Explore Low-Dimensional Structures for Constrained and Controllable Diffusion Models in Scientific Applications

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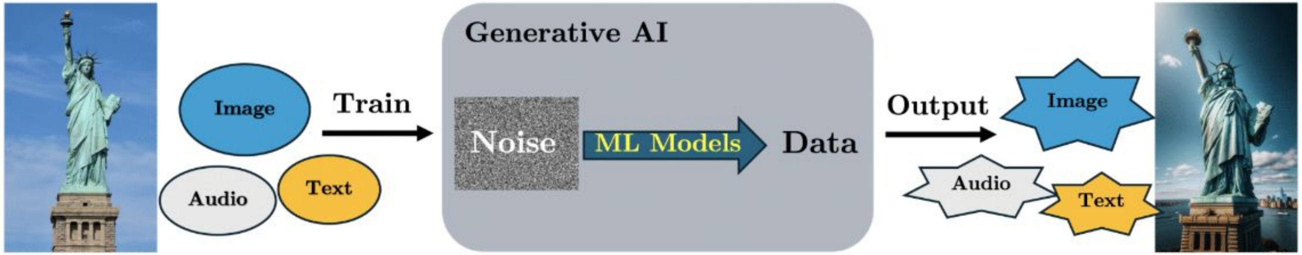
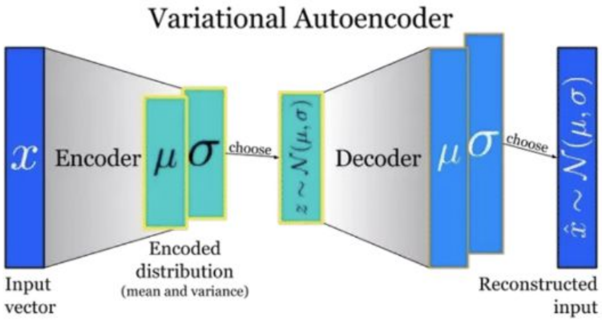
This Tutorial

- Session I: Introduction of Basic Low-dimensional Models
- Session II: Understanding Low-Dimensional Structures in Representation Learning
- Session III: Understanding Low-Dimensional Structures in Diffusion Generative Models
    - Low-Dimensional Models for Understanding Generalization in Diffusion Models - Qing Qu
    - ***Explore Low-Dimensional Structures for Constrained and Controllable Diffusion Models in Scientific Applications - Liyue Shen***
- Session IV: Designing Deep Networks for Pursuing Low-Dimensional Structures
- Session V: Panel Discussion

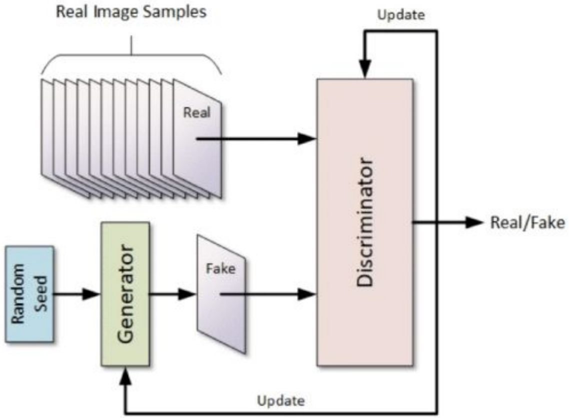
Recap: The Family of Generative Models



Generative models in the past:

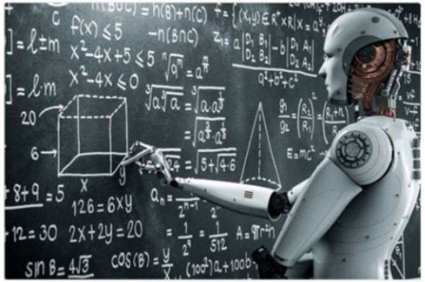


(a) VAE (Kingma & Wellings, 2013): poor generation quality.



(b) GAN (Goodfellow et al. 2014): unstable to train on large dataset.

Why is Diffusion Model?

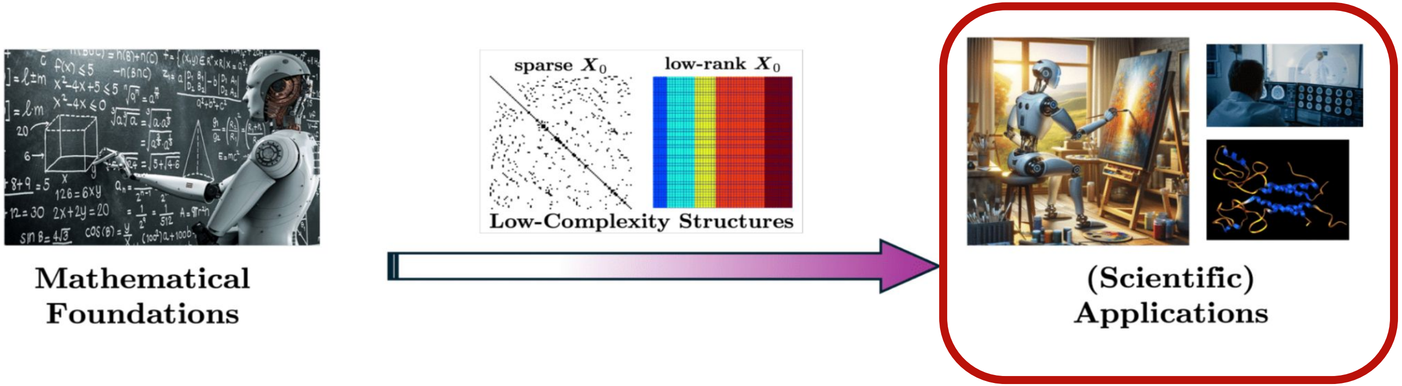


Mathematical
Foundations

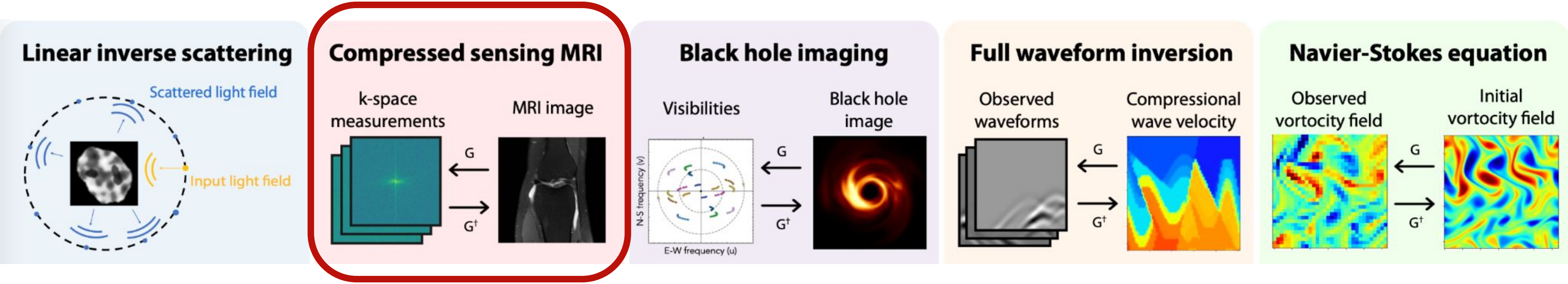
(Scientific)
Applications

Low-dimensional structures are the key to address real-world high-dimensional data with small data regime in scientific applications

Application of Diffusion Model: Solving Inverse Problems



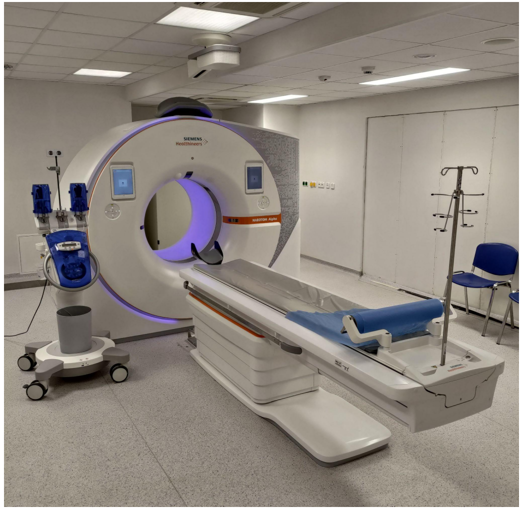
Inverse problems are common and important in scientific applications

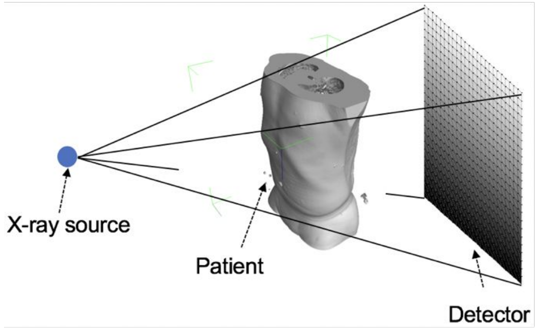


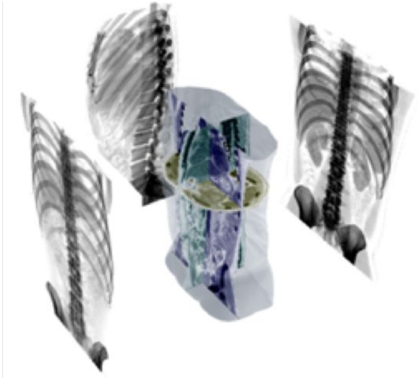
Zheng et al., InverseBench: Benchmarking Plug-and-Play Diffusion Models for Inverse Problems in Physical Sciences, ICLR 2025.

Medical Imaging

- **X-ray Computed Tomography (CT) imaging**
  - Reconstruct cross-sectional images of internal structures from X-ray projections at multiple views



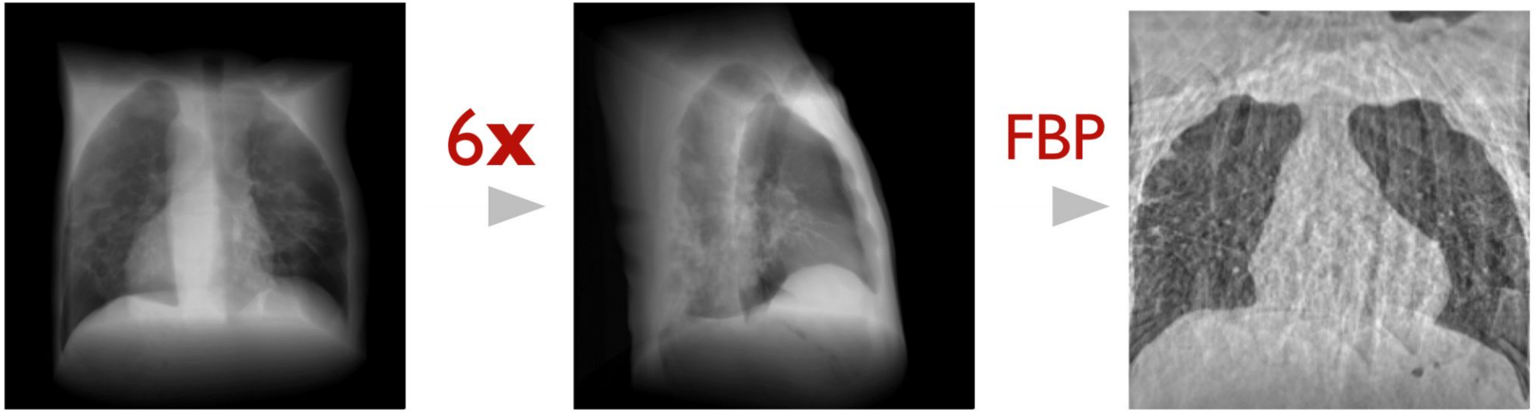




Shen et al., Patient-Specific Reconstruction of Volumetric Computed Tomography Images from a Single Projection View via Deep Learning, Nature BME 2019.

Medical Imaging

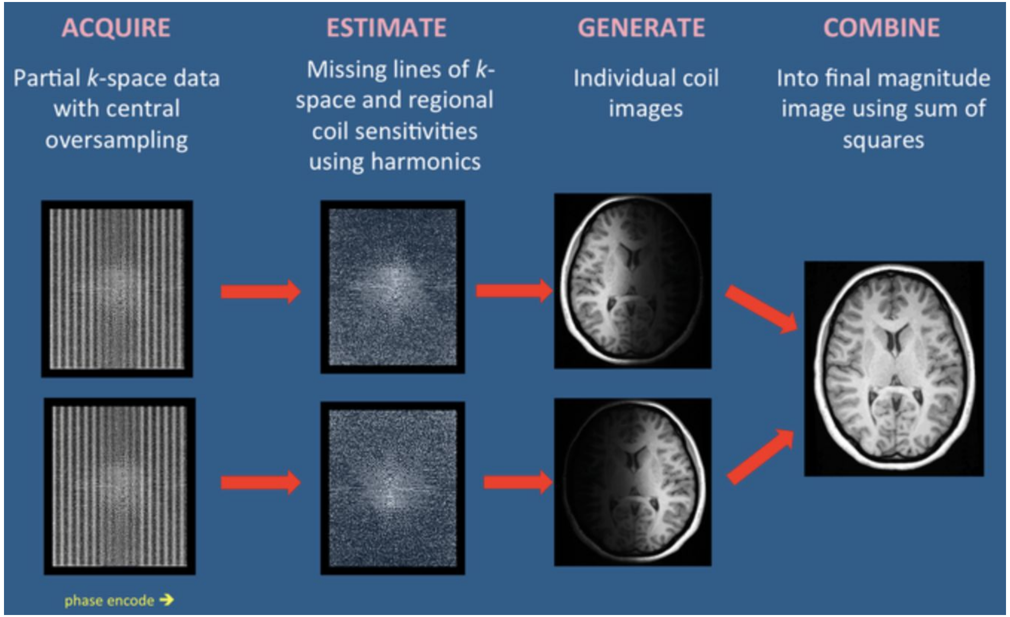
- X-ray Computed Tomography (CT) imaging
  - Reconstruct cross-sectional images of internal structures from X-ray projections at multiple views
- Reduce radiation dose in CT scanning
  - Sample sparse projections from fewer views



Dense-view (180) Sparse-view (30) Reconstruction

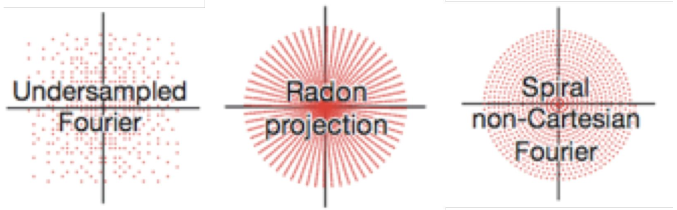
Medical Imaging

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



Medical Imaging

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



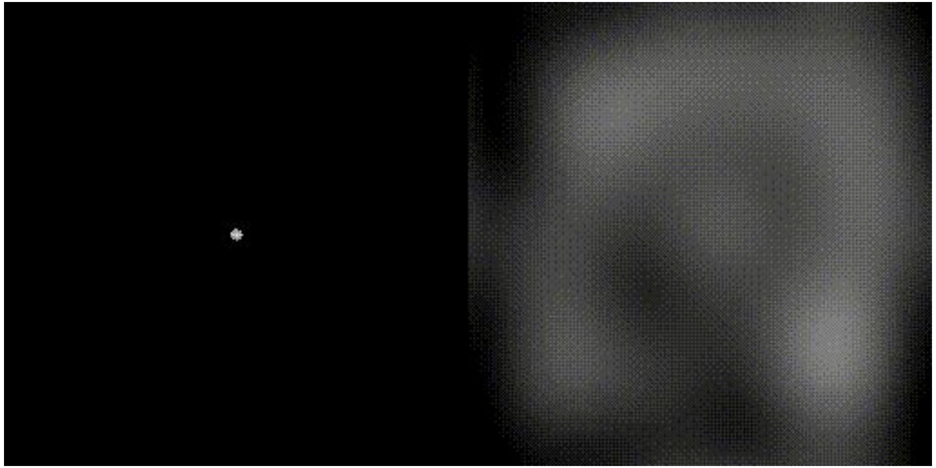


Image credit: https://mriquestions.com/k-space-trajectories.html

Inverse Problem in Medical Imaging

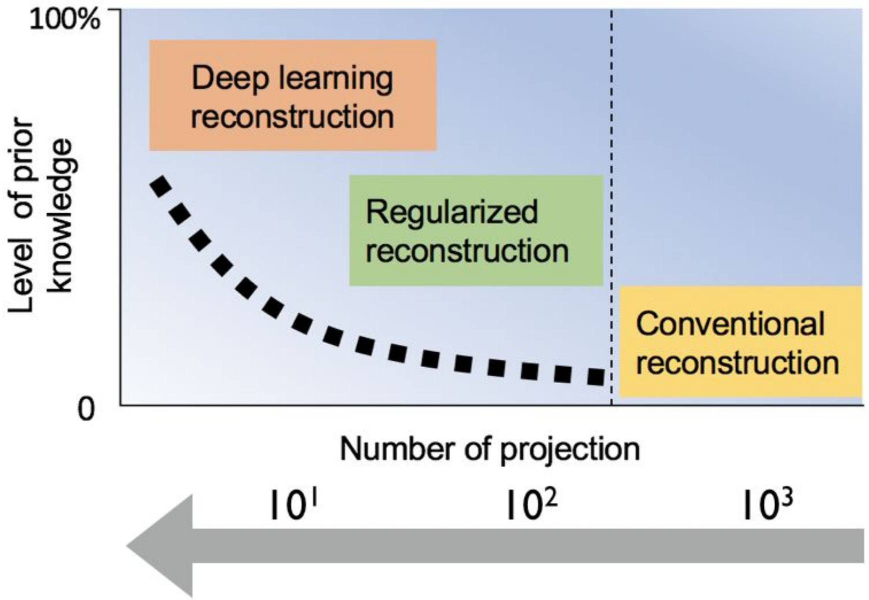
- Medical imaging process can be formulated as:

$$\mathbf{y} = \mathcal{A}(\mathbf{x}) + \mathbf{n} \longrightarrow \text{Noise}$$

Inverse problem: reconstruct original image from sparse measurements

Leverage Prior Knowledge for Solving Ill-posed Inverse Problem

- Conventional reconstruction: require dense sampling
- Regularized reconstruction: sparsity in transformed domain
- Deep learning reconstruction: learned prior from a data-driven way

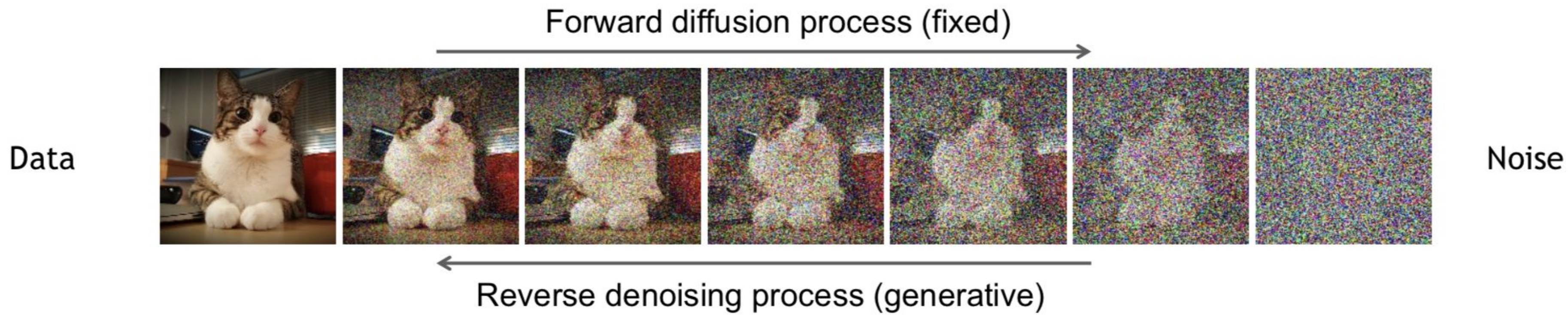


Diffusion model:

Provide prior knowledge of data distribution for solving inverse problems

Shen et al., Patient-Specific Reconstruction of Volumetric Computed Tomography Images from a Single Projection View via Deep Learning, Nature BME 2019.

