Measurement-conditioned Denoising Diffusion Probabilistic Model for Under-sampled Medical Image Reconstruction

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Abstract

We propose a novel and unified method, measurement-conditioned denoising diffusion probabilistic model (MC-DDPM), for under-sampled medical image reconstruction based on DDPM. Different from previous works, MC-DDPM is defined in measurement domain (e.g. k-space in MRI reconstruction) and conditioned on under-sampling mask. We apply this method to accelerate MRI reconstruction and the experimental results show excellent performance, outperforming full supervision baseline and the state-of-the-art score-based reconstruction method. Due to its generative nature, MC-DDPM can also quantify the uncertainty of reconstruction. Our code is available on github.

1 Introduction

Reconstruction from under-sampled measurements in medical imaging has been deeply studied over the years, including reconstruction of accelerated magnetic resonance imaging (MRI) [Aggarwal et al., 2018, Hammernik et al., 2018, Eo et al., 2018, Han et al., 2019], sparse view or limited angles computed tomography (CT) [Han and Ye, 2018, Zhang et al., 2019, Wang et al., 2019] and digital breast tomosynthesis (DBT). Most of works aim to obtain one sample of the posterior distribution \( p(x | y) \) where \( x \) is the reconstructed target image and \( y \) is the under-sampled measurements.

Recently, denoising diffusion probabilistic models (DDPM) [Sohl-Dickstein et al., 2015, Ho et al., 2020], which is a new class of unconditional generative model, have demonstrated superior performance and have been widely used in various image processing tasks. DDPM utilizes a latent variable model to reverse a diffusion process, where the data distribution is perturbed to the noise distribution by gradually adding Gaussian noise. Similar to DDPM, score-based generative models [Hyvärinen and Dayan, 2005, Song and Ermon, 2019] also generate data samples by reversing a diffusion process. Both DDPM and score-based models are proved to be discretizations of different continuous stochastic differential equations by [Song et al., 2020]. The difference between them lies in the specific setting of diffusion process and sampling algorithms. They have been applied to the

1https://github.com/Theodore-PKU/MC-DDPM
Figure 1: Overview of the proposed method illustrated by the example of under-sampled MRI reconstruction. Diffusion process: starting from the non-sampled k-space \( y_{M^c,0} \), Gaussian noise is gradually added until time \( T \). Reverse process: starting from total noise, \( y_{M^c,0} \) is generated step by step. The details of notations is presented in Sect. 3.

In this paper, We design our method based on DDPM rather than score-based generative model because DDPM is more flexible to control the noise distribution. We propose a novel and unified method, measurement-conditioned DDPM (MC-DDPM) for under-sampled medical image reconstruction based on DDPM (Fig.1 illustrates the method by the example of under-sampled MRI reconstruction), where the under-sampling is in the measurement space (e.g. k-space in MRI reconstruction) and thus the conditional diffusion process is also defined in the measurement space. Two points distinguish our method from previous works [Jalal et al., 2021, Song et al., 2021, Chung et al., 2021]: (1) the diffusion and sampling process are defined in measurement domain rather than image domain; (2) the diffusion process is conditioned on under-sampling mask so that data consistency is contained in the model naturally and inherently, and there is no need to execute extra data consistency when sampling. The proposed method allows us to sample multiple reconstruction results from the same measurements \( y \). Thus, we are able to quantify uncertainty for \( q(x|y) \), such as pixel-variance. Our experiments on accelerated MRI reconstruction show MC-DDPM can generate samples of high quality of \( q(x|y) \) and it outperforms baseline models and proposed method by [Chung et al., 2021] in evaluation metrics.

This paper is organized as follows: relevant background on DDPM and the under-sampled medical image reconstruction task is in Sect. 2; details of the proposed method MC-DDPM is presented in Sect. 3; specifications about the implementation of the application to accelerated MRI reconstruction, experimental results and discussion are given in Sect. 4; we conclude our work in Sect. 5.

2 Background

2.1 Denoising Diffusion Probabilistic Model

DDPM [Ho et al., 2020] is a certain parameterization of diffusion models [Sohl-Dickstein et al., 2015], which is a class of latent variable models using a Markov chain to convert the noise distribution to the data distribution. It has the form of \( p_0(x_0) := \int p_0(x_{0:T}) \, dx_{1:T} \), where \( x_0 \) follows the data
distribution \( q(\mathbf{x}_0) \) and \( \mathbf{x}_1, \ldots, \mathbf{x}_T \) are latent variables of the same dimensionality as \( \mathbf{x}_0 \). The joint distribution \( p_0(\mathbf{x}_{0:T}) \) is defined as a Markov chain with learned Gaussian transitions starting from \( p(\mathbf{x}_T) = \mathcal{N}(0, I) \):

\[
p_0(\mathbf{x}_{0:T}) := p(\mathbf{x}_T) \prod_{t=1}^{T} p_0(\mathbf{x}_{t-1} | \mathbf{x}_t), \quad p_0(\mathbf{x}_{t-1} | \mathbf{x}_t) := \mathcal{N}(\mathbf{\mu}_t(\mathbf{x}_t, t), \sigma_t^2 I). \tag{1}
\]

