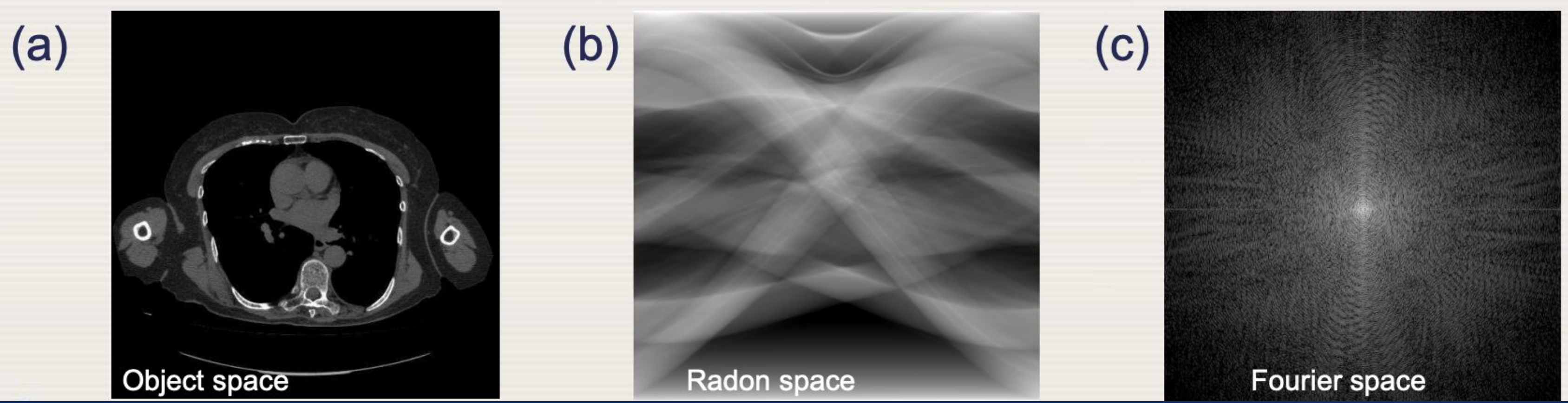
$$I(d) = I_0 e^{-\int_0^d \mu(x)dx}$$

$$I(d) = I_0 e^{-\sum_{i=1}^{i=n} \mu_i \Delta x}$$

$$\ln\left(\frac{I_0}{I(d)}\right) = \sum_{i=1}^{i=n} \mu_i \Delta x$$

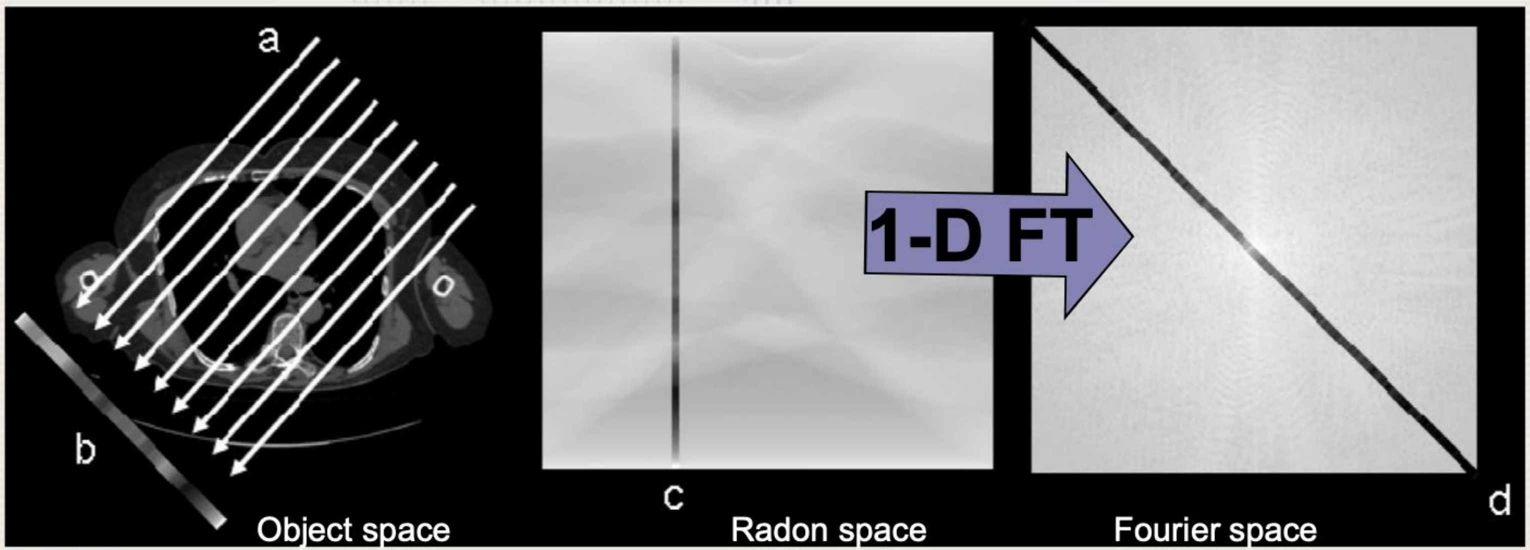
CT imaging: Filtered backprojection

- Three domains associated with CT image reconstruction:
  - Object space
    - Linear attenuation values
  - Radon space
    - Projection values recorded under many angles
    - This domain is also referred to as sinogram space where Cartesian coordinates are used
  - Fourier space
    - Can be derived from object space by a 2D Fourier transform



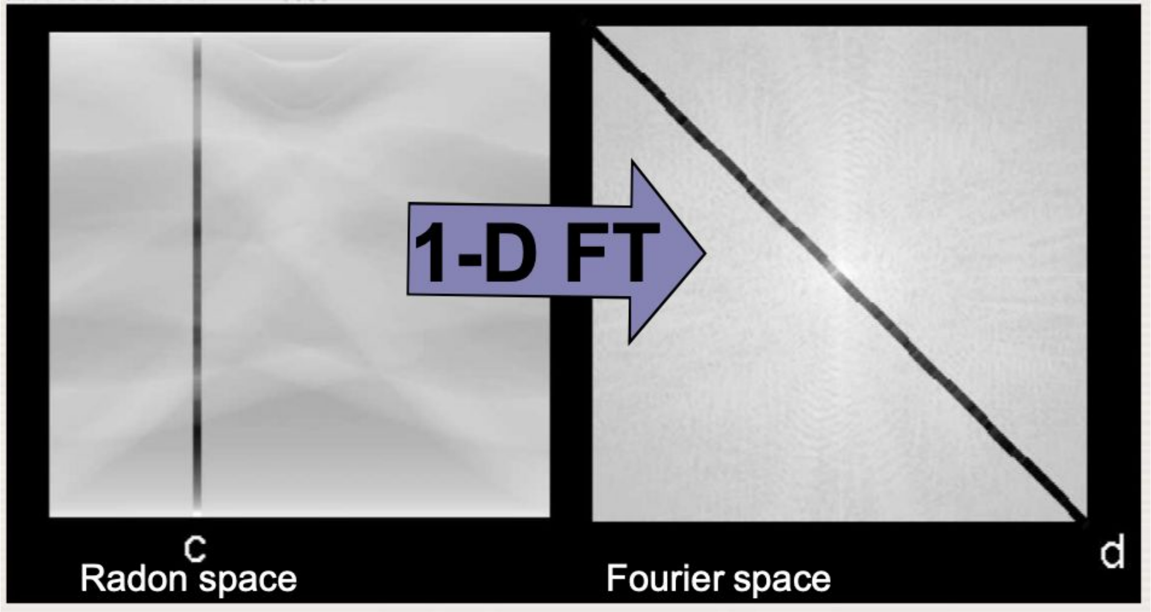
CT imaging: Filtered backprojection

- Central-slice theorem (Fourier-slice theorem):
  - One specific projection angle in object space
  - The projection that is recorded by the CT scanner
  - This projection corresponds with one line in Radon space
  - One angulated line in Fourier space is created from a 1-D transform of the recorded line in the sinogram



CT imaging: Filtered backprojection

- Central-slice theorem (Fourier-slice theorem):
    - 1D Fourier transform of the projection profile yields an angulated line in (Cartesian) Fourier space at the angle of the projection

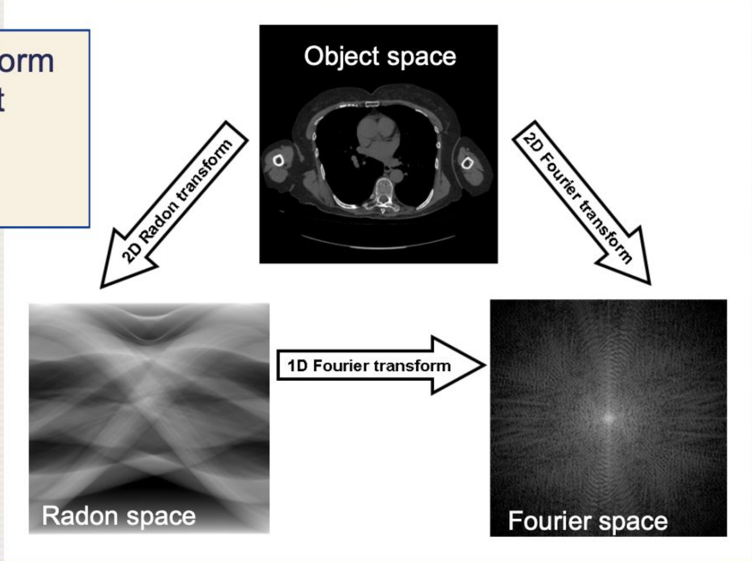


CT imaging: Filtered backprojection

- The interrelationships between the three domains:
  - Object space, Radon space, and Fourier space

A 2D Radon transform converts the object space into Radon space.

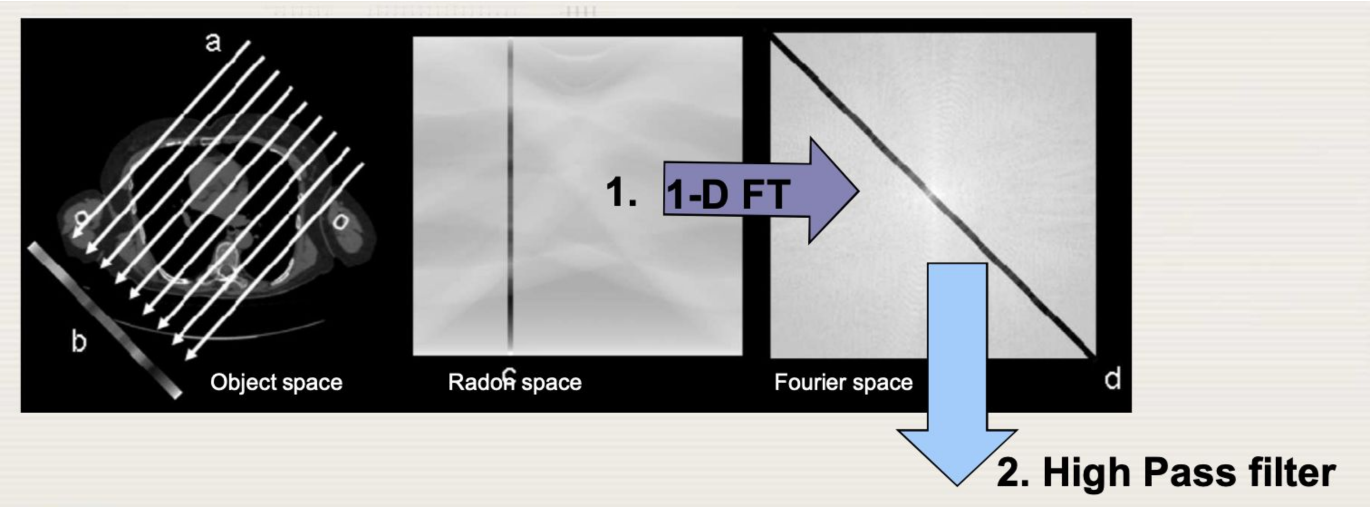
The creation of 2D Radon space is carried out during a CT scan: projections are recorded and they are stored as raw data in 2D Radon space.