Recap: Diffusion Models

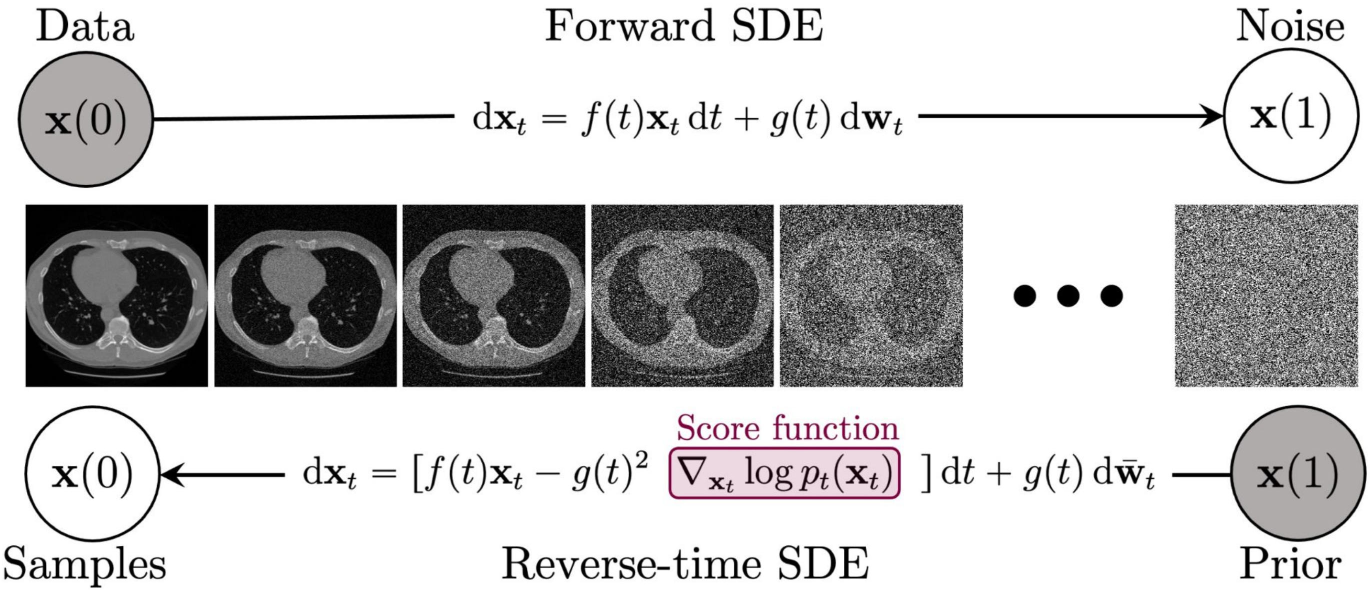


- Forward diffusion process with noise added
- Reverse denoising process for generative diffusion sampling

Ho et al., Denoising Diffusion Probabilistic Models, NeurIPS 2020.

Recap: Score-based Diffusion Models

- Forward diffusion process as stochastic differential equation (SDE)
- Generative reverse stochastic differential equation



Diffusion models learn data prior by modeling data distribution through unsupervised training

Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

Diffusion Models for Solving Inverse Problems

$$\mathbf{y} = \mathcal{A}(\mathbf{x}) + \mathbf{n} \longrightarrow \text{Noise}$$

- From Bayes' rule:

$$p(\mathbf{x} \mid \mathbf{y}) = p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x}) / \int p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x})\mathrm{d}\mathbf{x}.$$

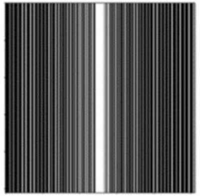
- Compute the posterior score function:

$$\nabla_{\mathbf{x}} \log p(\mathbf{x} \mid \mathbf{y}) = \nabla_{\mathbf{x}} \log p(\mathbf{x}) + \nabla_{\mathbf{x}} \log p(\mathbf{y} \mid \mathbf{x})$$

Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

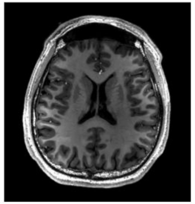
Diffusion Models for Solving Inverse Problems

$$\mathbf{y} = \mathcal{A}(\mathbf{x}) + \mathbf{n}$$ Noise



Measurements

Imaging System



High-quality Images

- From Bayes' rule:

$$p(\mathbf{x} \mid \mathbf{y}) = p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x}) / \int p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x})\mathrm{d}\mathbf{x}.$$

- Compute the posterior score function:

$$\nabla_{\mathbf{x}} \log p(\mathbf{x} \mid \mathbf{y}) = \boxed{\nabla_{\mathbf{x}} \log p(\mathbf{x})} + \nabla_{\mathbf{x}} \log p(\mathbf{y} \mid \mathbf{x})$$

Score function of data distribution

Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

Diffusion Models for Solving Inverse Problems

$$\mathbf{y} = \mathcal{A}(\mathbf{x}) + \mathbf{n}$$

- From Bayes' rule:

$$p(\mathbf{x} \mid \mathbf{y}) = p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x}) / \int p(\mathbf{x})p(\mathbf{y} \mid \mathbf{x})\mathrm{d}\mathbf{x}.$$

- Compute the posterior score function:

$$\nabla_{\mathbf{x}} \log p(\mathbf{x} \mid \mathbf{y}) = \nabla_{\mathbf{x}} \log p(\mathbf{x}) + \boxed{\nabla_{\mathbf{x}} \log p(\mathbf{y} \mid \mathbf{x})}$$

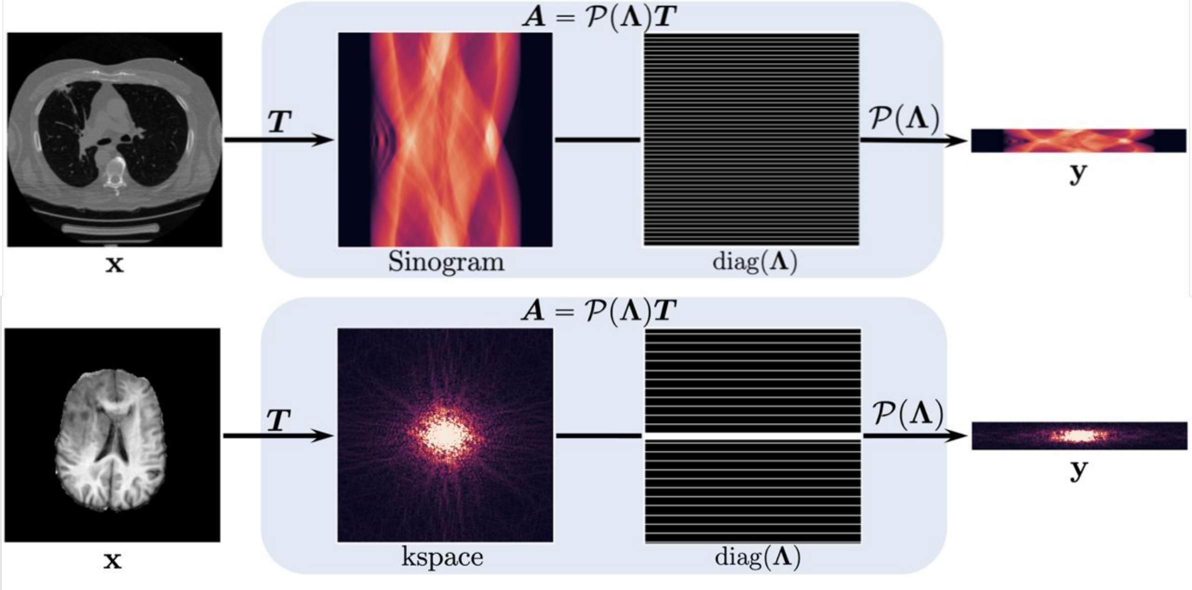
Known forward process

Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

Forward Process of Sparse-sampling Medical

- **Forward model:**
  - Physics-based transformation
  - Sparse sampling mask of observed measurements

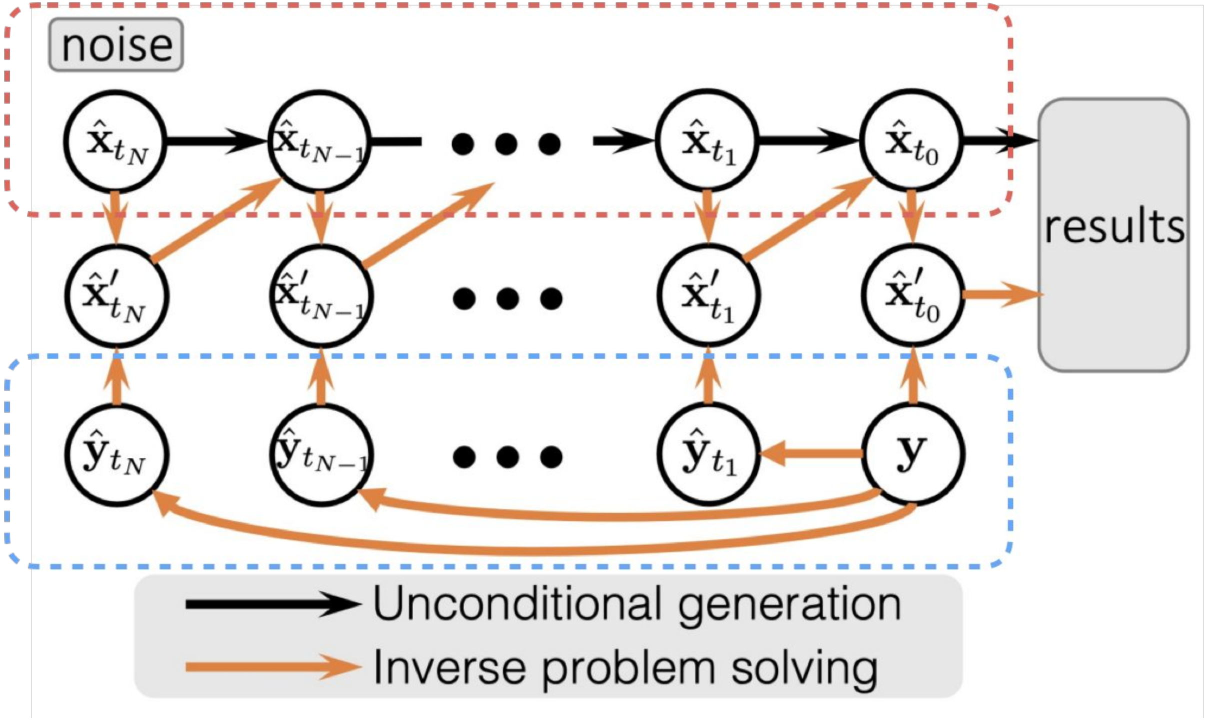
x: image
y: observed measurements
A: forward model
T: transformation
Λ: sampling mask
P: dimension reduction operator



Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

Diffusion Models for Solving Inverse Problems

$p(\mathbf{x})$



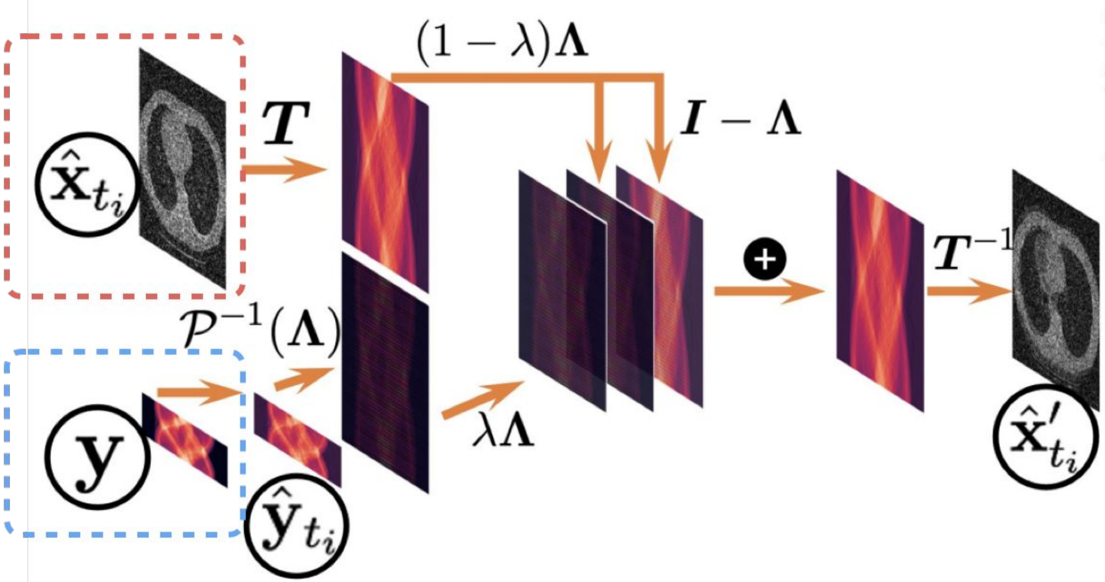
$p(\mathbf{x} \mid \mathbf{y})$

Posterior sampling consistent with data distribution prior and observed measurements

Song* and Shen* et al., Solving inverse problems in medical imaging with score-based generative models, ICLR 2022.

Optimization Objective

$$\hat{\mathbf{x}}'_{t_i} = \arg\min_{\boldsymbol{z}\in\mathbb{R}^n}\{(1-\lambda)\|\boldsymbol{z}-\hat{\mathbf{x}}_{t_i}\|_{\boldsymbol{T}}^2 + \min_{\boldsymbol{u}\in\mathbb{R}^n}\lambda\|\boldsymbol{z}-\boldsymbol{u}\|_{\boldsymbol{T}}^2\} \quad s.t. \quad \boldsymbol{A}\boldsymbol{u} = \hat{\mathbf{y}}_{t_i}$$

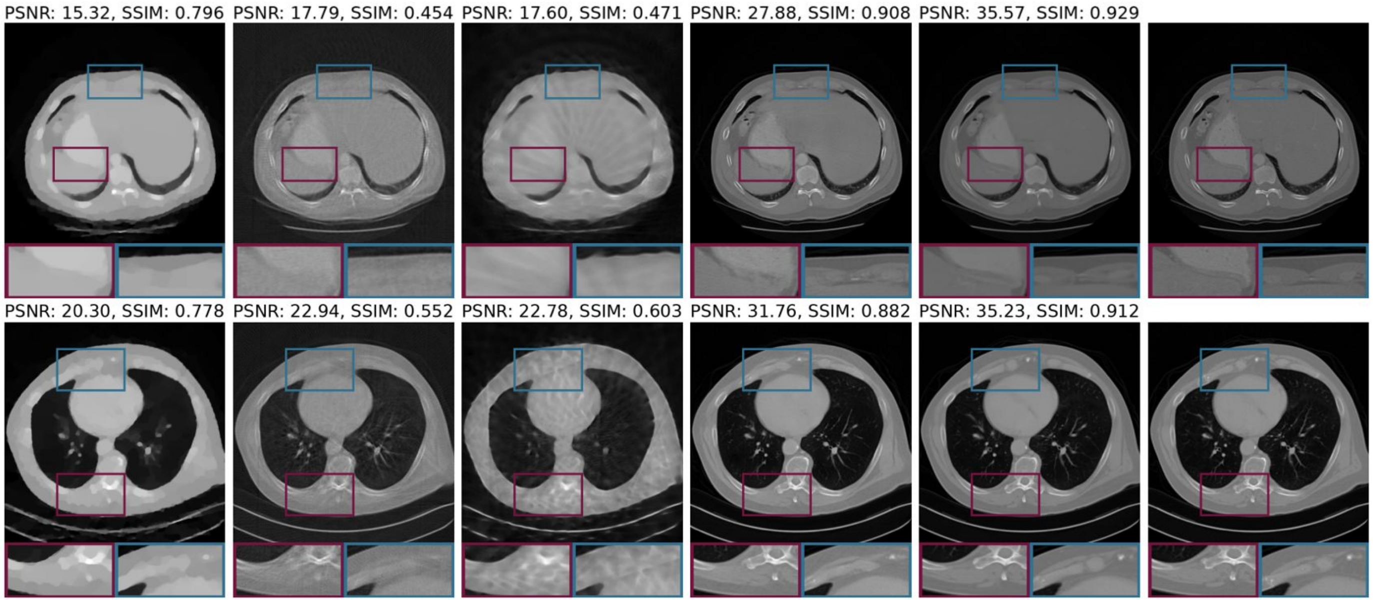


x: image
y: observed measurements
A: forward model
T: transformation
Λ: sampling mask
P: dimension reduction operator

Posterior sampling consistent with data distribution prior and observed measurements

Advantages of Diffusion Inverse Solvers

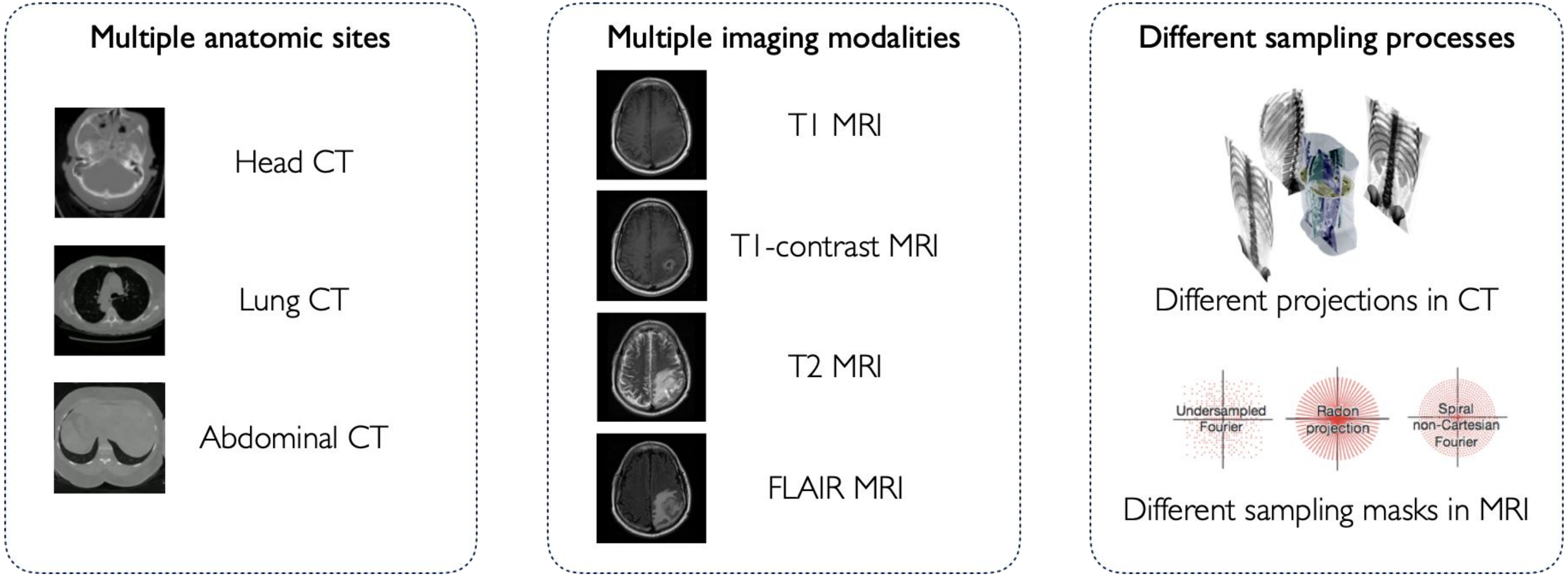
- No assumption of measurements sampling during training
- Comparable or better performance to supervised learning methods



(a) FISTA-TV (b) cGAN (c) Neumann (d) SIN-4c-PRN (e) Ours (f) Ground truth

Advantages of Diffusion Inverse Solvers

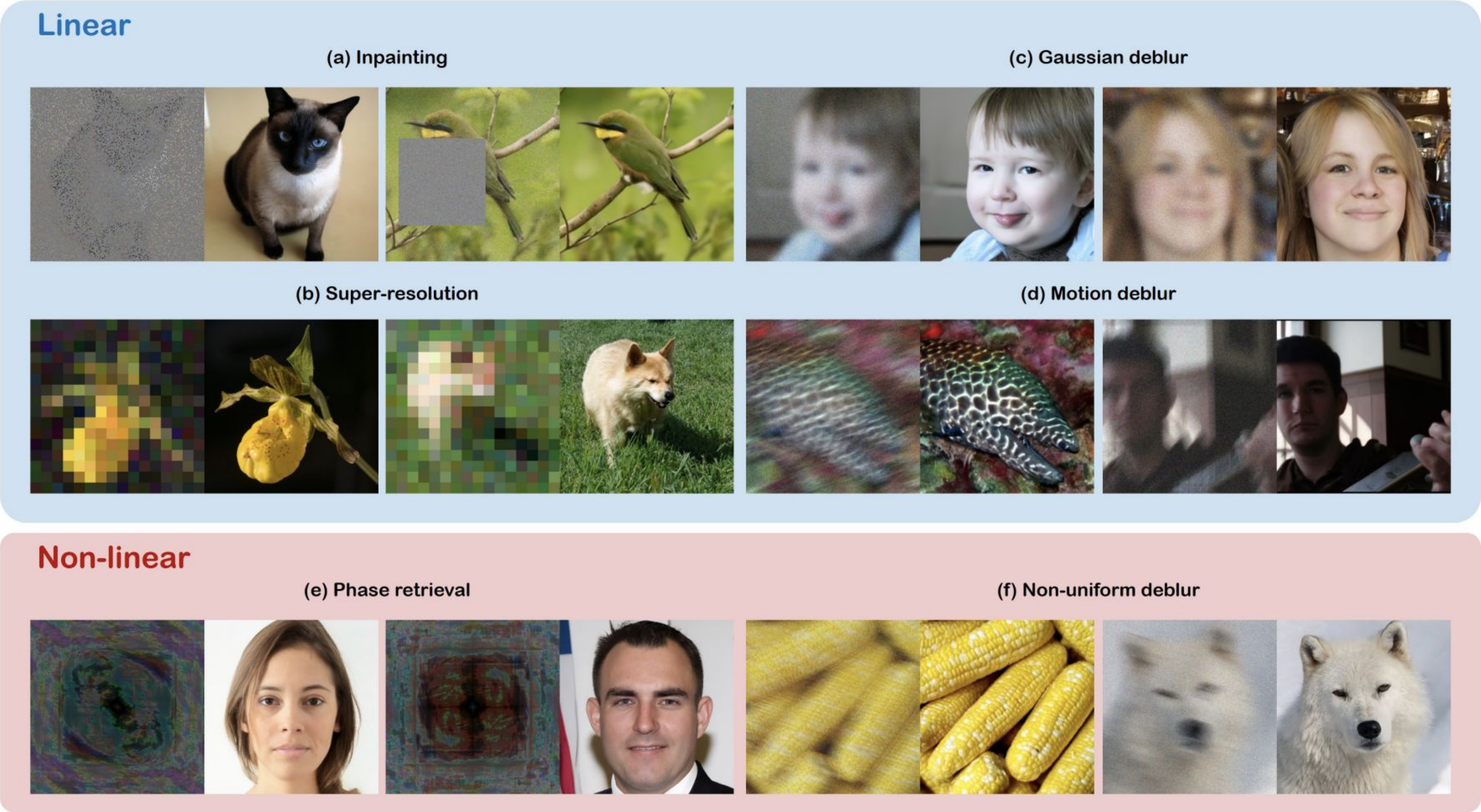
- **Generalizable to solve different inverse problems at inference time**
  - Different number of projections in CT reconstruction
  - Different acceleration factors in MRI reconstruction
  - A single training model captures data distribution prior of multi-anatomic sites and multi-modal images



Diffusion Inverse Solvers in Medical Imaging

- **Lots of literatures:**
  - Song et al., “Solving Inverse Problems in Medical Imaging with Score-Based Generative Models”, ICLR, 2022
  - Jalal et al., “Robust Compressed Sensing MRI with Deep Generative Priors”, NeurIPS, 2021
  - Chung and Ye, “Score-based diffusion models for accelerated MRI”, Medical Image Analysis, 2022
  - Chung et al., “Come-Closer-Diffuse-Faster: Accelerating Conditional Diffusion Models for Inverse Problems through Stochastic Contraction”, CVPR, 2022
  - Peng et al., “Towards performant and reliable undersampled MR reconstruction via diffusion model sampling”, arXiv, 2022
  - Xie and Li, “Measurement-conditioned Denoising Diffusion Probabilistic Model for Under-sampled Medical Image Reconstruction”, arXiv, 2022
  - Luo et al, “MRI Reconstruction via Data Driven Markov Chain with Joint Uncertainty Estimation”, arXiv, 2022
  - ……

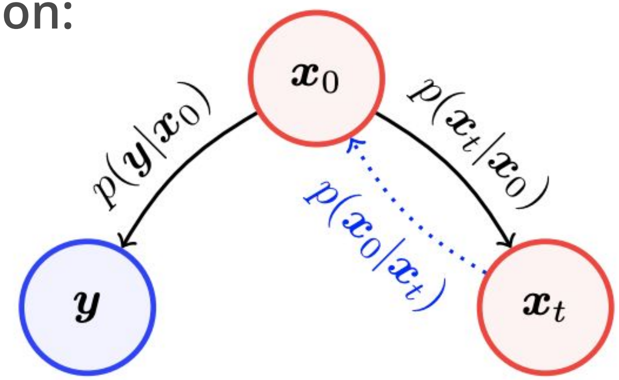
Diffusion Inverse Solvers beyond Medical Imaging



Chung et al., Diffusion Posterior Sampling for General Noisy Inverse Problems, ICLR 2023.