The sampling process of \( p_0(\mathbf{x}_0) \) is: to sample \( \mathbf{x}_T \) from \( \mathcal{N}(0, I) \) firstly; then, to sample \( \mathbf{x}_{t-1} \) from \( p_0(\mathbf{x}_{t-1} | \mathbf{x}_t) \) until \( \mathbf{x}_0 \) is obtained. It can be regarded as a reverse process of the diffusion process, which converts the data distribution to the noise distribution \( \mathcal{N}(0, I) \). In DDPM the diffusion process is fixed to a Markov chain that gradually adds Gaussian noise to the data according to a variance schedule \( \beta_1, \ldots, \beta_T \):

\[
q(\mathbf{x}_1; \mathbf{x}_0) := \prod_{t=1}^{T} q(\mathbf{x}_t | \mathbf{x}_{t-1}), \quad q(\mathbf{x}_t | \mathbf{x}_{t-1}) := \mathcal{N}(\alpha_t \mathbf{x}_{t-1}, \beta_t^2 I),
\]

where \( \alpha_t^2 + \beta_t^2 = 1 \) for all \( t \) and \( \beta_1, \ldots, \beta_T \) are fixed to constants and their value are set specially so that \( q(\mathbf{x}_T; \mathbf{x}_0) \approx \mathcal{N}(0, I) \).

### 2.2 Under-sampled Medical Image Reconstruction

Suppose \( \mathbf{x} \in \mathbb{R}^n \) represents a medical image and \( \mathbf{y} \in \mathbb{R}^m, m < n \) is the under-sampled measurements which is obtained by the following forward model:

\[
\mathbf{y} = \mathbf{P}_\Omega \mathbf{A} \mathbf{x} + \mathbf{\epsilon}, \tag{3}
\]

where \( \mathbf{A} \in \mathbb{R}^{n \times n} \) is the measuring matrix and usually is invertible, \( \mathbf{P}_\Omega \in \mathbb{R}^{m \times n} \) is the undersampling matrix with the given sampling pattern \( \Omega \) and \( \mathbf{\epsilon} \) is the noise. For example, \( \mathbf{x} \) is a CT image, \( \mathbf{A} \) is the Radon transform matrix and \( \mathbf{y} \) is the sinogram of limited angles. Under-sampled medical image reconstruction is to reconstruct \( \mathbf{x} \) from \( \mathbf{y} \) as possible. Assuming \( \mathbf{x} \) follows a distribution of \( q(\mathbf{x}) \) and given \( \mathbf{P}_\Omega \), according to Bayesian Formula, we can derive the posterior distribution as follows (usually \( \mathbf{P}_\Omega \) is neglected):

\[
q(\mathbf{x} | \mathbf{y}, \mathbf{P}_\Omega) = \frac{q(\mathbf{x}, \mathbf{y} | \mathbf{P}_\Omega)}{q(\mathbf{y})} = \frac{q(\mathbf{y} | \mathbf{x}, \mathbf{P}_\Omega) q(\mathbf{x})}{q(\mathbf{y})}. \tag{4}
\]

Therefore, the task of under-sampled medical image reconstruction to reconstruct the posterior distribution.

### 3 Method: Measurement-conditioned DDPM

Inspired by DDPM, we propose measurement-conditioned DDPM (MC-DDPM) which is designed for under-sampled medical image reconstruction. In this section, we formulate the MC-DDPM, including the diffusion process and its reverse process, training objective and sampling algorithm. For the convenience, we use new notations different from Eq.\(^2\) to represent the under-sampled forward model:

\[
\mathbf{y}_M = \mathbf{M} \mathbf{A} \mathbf{x} + \mathbf{\epsilon}_M. \tag{5}
\]

where \( \mathbf{M} \in \mathbb{R}^{n \times n} \) is a diagonal matrix whose diagonal elements are either 1 or 0 depending on the sampling pattern \( \Omega \). \( \mathbf{y}_M \) and \( \mathbf{\epsilon}_M \) are both \( n \)-dimension vectors and their components at non-sampled positions are 0. The merit of the new notations is that we can further define \( \mathbf{M}^c = \mathbf{I} - \mathbf{M} \) (the superscript \( c \) means complement) and \( \mathbf{y}_{M^c} = \mathbf{M}^c \mathbf{A} \mathbf{x} \) which represents the non-sampled measurements. In this paper, we assume \( \mathbf{\epsilon}_M = 0 \). Then, we have \( \mathbf{y}_M + \mathbf{y}_{M^c} = \mathbf{A} \mathbf{x} \), i.e. \( \mathbf{y}_M + \mathbf{y}_{M^c} \) is the full-sampled measurements. In addition, the posterior distribution of reconstruction can be rewritten as \( q(\mathbf{x} | \mathbf{M}, \mathbf{y}_M) \). Through this paper, the subscript \( \mathbf{M} \) or \( \mathbf{M}^c \) in notations indicates that only components at under-sampled or non-sampled positions are not 0.

\(^2\)Assuming the sampling pattern \( \Omega \) is \( \{s_1, \ldots, s_m\} \subseteq \{1, \ldots, n\} \), the element of \( \mathbf{P}_\Omega \) at position \((i, s_i)\), \( i = 1, \ldots, m \), is 1 and other elements are all 0.