- ❑According to the central slice theorem, many 1D Fourier transforms of transmission profiles under many angles allow for creating the Fourier space of the object space.
- ❑The number of 1D transforms is equal to the number of registered profiles

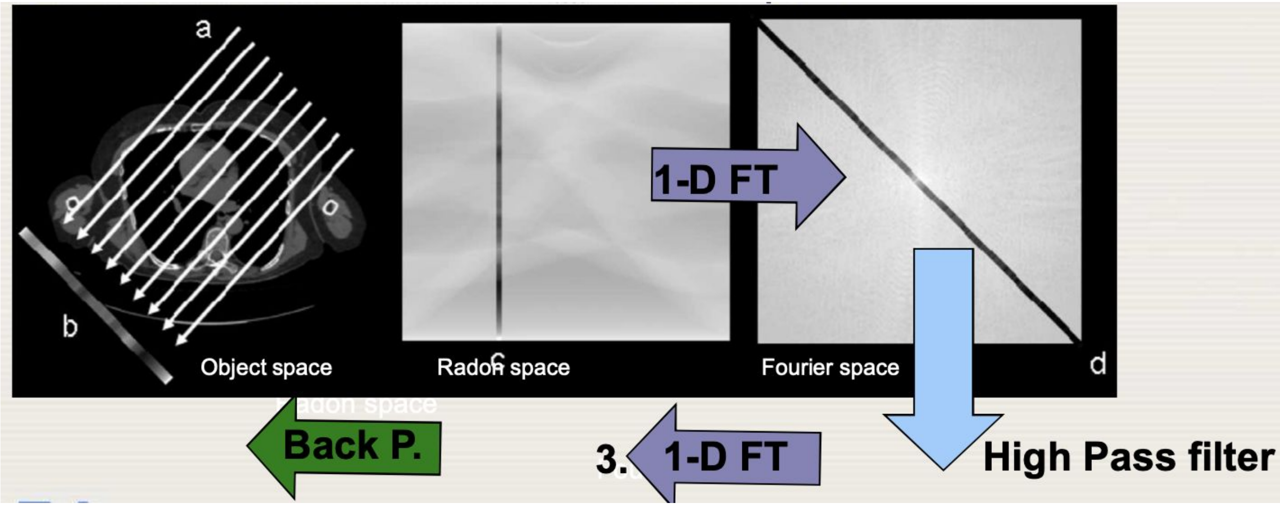
CT imaging: Filtered backprojection

- Mathematical operations of filtered backprojection (FBP)
  a. A Fourier transform of Radon space should be performed (requiring many 1D Fourier transforms)
  b. A high-pass filter should be applied to each one of the 1D Fourier transforms



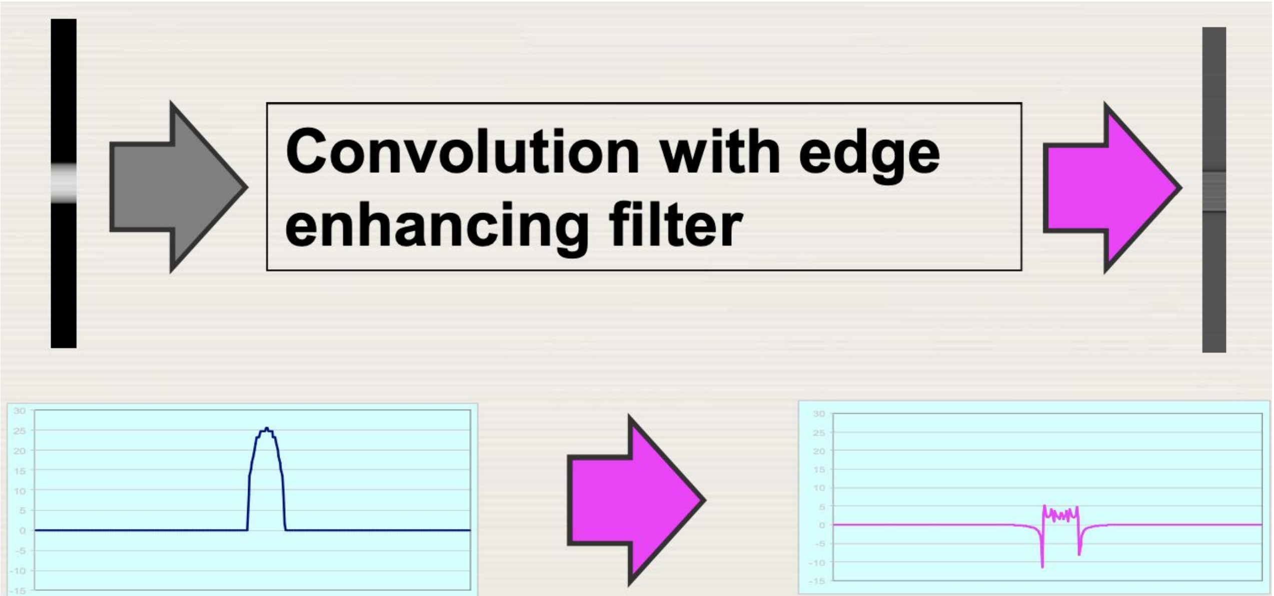
CT imaging: Filtered backprojection

- Mathematical operations of filtered backprojection (FBP)
  a. A Fourier transform of Radon space should be performed (requiring many 1D Fourier transforms)
  b. A high-pass filter should be applied to each one of the 1D Fourier transforms
  c. An inverse Fourier transform should be applied to the high pass filtered Fourier transforms in order to obtain a Radon space with modified projection profiles
  d. Backprojection of the filtered profiles yields the reconstruction of the measured object



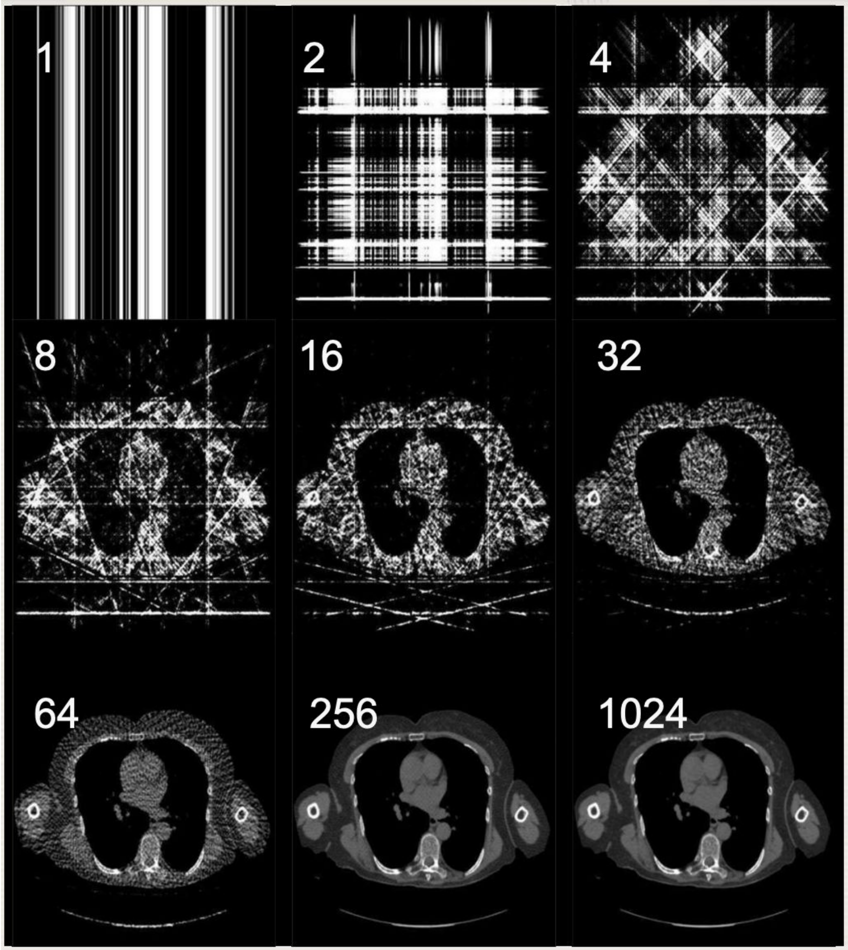
CT imaging: Filtered backprojection

- Mathematics shows that the high pass filter that is applied to the Fourier domain can be substituted by a convolution of profiles with an appropriate kernel directly in the Radon domain



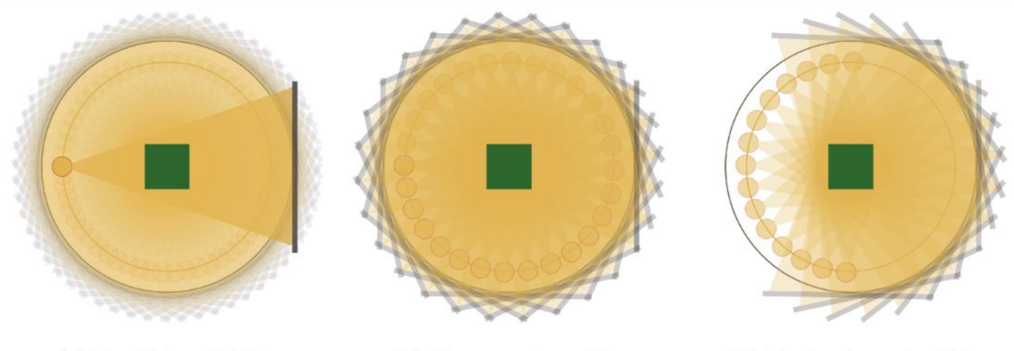
CT imaging: Filtered backprojection

- Successive filtered backprojections with 1, 2, 4, 8, 16, 32, 64, 256, and 1024 backprojections
- This shows how successive filtered backprojections under different angles can be used to achieve a good reconstruction of the space domain

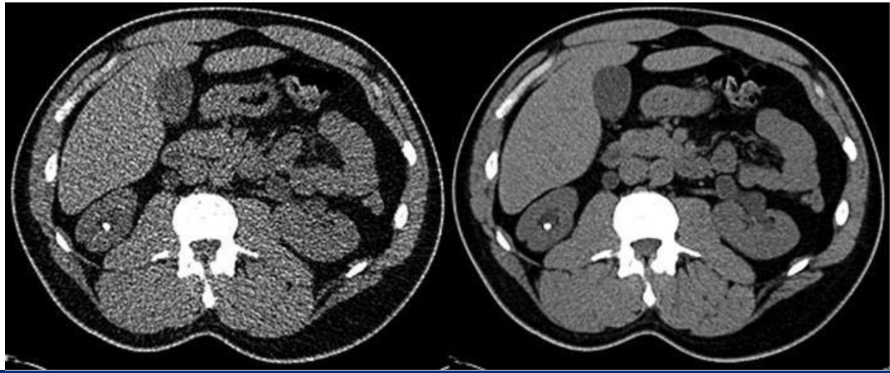


Motivation

- Reduce Radiation Dose
  - CT scans expose the patient to ionizing radiation, which can have cumulative health effects
  - Sparse-view CT reconstruction:
    - Reduces the number of projections, leading to a lower overall radiation dose while maintaining diagnostic image quality
  - Low-dose CT reconstruction:
    - Reduce the amount of radiation delivered to the patient while maintaining sufficient image quality for accurate diagnosis



(a) Traditional CT (b) Sparse-view CT (c) Limited-angle CT



Today's agenda

- Motivation and physics background
  - Computed Tomography (CT) imaging
    - X-ray projection, attenuation and acquisition
    - Hounsfield units
    - Filtered backprojection
    - Sparse-view CT and low-dose CT
  - Magnetic Resonance Imaging (MRI)
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

**Some slides in this section are adapted from: [Diagnostic Radiology Physics: A Handbook for Teachers and Students, Chapter 11 Computed Tomography]*

Today's agenda

- Motivation and physics background
    - Computed Tomography (CT) imaging
    - Magnetic Resonance Imaging (MRI)
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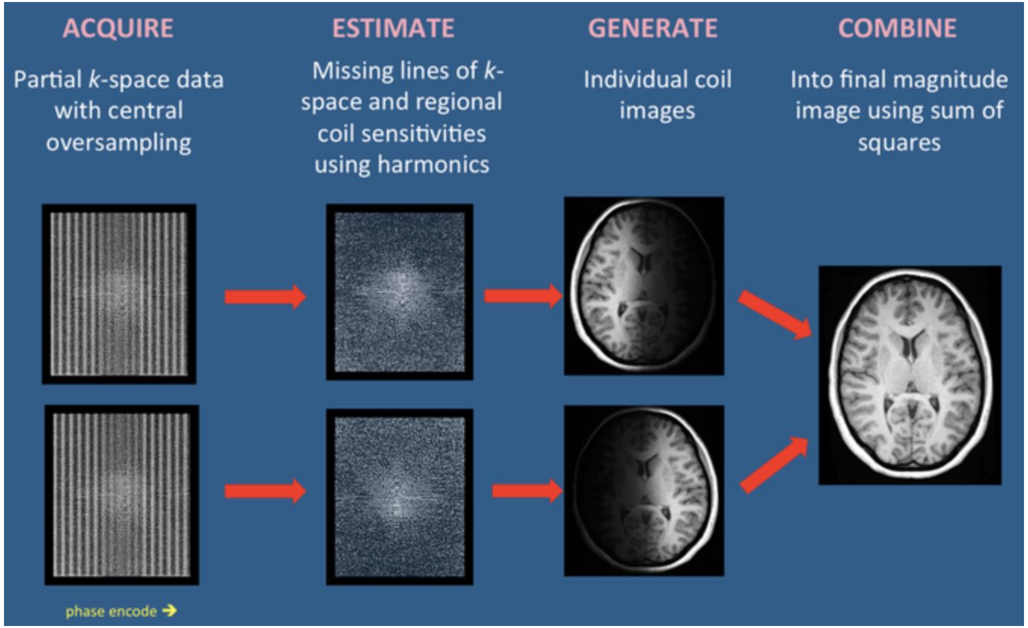
- Challenges

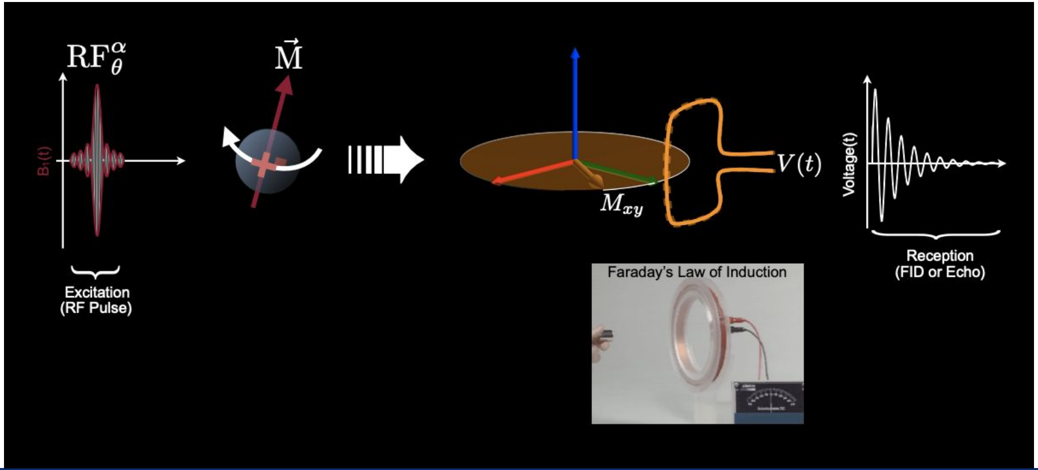
Biomedical imaging

- Magnetic Resonance Imaging (MRI)
  - Reconstruct cross-sectional images of internal structures from measurements in frequency space