Diffusion Posterior Sampling for General Inverse Problems

Posterior mean estimation:



$$\nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{x}_t|\boldsymbol{y}) = \nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{x}_t) + \boxed{\nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{y}|\boldsymbol{x}_t)}$$

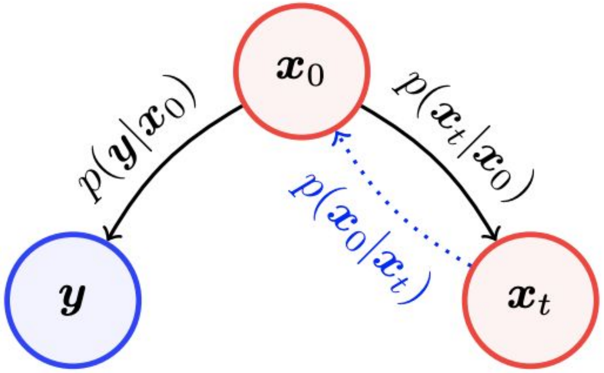
$$\hat{\boldsymbol{x}}_0 := \mathbb{E}[\boldsymbol{x}_0|\boldsymbol{x}_t] = \frac{1}{\sqrt{\bar{\alpha}(t)}}(\boldsymbol{x}_t + (1-\bar{\alpha}(t))\nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{x}_t))$$

$$p(\boldsymbol{y}|\boldsymbol{x}_t) \simeq p(\boldsymbol{y}|\hat{\boldsymbol{x}}_0), \quad \text{where} \quad \hat{\boldsymbol{x}}_0 := \mathbb{E}[\boldsymbol{x}_0|\boldsymbol{x}_t] = \mathbb{E}_{\boldsymbol{x}_0 \sim p(\boldsymbol{x}_0|\boldsymbol{x}_t)}[\boldsymbol{x}_0]$$

Chung et al., Diffusion Posterior Sampling for General Noisy Inverse Problems, ICLR 2023.

Diffusion Posterior Sampling for General Inverse Problems

Take backpropagation through network:

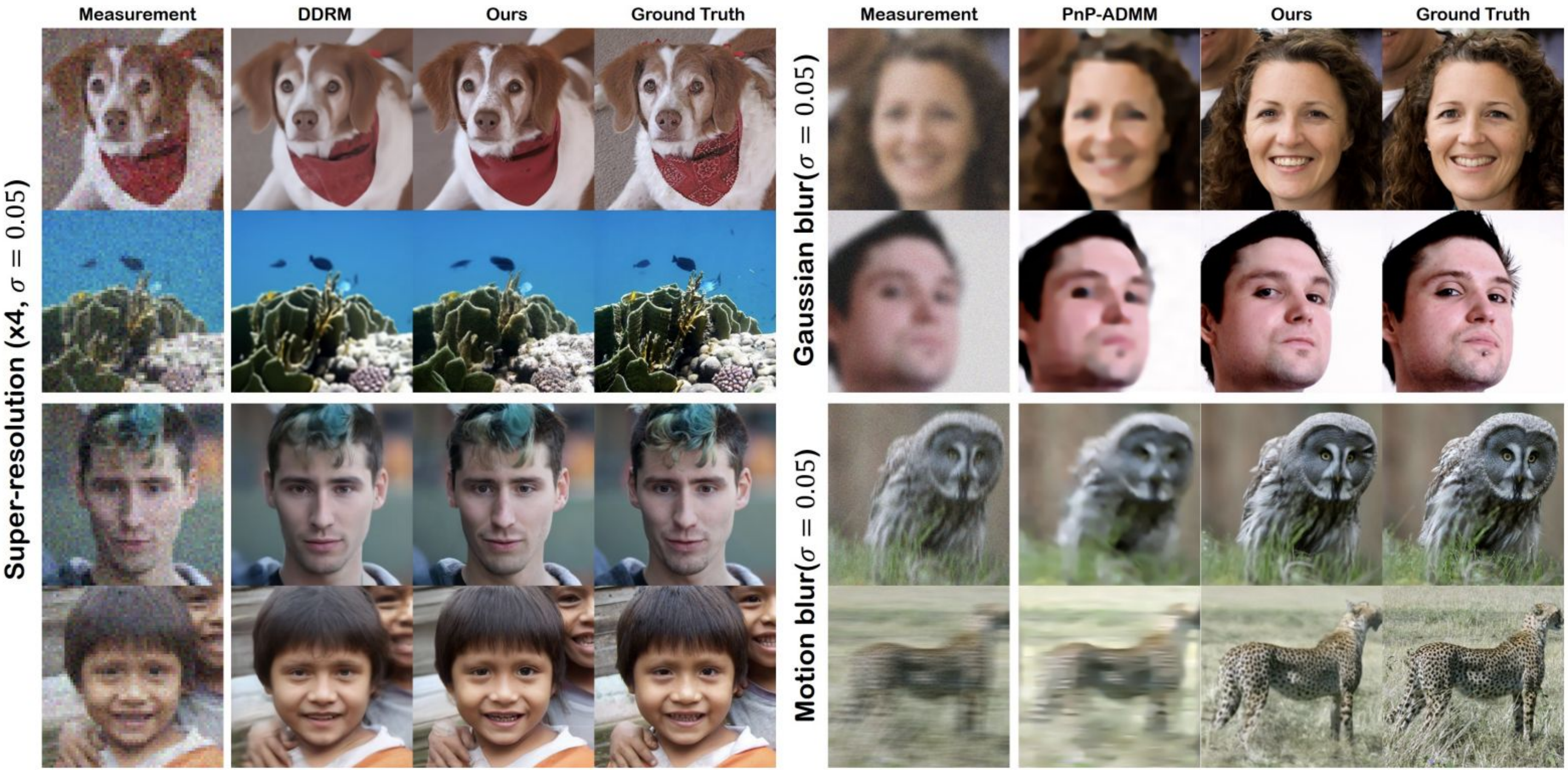


$$\nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{x}_t|\boldsymbol{y}) = \nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{x}_t) + \boxed{\nabla_{\boldsymbol{x}_t} \log p_t(\boldsymbol{y}|\boldsymbol{x}_t)}$$

$$\begin{aligned}\nabla_{\boldsymbol{x}_t} \log p(\boldsymbol{y}|\boldsymbol{x}_t) &\simeq \nabla_{\boldsymbol{x}_t} \log p(\boldsymbol{y}|\hat{\boldsymbol{x}}_0) \\ &\simeq -\frac{1}{\sigma^2}\nabla_{\boldsymbol{x}_t}\|\boldsymbol{y} - \mathcal{A}(\hat{\boldsymbol{x}}_0(\boldsymbol{x}_t))\|_2^2\end{aligned}$$

Chung et al., Diffusion Posterior Sampling for General Noisy Inverse Problems, ICLR 2023.

Diffusion Posterior Sampling for General Inverse Problems



Chung et al., Diffusion Posterior Sampling for General Noisy Inverse Problems, ICLR 2023.

Diffusion Inverse Solvers

Category	Method	SVD	Pseudo inverse	Linear	Gradient
Linear guidance	DDRM	✓	✓	✓	--
	DDNM	✗	✓	✓	--
	ΠGDM	✗	✓	✗	--
General guidance	DPS	✗	✗	✗	✓
	LGD	✗	✗	✗	✓
	DPG	✗	✗	✗	✗
	SCG	✗	✗	✗	✗
	EnKG	✗	✗	✗	✗
Variable-splitting	DiffPIR	✗	✗	✗	✓
	PnP-DM	✗	✗	✗	✓
	DAPS	✗	✗	✗	✓
Variational Bayes	RED-diff	✗	✗	✗	✓
Sequential Monte Carlo	FPS	✗	✗	✓	--
	MCGDiff	✓	✓	✓	--

Zheng et al., InverseBench: Benchmarking Plug-and-Play Diffusion Models for Inverse Problems in Physical Sciences, ICLR 2025.

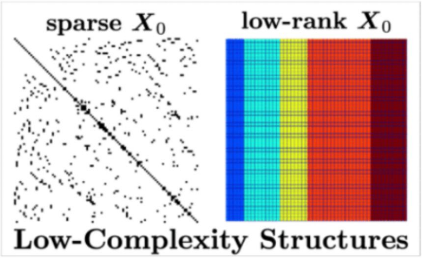
Challenges of Diffusion Inverse Solvers in Scientific Applications

Efficiency

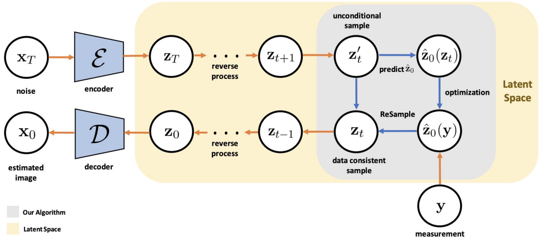
(Scientific) Applications

Generalizability

Controllability



Challenges of Diffusion Inverse Solvers in Scientific Applications

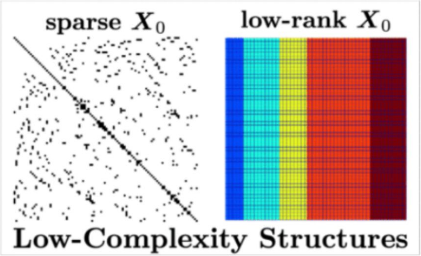


Efficiency

(Scientific)
Applications

Generalizability

Controllability

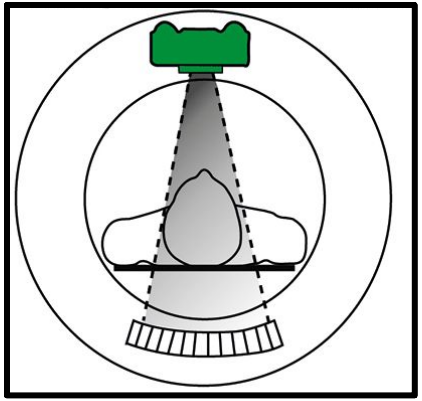


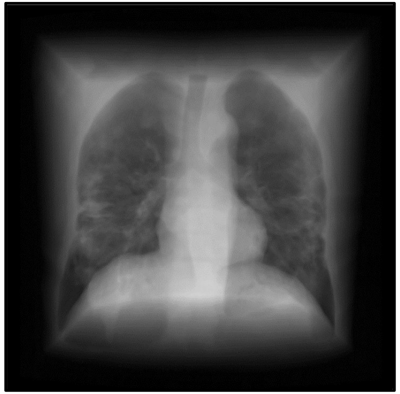
Limitations of Diffusion Inverse Solvers

- **Requires large-scale training data**
  - 50k ~ 300k images
- **Slow training and sampling process**
  - ~1000 sampling steps
- **Expensive GPU memory cost for high-dimensional data**
  - Most models only apply to 2D images
- **……**

Limitations of Diffusion Inverse Solvers

- Real-world applications is mostly about **high-dimensional and high-resolution** data!
  - 3D volumetric CT images with standard resolution of 512^3



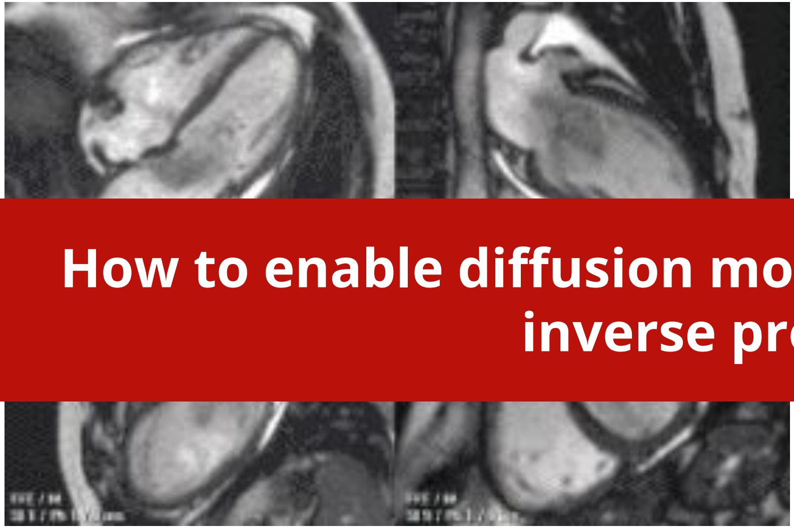


Projections

CT volumetric image

Limitations of Diffusion Inverse Solvers

- Real-world applications is mostly about high-dimensional and high-resolution data!
  - 3D volumetric CT images with standard resolution of 512^3
  - 4D MRI images with time sequence
  - High-resolution satellite images with thousands of pixels
  - ....

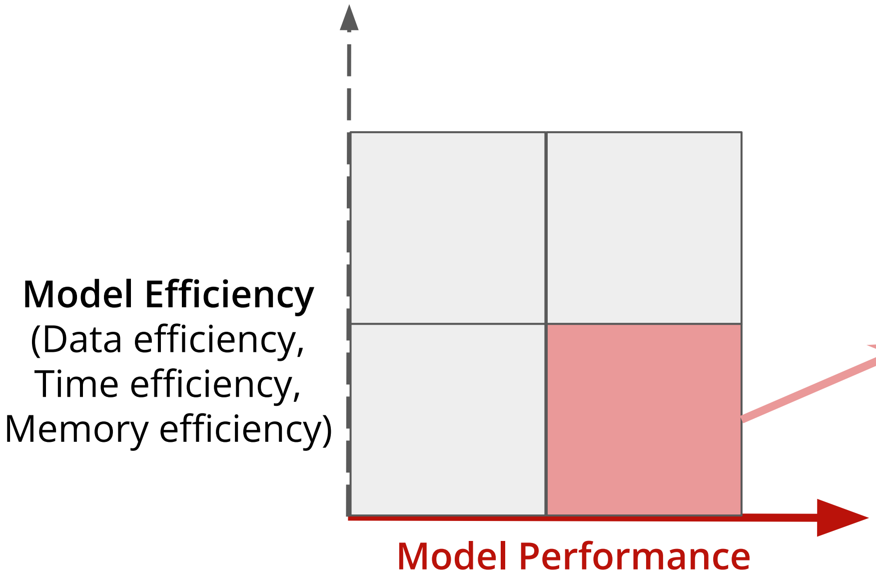


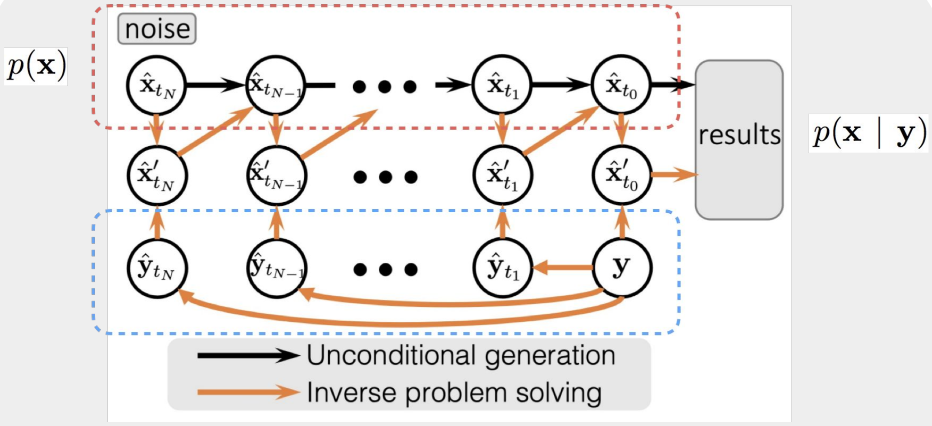
How to enable diffusion model for solving large-scale inverse problems?

Image credit: https://en.wikipedia.org/wiki/Cardiac_magnetic_resonance_imaging,
https://www.euspaceimaging.com/blog/2020/04/30/30-cm-satellite-imagery-as-an-alternative-to-aerial-data/

Enhance Diffusion Model Efficiency

- Focus on improving model performance
- Achieve impressive results for 2D images

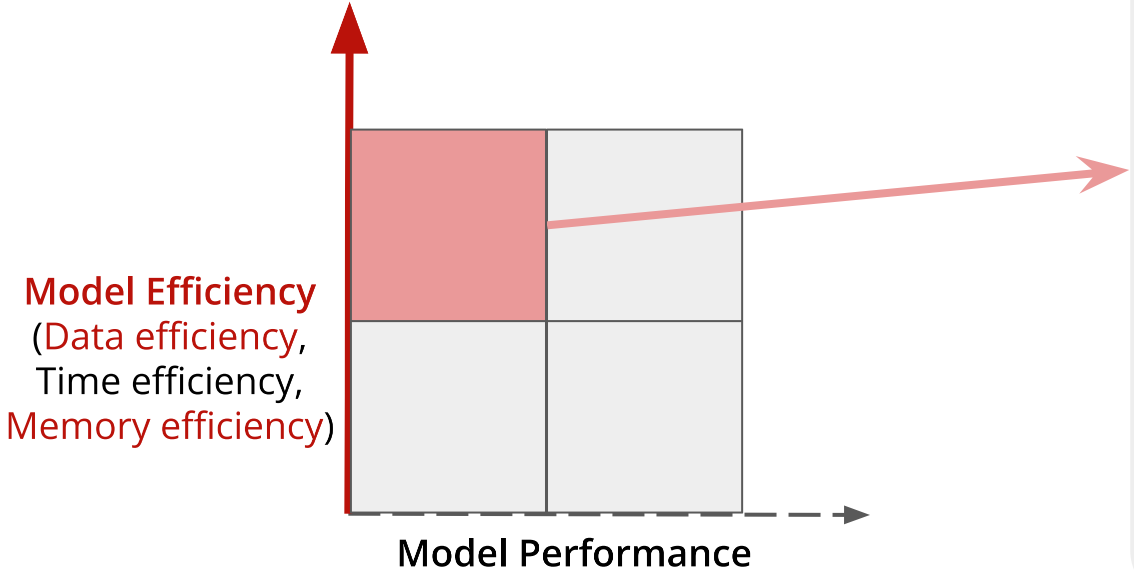


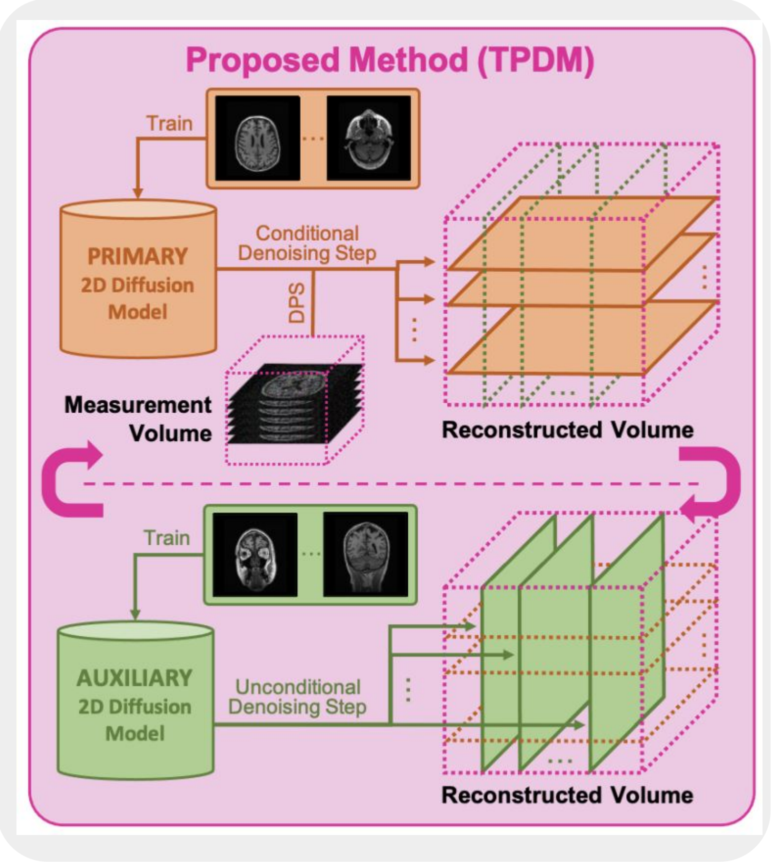


DPS, MCG, DDRM, DDNM, DDS ……

Enhance Diffusion Model Efficiency

- Improve data and memory efficiency for tackling high-dimensional data
  - Solve 3D imaging problems by using 2D diffusion priors