\(^3\)Specifically, \( M_{i,s_i} = 1 \) if \( i \in \Omega \). Otherwise its value is 0.
The purpose of reconstruction task is to estimate \( q(x \mid M, y_M) \). Since \( y_M \) is known and \( x = A^{-1} (y_M + y_{M^c}) \), the problem is transformed to estimate \( q(y_{M^c} \mid M, y_M) \). Because \( M \) and \( M^c \) are equivalent as the condition, we can replace \( q(y_{M^c} \mid M, y_M) \) by \( q(y_{M^c} \mid M^c, y_M) \). Based on this observation, we propose MC-DDPM which solves the reconstruction problem by generating samples of \( q(y_{M^c} \mid M^c, y_M) \). MC-DDPM is defined in measurement domain, instead of image domain as usual DDPM, and is conditioned on the non-sampling matrix \( M^c \) and sampled measurements \( y_M \). It has the following form:

\[
p_q (y_{M^c,0} \mid M^c, y_M) := \int p_\theta (y_{M^c,0:T} \mid M^c, y_M) \, dy_{M^c,1:T},
\]

where \( y_{M^c,0} = y_{M^c} \). \( p_\theta (y_{M^c,0:T} \mid M^c, y_M) \) is defined as follows:

\[
p_\theta (y_{M^c,0:T} \mid M^c, y_M) := p (y_{M^c,T} \mid M^c, y_M) \prod_{t=1}^T p_\theta (y_{M^c,t-1} \mid y_{M^c,t}, M^c, y_M),
\]

\[
p_\theta (y_{M^c,t-1} \mid y_{M^c,t}, M^c, y_M) := \mathcal{N} (\mu_\theta (y_{M^c,t-1}, t, M^c, y_M), \sigma_\theta^2 M^c),
\]

where \( \sigma_\theta^2 M^c \) is the covariance matrix and it means the noise is only added at non-sampled positions because for all \( t \) the components of \( y_{M^c,t} \) at under-sampled positions are always 0. If the conditions \( (M^c, y_M) \) in equations above is removed, they degrade to the form of Eq. 8.

Similar to DDPM, the sampling process of \( p_\theta (y_{M^c,0} \mid M^c, y_M) \) is a reverse process of the diffusion process which is also defined in measurement domain. Specifically, the Gaussian noise is gradually added to the non-sampled measurements \( y_{M^c,0} \). The diffusion process has the following form:

\[
q (y_{M^c,1:T} \mid y_{M^c,0}, M^c, y_M) := \prod_{t=1}^T q (y_{M^c,t} \mid y_{M^c,t-1}, M^c, y_M),
\]

\[
q (y_{M^c,t} \mid y_{M^c,t-1}, M^c, y_M) := \mathcal{N} (\tilde{\alpha}_t y_{M^c,t-1}, \tilde{\beta}_t^2 M^c),
\]

(7)

(8)

There are two points worthy of noting: (1) \( \alpha_t, \beta_t \) are not restricted to satisfy \( \alpha_t^2 + \beta_t^2 = 1 \); (2) formally, we add \( y_M \) as one of the conditions, but it has no effect on the diffusion process in fact. Let \( \tilde{\alpha}_t = \prod_{i=1}^t \alpha_i, \tilde{\beta}_t^2 = \sum_{i=1}^t \frac{\alpha_i^2}{\alpha_t^2} \beta_i^2 \), and we additionally define \( \tilde{\alpha}_0 = 1, \tilde{\beta}_0 = 0 \). Then, we can derive that:

\[
q (y_{M^c,t} \mid y_{M^c,0}, M^c, y_M) = \mathcal{N} (\tilde{\alpha}_t y_{M^c,0}, \tilde{\beta}_t^2 M^c),
\]

(9)

Next, we discuss how to train MC-DDPM \( p_\theta (y_{M^c,0} \mid M^c, y_M) \). Firstly, let \( p (y_{M^c,T} \mid M^c, y_M) = \mathcal{N} (0, \beta_T^2 M^c) \) so that it is nearly equal to \( q (y_{M^c,T} \mid y_{M^c,0}) \). Training of \( p_\theta (y_{M^c,0} \mid M^c, y_M) \) is performed by optimizing the variational bound on negative log likelihood:

\[
E \left[ - \log p_\theta (y_{M^c,0} \mid M^c, y_M) \right] \leq E_q \left[ - \log \frac{p_\theta (y_{M^c,0:T} \mid M^c, y_M)}{q (y_{M^c,1:T} \mid y_{M^c,0}, M^c, y_M)} \right]
\]

\[
= E_q \left[ - \log p (y_{M^c,T} \mid M^c, y_M) - \sum_{t \geq 1} \log \frac{p_\theta (y_{M^c,t-1} \mid y_{M^c,t}, M^c, y_M)}{q (y_{M^c,t} \mid y_{M^c,t-1}, M^c, y_M)} \right] =: L.
\]

Assuming that

\[
\mu_\theta (y_{M^c,t-1}, t, M^c, y_M) = \frac{1}{\alpha_t} \left( y_{M^c,t} - \frac{\beta_t^2}{\beta_t^2} \varepsilon_\theta (y_{M^c,t-1}, t, M^c, y_M) \right),
\]