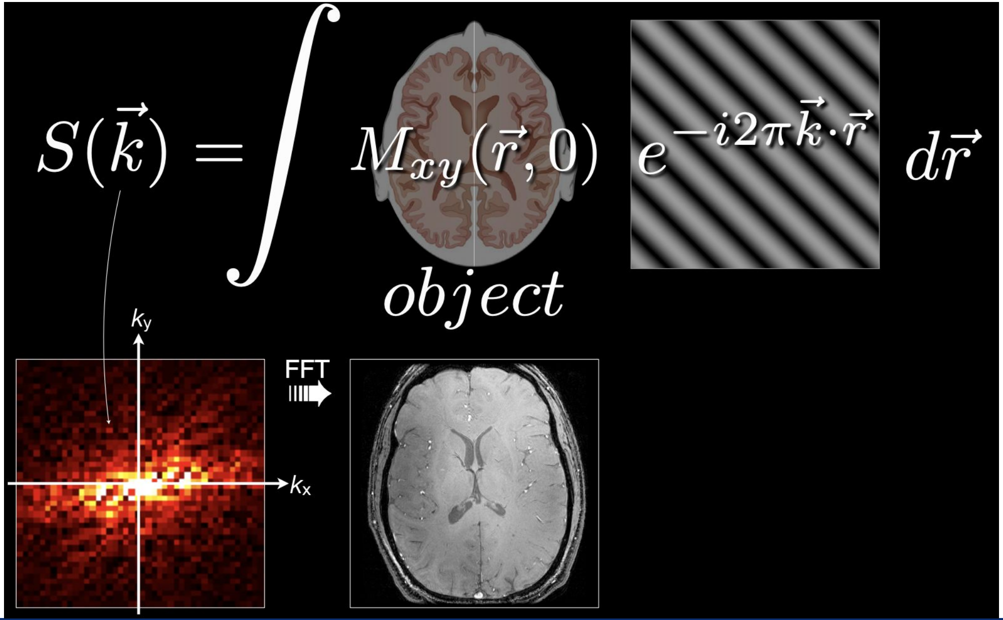
MRI: Signal reception

- MRI is a classic excitation-reception paradigm
- On-resonance RF energy perturbs the bulk magnetization
- This generates transverse magnetization
- Transverse magnetization can be detected by a coil
- A voltage signal is recorded, where the echo encodes the spatial information and image contrast



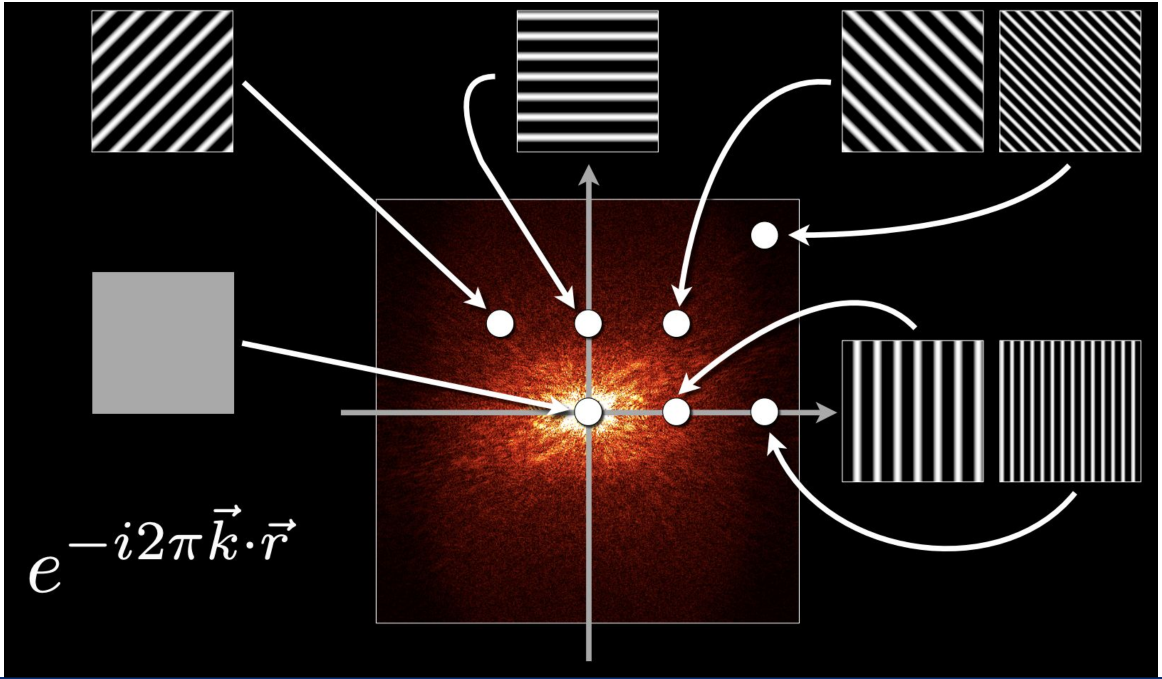
MRI: Signal equation

- RF pulses generate Mxy with contrast
- Gradients encode spatial information
- MR scanner collect raw data in Fourier space (k-space)



MRI: k-space

- k-space is the raw data collected by the scanner
  - A point in k-space tells the presence/absence of a spatial frequency (pattern) in the acquired image
  - k-space has units of cm-1 or mm-1 [i.e. spatial frequency]



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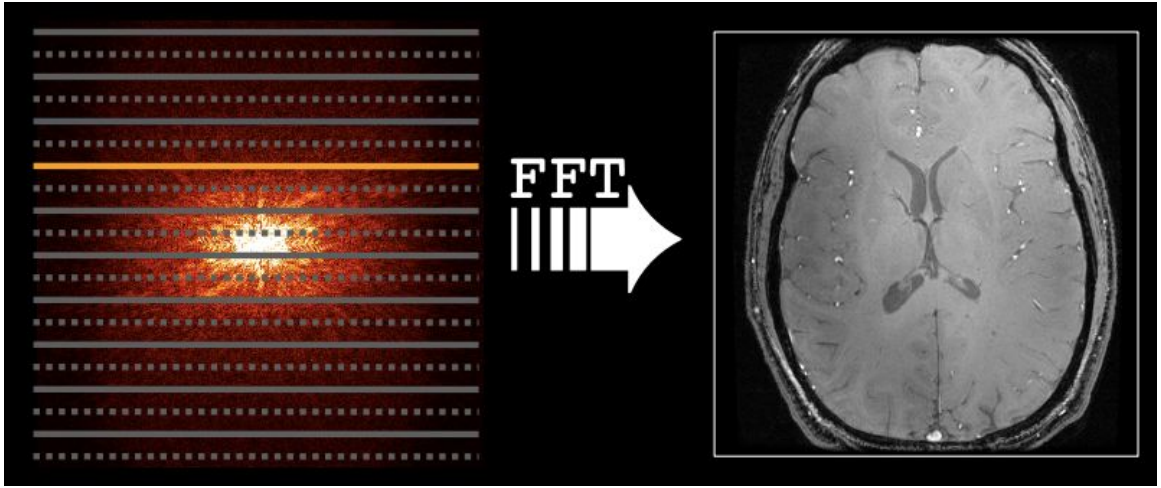
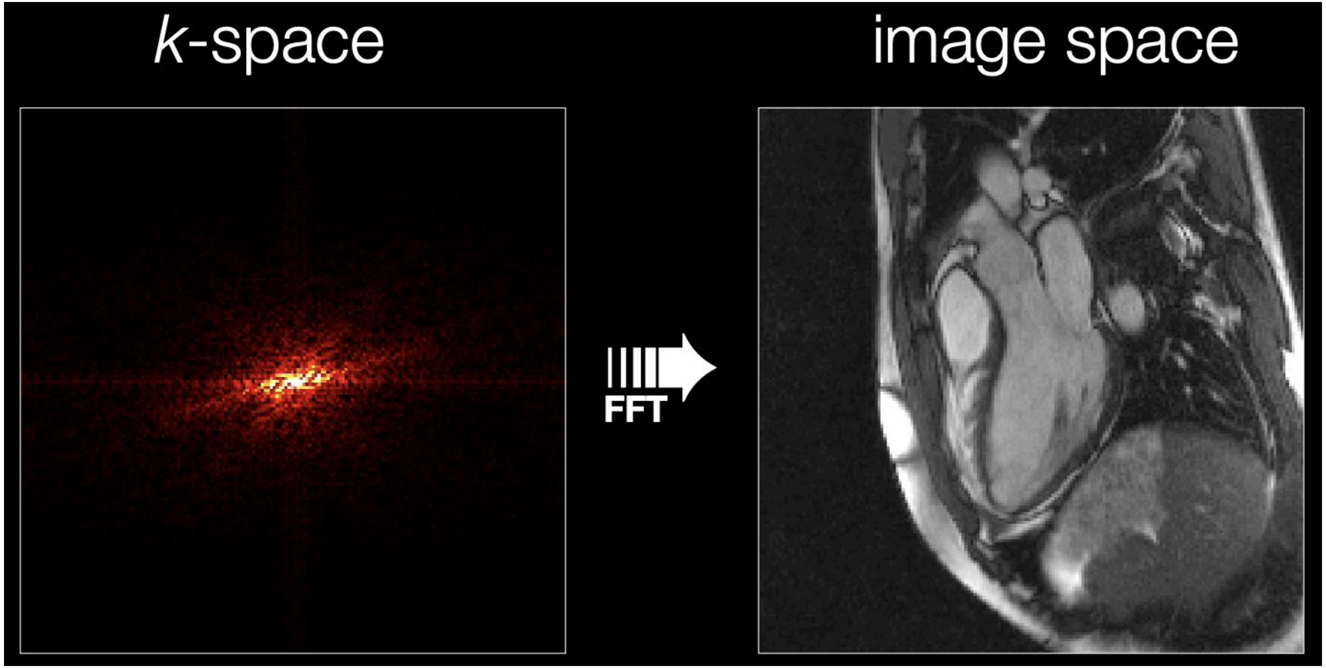
  - A point in k-space tells the presence/absence of a spatial frequency (pattern) in the acquired image
  - k-space has units of cm-1 or mm-1 [i.e. spatial frequency]
  - Each echo measures many of the spatial frequencies that comprise the object
  - A line of k-space is filled by an echo



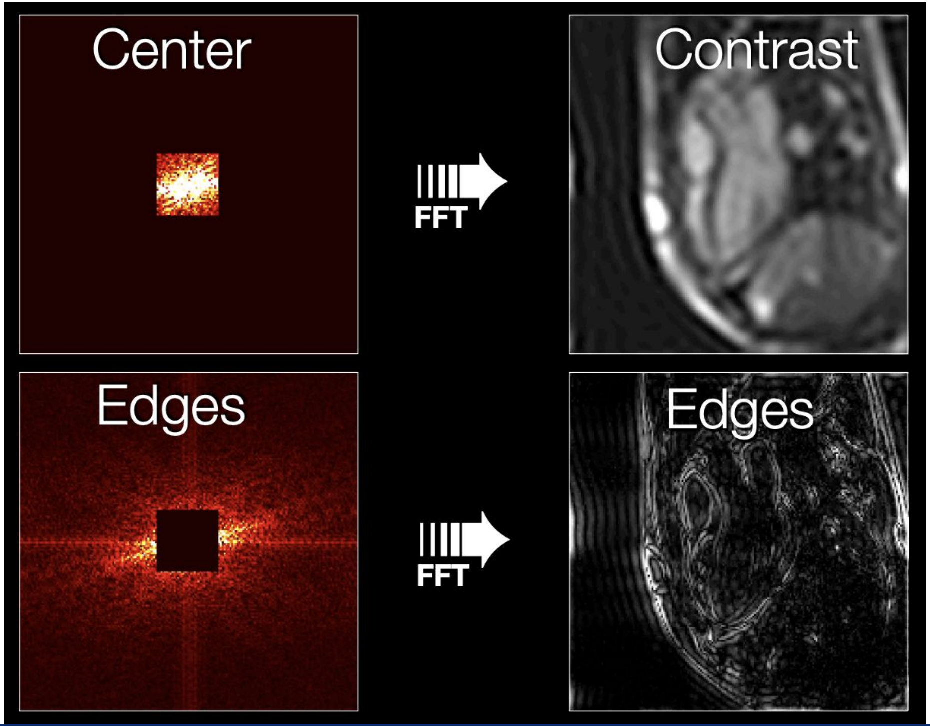
MRI: k-space

- k-space and image space can be related through Fourier Transform



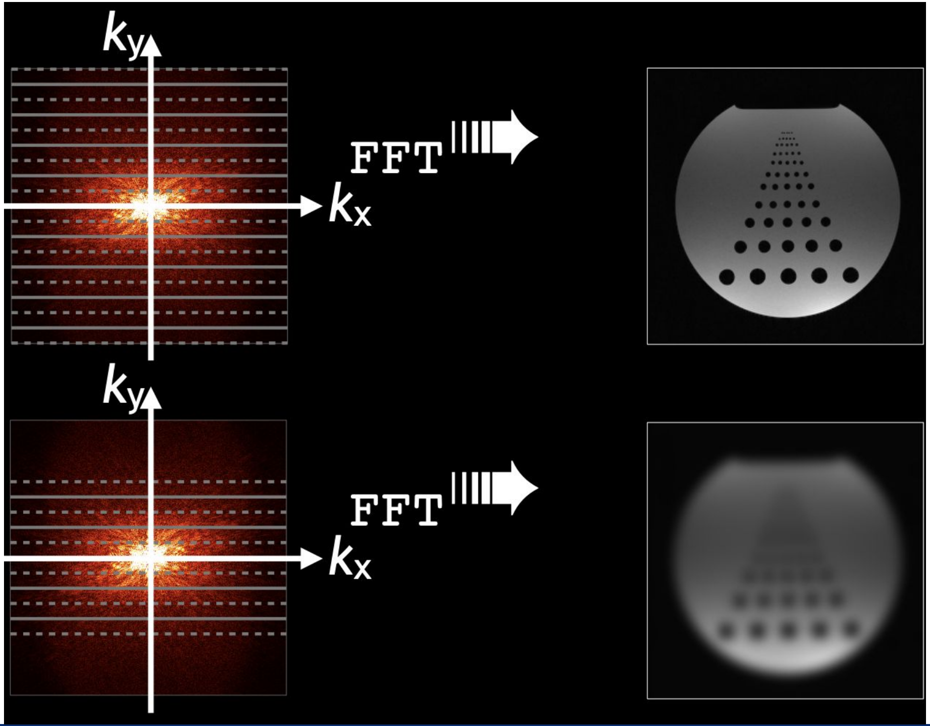
MRI: k-space

- The center of k-space contains image contrast (low-frequency components)
- The periphery of k-space contains edge information (high-frequency components)