Chung, et al., Solving 3D Inverse Problems using Pre-trained 2D Diffusion Models, CVPR 2023.
Lee, et al., Improving 3D Imaging with Pre-Trained Perpendicular 2D Diffusion Models, ICCV 2023

DiffusionMBIR: Model-based Iterative

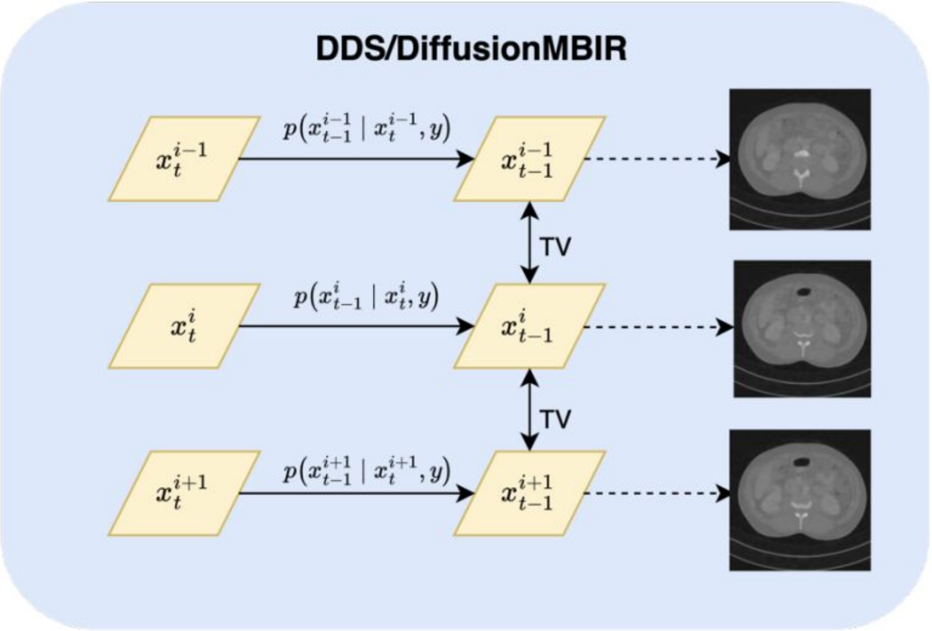
- Solve 3D imaging problems by using 2D diffusion priors
- Regularized objective:

$$\min_{\boldsymbol{x}} \frac{1}{2}\|\boldsymbol{y} - \boldsymbol{A}\boldsymbol{x}\|_2^2 + \|\boldsymbol{D}_z \boldsymbol{x}\|_1,$$

- Iterative solver:
  - Parallel denoising for each slice
  - Z-directional TV prior to impose consistency

$$\boldsymbol{x}'_{i-1} \leftarrow \mathrm{Solve}(\boldsymbol{x}_i, \boldsymbol{s}_{\theta^*}),$$

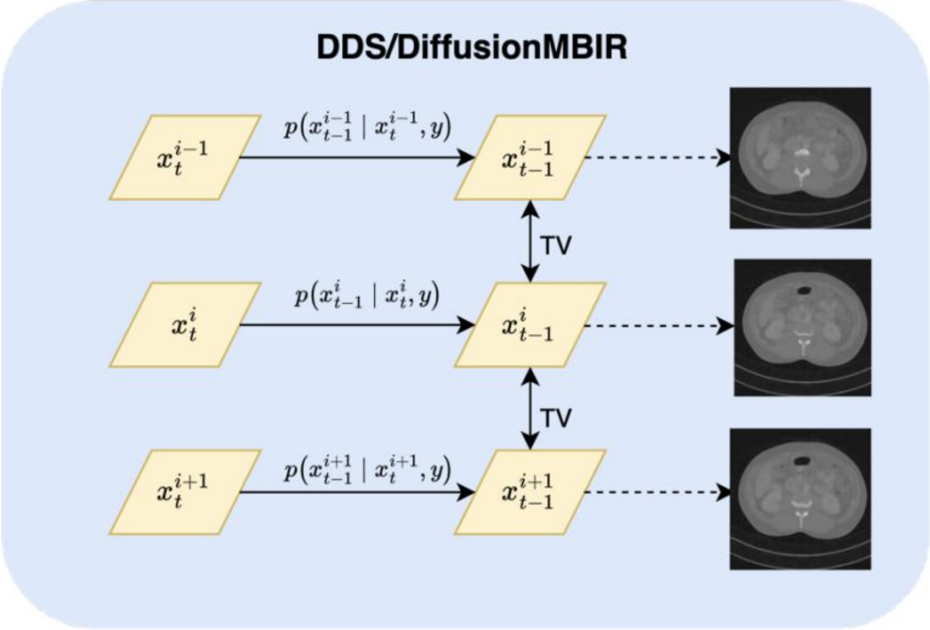
$$\boldsymbol{x}_{i-1} \leftarrow \operatorname*{argmin}_{\boldsymbol{x}'_{i-1}} \frac{1}{2}\|\boldsymbol{y} - \boldsymbol{A}\boldsymbol{x}'_{i-1}\|_2^2 + \|\boldsymbol{D}_z \boldsymbol{x}'_{i-1}\|_1.$$



Chung, et al., Solving 3D Inverse Problems using Pre-trained 2D Diffusion Models, CVPR 2023.

Slice-by-slice Reconstruction with 2D Diffusion Priors

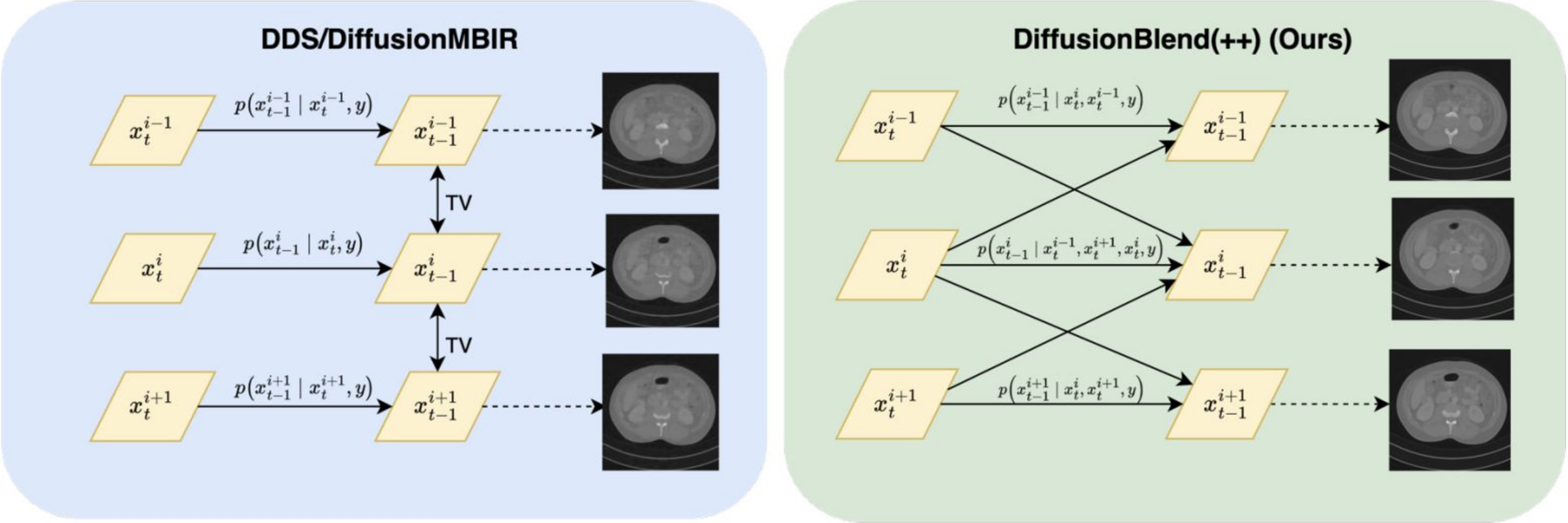
- **Limitation:**
  - Rely on additional regularization or impractical assumption
  - Compromise model performance on cross-slice consistency
  - Increase inference time (TPDM: 24 to 36 hours per volume!)



Song* and Hu*, et al., DiffusionBlend: Learning 3D Image Prior through Position-aware Diffusion Score Blending for 3D Computed Tomography Reconstruction, NeurIPS 2024

DiffusionBlend: Position-aware Diffusion Score Blending

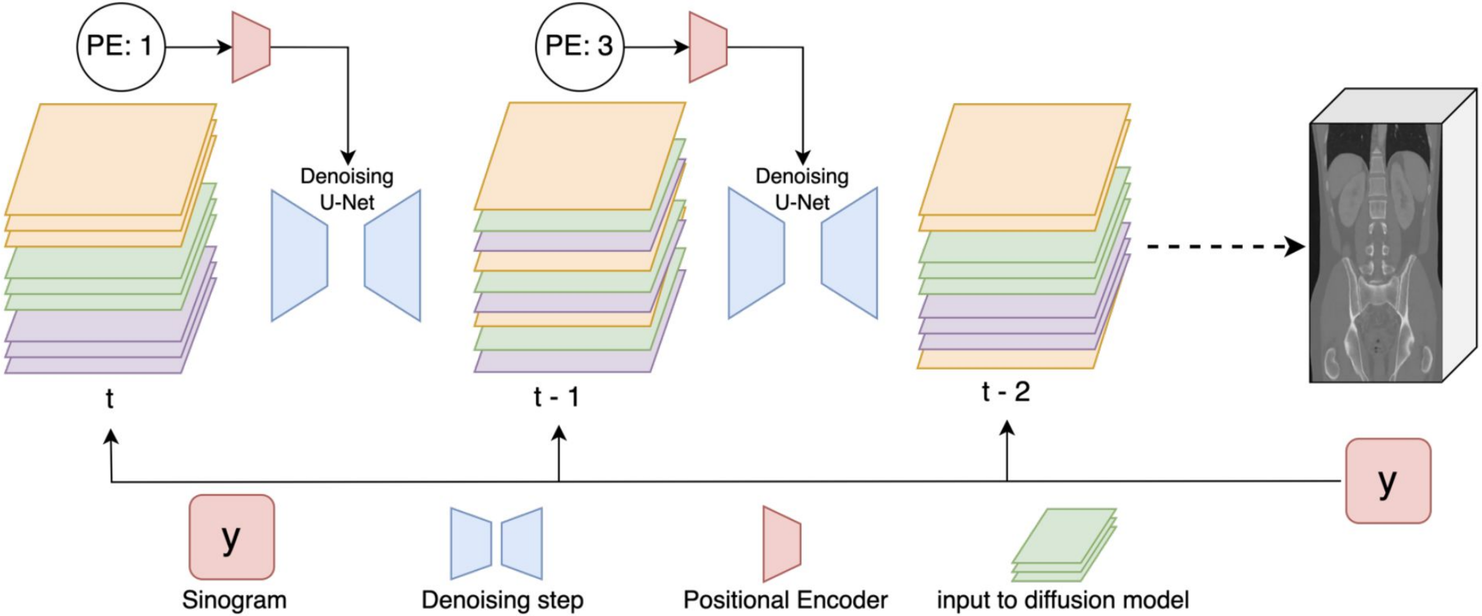
- Learn 3D-patch image prior by incorporating cross-slice dependency
- Blend learned diffusion score between groups of slices



Song* and Hu*, et al., DiffusionBlend: Learning 3D Image Prior through Position-aware Diffusion Score Blending for 3D Computed Tomography Reconstruction, NeurIPS 2024

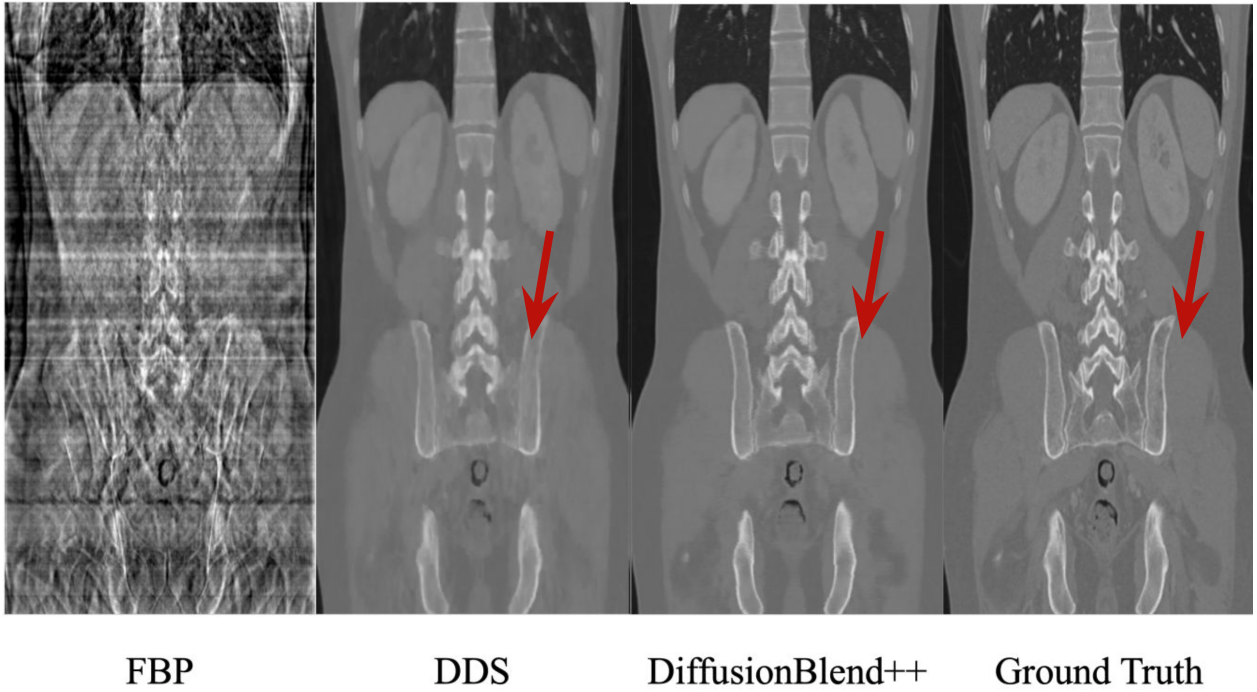
DiffusionBlend: Position-aware Diffusion Score Blending

- Enforce cross-slice consistency for 3D volume without hand-crafted regularization
- Positional encoding: separation between the slices



DiffusionBlend: Position-aware Diffusion Score Blending

- Enable 3D CT reconstruction with high-dimensional 3D image (256×256×500)
- Enhance cross-slice consistency on z-axis



Song* and Hu*, et al., DiffusionBlend: Learning 3D Image Prior through Position-aware Diffusion Score Blending for 3D Computed Tomography Reconstruction, NeurIPS 2024

DiffusionBlend: Position-aware Diffusion Score Blending

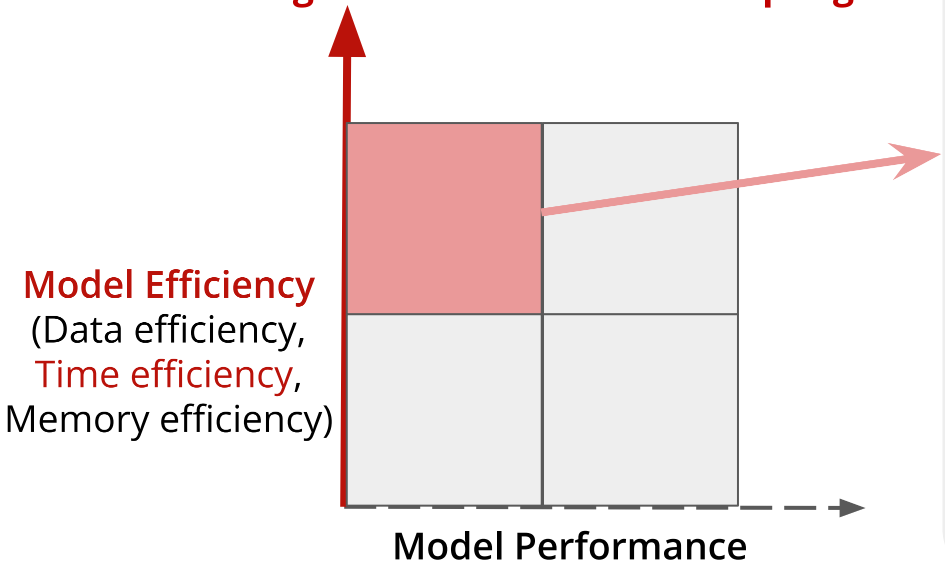
- Achieve SOTA in DIS methods for (ultra-)sparse-view CT reconstruction

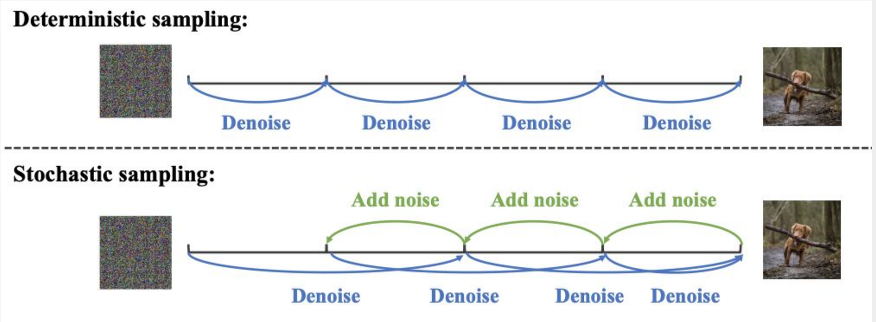
Method	Sparse-View CT Reconstruction on AAPM						Sparse-View CT Reconstruction on LIDC					
	8 views		6 views		4 views		8 Views		6 Views		4 Views	
	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑
FBP	14.64	0.325	13.18	0.268	11.16	0.236	14.78	0.206	14.10	0.181	13.10	0.165
FBP-UNet	27.34	0.878	25.12	0.827	24.10	0.810	28.87	0.858	26.59	0.793	25.37	0.744
DiffusionMBIR	29.86	0.908	28.12	0.875	25.68	0.843	33.29	0.922	31.69	0.903	29.21	0.868
TPDM	-	-	-	-	-	-	28.12	0.833	25.78	0.804	22.29	0.735
DDS 2D	33.64	0.950	32.33	0.939	30.25	0.916	31.60	0.898	29.99	0.871	28.03	0.830
DDS	33.97	0.934	32.95	0.879	30.89	0.932	32.51	0.920	30.83	0.898	27.61	0.828
DiffusionBlend (Ours)	36.45	0.958	35.23	0.952	33.98	0.944	34.47	0.934	31.48	0.908	28.24	0.859
DiffusionBlend++ (Ours)	**37.87**	**0.968**	**36.66**	**0.963**	**34.27**	**0.955**	**35.66**	**0.947**	**33.97**	**0.935**	**31.38**	**0.913**

Song* and Hu*, et al., DiffusionBlend: Learning 3D Image Prior through Position-aware Diffusion Score Blending for 3D Computed Tomography Reconstruction, NeurIPS 2024

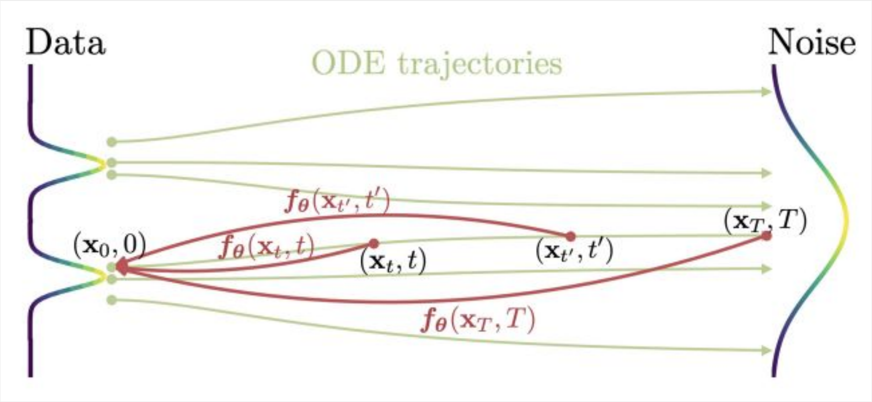
Enhance Diffusion Model Efficiency

- Improve time efficiency
  - Enable sampling as few as 1~4 steps for image generation
  - **How to improve time efficiency for high-dimensional data sampling?**





Distillation of diffusion model



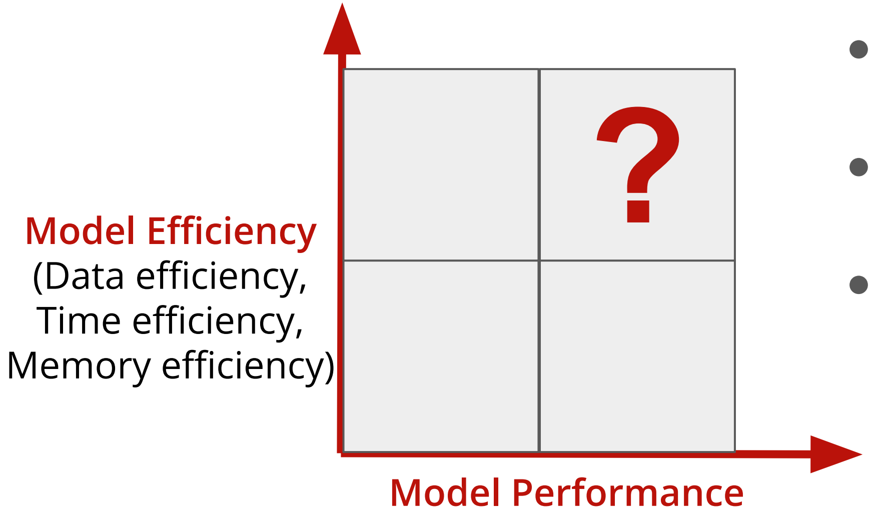
Consistency model

Meng et al., On Distillation of Guided Diffusion Models, CVPR 2023
Song et al., Consistency Models, ICML 2023

Enable Diffusion Model for High-dimensional High-resolution Data

Open Question:

Can we achieve better model efficiency while maintaining model performance?