(10)

and supposing \( y_{M^c,t} = \tilde{\alpha}_t y_{M^c,0} + \varepsilon, \varepsilon \sim \mathcal{N} (0, \beta_t^2 M^c) \) (Eq. 8), after reweighting \( L \) can be simplified as follows:

\[
L_{\text{simple}} = E_{y_{M^c,0} \mid t, \varepsilon} \| \varepsilon - \varepsilon_\theta (\tilde{\alpha}_t y_{M,0} + \beta_t \varepsilon, t, M^c, y_M) \|_2^2, \varepsilon \sim \mathcal{N} (0, M^c),
\]

(11)
We show the results of PD with MC-DDPPM to accelerated MRI reconstruction where \( f \) is a deep neural network and \( y_M \) is the under-sampled k-space data. The specific design for \( \varepsilon_\theta (y_{M^c,t}, t, M^c, y_M) \) in our experiments is given as follows:

\[
\varepsilon_\theta (y_{M^c,t}, t, M^c, y_M) = M^c f \left( g \left( A^{-1} (y_{M^c,t} + y_M), A^{-1} y_M, t, \theta \right) \right),
\]

where \( f \) is a deep neural network and \( g (\cdot, \cdot) \) is the concatenation operation. Because MR image \( x \) is in complex filed, we use \(|x|\), the magnitude of it, as the final image. Pixel-wise variance is also computed using magnitude images.

### 4 Experiments

We apply MC-DDPPM to accelerated MRI reconstruction where \( A \) is 2d Fourier transform and \( y_M \) is the under-sampled k-space data. We train the network with k-space data which were computed from \( 320 \times 320 \) size complex images. We base the implementation of guided-DDPM [Dhariwal and Nichol, 2021] and also follow similar setting for the diffusion process in [Dhariwal and Nichol, 2021] but multiply \( \beta_t \) by 0.5 so that \( \beta_T \approx 0.5 \). All networks were trained with learning rate of 0.0001. More details of experiments is in supplementary materials.

To verify superiority, we perform comparison studies with baseline methods (U-Net [Ronneberger et al., 2015]) used in [Zbontar et al., 2018]. The evaluation metrics, peak signal-to-noise ratio (PSNR) and structural similarity index (SSIM), of score-based reconstruction method proposed in [Chung et al., 2021] are also used for comparison since their experiments are conducted on the same dataset.

### 4.1 Experimental Setting

All experiments are performed with fastMRI single-coil knee dataset [Zhontar et al., 2018], which is publicly available and is divided into two parts, proton-density with (PDFS) and without fat suppression (PD). We trained the network with k-space data which were computed from \( 320 \times 320 \) size complex images. We base the implementation of guided-DDPM [Dhariwal and Nichol, 2021] and also follow similar setting for the diffusion process in [Dhariwal and Nichol, 2021] but multiply \( \beta_t \) by 0.5 so that \( \beta_T \approx 0.5 \). All networks were trained with learning rate of 0.0001. More details of experiments is in supplementary materials.

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### 4.2 Experimental Results

We show the results of PD with \( 4 \times \) (the first row) and \( 8 \times \) (the second row) acceleration in Fig. 2. More results are shown in supplementary materials. We compare our method to zero-filled reconstruction (ZF) and U-Net. Since MC-DDPM can produce multiple reconstruction samples, we use the mean of 20 samples as the object for comparison. We observe that the proposed method performs best both in \( 4 \times \) and \( 8 \times \) accelerations, where we see virtually more realistic structures and less error in the zoomed-in image than ZF and U-Net. In the last column of Fig. 2 we show the standard results are shown in supplementary materials. We compare our method to zero-filled reconstruction (ZF) and U-Net. Since MC-DDPM can produce multiple reconstruction samples, we use the mean of 20 samples as the object for comparison. We observe that the proposed method performs best both in \( 4 \times \) and \( 8 \times \) accelerations, where we see virtually more realistic structures and less error in the zoomed-in image than ZF and U-Net. In the last column of Fig. 2 we show the standard
Figure 2: Reconstruction results of $4 \times$ (the first row) and $8 \times$ (the second row) on PD data: (a) ground-truth, (b) zero-filled reconstruction, (c) U-Net, (d) the mean of samples generated by proposed method, (e) the standard deviation of the samples: range is set to $[0, 0.2]$. Blue box: Zoom in version of the indicated red box. Green box: Difference magnitude of the inset. White numbers indicate PSNR and SSIM, respectively.

Table 1: Quantitative metrics. Numbers in bold face indicate the best metric out of all the methods. The enhancement in the last two columns is computed based on U-Net.

|       | PD |       |       | PDFS |       |       | Enhancement |
|-------|----|-------|-------|------|-------|-------|-------------|
|       | ZF | U-Net | Ours  | ZF   | U-Net | Ours  | Chung et al. [2021] | Ours |
| $\times 4$ | PSNR | 29.62 | 34.04 | **36.69** | 26.32 | 28.30 | **33.00** | +0.06 | +3.68 |
|       | SSIM | 0.745 | 0.834 | **0.905** | 0.545 | 0.648 | **0.735** | +0.002 | +0.079 |
| $\times 8$ | PSNR | 25.94 | 31.13 | **33.49** | 24.90 | 26.17 | **31.75** | +1.01 | +3.97 |
|       | SSIM | 0.667 | 0.750 | **0.862** | 0.513 | 0.580 | **0.702** | +0.028 | +0.117 |