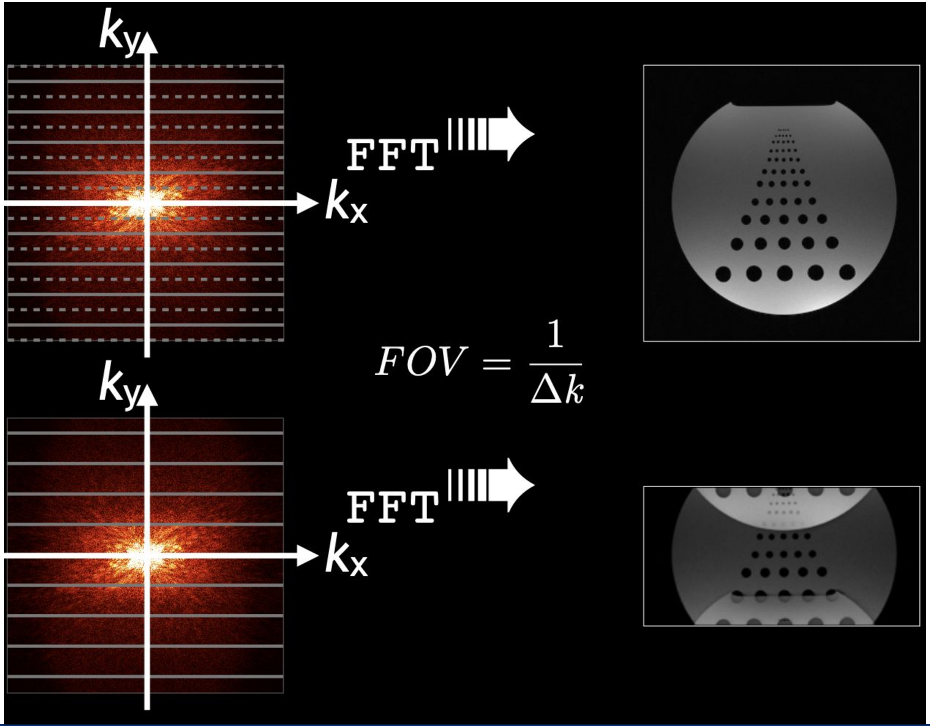
MRI: k-space

- Acquiring fewer high phase encodes decreases the resolution



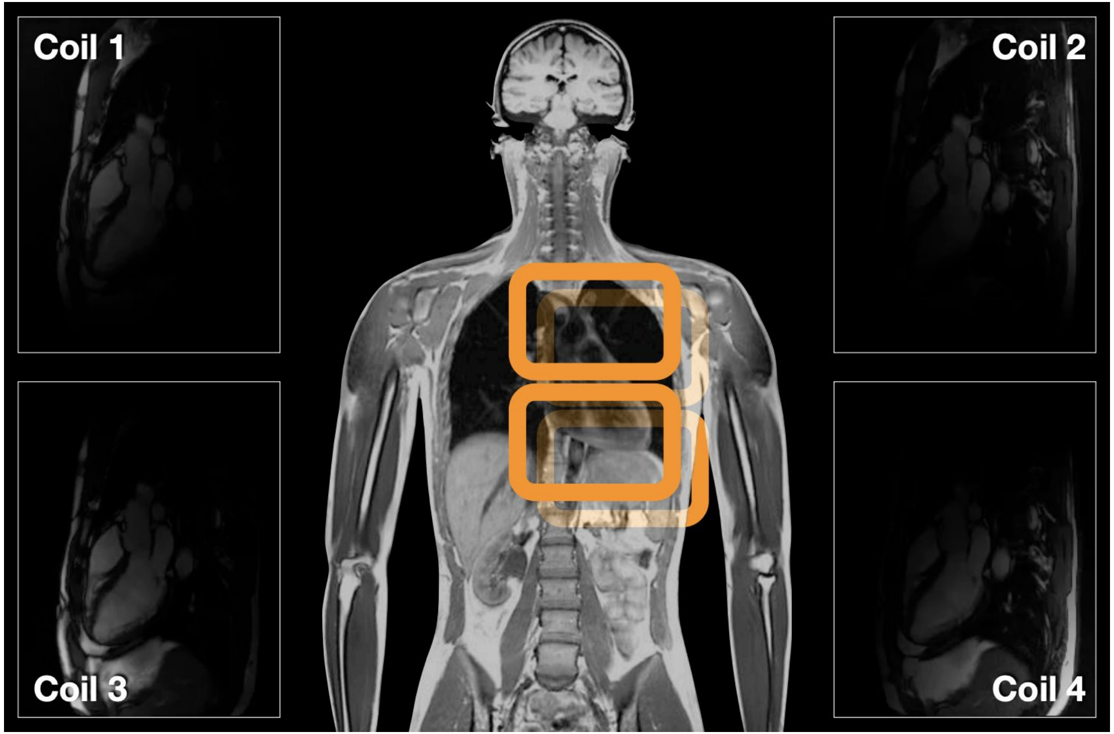
MRI: k-space

- Uniformly skipping lines in k-space causes aliasing



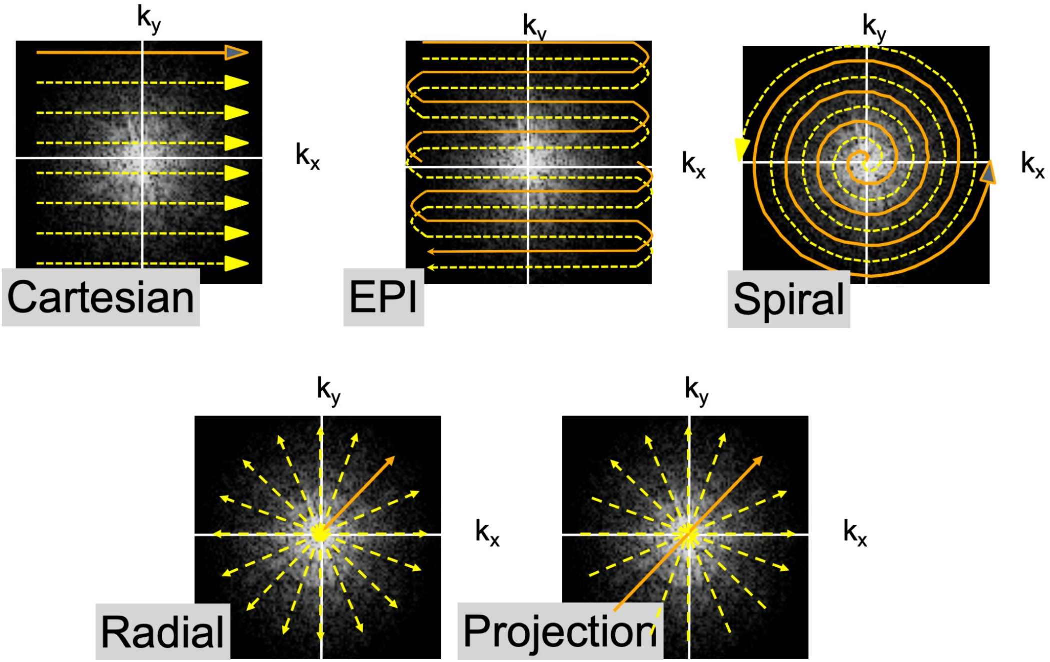
MRI: Multi-coil

- Each coil element has a unique sensitivity profile



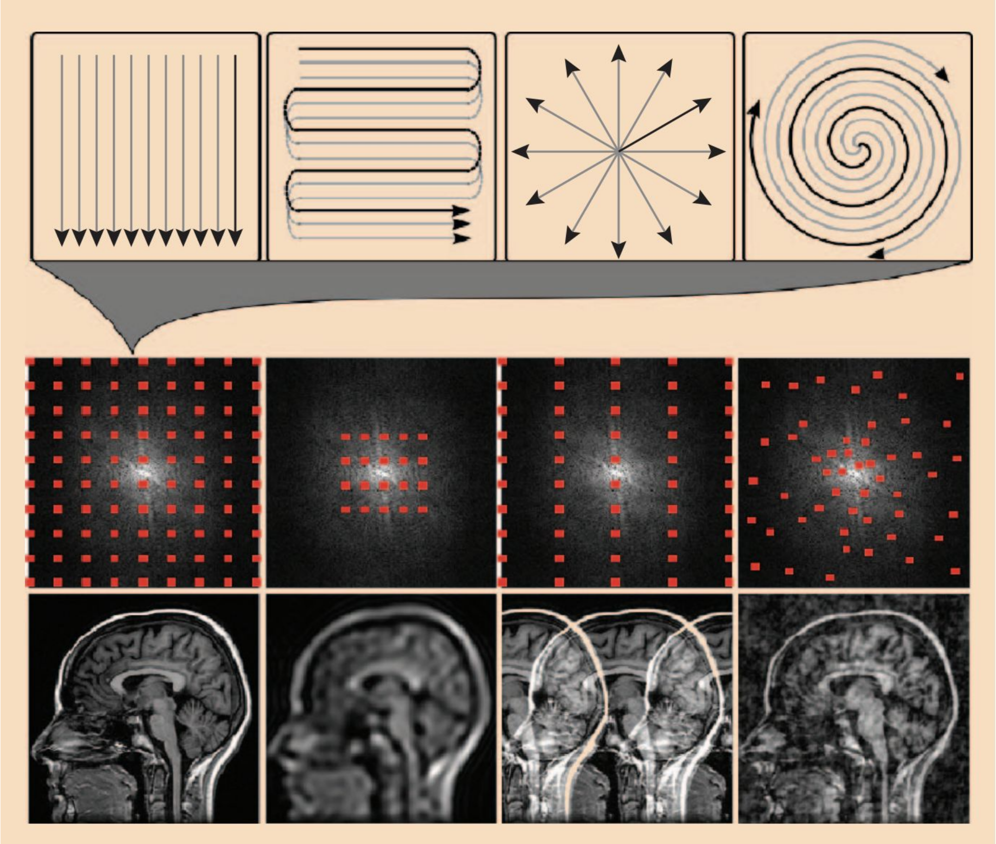
Motivation

- MRI is slow:
  - Fully sampling k-space data can take around 5-10 mins
- Alternate k-space trajectory for fast sampling k-space raw data



Motivation

- Sparse-sampling MRI reconstruction:
  - Accelerate MRI scanning and acquisition process
  - The Nyquist criterion sets the required k-space coverage, which can be achieved using various sampling trajectories
  - Violation of the Nyquist criterion causes noise and artifacts in the reconstructions, which depend on the sampling pattern



Today's agenda

- Motivation and physics background
  - Computed Tomography (CT) imaging
  - Magnetic Resonance Imaging (MRI)
    - Signal reception
    - k-space acquisition and sampling
    - Multi-coil acquisition
    - Sparse-sampling MRI reconstruction
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

**Some slides in this section are adapted from: [Stanford RAD229: MRI Signals and Sequences]*

Today's agenda

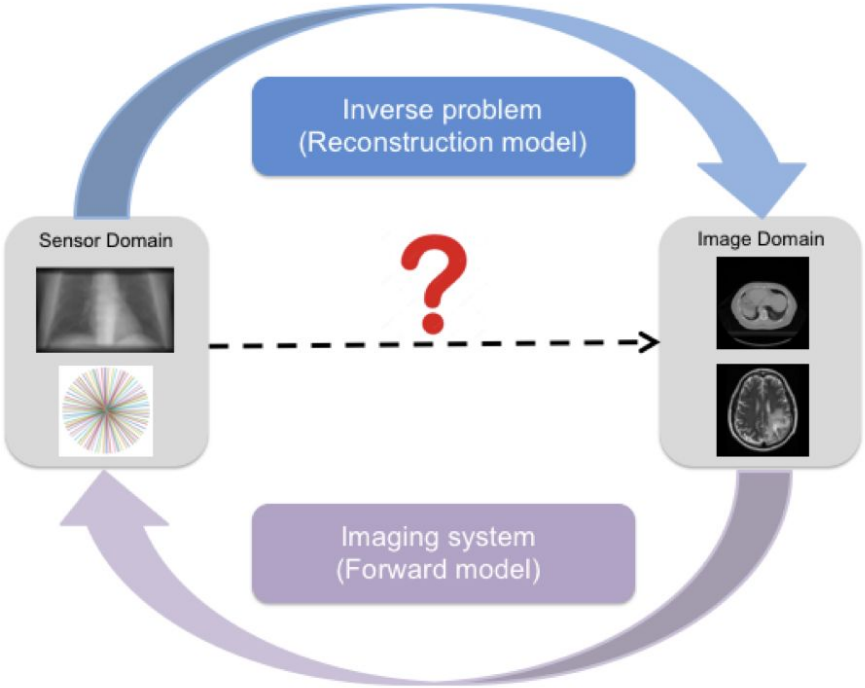
- Motivation and physics background
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