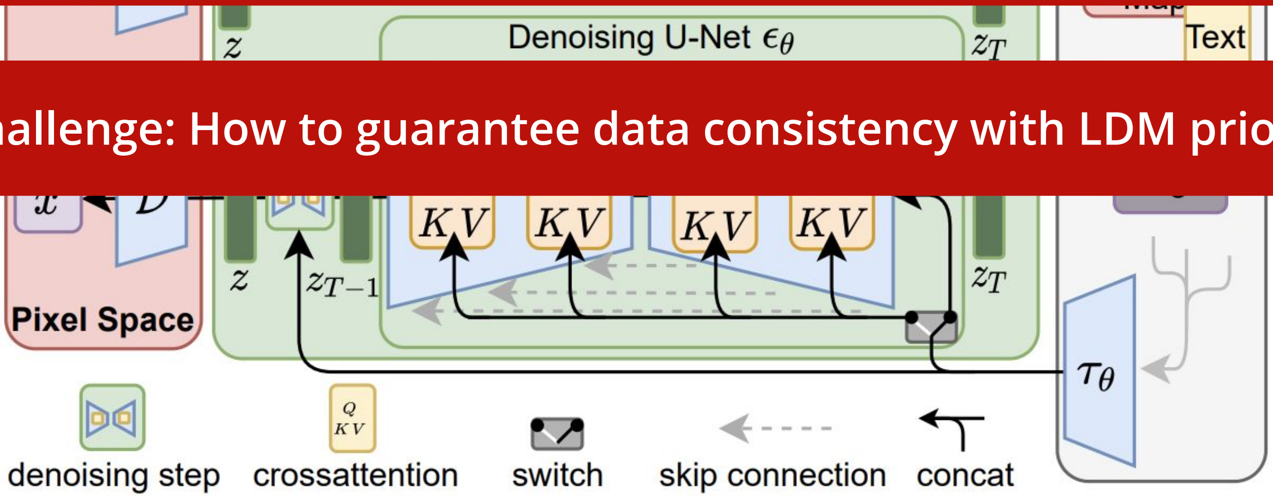


- **Improve data efficiency:**
  - Require less training data
- **Improve memory efficiency:**
  - Reduce memory cost
- **Improve time efficiency:**
  - Faster training/sampling process

Latent Diffusion Model (LDM)

- Train diffusion model in low-dimensional latent space
  - Encoder-decoder models project data to low-dimensional latent space
  - Enable diffusion model training on limited computational resources while retaining quality and flexibility

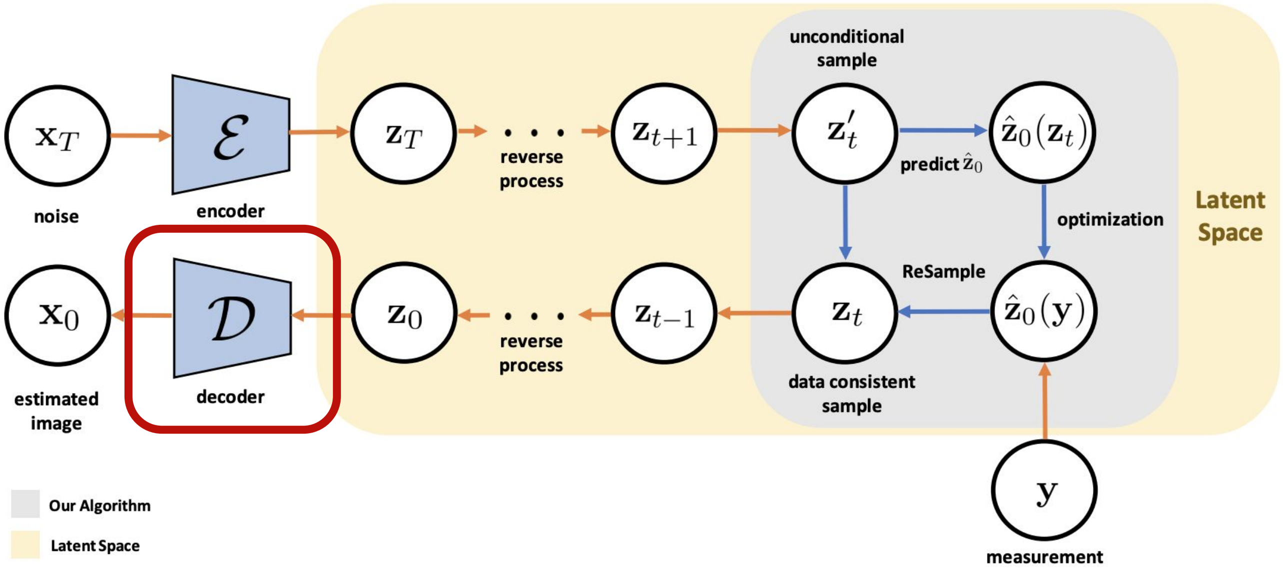
Can the efficient LDMs be used as prior for solving inverse problems?



Challenge: How to guarantee data consistency with LDM prior?

Challenge: Guarantee Data Consistency with LDM

- Non-linearity from pretrained decoder
- ReSample: solve general (linear and nonlinear) inverse problems with pre-trained LDMs

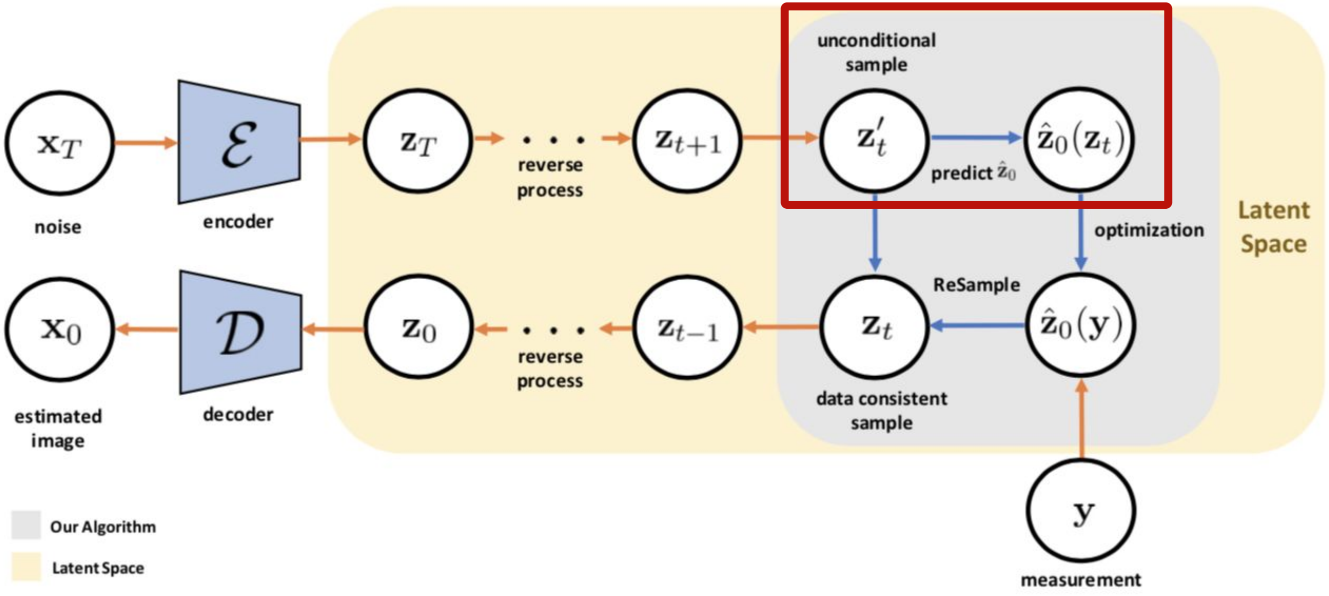


Song* and Kwon* et al., Solving Inverse Problems with Latent Diffusion Models via Hard Data Consistency, ICLR 2024

ReSample

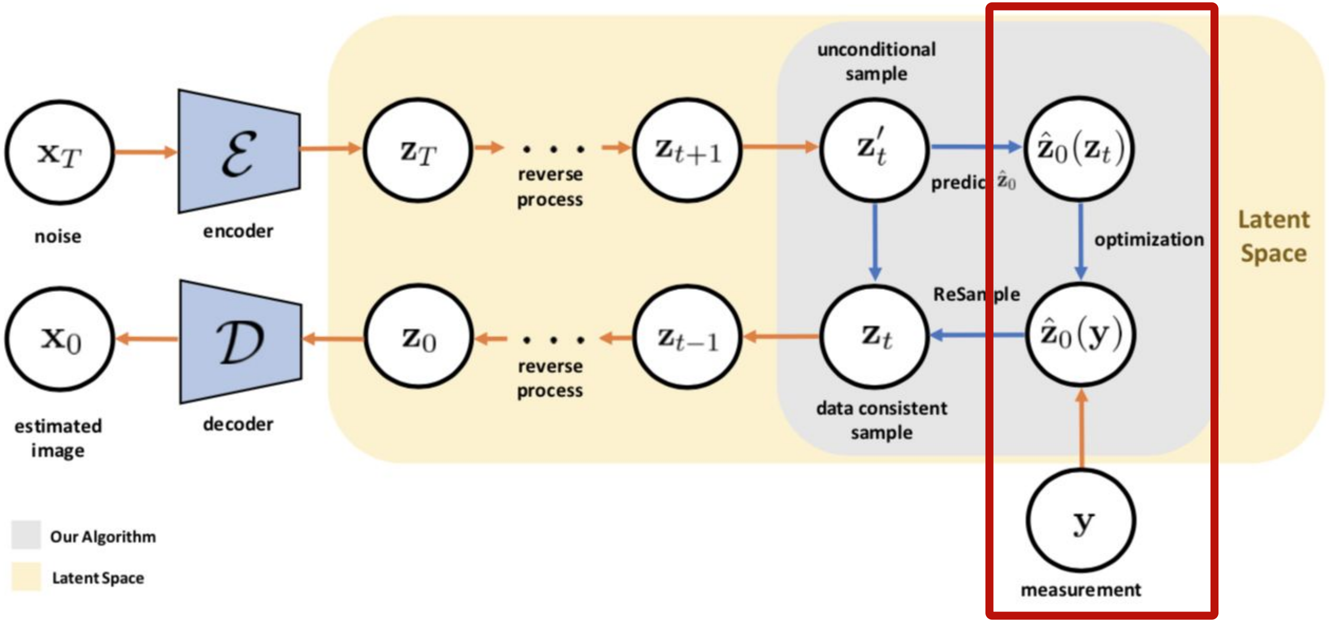
- Posterior mean estimation:

$$\hat{\mathbf{z}}_0(\mathbf{z}_t) = \mathbb{E}[\mathbf{z}_0|\mathbf{z}_t] = \frac{1}{\sqrt{\bar{\alpha}_t}}(\mathbf{z}_t + (1-\bar{\alpha}_t)\nabla \log p(\mathbf{z}_t))$$



ReSample

- Optimization objective: $$\hat{\mathbf{z}}_0(\mathbf{y}) = \arg\min_{\mathbf{z}} \left(\frac{1}{2}\|\mathbf{y} - \mathcal{A}(\mathcal{D}(\mathbf{z}))\|_2^2\right)$$

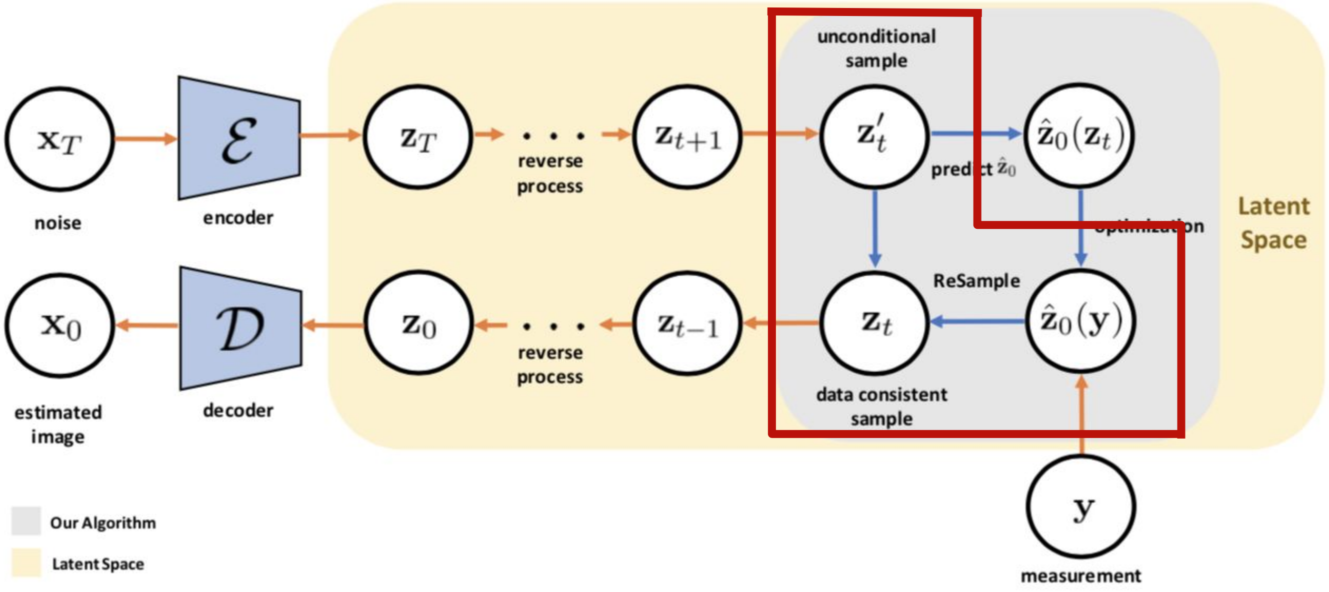


Song* and Kwon* et al., Solving Inverse Problems with Latent Diffusion Models via Hard Data Consistency, ICLR 2024

ReSample

- Stochastic resampling combines prior consistency and data consistency

$$\mathbf{z}_t = \text{StochasticResample}(\hat{\mathbf{z}}_0(\mathbf{y}), \mathbf{z}'_t, \gamma)$$



ReSample

Proposition 1 (Stochastic Encoding). *Since the sample $\hat{\mathbf{z}}_t$ given $\hat{\mathbf{z}}_0(\mathbf{y})$ and measurement $\mathbf{y}$ is conditionally independent of $\mathbf{y}$, we have that*

$$p(\hat{\mathbf{z}}_t|\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y}) = p(\hat{\mathbf{z}}_t|\hat{\mathbf{z}}_0(\mathbf{y})) = \mathcal{N}(\sqrt{\bar{\alpha}_t}\hat{\mathbf{z}}_0(\mathbf{y}), (1-\bar{\alpha}_t)\mathbf{I}).$$

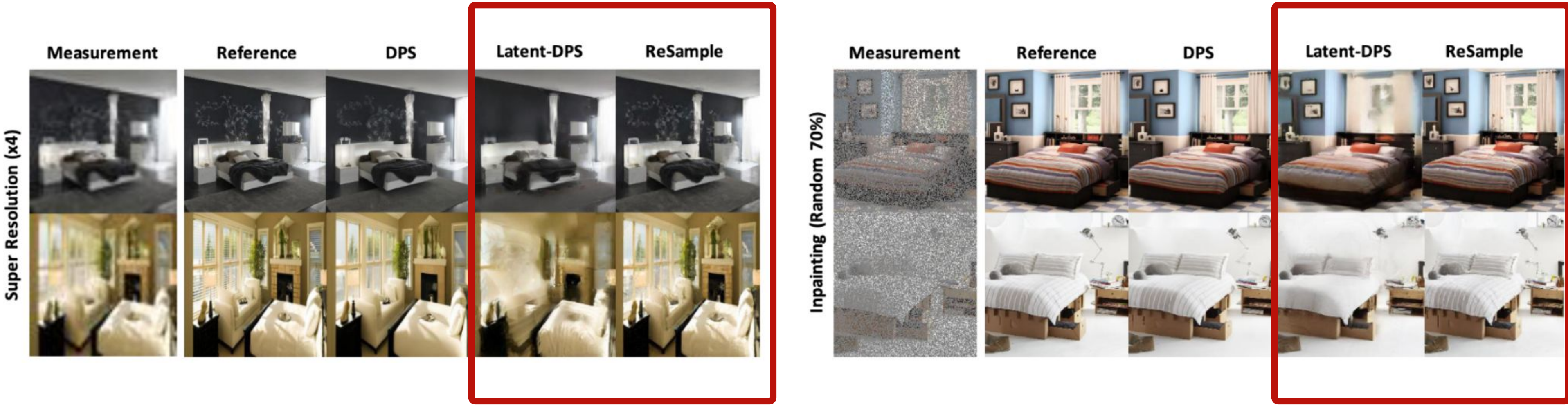
Proposition 2 (Stochastic Resampling). *Suppose that $p(\mathbf{z}'_t|\hat{\mathbf{z}}_t,\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y})$ is normally distributed such that $p(\mathbf{z}'_t|\hat{\mathbf{z}}_t,\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y}) = \mathcal{N}(\mu_t,\sigma_t^2)$. If we let $p(\hat{\mathbf{z}}_t|\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y})$ be a prior for μ_t, then the posterior distribution $p(\hat{\mathbf{z}}_t|\mathbf{z}'_t,\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y})$ is given by*

$$p(\hat{\mathbf{z}}_t|\mathbf{z}'_t,\hat{\mathbf{z}}_0(\mathbf{y}),\mathbf{y}) = \mathcal{N}\left(\frac{\sigma_t^2\sqrt{\bar{\alpha}_t}\hat{\mathbf{z}}_0(\mathbf{y}) + (1-\bar{\alpha}_t)\mathbf{z}'_t}{\sigma_t^2+(1-\bar{\alpha}_t)}, \frac{\sigma_t^2(1-\bar{\alpha}_t)}{\sigma_t^2+(1-\bar{\alpha}_t)}\mathbf{I}\right).$$

Hyperparameter controlling the tradeoff between data consistency and prior consistency

ReSample

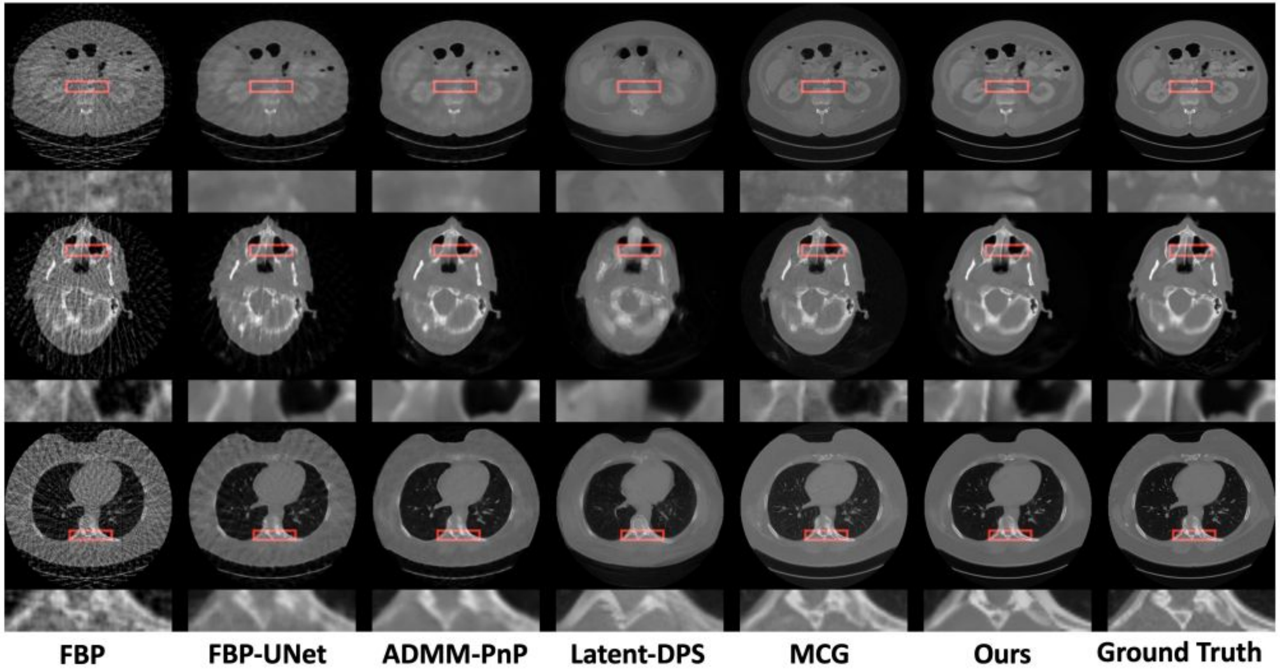
- **Results in natural images:**
  - Tasks: super resolution, inpainting, Gaussian deblurring, non-linear deblurring
  - Datasets: FFHQ dataset, CelebA-HQ dataset, LSUN-Bedroom dataset