deviation of the samples. As the acceleration factor is increased, we see that the uncertainty increases correspondingly. Quantitative metrics in Table. 1 also confirm the superiority of our method. In the last two columns of Table. 1, we compare MC-DDPM to the score-based reconstruction method proposed in [Chung et al., 2021]. Because the testing volumes are randomly selected both in our experiments and in [Chung et al., 2021], it is impossible to compare directly. As a substitution, we compare the enhancement of evaluation metrics which is computed by the result of proposed method subtracting the result of U-Net. Due to the experiments in [Chung et al., 2021] were conducted on the whole dataset (both PD and PDFS), we compute the average enhancement of PD and PDFS as our final result. Our method outperforms [Chung et al., 2021] by 3.62/0.077 ($4 \times$) and 2.96/0.089 ($8 \times$) in PSNR/SSIM.

We also explore the effects of sampling steps and number of samples on reconstruction quality, which are illustrated in Fig. 3 and Fig. 4. The two experiments are conducted on one volume of PDFS with $4 \times$ and $8 \times$ acceleration, and PSNR is computed on the mean of generated samples. We discover that: (1) even the sampling steps decrease to 250, PSNR only reduces a little; (2) the quality of the mean of samples is enhanced when the number of samples increases and seems to converge. Taking the efficiency into account, 20 samples with 250 sampling steps may be a good choice.
4.3 Discussion

It is very common in medical imaging that the measurement is under sampled to reduce the cost or dosage. Therefore, it is important to define the conditional diffusion process in the measurement space for a reconstruction task. In this project, although our experiments are conducted using MR images, our method can be applied to other under-sampled medical image reconstruction tasks, such as limited angle or sparse view CT Reconstruction. In our MC-DDPM, the variance schedule \( \beta_t \) is an important hyper-parameter that is potentially related to the sampling quality and efficiency. Further investigation on hyper-parameter \( \beta_t \) is planned in our future study.

5 Conclusion

In this paper we present a novel and unified mathematical framework, MC-DDPM, for medical image reconstruction using under-sampled measurements. Our method applies diffusion process in measurement domain with conditioned under-sampling mask, and provides an estimate of uncertainty as output. The superior performance of our method is demonstrated using accelerated MRI reconstruction, although MC-DDPM should potentially work for other under-sampled medical image reconstruction tasks.

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We can rewrite the equation above recursively:

\[
\bar{\alpha}_t = \prod_{i=1}^{t} \alpha_i \beta_t^2 = \sum_{i=1}^{t} \frac{\alpha_i^2}{\alpha_t^2} \beta_t^2, \tag{13}
\]

where \(\bar{\alpha}_0 = 1\) and \(\beta_0 = 0\).

**Eq. 8**

\[
q(\mathbf{y}_{M^c,t} | \mathbf{y}_{M^c,0}, \mathbf{M}^c, \mathbf{y}_M) = \mathcal{N}(\bar{\alpha}_t \mathbf{y}_{M^c,0}, \bar{\beta}_t^2 \mathbf{M}^c).
\]

**Proof.** According to Eq. 7, we have that:

\[
\mathbf{y}_{M^c,t} = \alpha_t \mathbf{y}_{M^c,t-1} + \beta_t \mathbf{t}_t, \mathbf{t}_t \sim \mathcal{N}(0, \mathbf{M}^c).
\]

We can rewrite the equation above recursively:

\[
\mathbf{y}_{M^c,t} = \alpha_t \mathbf{y}_{M^c,t-1} + \beta_t \mathbf{t}_t
\]

\[
= \alpha_t (\alpha_{t-1} \mathbf{y}_{M^c,t-2} + \beta_{t-1} \mathbf{t}_t) + \beta_t \mathbf{t}_t
\]

\[
= \alpha_t \alpha_{t-1} \mathbf{y}_{M^c,t-2} + \alpha_t \beta_{t-1} \mathbf{t}_{t-1} + \beta_t \mathbf{t}_t
\]

\[
= \left( \prod_{i=t-1}^{t} \alpha_i \right) \mathbf{y}_{M^c,t-2} + \sum_{i=t-1}^{t-1} \left( \prod_{j=i+1}^{t} \alpha_j \right) \beta_i \mathbf{t}_i + \beta_t \mathbf{t}_t
\]

\[
= \left( \prod_{i=1}^{t} \alpha_i \right) \mathbf{y}_{M^c,0} + \sum_{i=1}^{t} \left( \prod_{j=i+1}^{t} \alpha_j \right) \beta_i \mathbf{t}_i + \beta_t \mathbf{t}_t
\]

\[
= \bar{\alpha}_t \mathbf{y}_{M^c,0} + \sum_{i=1}^{t} \frac{\bar{\alpha}_t}{\alpha_i} \beta_i \mathbf{t}_i
\]

Because \(\mathbf{t}_i, i = 1, ..., t\) are all sampled from \(\mathcal{N}(0, \mathbf{M}^c)\) and independent of each other, \(\sum_{i=1}^{t} \frac{\bar{\alpha}_t}{\alpha_i} \beta_i \mathbf{t}_i\) can be regarded as sampled from \(\mathcal{N}(0, \bar{\beta}_t^2 \mathbf{M}^c)\) according to the definition of \(\bar{\beta}_t\). Therefore, we have that:

\[
\mathbf{y}_{M^c,t} = \bar{\alpha}_t \mathbf{y}_{M^c,0} + \bar{\beta}_t^2 \mathbf{e}, \mathbf{e} \sim \mathcal{N}(0, \mathbf{M}^c),
\]

i.e.