Motivation

- Sparse-sampling CT image reconstruction
  - Reduce X-ray radiation dose
- Sparse-sampling MRI image reconstruction
  - Reduce scan time
    - Patient comfort
    - Scan cost / throughput
    - Motion artifacts
  - Improve spatial resolution (collect higher k-space lines)
  - Improve temporal resolution trade-off in dynamic MRI

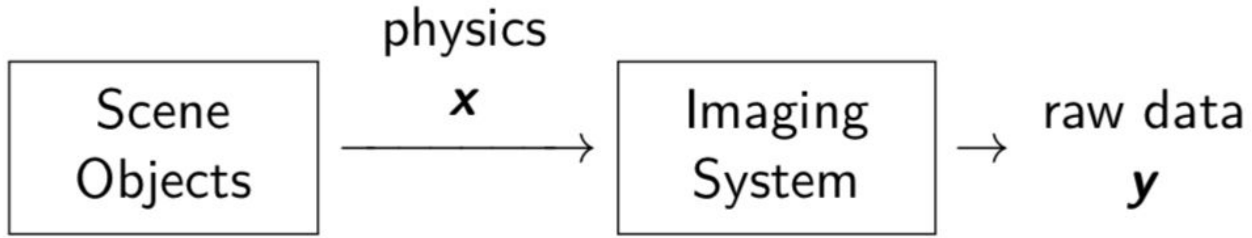
Inverse problem

- Sparse-sampling medical image reconstruction
  - Ill-posed inverse problem



Inverse problem

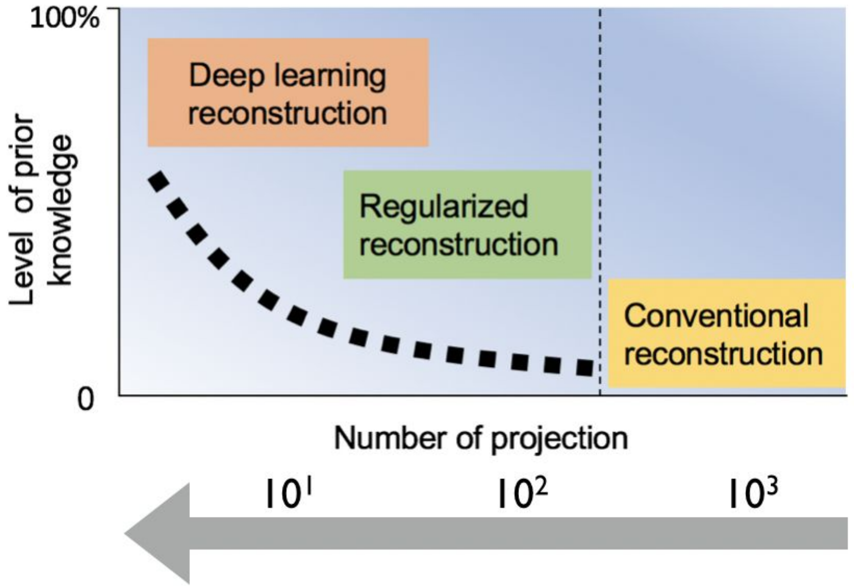
- Forward problem (data acquisition):



- Inverse problem (image formation):

Generations of medical image reconstruction methods

- 70's "Analytical" methods (integral equations)
  - FBP for PET / X-ray CT, IFFT for MRI, ...
- 80's Algebraic methods (as in "linear algebra")
  - Solve y = Ax
- 90's Statistical methods
  - Least square / Maximum likelihood methods
  - Regularized / Bayesian methods
- 00's Compressed sensing methods
  - Mathematical sparsity models
- 10's Adaptive / data-driven methods
  - Machine learning, deep learning, ...



Inverse problem via MAP estimation

Unknown image $\boldsymbol{x}$ → System model $\mathrm{p}(\boldsymbol{y} \mid \boldsymbol{x})$ → Data $\boldsymbol{y}$ → Estimator → Recon. image $\hat{\boldsymbol{x}}$

- If there is a prior p(x), then the MAP estimate is:

$$\hat{\boldsymbol{x}} = \arg\max_{\boldsymbol{x}} \mathrm{p}(\boldsymbol{x} \mid \boldsymbol{y}) = \arg\max_{\boldsymbol{x}} \log \mathrm{p}(\boldsymbol{y} \mid \boldsymbol{x}) + \log \mathrm{p}(\boldsymbol{x})$$

- For gaussian measurement errors and a linear forward model:

$$-\log \mathrm{p}(\boldsymbol{y} \mid \boldsymbol{x}) \equiv \frac{1}{2} \|\boldsymbol{y} - \boldsymbol{A}\boldsymbol{x}\|_{\boldsymbol{W}}^2$$

where $\|\boldsymbol{y}\|_{\boldsymbol{W}}^2 = \boldsymbol{y}'\boldsymbol{W}\boldsymbol{y}$

and $\boldsymbol{W}^{-1} = \mathrm{Cov}\{\boldsymbol{y} \mid \boldsymbol{x}\}$ is known

($\boldsymbol{A}$ from physics, $\boldsymbol{W}$ from statistics)

Prior for MAP estimation

- If all images x are "plausible" (have non-zero probability) then:

$$\mathrm{p}(\boldsymbol{x}) \propto e^{-\mathrm{R}(\boldsymbol{x})} \implies -\log \mathrm{p}(\boldsymbol{x}) \equiv \mathrm{R}(\boldsymbol{x})$$

- MAP ≡ regularized weighted least-squares (WLS) estimation:

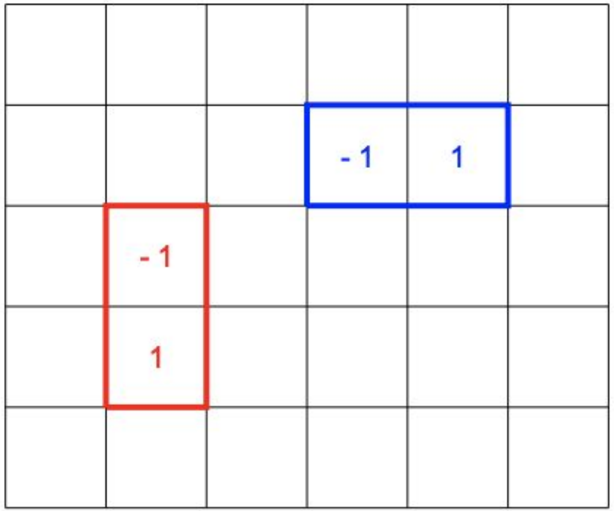
$$\begin{aligned}\hat{\boldsymbol{x}} &= \arg\max_{\boldsymbol{x}} \ \log \mathrm{p}(\boldsymbol{y} \mid \boldsymbol{x}) + \log \mathrm{p}(\boldsymbol{x}) \\ &= \arg\min_{\boldsymbol{x}} \ \frac{1}{2} \|\boldsymbol{y} - \boldsymbol{A}\boldsymbol{x}\|_{\boldsymbol{W}}^2 + \mathrm{R}(\boldsymbol{x})\end{aligned}$$

- Regularizer R(x):
  - Carry on data characteristics
  - Essential for high-quality solutions to ill-conditioned / ill-posed inverse problems

Total-variation (TV) regularization

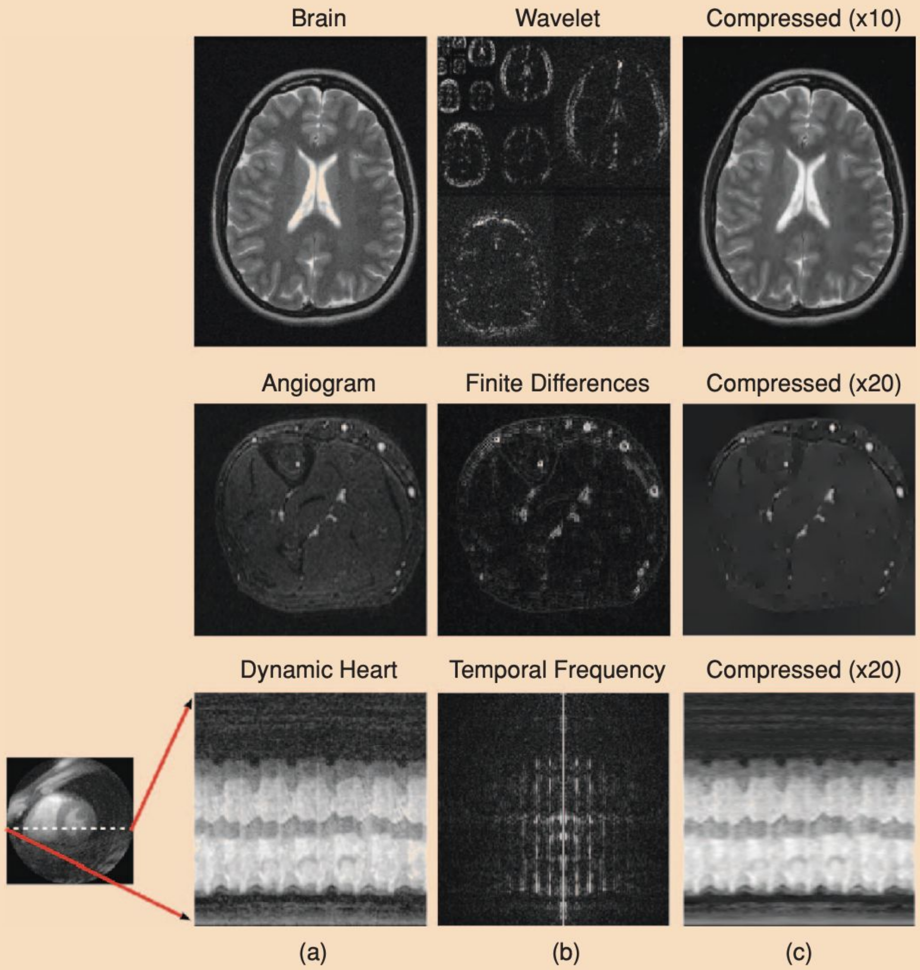
- Neighboring pixels tend to have similar values except near edges (“gradient sparsity”)

$$
\begin{aligned}
R(\boldsymbol{x}) &= \beta \mathrm{TV}(\boldsymbol{x}) = \beta \left\| \boldsymbol{\Delta x} \right\|_1 \\
&= \beta \sum_j |x_j - x_{j-1}|
\end{aligned}
$$



Compressed sensing in MRI

- Transform sparsity:
  - The desired image should have a sparse representation in a known transform domain (i.e., it must be compressible by transform coding)
- Transform sparsity of MRI images:
  - Fully sampled images are mapped by a sparsifying transform to a transform domain
  - The several largest coefficients are preserved while all others are set to zero
  - The transform is inverted forming a reconstructed image



Today's agenda

- Motivation and physics background
- Conventional reconstruction method
  - Inverse problem
  - MAP estimation
  - Prior / regularizer
  - Compressed sensing
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

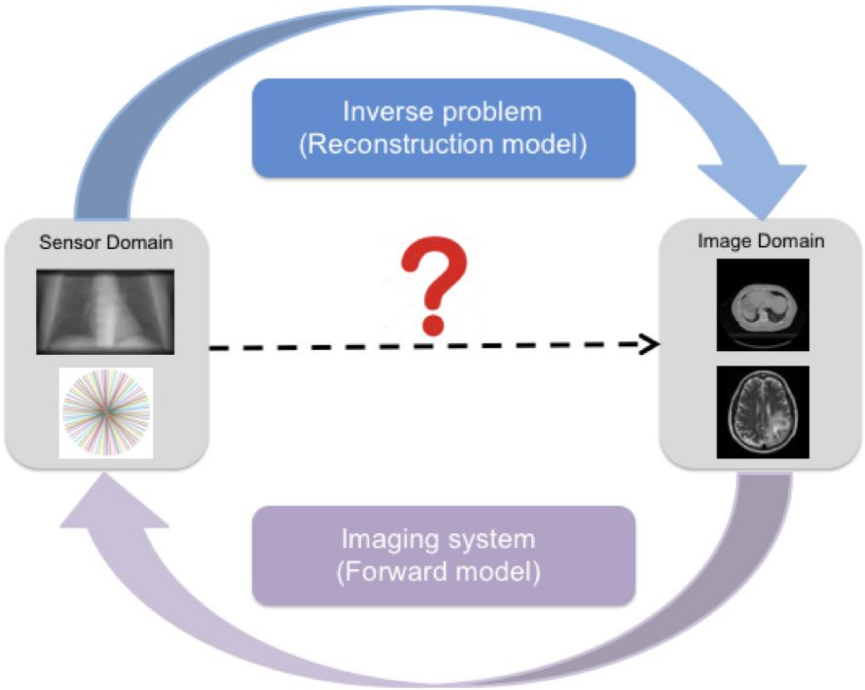
**Some slides in this section are adapted from: Medical imaging inverse problems using optimization and machine learning, Jeffrey A. Fessler, 2019*

Today's agenda

- Motivation and physics background
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