Song* and Kwon* et al., Solving Inverse Problems with Latent Diffusion Models via Hard Data Consistency, ICLR 2024

ReSample

- Data efficiency: use pre-trained encoder / decoder from natural images
- Fine-tune latent diffusion models using 2000 CT images



Song* and Kwon* et al., Solving Inverse Problems with Latent Diffusion Models via Hard Data Consistency, ICLR 2024

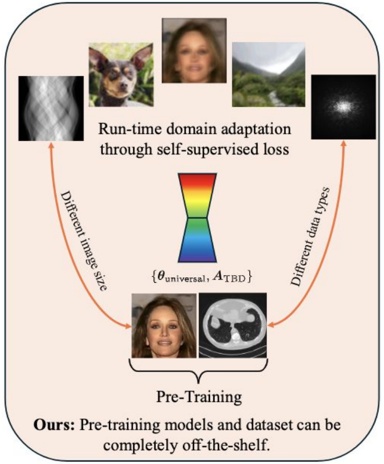
ReSample

- Achieve SOTA results for sparse-view CT image reconstruction using low-dimensional prior in latent space
- Outperform pixel-space diffusion models trained with more data samples

Method	Abdominal		Head		Chest	
	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑
Latent-DPS	26.80 ±1.09	0.870 ±0.026	28.64 ±5.38	0.893 ±0.058	25.67±1.14	0.822 ±0.033
MCG (Chung et al., 2022)	29.41 ±3.14	0.857 ±0.041	28.28 ±3.08	0.795 ±0.116	27.92 ±2.48	0.842 ±0.036
DPS (Chung et al., 2023a)	27.33 ±2.68	0.715 ± 0.031	24.51 ±2.77	0.665 ±0.058	24.73 ±1.84	0.682 ±0.113
PnP-UNet (Gilton et al., 2021)	32.84 ±1.29	0.942 ±0.008	33.45 ±3.25	0.945 ±0.023	29.67 ±1.14	0.891 ±0.011
FBP	26.29 ±1.24	0.727 ±0.036	26.71 ±5.02	0.725 ±0.106	24.12 ±1.14	0.655 ±0.033
FBP-UNet (Jin et al., 2017)	32.77 ±1.21	0.937 ±0.013	31.95 ±3.32	0.917 ±0.048	29.78 ±1.12	0.885 ±0.016
ReSample (Ours)	**35.91** ±1.22	**0.965** ±0.007	**37.82** ±5.31	**0.978** ±0.014	**31.72** ±0.912	**0.922** ±0.011

Song* and Kwon* et al., Solving Inverse Problems with Latent Diffusion Models via Hard Data Consistency, ICLR 2024

Challenges of Diffusion Inverse Solvers in Scientific Applications

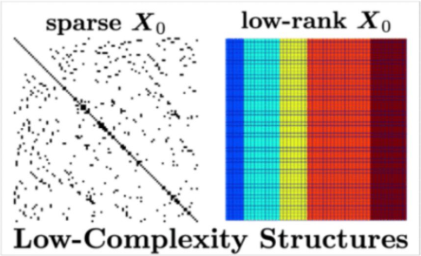


Efficiency

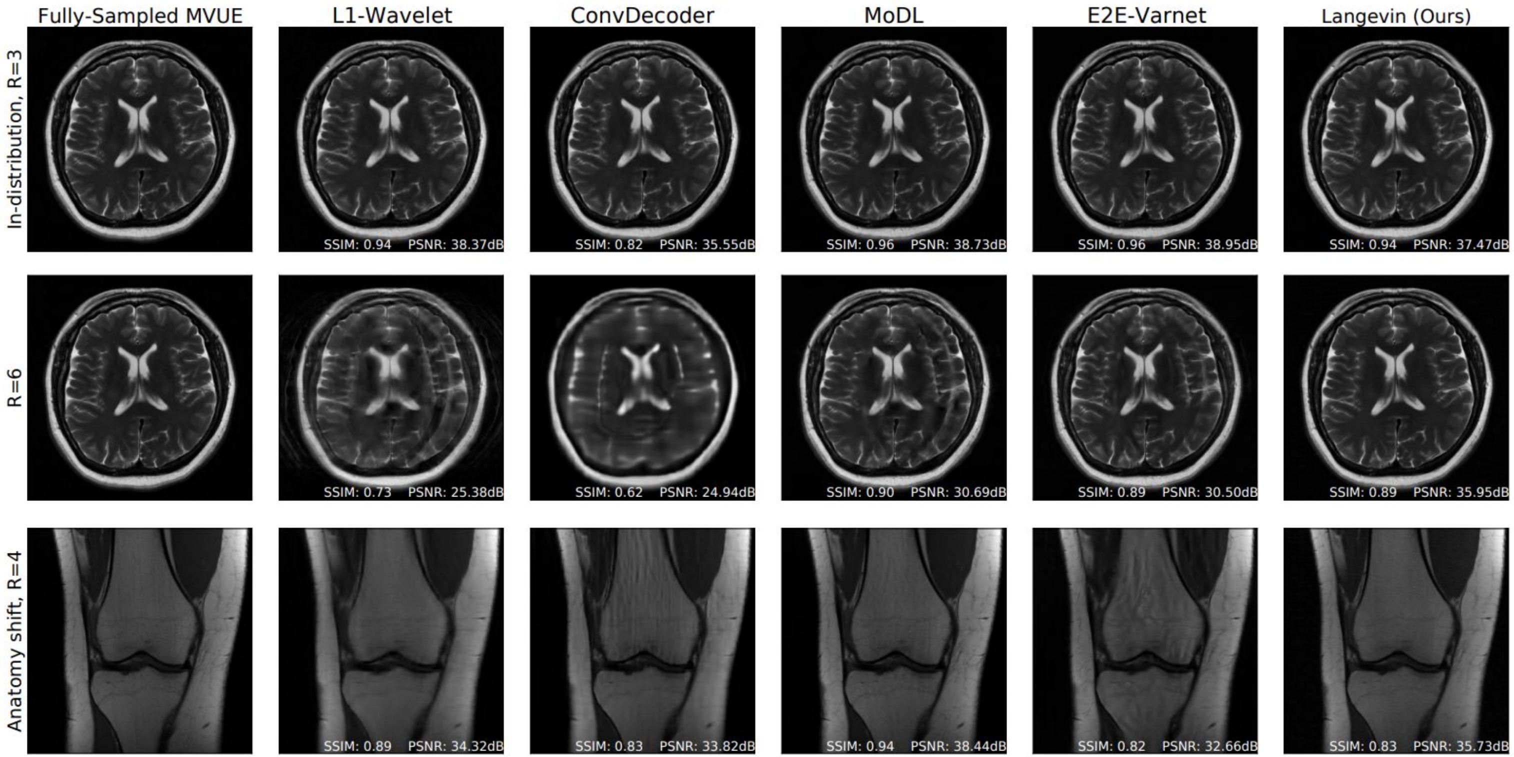
(Scientific) Applications

Generalizability

Controllability



Generalizability of Diffusion Priors

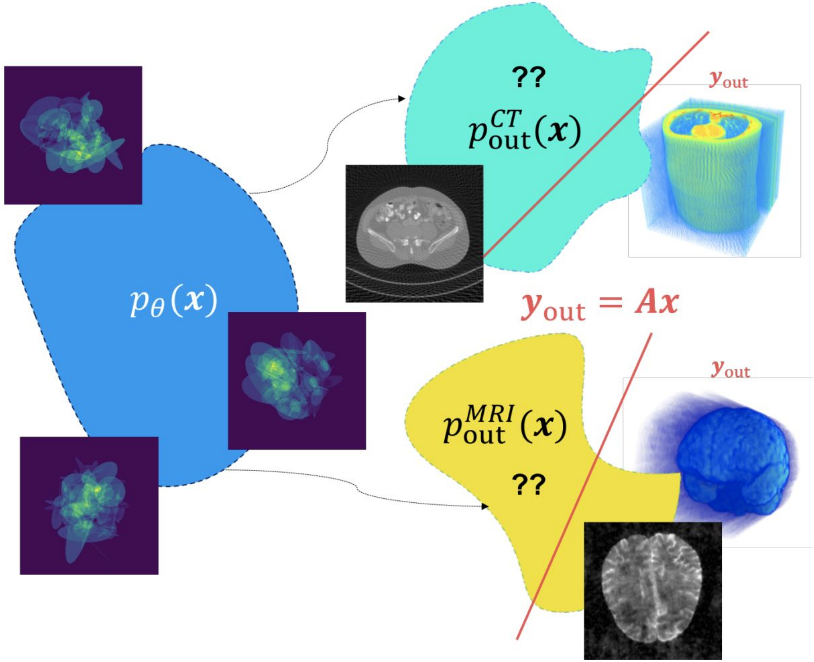


How generalizable is the learned diffusion prior?

Jalal et al., Robust Compressed Sensing MRI with Deep Generative Priors, NeurIPS, 2021

Out-of-Distribution (OOD) Inverse Problems

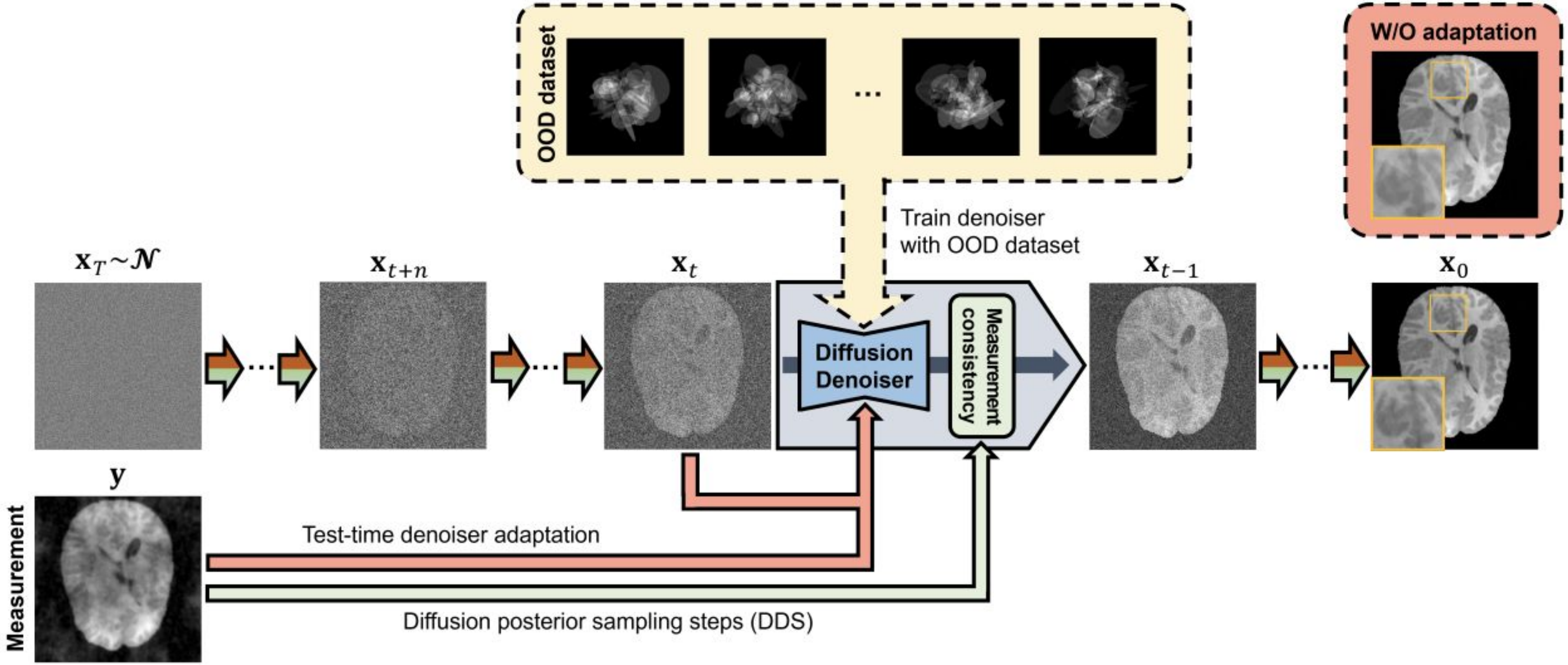
- Pretrained diffusion model learns prior
- At test-time, obtain measurements from unknown OOD distributions



Chung, et al., Deep Diffusion Image Prior for Efficient OOD Adaptation in 3D Inverse Problems, ECCV 2024

Steerable Conditional Diffusion for OOD Adaptation

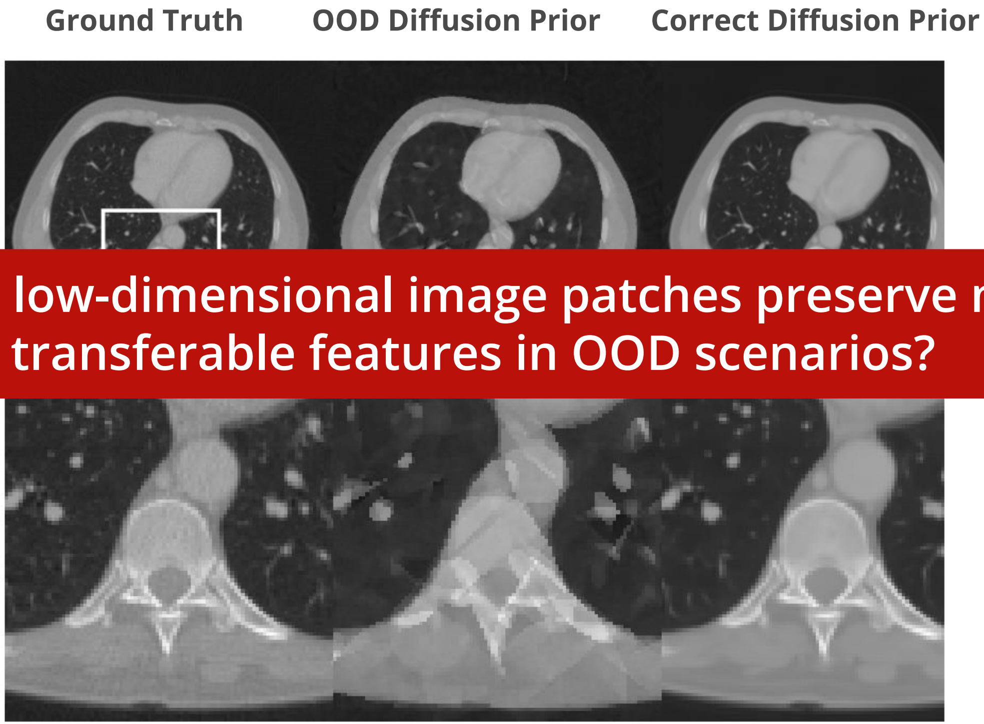
- Self-supervised loss for LoRA adaptation
- Enables DIS model adaptation for OOD tasks using a single corrupted measured data



Barbano, et al., Steerable Conditional Diffusion for Out-of-Distribution Adaptation in Medical Image Reconstruction, TMI 2025

Steerable Conditional Diffusion for OOD Adaptation

- Training: synthetic ellipses images
- Test: computed tomography images

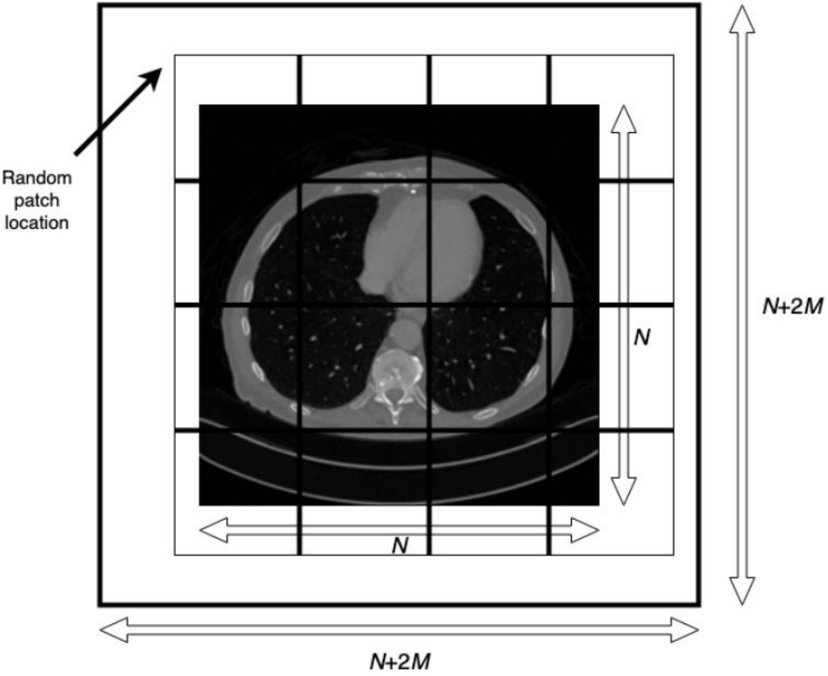


Would low-dimensional image patches preserve more transferable features in OOD scenarios?

Barbano, et al., Steerable Conditional Diffusion for Out-of-Distribution Adaptation in Medical Image Reconstruction, TMI 2025

PaDIS: Patch-based Diffusion Inverse Solver

- Learn score function of whole image through scores of patches with positional encoding
- Zero-padding boundary region to enable shifting patch locations



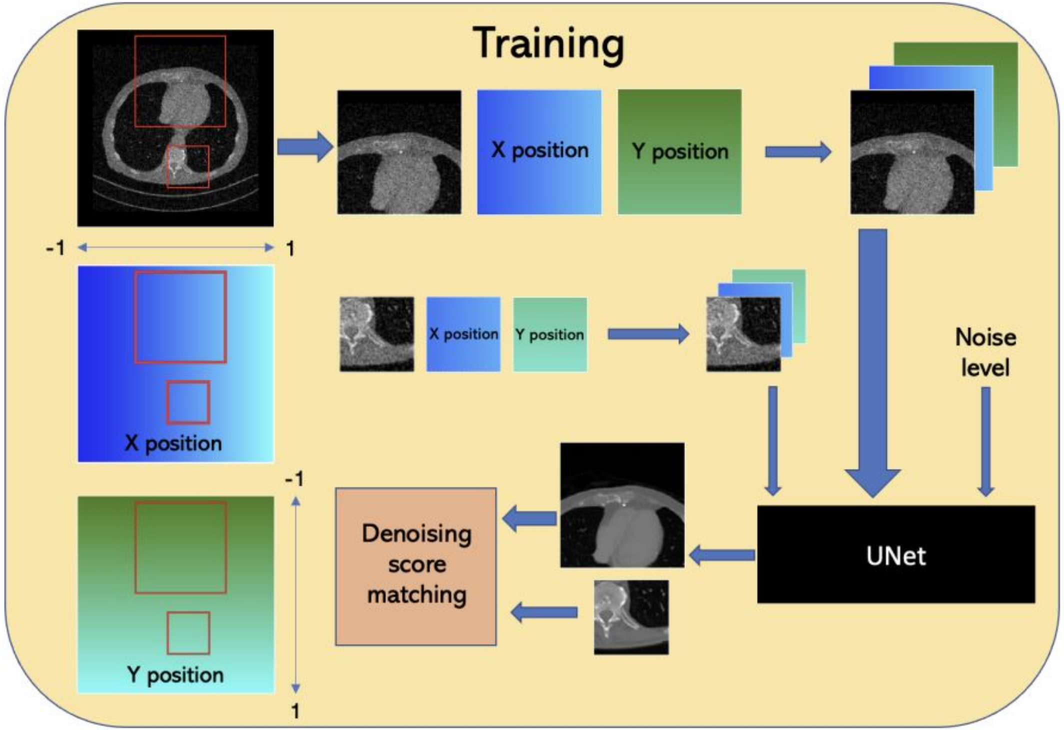
$$p(\boldsymbol{x}) = \prod_{i,j=1}^{i,j=M} p_{i,j,B}(\boldsymbol{x}_{i,j,B}) \prod_{r=1}^{(k+1)^2} p_{i,j,r}(\boldsymbol{x}_{i,j,r})/Z,$$

$$\nabla \log p(\boldsymbol{x}) = \sum_{i,j=1}^{i,j=M} \left(\boldsymbol{s}_{i,j,B}(\boldsymbol{x}_{i,j,B}) + \sum_{r=1}^{(k+1)^2} \boldsymbol{s}_{i,j,r}(\boldsymbol{x}_{i,j,r}) \right)$$

Hu, et al., Learning Image Priors through Patch-based Diffusion Models for Solving Inverse Problems, NeurIPS 2024