\[
q(\mathbf{y}_{M^c,t} | \mathbf{y}_{M^c,0}, \mathbf{M}^c, \mathbf{y}_M) = \mathcal{N}(\bar{\alpha}_t \mathbf{y}_{M^c,0}, \bar{\beta}_t^2 \mathbf{M}^c).
\]

\[\square\]

**Eq. 9**

\[
q(\mathbf{y}_{M^c,t-1} | \mathbf{y}_{M^c,t}, \mathbf{y}_{M^c,0}, \mathbf{M}, \mathbf{y}_M) = \mathcal{N}(\bar{\mu}_t, \bar{\beta}_t \mathbf{M}^c),
\]

where

\[
\bar{\mu}_t = \frac{\alpha_t \beta_{t-1}^2}{\beta_t^2} \mathbf{y}_{M^c,t} + \frac{\alpha_{t-1} \beta_t^2}{\beta_t^2} \mathbf{y}_{M^c,0}, \bar{\beta}_t = \frac{\beta_t \beta_{t-1}}{\beta_t}.
\]
Proof. Utilizing Bayesian Formula, we can derive that:

\[
\begin{align*}
q (Y_{m^*,t} | Y_{m^*,t-1}, Y_{M^*,0}, M, y_M) &= q (Y_{m^*,t-1}, Y_{m^*,t} | Y_{M^*,0}, M, y_M) \\
&= q (Y_{m^*,t-1} | Y_{M^*,0}, M, y_M) q (Y_{m^*,t} | Y_{M^*,0}, M, y_M) \\
&= q (Y_{m^*,t-1}, M, y_M) q (Y_{m^*,t} | Y_{M^*,0}, M, y_M) \\
&= q (Y_{m^*,t} | Y_{M^*,0}, M, y_M) q (Y_{m^*,t-1} | Y_{M^*,0}, M, y_M)
\end{align*}
\]

According to Eq. 7, Eq. 8, it is easy to write the explicit expressions for the three distributions in last equation. Since the components of \( Y_{M^*,0}, Y_{M^*,t-1} \) and \( Y_{M^*,t} \) at under-sampled positions are all 0, we only need to consider the non-sampled part of \( q (Y_{m^*,t-1} | Y_{m^*,t}, Y_{M^*,0}, M, y_M) \). For convenience, we use \( y_t \) to represent the non-sampled part of \( y_{m^*,t} \) and neglect the condition \((M, y_M)\) in derivation. Then, we have:

\[
\begin{align*}
q (Y_{m^*,t} | Y_{m^*,t-1}, M, y_M) &= q (y_t | y_{t-1}) = \frac{1}{\sqrt{(2\pi)^d \beta^2 t}} \exp \left\{ -\frac{\|y_t - \alpha_t y_{t-1}\|^2}{2\beta^2_t} \right\} ; \\
q (Y_{m^*,t-1} | Y_{m^*,0}, M, y_M) &= q (y_{t-1} | y_0) = \frac{1}{\sqrt{(2\pi)^d \beta^2 t_{t-1}}} \exp \left\{ -\frac{\|y_{t-1} - \bar{\alpha}_t y_0\|^2}{2\beta^2_{t-1}} \right\} ; \\
q (Y_{m^*,t} | Y_{m^*,0}, M, y_M) &= q (y_t | y_0) = \frac{1}{\sqrt{(2\pi)^d \beta^2 t}} \exp \left\{ -\frac{\|y_t - \bar{\alpha}_t y_0\|^2}{2\beta^2_t} \right\} ;
\end{align*}
\]

where \( d = n - m \). Next, we derive the distribution of \( q (y_{t-1} | y_t, y_0) \) according to the three Gaussian distributions above.

Firstly, the coefficient is:

\[
\frac{1}{\sqrt{(2\pi)^d \beta^2 t}} \frac{1}{\sqrt{(2\pi)^d \beta^2 t_{t-1}}} = \frac{1}{\sqrt{(2\pi)^d (\beta^2 t_{t-1} / \beta^2 t)}} = \frac{1}{\sqrt{(2\pi)^d (\beta_{t-1} / \beta_t)^2}}.
\]

Secondly, the exponential part is (neglecting the negative sign):

\[
\frac{\|y_t - \alpha_t y_{t-1}\|^2}{2\beta^2_t} + \frac{\|y_{t-1} - \bar{\alpha}_t y_0\|^2}{2\beta^2_{t-1}} - \frac{\|y_t - \bar{\alpha}_t y_0\|^2}{2\beta^2_t} = \beta^2_{t-1} \beta^2_t \frac{\|y_t - \alpha_t y_{t-1}\|^2}{2\beta^2_t} + \beta^2_t \beta^2_{t-1} \frac{\|y_{t-1} - \bar{\alpha}_t y_0\|^2}{2\beta^2_{t-1}} - \beta^2_{t-1} \beta^2_t \frac{\|y_t - \bar{\alpha}_t y_0\|^2}{2\beta^2_{t-1} \beta^2_t} = \frac{a \|y_{t-1}\|^2 + b y_{t-1}^T y_t + c y_{t-1}^T y_0 + d \|y_t\|^2 + e y_t^T y_0 + f \|y_0\|^2}{2\beta^2_t \beta^2_{t-1} \beta^2_t},
\]