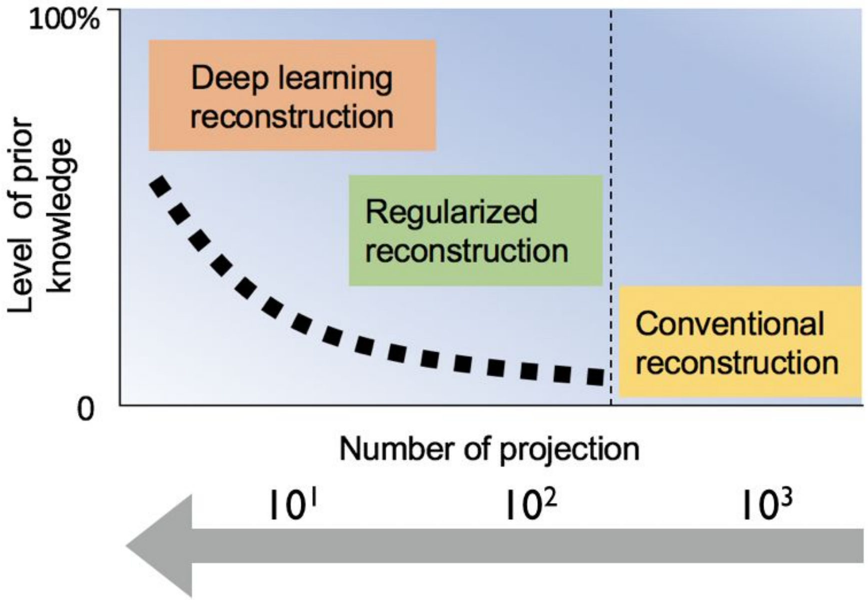
Sparse-sampling image reconstruction

- Ill-posed inverse problem



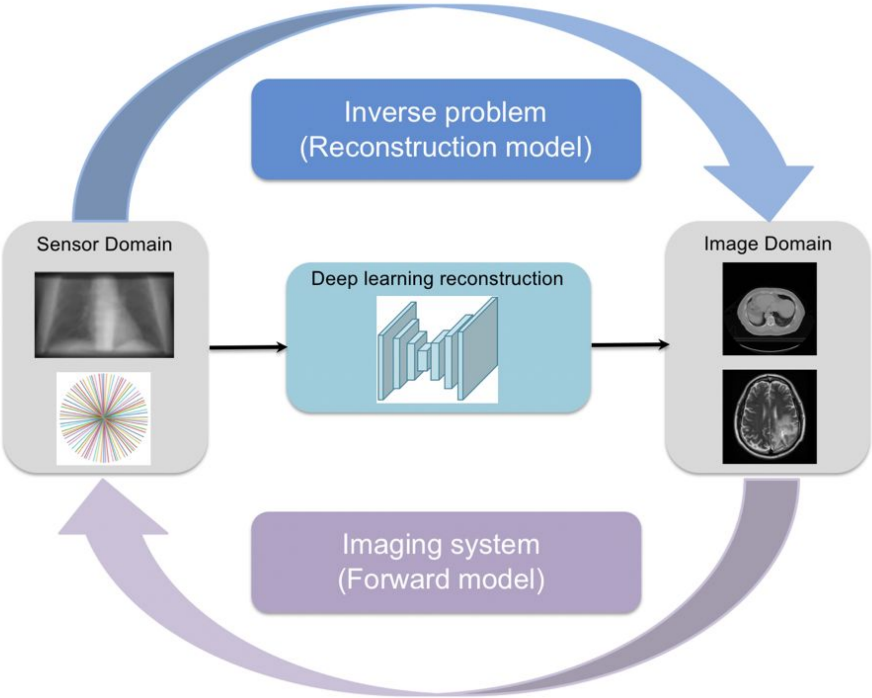
Sparse-sampling image reconstruction

- Leverage prior knowledge for solving ill-posed inverse problem
  - Conventional reconstruction: require dense sampling
  - Regularized reconstruction: sparsity in transformed domain
  - Deep learning reconstruction: learn implicit prior from data-driven



Deep learning-based image reconstruction

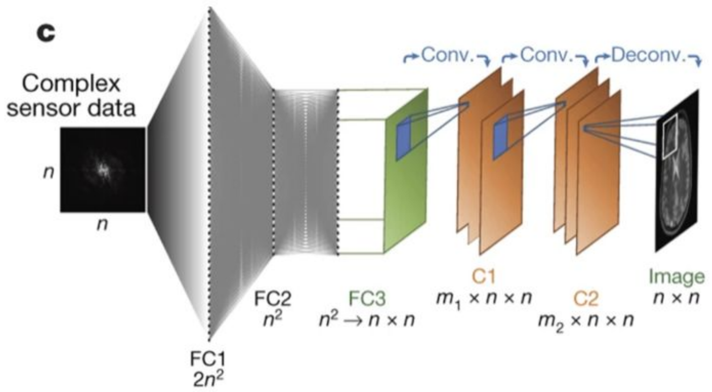
- Network learns cross-domain mapping function in a data-driven way



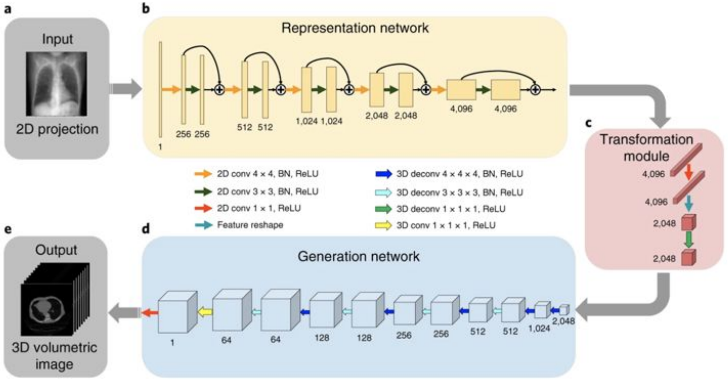
Deep learning-based image reconstruction

- Network learns cross-domain mapping function in a data-driven way

Sparse-sampling MRI reconstruction
Zhu et al. 2018



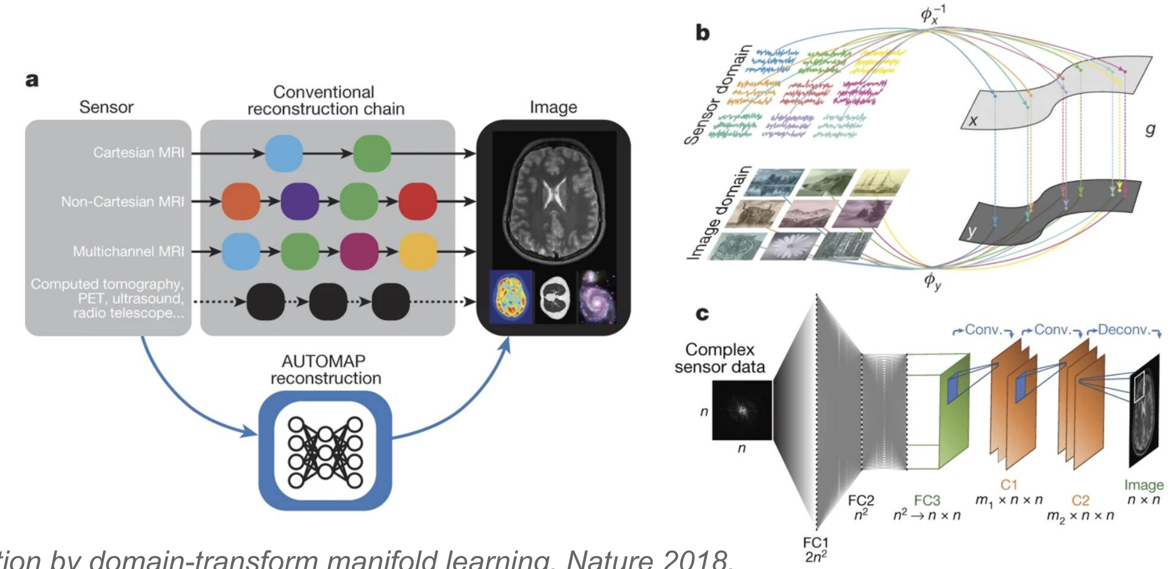
Sparse-view CT reconstruction
Shen et al. 2019



Zhu, et al., Image reconstruction by domain-transform manifold learning, Nature 2018.
Shen, et al., Patient-specific reconstruction of volumetric computed tomography images from a single projection view via deep learning, Nature BME 2019.

AUTOMAP image reconstruction, 2018

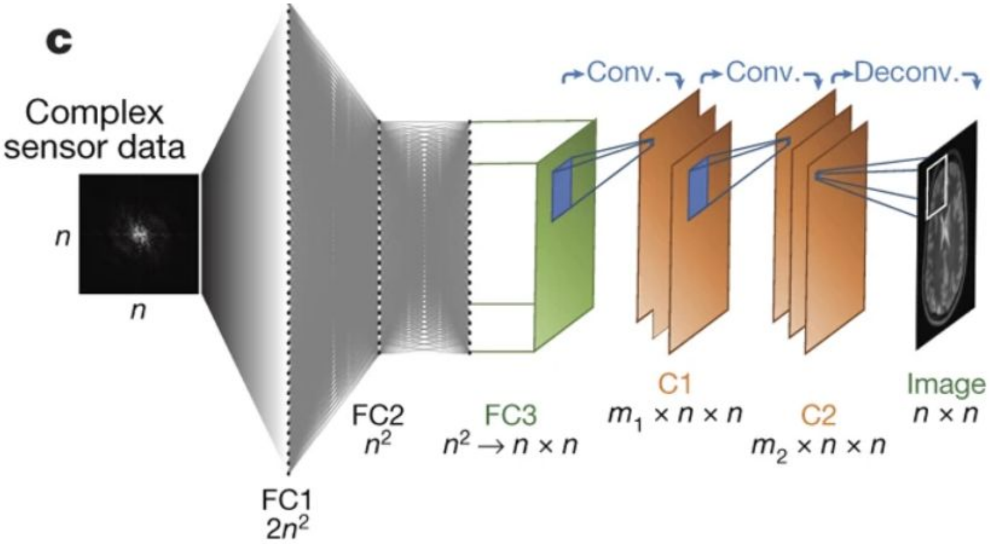
- A unified image reconstruction framework that learns the reconstruction relationship between sensor and image domain without expert knowledge
- A mapping between sensor domain and image domain is determined via supervised learning of sensor and image domain pairs



Zhu, et al., Image reconstruction by domain-transform manifold learning, Nature 2018.

AUTOMAP image reconstruction, 2018

- Deep neural network architecture:
  - FC1 - FC3: Fully connected layers with hyperbolic tangent activations
  - C1 - C2: Convolutional layers with rectifier nonlinearity activations that form a convolutional autoencoder



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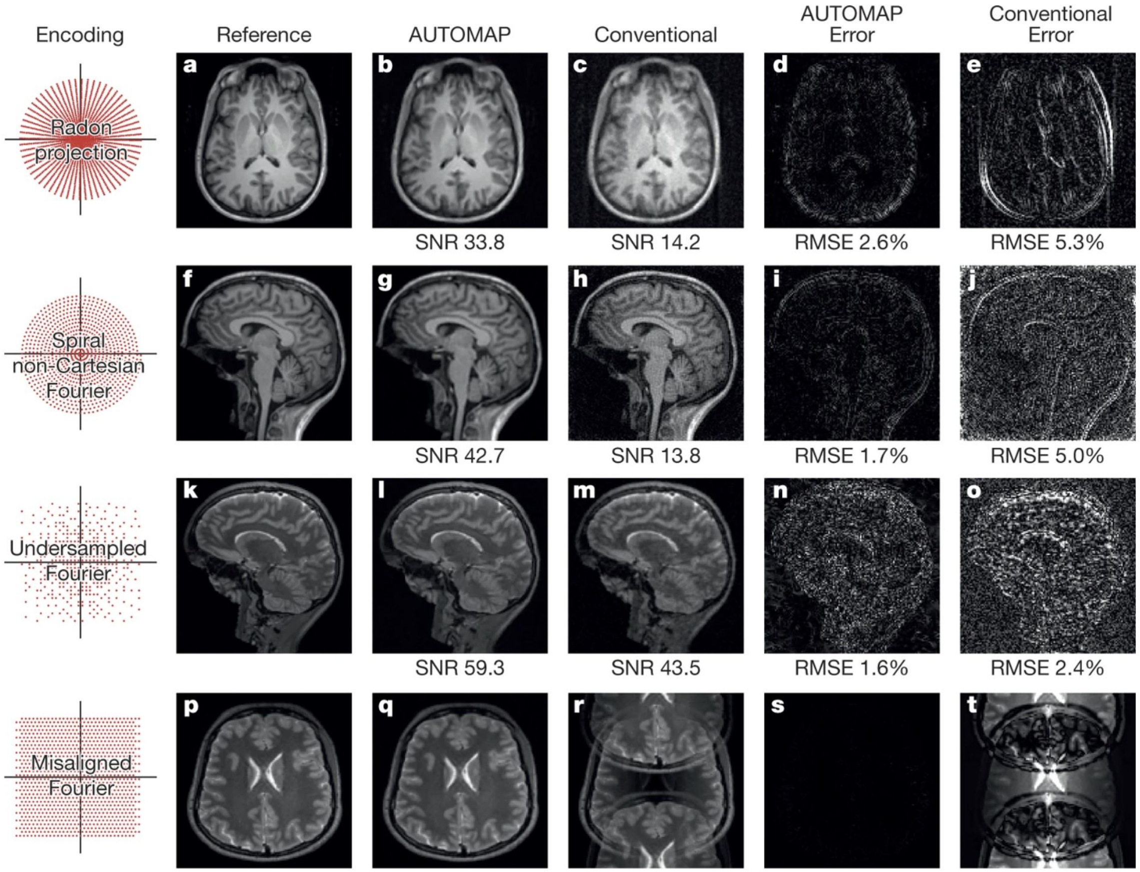
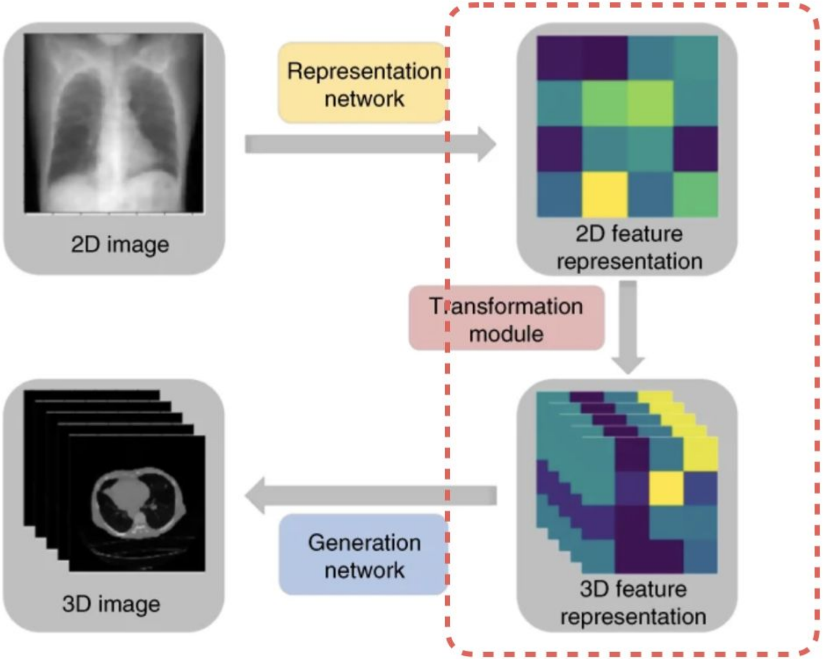