PaDIS: Patch-based Diffusion Inverse Solver

- Improve training efficiency

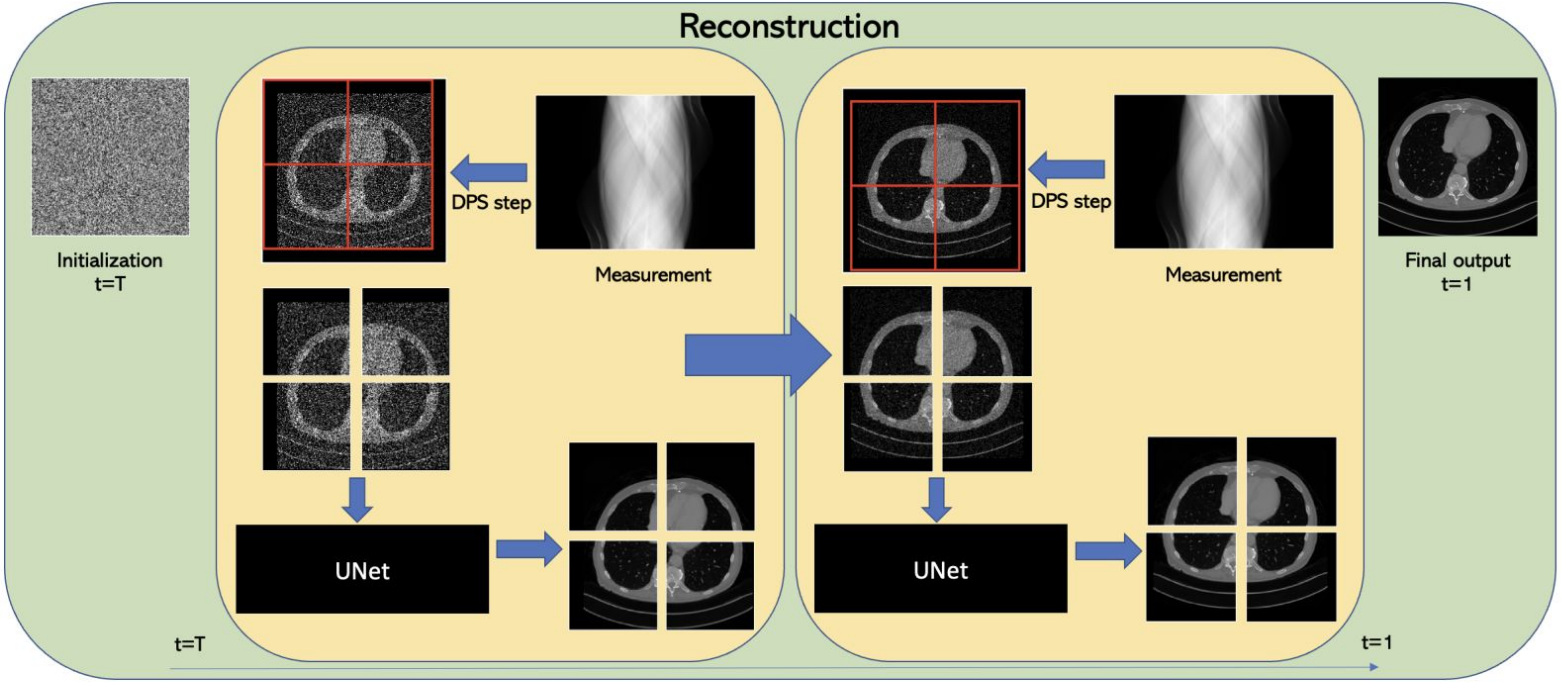


- Memory efficiency
  - Only input image patches
- Data efficiency
  - 2000~3000 training samples
- Training Time efficiency
  - Patch image model: ~12 hours
  - Whole image model: 24~36 hours

Hu, et al., Learning Image Priors through Patch-based Diffusion Models for Solving Inverse Problems, NeurIPS 2024

PaDIS: Patch-based Diffusion Inverse Solver

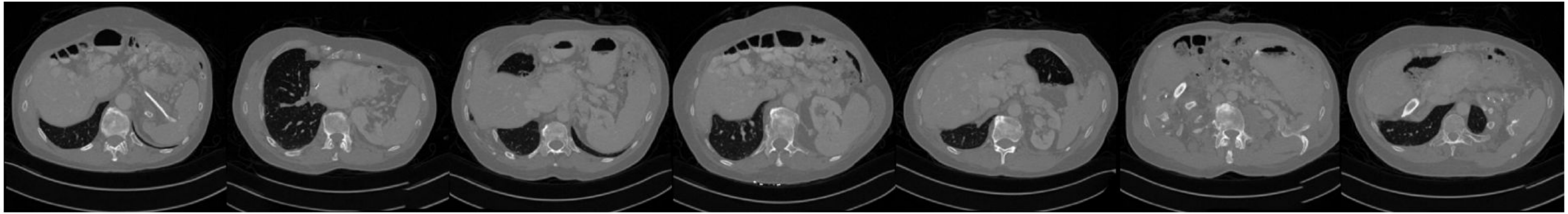
- Random partition in each sampling step
- No boundary artifacts because of shifting patch locations



Hu, et al., Learning Image Priors through Patch-based Diffusion Models for Solving Inverse Problems, NeurIPS 2024

PaDIS: Patch-based Diffusion Inverse Solver

- Generate entire images via positional encoding



Hu, et al., Learning Image Priors through Patch-based Diffusion Models for Solving Inverse Problems, NeurIPS 2024

PaDIS: Patch-based Diffusion Inverse Solver

- For in-distribution inverse problems
- Comparable or even better results as whole-image DIS models

Method	CT, 20 Views		CT, 8 Views		Deblurring		Superresolution	
	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑
Baseline	24.93	0.595	21.39	0.415	24.54	0.688	25.86	0.739
ADMM-TV	26.82	0.724	23.09	0.555	28.22	0.792	25.66	0.745
PnP-ADMM [42]	26.86	0.607	22.39	0.489	28.82	0.818	26.61	0.785
PnP-RED [46]	27.99	0.622	23.08	0.441	29.91	0.867	26.36	0.766
Whole image diffusion	32.84	0.835	25.74	0.706	30.19	0.853	29.17	0.827
Langevin dynamics [1]	33.03	0.846	27.03	0.689	30.60	0.867	26.83	0.744
Predictor-corrector [19]	32.35	0.820	23.65	0.546	28.42	0.724	26.97	0.685
VE-DDNM [7]	31.98	0.861	27.71	0.759	-	-	26.01	0.727
Patch Averaging [23]	33.35	0.850	28.43	0.765	29.41	0.847	27.67	0.802
Patch Stitching [66]	32.87	0.837	26.71	0.710	29.69	0.849	27.50	0.780
PaDIS (Ours)	**33.57**	**0.854**	**29.48**	**0.767**	**30.80**	**0.870**	**29.47**	**0.846**

Hu, et al., Learning Image Priors through Patch-based Diffusion Models for Solving Inverse Problems, NeurIPS 2024

PaDIS: Patch-based Diffusion Inverse Solver

- For out-of-distribution (OOD) inverse problems with mismatching distribution (training data: synthetic ellipses, testing data: CT images)
- Low-dimensional patch-based diffusion model training enhance generalization and robustness for OOD tasks

Method	CT, 20 Views		CT, 60 Views		Deblurring		Superresolution	
	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑	PSNR↑	SSIM↑
Baseline	24.93	0.613	30.15	0.784	23.93	0.666	25.42	0.724
ADMM-TV	26.81	0.750	31.14	0.862	27.58	0.773	25.22	0.729
PnP-ADMM (Xu et al., 2020)	30.20	0.838	36.75	0.932	28.98	0.815	27.29	0.796
PnP-RED (Hu et al., 2022)	27.12	0.682	32.68	0.876	28.37	0.793	27.73	0.809
Whole image, naive	28.11	0.800	33.10	0.911	25.85	0.742	25.65	0.742
Patches, naive (Hu et al., 2024)	27.44	0.719	33.97	0.934	26.77	0.782	26.12	0.759
Self-supervised, whole (Barbano et al., 2023)	33.19	0.861	40.47	0.957	29.50	0.831	27.07	0.701
Self-supervised, patch (Ours)	**33.77**	**0.874**	**41.45**	**0.969**	**30.34**	**0.860**	**28.10**	**0.827**
Whole image, correct*	33.99	0.886	41.67	0.969	29.87	0.851	28.33	0.801
Patches, correct*	34.02	0.889	41.70	0.967	30.12	0.865	28.49	0.835

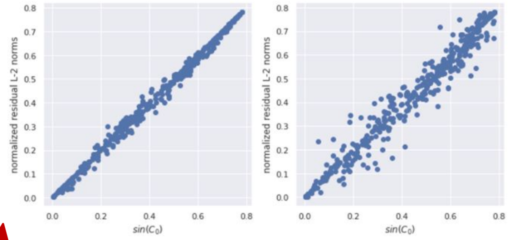
*not available in practice for mismatched distribution inverse problems

Hu, et al., Test-Time Adaptation Improves Inverse Problem Solving with Patch-Based Diffusion Models, TCI 2025

Challenges of Diffusion Inverse Solvers in Scientific Applications

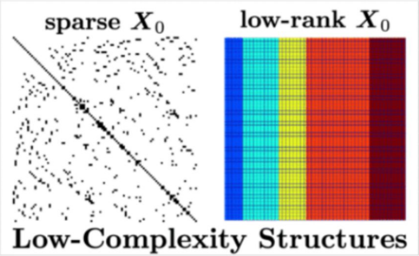
Efficiency

(Scientific) Applications



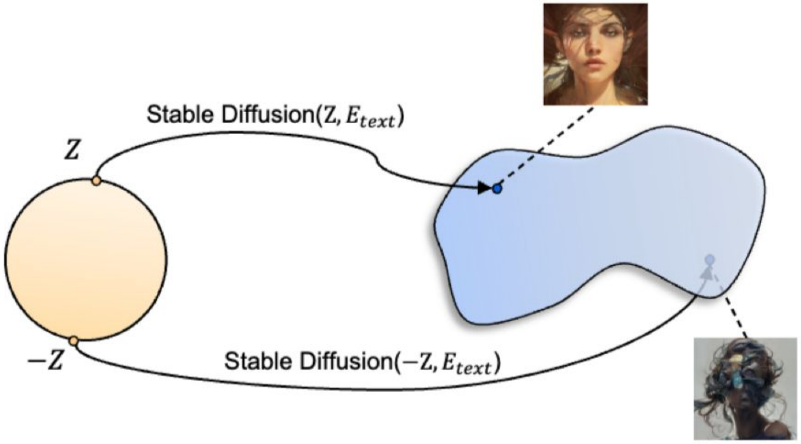
Generalizability

Controllability

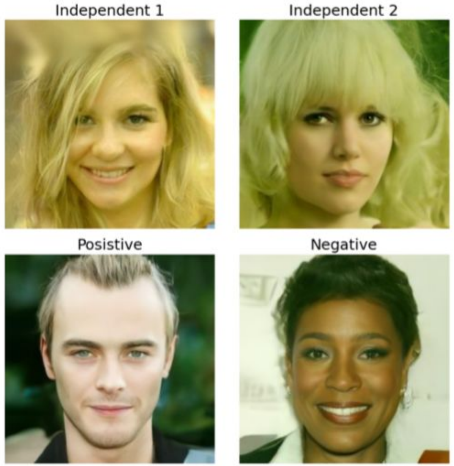


Motivations

- Diffusion models provide potential sampling from posterior distribution
- **Initial noise space of diffusion model offers an inherent (low-dimensional) latent structures of high-dimensional data!**



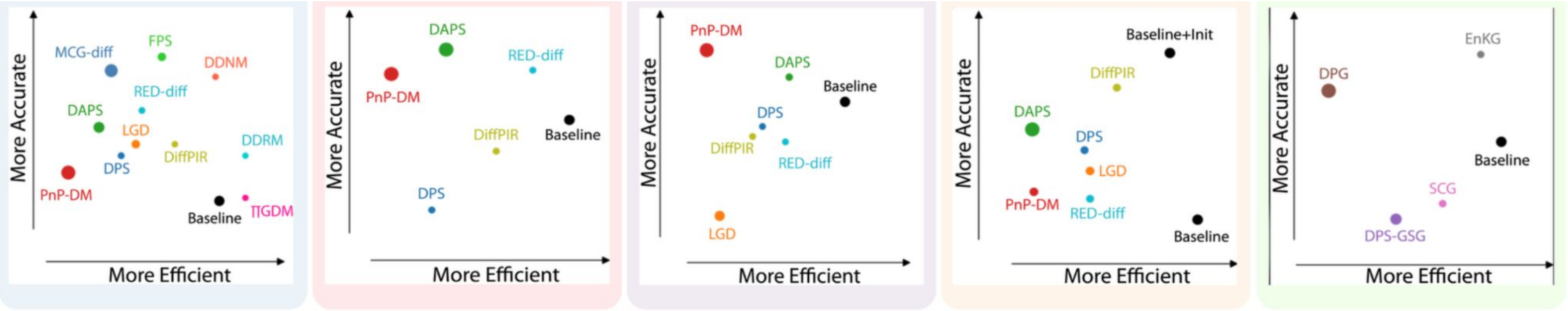
(a) Stable Diffusion



(b) CelebA-HQ

Motivations

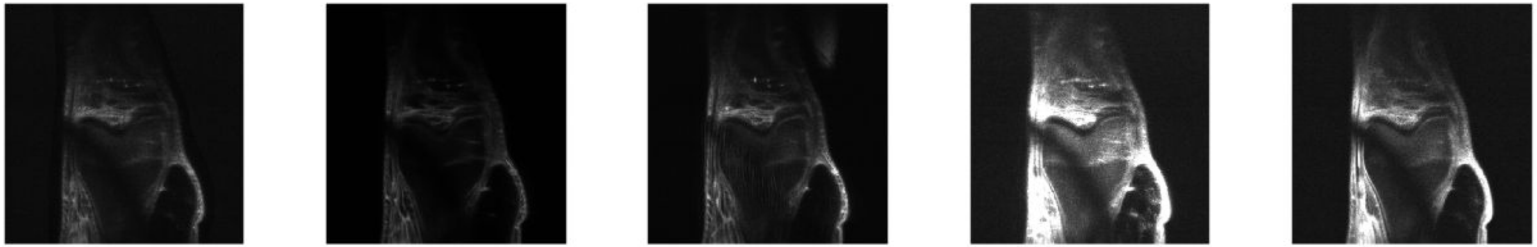
- Diffusion models provide potential sampling from posterior distribution
- **Initial noise space of diffusion model offers an inherent (low-dimensional) latent structures of high-dimensional data!**
- Uncertainty estimation is desired in real-world applications
  - Existing benchmarks focus on measuring accuracy of a random sample against groundtruth



Zheng et al., InverseBench: Benchmarking Plug-and-Play Diffusion Models for Inverse Problems in Physical Sciences, ICLR 2025.

Motivations

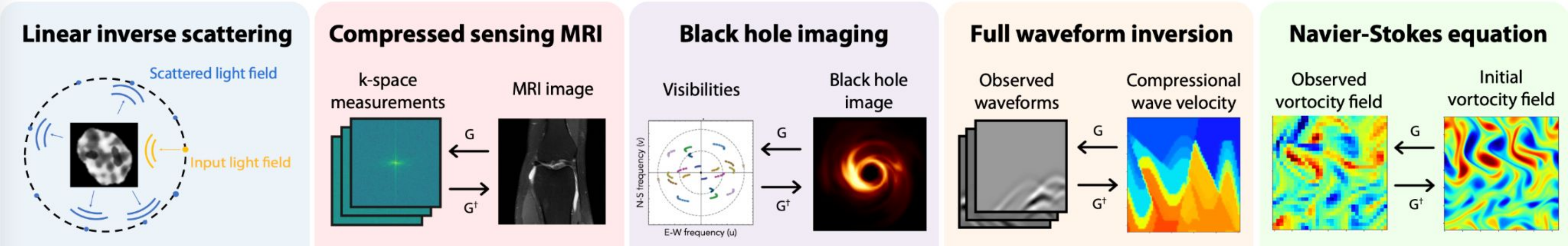
- Diffusion models provide potential sampling from posterior distribution
- **Initial noise space of diffusion model offers an inherent (low-dimensional) latent structures of high-dimensional data!**
- Uncertainty estimation is desired in real-world applications
  - Existing benchmarks focus on measuring accuracy of a random sample against groundtruth
  - Diffusion posterior sampling from initial noise space offers more statistical information about sampled posterior distribution



Motivations

- Diffusion models provide sampling from posterior distribution
- Initial noise space of diffusion model offers an inherent low-dimensional latent structures of high-dimensional data!
- Scientific applications always require to control sampled data satisfying certain (physical) constraints

How to guarantee controllable and constrained sampling with diffusion models?



Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Controllable and Constrained Sampling: Toy Example

- Given a target image, how to conduct constrained sampling around target image with controlled mean and variance

Target Image

Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Controllable and Constrained Sampling: Toy Example

- **Exploring initial noise perturbation with a controller algorithm can achieve this constrained sampling!**

Target Image

Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

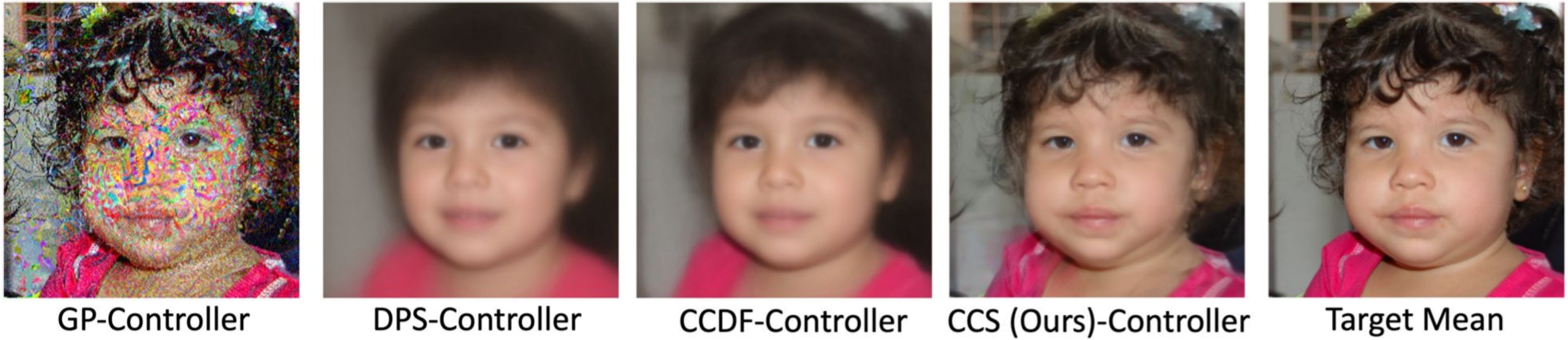
Controllable and Constrained Sampling: Toy Example

- Despite diverse samples, the sample mean closely matches the desired target image (at the constrained distance)

Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

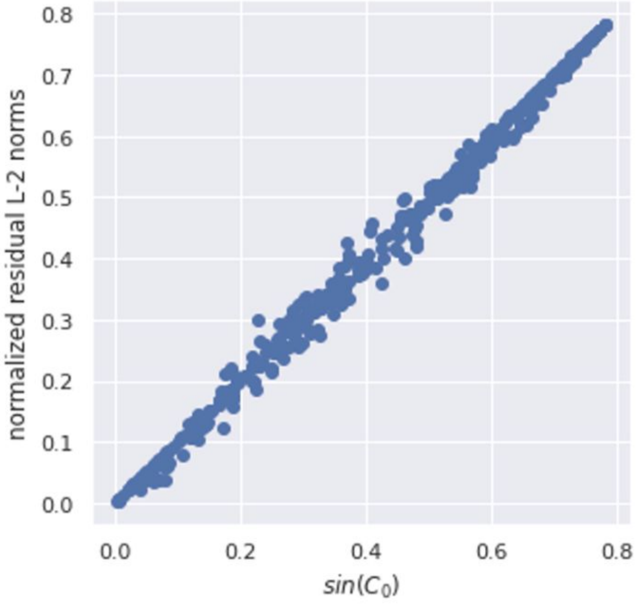
Controllable and Constrained Sampling: Toy Example

- Compared with other methods, CCS gives sample mean that better matches the desired target image (at the constrained distance)

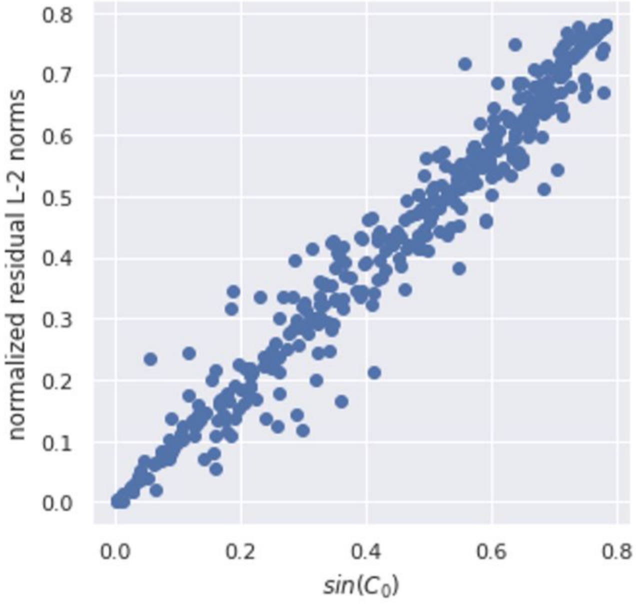


Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

- Linearity between the magnitude of initial noise perturbation and sample-target image distance