where

\[
\begin{align*}
a &= \beta^2_{t-1} \beta^2_t \alpha^2_t + \beta^2_t \beta^2_{t-1}; \\
b &= -2\beta^2_{t-1} \beta^2_t \alpha_t; \\
c &= -2\beta^2_t \beta^2_{t-1} \alpha_t; \\
d &= \beta^2_{t-1} \beta^2_t - \beta^2_t \beta^2_{t-1}; \\
e &= 2\beta^2_t \beta^2_{t-1} \alpha_t; \\
f &= \beta^2_t \beta^2_{t-1} \alpha_t - \beta^2_t \beta^2_{t-1} \alpha^2_t.
\end{align*}
\]
According to the definitions of $\tilde{\alpha}_t$ and $\tilde{\beta}_t$, we can derive the following useful equation:

$$\tilde{\beta}_t^2 \alpha_t^2 + \beta_t^2 = \tilde{\beta}_t^2.$$  

The equation above can be used to simplify $a$, $d$ and $f$. We have the following results:

$$a = \tilde{\beta}_t^4, d = \alpha_t^2 \tilde{\beta}_t^4, f = \alpha_t^2 \tilde{\beta}_t^4.$$  

Therefore, we derive that:

$$a \|y_{t-1}\|_2^2 + b y_{t-1}^T y_t + c y_{t-1}^T y_0 + d \|y_t\|_2^2 + c y_t^T y_0 + f \|y_0\|_2^2$$

$$= \frac{\tilde{\beta}_t^4 \|y_{t-1}\|_2^2 - 2 \tilde{\beta}_t^2 \tilde{\alpha}_t y_{t-1}^T y_t - 2 \tilde{\beta}_t^2 \tilde{\alpha}_t - 1 y_{t-1}^T y_0 + \tilde{\alpha}_t \tilde{\beta}_t^4 \|y_t\|_2^2 + 2 \beta_t^2 \tilde{\beta}_t^4 \tilde{\alpha}_t^2 y_{t-1}^T y_0 + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^4 \|y_0\|_2^2}{2 \tilde{\beta}_t^4 \beta_t^4}$$

$$= \frac{\tilde{\beta}_t^4 \|y_{t-1}\|_2^2 - 2 \tilde{\beta}_t^2 y_{t-1}^T (\tilde{\alpha}_t \tilde{\beta}_t^2 y_t + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^2 y_0) + \|\tilde{\alpha}_t \tilde{\beta}_t^2 y_t + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^2 y_0\|_2^2}{2 \tilde{\beta}_t^4 \beta_t^4}$$

$$= \frac{\|\tilde{\beta}_t^2 y_{t-1} - (\tilde{\alpha}_t \tilde{\beta}_t^2 y_t + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^2 y_0)\|_2^2}{2 \tilde{\beta}_t^4 \beta_t^4}$$

$$= \frac{\|y_{t-1} - (\tilde{\alpha}_t \tilde{\beta}_t^2 y_t + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^2 y_0)\|_2^2}{2 \tilde{\beta}_t^4 \beta_t^4}.$$  

Finally, we obtain that:

$$q (y_{M^c, t-1} | y_{M^c, t}, y_{M^c, 0}, \text{M}, \text{yM}) = q (y_{t-1} | y_t, y_0)$$

$$= \frac{1}{\sqrt{2\pi}^d \left( \frac{\beta_t \beta_{t-1}}{\beta_t} \right)^{2d}} \exp \left\{ - \frac{\|y_{t-1} - (\tilde{\alpha}_t \tilde{\beta}_t^2 y_t + \tilde{\tilde{\alpha}}_t \tilde{\beta}_t^2 y_0)\|_2^2}{2 \tilde{\beta}_t^4 \beta_{t-1}^2} \right\}.$$  

i.e.

$$q (y_{M^c, t-1} | y_{M^c, t}, y_{M^c, 0}, \text{M}, \text{yM}) = \mathcal{N} \left( \tilde{\mu}_t, \tilde{\beta}_t \text{M}^c \right),$$

where $\tilde{\mu}_t = \frac{\alpha_t \beta_t}{\beta_t^2} y_{M^c, t} + \frac{\tilde{\alpha}_t \beta_t}{\beta_t^2} y_{M^c, 0}, \tilde{\beta}_t = \frac{\beta_t \beta_{t-1}}{\beta_t}.$

Training Objective In DDPM [Ho et al., 2020], the training of $p_\theta$ ($x_0$) is performed by optimizing the variational bound on negative log likelihood:

$$E [-\log p_\theta (x_0)] \leq E_q \left[-\log \frac{p_\theta (x_0 | T)}{q(x_1:T | x_0)}\right]$$

$$= E_q \left[-\log p(x_T) - \sum_{t=1}^{T} \log \frac{p_\theta (x_t | x_{t-1})}{q(x_t | x_{t-1})} \right] =: L.$$  