PatRecon, 2019

- Goal: Reconstruct 3D CT from sparse-sampling projections of different angles

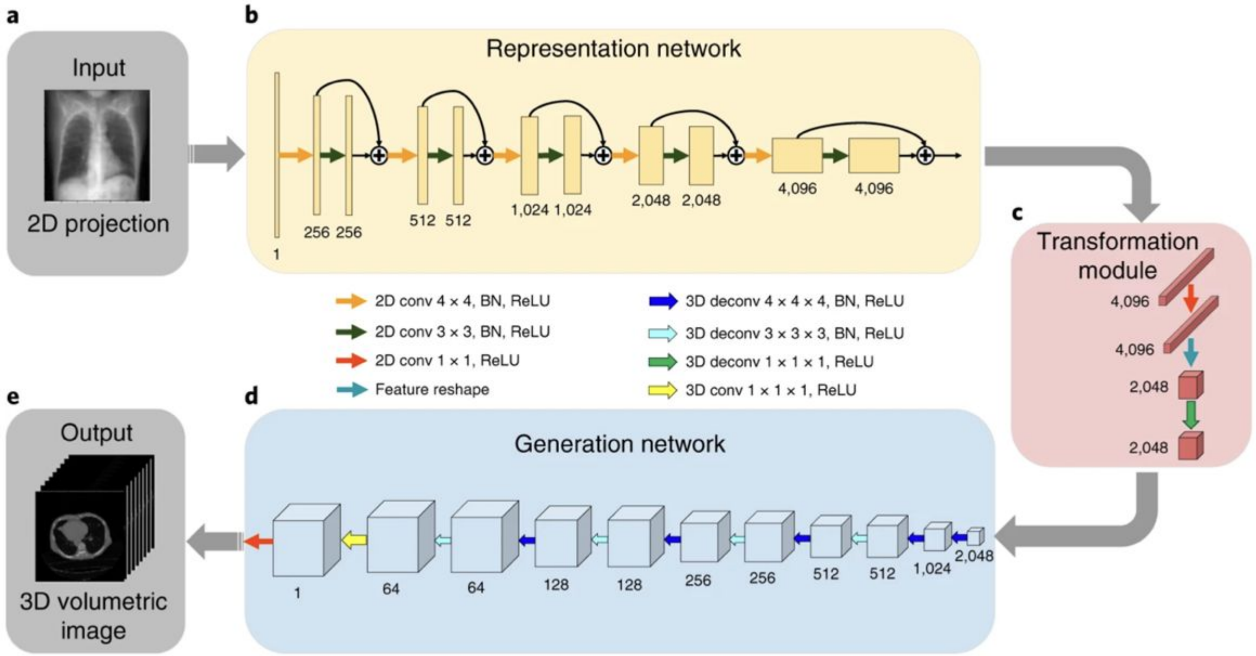


Reason 2D-3D cross-domain transformation in feature space

Shen, et al., Patient-specific reconstruction of volumetric computed tomography images from a single projection view via deep learning, Nature BME 2019.

PatRecon, 2019

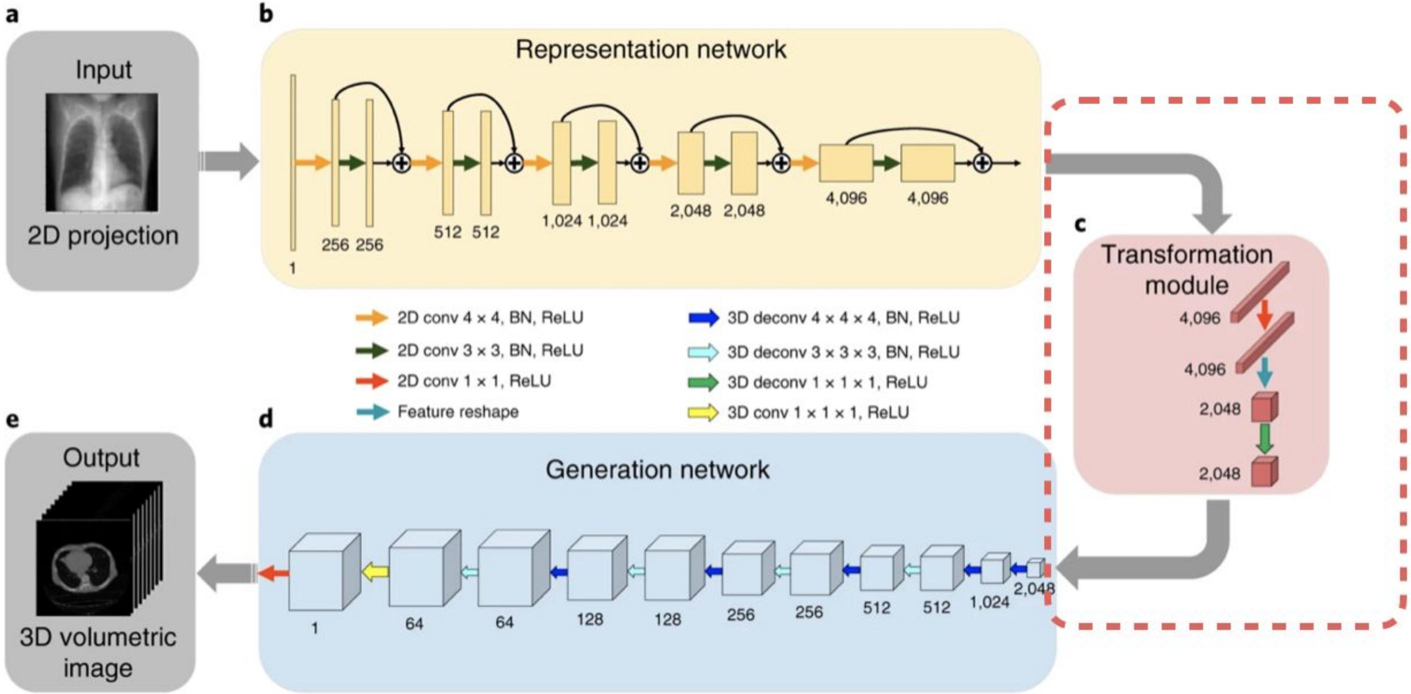
- Encoder-decoder framework
  - Representation network
  - Transformation module
  - Generation network



Shen, et al., Patient-specific reconstruction of volumetric computed tomography images from a single projection view via deep learning, Nature BME 2019.

PatRecon, 2019

- Patient-specific reconstruction of volumetric computed tomography images from ultra-sparse-view projections via deep learning



Reason 2D-3D cross-domain transformation in feature space

Fully data-driven!

Follow up …

- Emerging follow-up works:
  - Ying, et al., CVPR 2019
  - Kasten, et al., MLMIR 2020
  - Lei, et al., PMB 2020
  - Lu, et al., Nature BME 2021
  - Tao, et al., TMI 2021
  - Lyu, et al., MedIA 2021
  - Zhang, et al., TCI 2021
  - Sde-Chen, et al., ICCV 2021
  - Eulig, et al., Med Phys 2021
  - Zhou, et al., MedIA 2022
  - ……

Follow up …

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  - ……

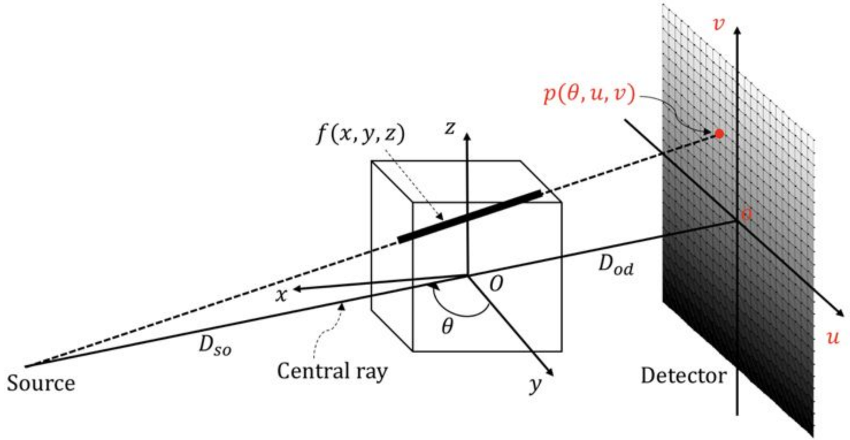
How to combine physics knowledge with deep learning models?

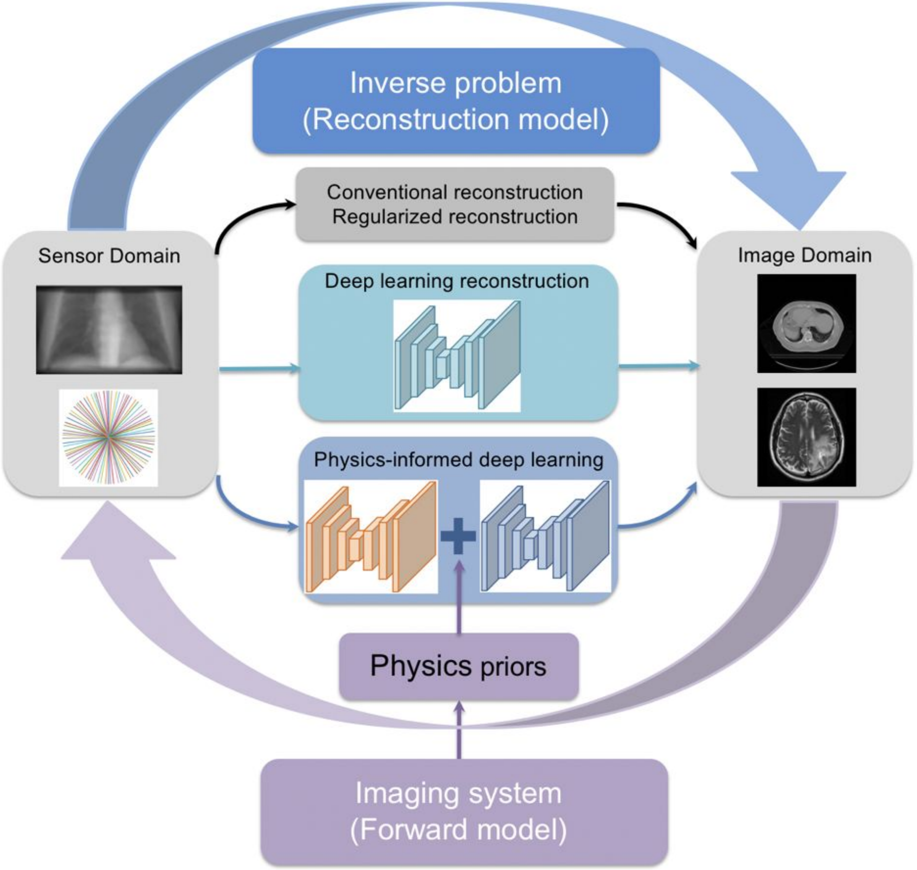
Today's agenda

- Motivation and physics background
- Conventional reconstruction method
- Deep learning-based reconstruction method
- Physics-informed learning
- Challenges

Physics priors from imaging system (forward model)

- Physics priors:
  - Transform (CT, MRI …)
  - Geometry (fan-beam, cone-beam…)
  - Dimension (2D, 3D, 3D+time …)
  - …
- 3D cone-beam CT geometry