FFHQ dataset with pixel diffusion model

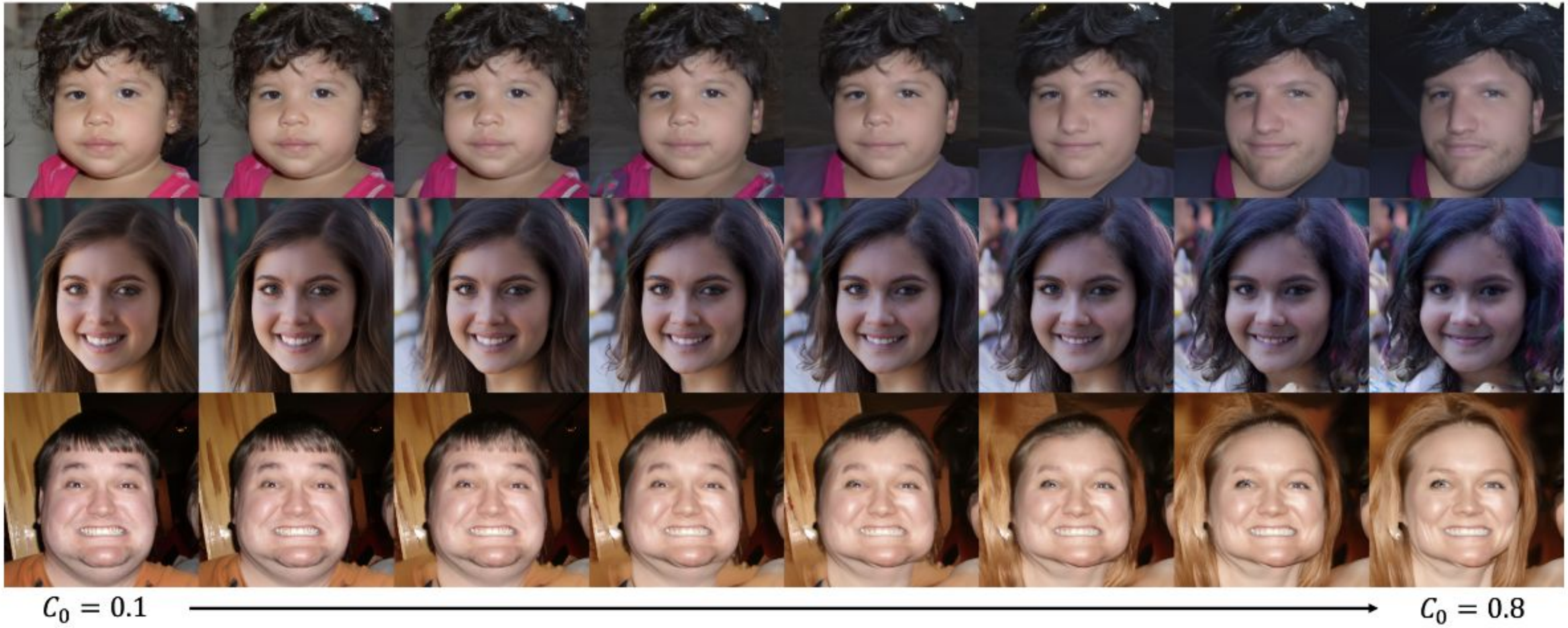


Celeba-HQ dataset with latent diffusion model

Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Controllable and Constrained Sampling with Diffusion Models

- Linearity when increasing the magnitude of initial noise perturbation



Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

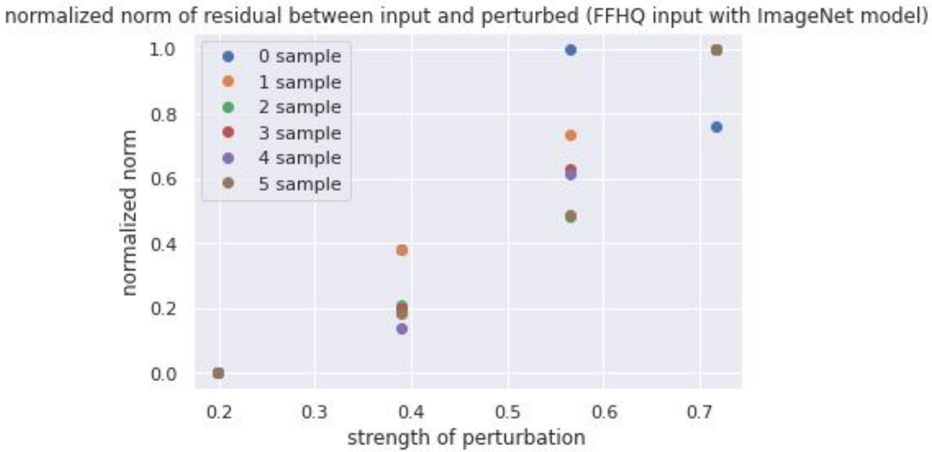
Implications of the Linearity Score

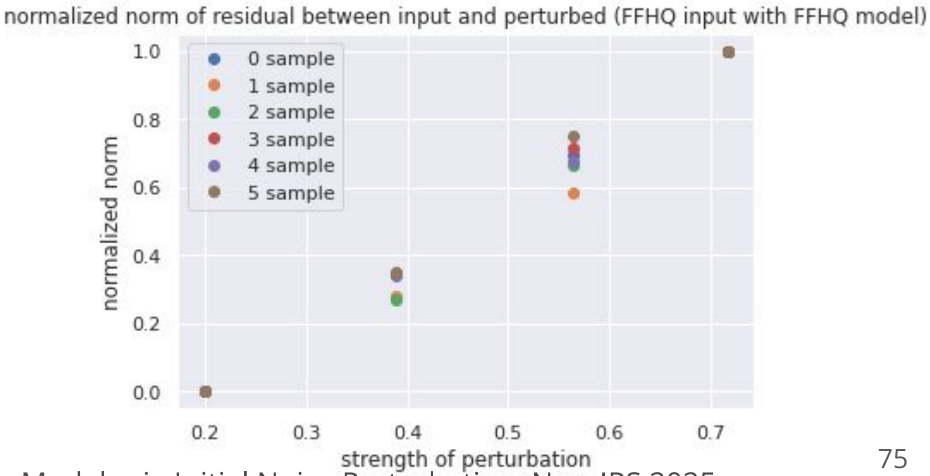
- However, the linearity of perturbation for different centers is different across initial noise manifold

Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Implications of the Linearity Score

- However, the linearity of perturbation for different centers is different across initial noise manifold
- Out-of-distribution (OOD) data shows lower linearity score
    - OOD data lies on a low-probability manifold

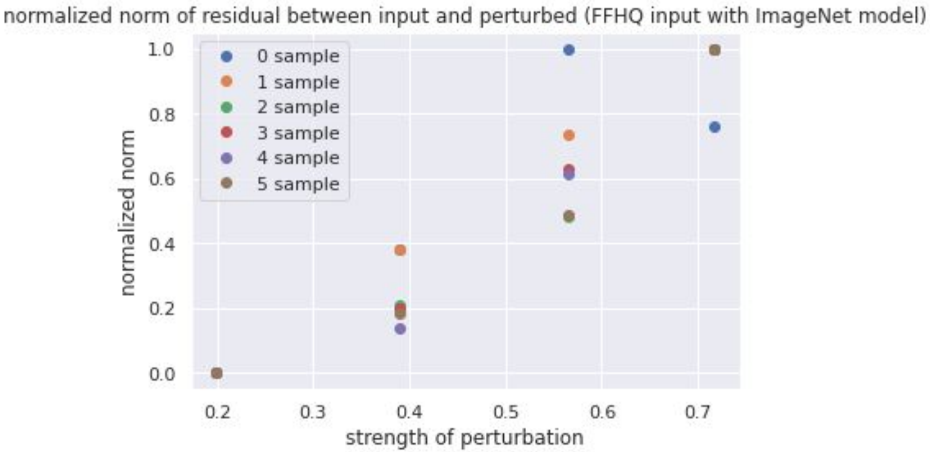


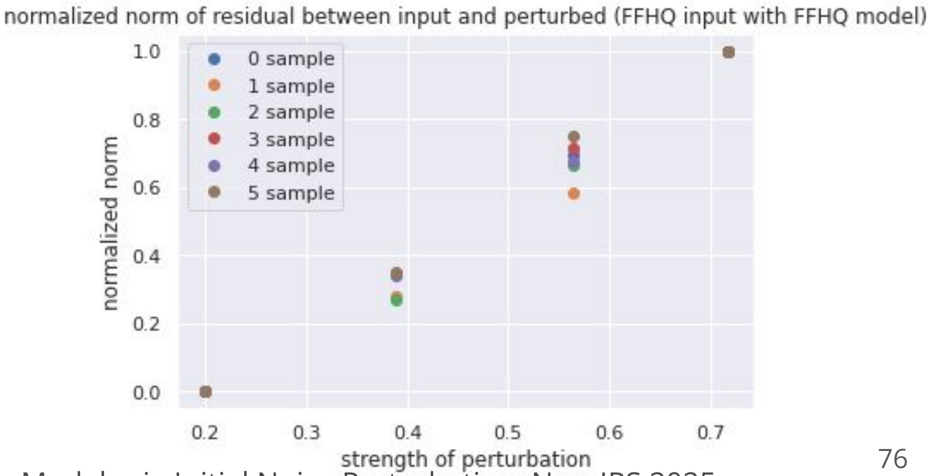


Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Implications of the Linearity Score

- However, the linearity of perturbation for different centers is different across initial noise manifold
- Out-of-distribution (OOD) data shows lower linearity score
  - OOD data lies on a low-probability manifold
- **The linearity score reveals inherent properties for understanding the low-dimensional geometry of learned data manifold**
  - Transition from memorization regime to generalization regime





Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Designing low-dimensional tokenizers

- **Pre-training considerations:**
  - Improved linearity enhances generalization capability
  - Perturbation in latent space [1,2]
- **Post-training considerations:**
  - Improved linearity enhances controllability
  - Decoder post-training for alignment [1,2]

[1] Qiu, et al., Image Tokenizer Needs Post-Training, arXiv 2025
[2] Zheng, et al., Diffusion Transformers with Representation Autoencoders, arXiv 2025
[3] Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

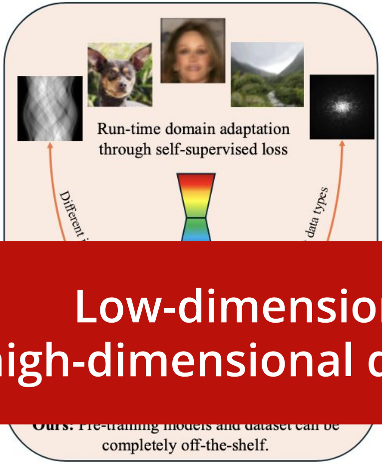
Designing low-dimensional tokenizers

- **Pre-training considerations:**
  - Improved linearity enhances generalization capability
  - Perturbation in latent space [1,2]
- **Post-training considerations:**
  - Improved linearity enhances controllability
  - Decoder post-training for alignment [1,2]
- **More thoughts…**
  - Improving linearity as much as possible? No!
  - If fully linear, a diffusion model collapses to a linear model
  - Tradeoff between fine-details and controllability/generalizability

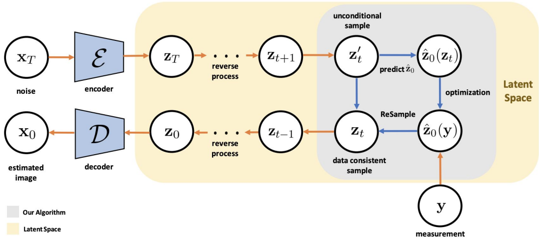
Our Blog Post:

[1] Qiu, et al., Image Tokenizer Needs Post-Training, arXiv 2025
[2] Zheng, et al., Diffusion Transformers with Representation Autoencoders, arXiv 2025
[3] Song, et al., CCS: Controllable and Constrained Sampling with Diffusion Models via Initial Noise Perturbation, NeurIPS 2025

Challenges of Diffusion Inverse Solvers in Scientific Applications



Efficiency

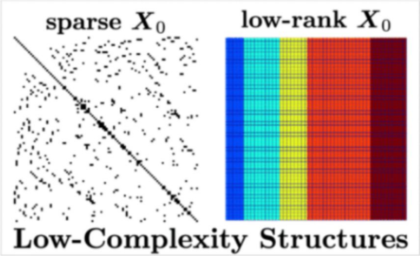


Low-dimensional structures are the key to address real-world high-dimensional data with small data regime in scientific applications

(Scientific)
Applications

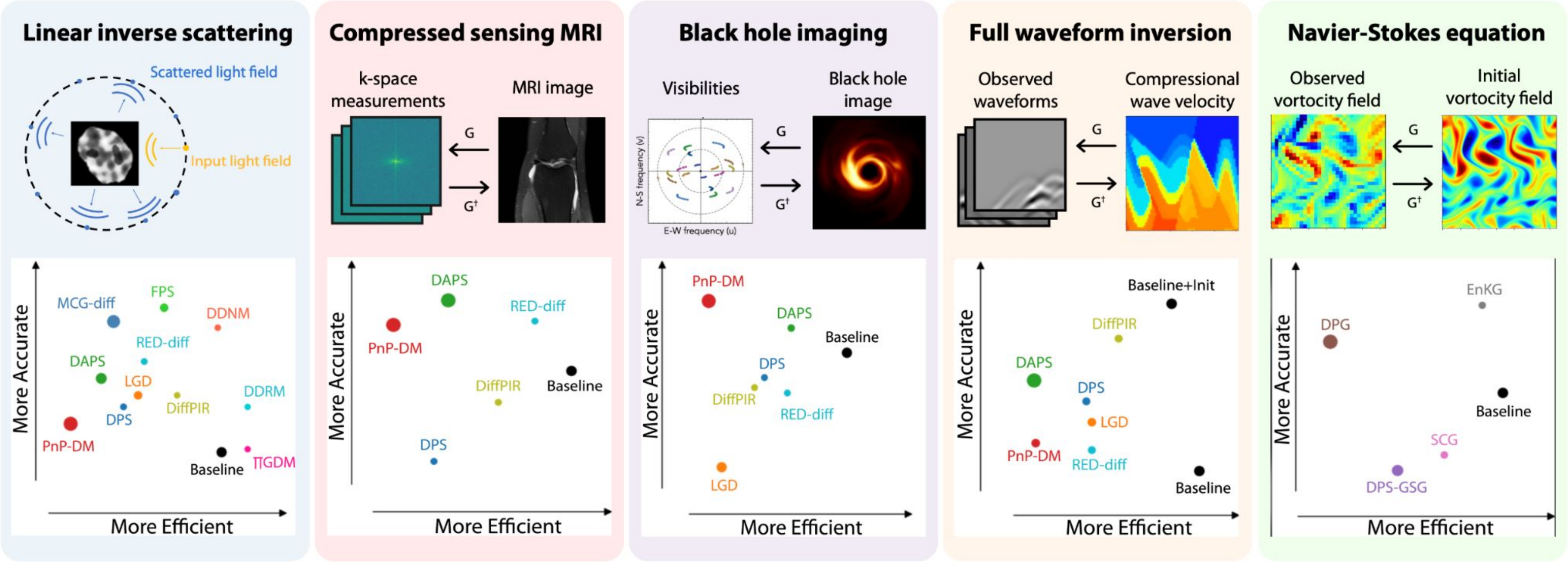
Generalizability

Controllability



DIS for Solving Various Inverse Problems in Scientific Applications

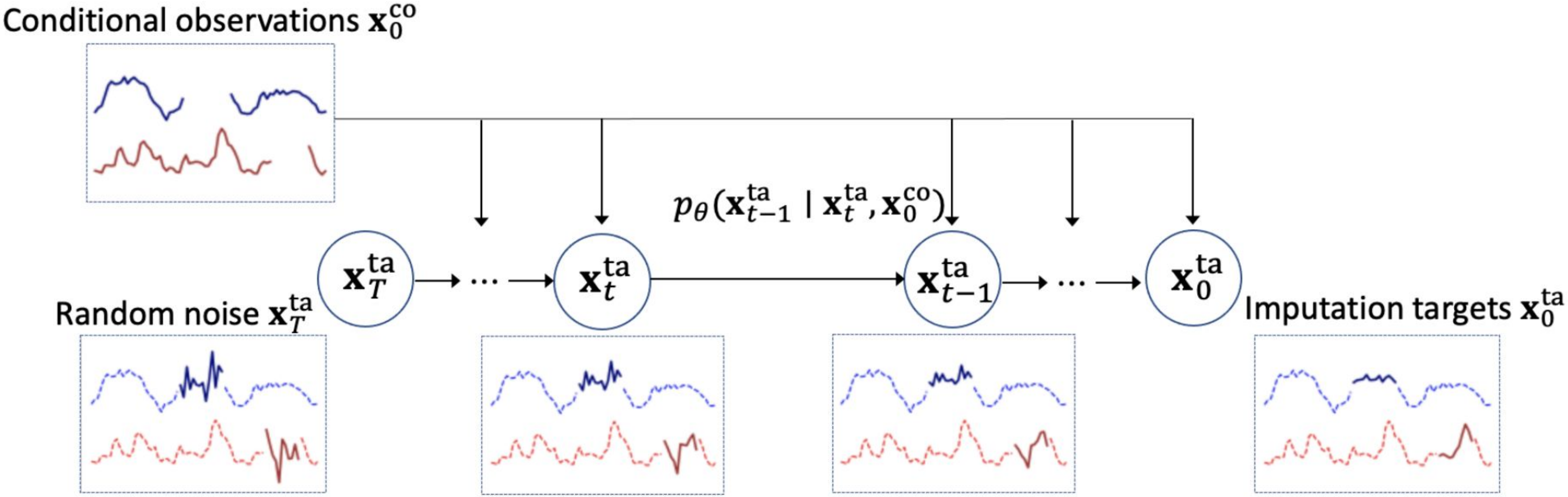
- Computational imaging
- Dynamic systems
- ……



Zheng et al., InverseBench: Benchmarking Plug-and-Play Diffusion Models for Inverse Problems in Physical Sciences, ICLR 2025

CSDI: Time Series Imputation

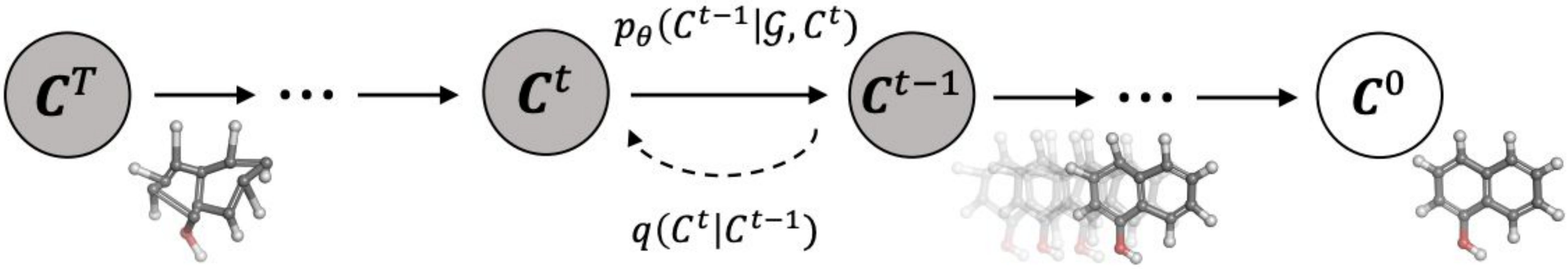
- Scientific applications in finance, meteorology and healthcare
- ……



Tashiro, et al., CSDI: Conditional Score-based Diffusion Models for Probabilistic Time Series Imputation, NeurIPS 202

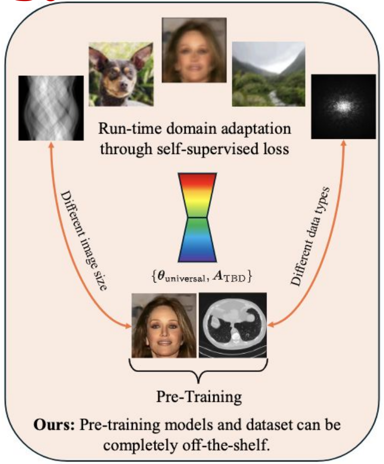
GeoDiff: Molecular Conformation Prediction

- Scientific applications in cheminformatics and drug discovery
- ……

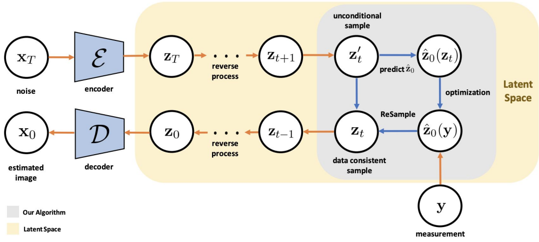


Tashiro, et al., GeoDiff: a Geometric Diffusion Model for Molecular Conformation Generation, ICLR 2022

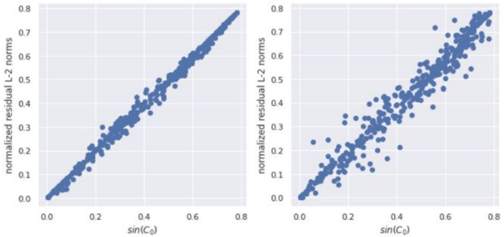
~~Challenges~~ Opportunities! of Diffusion Inverse Solvers in Scientific Applications



Efficiency



(Scientific) Applications



Generalizability

Controllability

Diffusion models can benefit numerous scientific applications!

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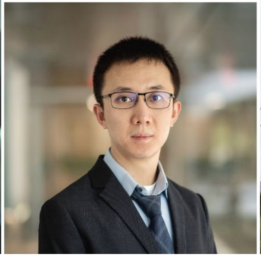
- Collaborators at U-M EECS / BME / Radiology / Radiation Oncology…
- Contact: liyues@umich.edu


Jeff Fessler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Bowen Song


Jason Hu


Chenwei Wu


Lixuan Chen


Soo-Min Kwon

NSF National Science Foundation

DARPA

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