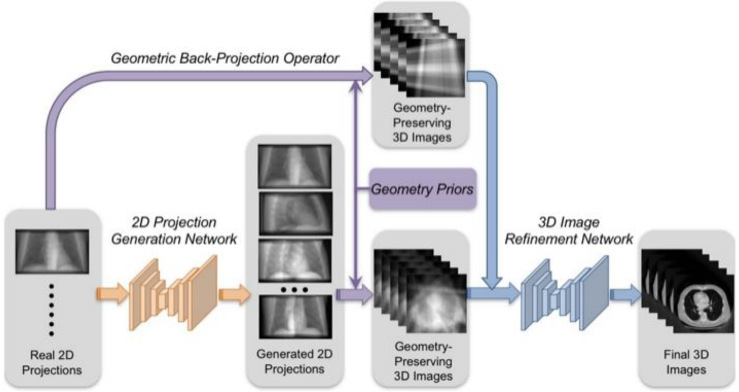




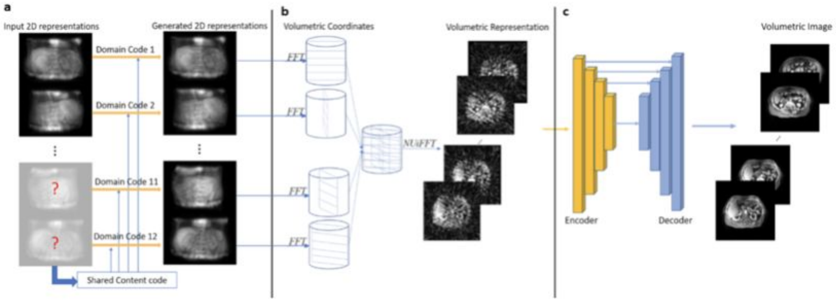
Physics-informed learning

- Dual-domain learning:
  - Physics priors relate and transfer information in different domains
  - Networks learn image synthesis and completion in both 2D and 3D domains

Sparse-view CT reconstruction



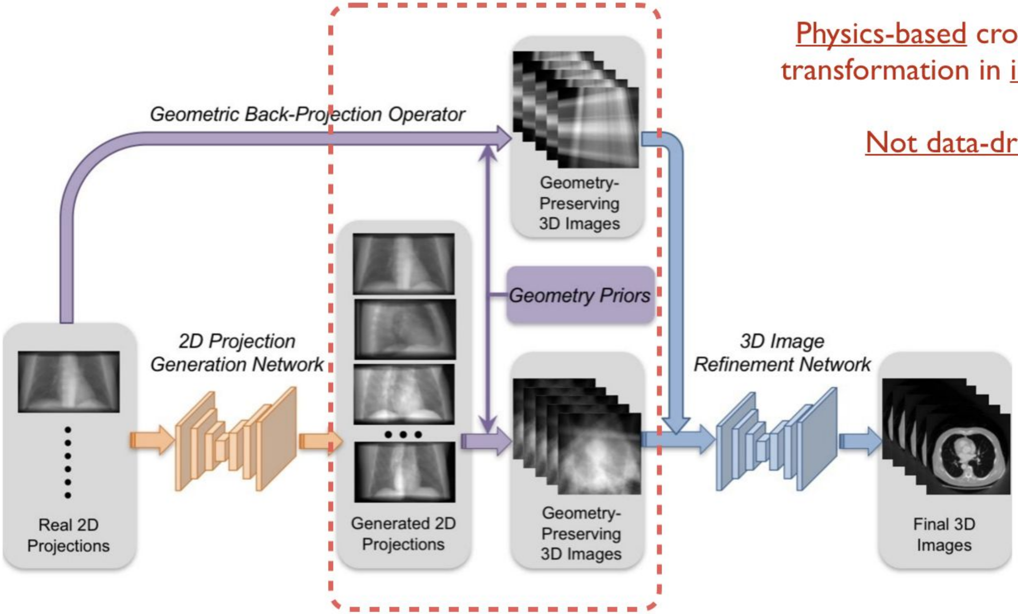
Sparse-sampling MRI reconstruction



Shen, et al., A geometry-informed deep learning framework for ultra-sparse computed tomography (CT) imaging, CIBM 2022.
Liu, et al., Real time volumetric MRI for 3D motion tracking via physics-aware deep learning, Med Phys 2022.

Physics-informed learning: Sparse-view CT reconstruction

- Dual-domain learning:
  - Physics priors relate and transfer information in different domains



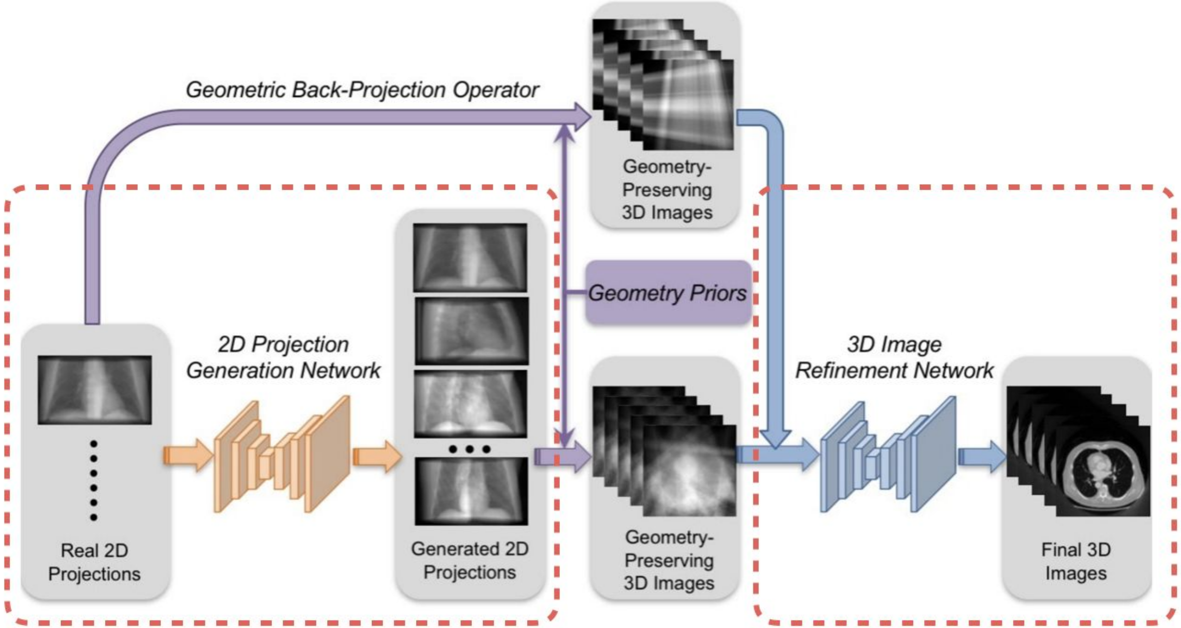
Physics-based cross-domain transformation in image space

Not data-driven!

Shen, et al., A geometry-informed deep learning framework for ultra-sparse computed tomography (CT) imaging, CIBM 2022.

Physics-informed learning: Sparse-view CT reconstruction

- Dual-domain learning:
  - Networks learn image synthesis and completion in both 2D and 3D domains



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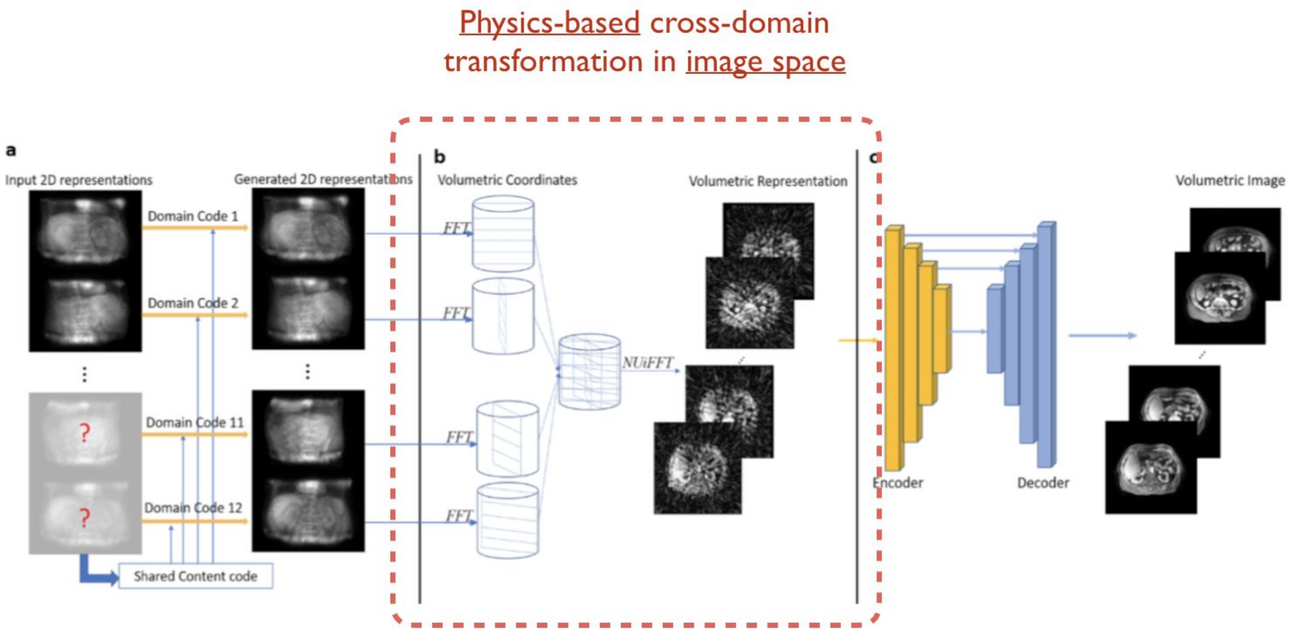

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Today's agenda

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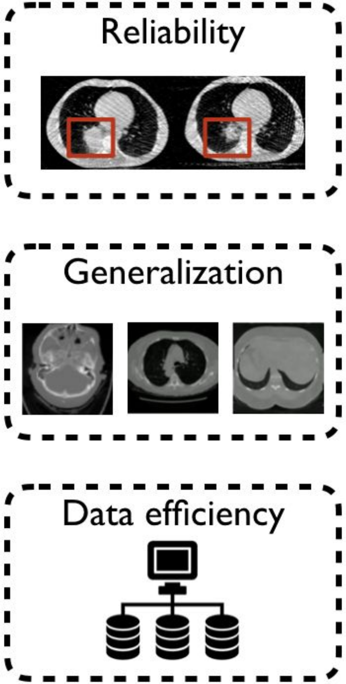
Challenges of deep learning-based image reconstruction

- The instabilities usually occur in several forms:
  a. Certain tiny, almost undetectable perturbations, both in the image and sampling domain, may result in severe artefacts in the reconstruction
  b. A small structural change, for example, a tumor, may not be captured in the reconstructed image
  c. More samples may yield poorer performance, with fixed training sampling pattern



On instabilities of deep learning in image reconstruction and the potential costs of AI

Vegard Antun, Francesco Renna, Clarice Poon, Ben Adcock, and Anders C. Hansen

+ See all authors and affiliations

PNAS December 1, 2020 117 (48) 30088-30095; first published May 11, 2020; https://doi.org/10.1073/pnas.1907377117

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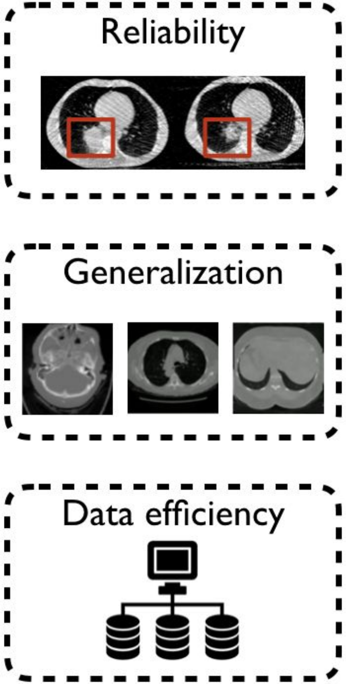
How to address these challenges?



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  c. More s

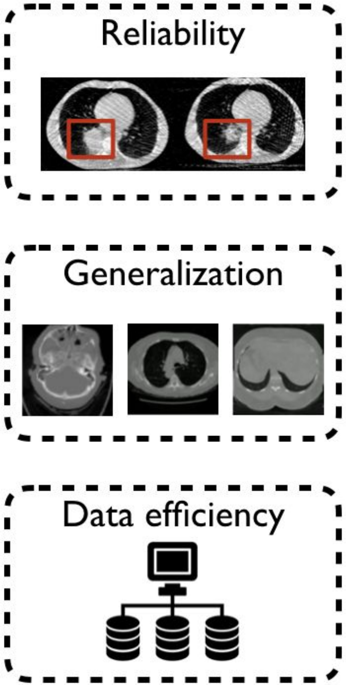
How to address these challenges?

New insight and paradigm for deep learning-based image reconstruction!
- Implicit neural representation learning
- Generative diffusion models

On instabilit
reconstruct

Vegard Antun, Fran
+ See all authors a

PNAS December 1, 2020 117



Antun, et al., On instabilities of deep learning in image reconstruction and the potential costs of AI, PNAS 2020.

Next time

- Implicit neural representation learning

Date	Lecture #	Topic	Papers	Instructor / Presenter
Tue 8/29	1	Introduction and course overview		Liyue Shen
Thu 8/31	2	Biomedical imaging with deep learning **[Fundamental]**		Liyue Shen
Tue 9/5	3	Implicit neural representation learning **[Advanced]**		Liyue Shen
Thu 9/7	4	Generative diffusion models **[Advanced]**		Liyue Shen
Tue 9/12	5	Medical image analysis **[Fundamental]**		Liyue Shen
Thu 9/14	6	Multimodal foundation models **[Advanced]**		Liyue Shen
Mon 9/18		Drop/add deadline for full term classes		
Tue 9/19	7	Implicit neural representation learning		
Thu 9/21	8	Implicit neural representation learning		
Tue 9/26	9	Implicit neural representation learning		
Thu 9/28	10	Implicit neural representation learning		
Tue 10/3	11	Generative diffusion models		
Thu 10/5	12	Generative diffusion models		
Tue 10/10	13	Generative diffusion models		
Thu 10/12	14	Generative diffusion models		
Tue 10/17		No class (fall study break)		
Thu 10/19	15	Self-supervised learning		
Tue 10/24	16	Self-supervised learning		
Thu 10/26	17	Multimodal learning		
Tue 10/31	18	Multimodal learning		
Thu 11/2	19	Transformer and LLM		
Tue 11/7	20	Transformer and LLM		