Similarly we can define $L$ for MC-DDPM as follows:

$$E [-\log p_\theta (y_{M^c, 0} | \text{M}^c, \text{yM})] \leq E_q \left[-\log \frac{p_\theta (y_{M^c, 0} | T) | \text{M}^c, \text{yM})}{q(y_{M^c, 1:T} | y_{M^c, 0}, \text{M}^c, \text{yM})} \right]$$

$$= E_q \left[-\log p(y_{M^c, T} | \text{M}^c, \text{yM}) - \sum_{t=1}^{T} \log \frac{p_\theta (y_{M^c, t-1} | y_{M^c, t}, \text{M}^c, \text{yM})}{q(y_{M^c, t} | y_{M^c, t-1}, \text{M}^c, \text{yM})} \right] =: L.$$  

Removing the constants in $L$, we can derive $L_{\text{vib}}$ as follows:

$$L_{\text{vib}} = E_q \left[ \frac{1}{2}\|\tilde{\mu}_t - \mu_\theta (y_{M^c, t}, \text{M}^c, \text{yM})\|_2^2 \right].$$
Table 2: Quantitative metrics (PSNR, SSIM, NMSE, MSE) which are computed on volumes. Numbers in bold face indicate the best metric out of all the methods.

|       | PD       | PDFS     |
|-------|----------|----------|
|       | ZF       | U-Net    | Ours     | ZF       | U-Net    | Ours     |
| × 4   | PSNR     | 29.62    | 34.04    | **36.69**| 26.32    | 28.30    | **33.00**|
|       | SSIM     | 0.745    | 0.834    | **0.905**| 0.545    | 0.648    | **0.735**|
|       | NMSE     | 0.0271   | 0.0107   | **0.0057**| 0.0776   | 0.0510   | **0.0164**|
|       | MSE      | 2.31e-10 | 7.64e-11 | **4.26e-11**| 5.11e-11 | 3.38e-11 | **1.08e-11**|
| × 8   | PSNR     | 25.94    | 31.13    | **33.49**| 24.90    | 26.17    | **29.76**|
|       | SSIM     | 0.667    | 0.750    | **0.862**| 0.513    | 0.580    | **0.702**|
|       | NMSE     | 0.0630   | 0.0203   | **0.0114**| 0.105    | 0.0814   | **0.0215**|
|       | MSE      | 5.66e-10 | 1.50e-10 | **9.00e-11**| 6.88e-11 | 5.58e-11 | **1.40e-11**|

Table 3: Quantitative metrics (PSNR, SSIM, NMSE, MSE) which are computed on slices. Numbers in bold face indicate the best metric out of all the methods.

|       | PD       | PDFS     |
|-------|----------|----------|
|       | ZF       | U-Net    | Ours     | ZF       | U-Net    | Ours     |
| × 4   | PSNR     | 27.15    | 31.32    | **33.98**| 23.07    | 25.15    | **29.76**|
|       | SSIM     | 0.678    | 0.785    | **0.867**| 0.438    | 0.536    | **0.614**|
|       | NMSE     | 0.0272   | 0.0118   | **0.0060**| 0.0898   | 0.0611   | **0.0174**|
|       | MSE      | 2.33e-10 | 7.71e-11 | **4.32e-11**| 5.29e-11 | 3.53e-11 | **1.11e-11**|
| × 8   | PSNR     | 23.51    | 28.46    | **30.97**| 21.70    | 23.01    | **28.60**|
|       | SSIM     | 0.592    | 0.695    | **0.813**| 0.399    | 0.468    | **0.571**|
|       | NMSE     | 0.0624   | 0.0222   | **0.0118**| 0.120    | 0.0961   | **0.0222**|
|       | MSE      | 5.29e-11 | 3.53e-11 | **1.11e-11**| 7.09e-11 | 5.58e-11 | **1.43e-11**|

where \( t \) is uniform between 1 and \( T \). Assuming that 
\[
\mu_\theta (y_{M^c,t}, t, M^c, y_M) = \frac{1}{\alpha_t} \left( y_{M^c,t} - \frac{\beta_t^2}{\beta_t} \varepsilon_\theta (y_{M^c,t}, t, M^c, y_M) \right),
\]

and supposing \( y_{M^c,t} = \bar{\alpha}_t y_{M^c,0} + \varepsilon, \varepsilon \sim \mathcal{N}(0, \beta_t^2 M^c) \) (Eq. 8), \( L_{v1b} \) can be simplified as follows:
\[
L_{v1b} = E_{y_{M^c,0}, t, \varepsilon} \frac{\beta_t^4}{2 \bar{\alpha}_t^2 \beta_t^2 \alpha_t^2} \| \varepsilon - \varepsilon_\theta (\bar{\alpha}_t y_{M^c,0} + \bar{\beta}_t \varepsilon, t, M^c, y_M) \|_2^2, \varepsilon \sim \mathcal{N}(0, M^c).
\]

After reweighting \( L_{v1b} \), we obtain the final training objective as follows:
\[
L_{simple} = E_{y_{M,0}, t, \varepsilon} \| \varepsilon - \varepsilon_\theta (\bar{\alpha}_t y_{M,0} + \bar{\beta}_t \varepsilon, t, M^c, y_M) \|_2^2, \varepsilon \sim \mathcal{N}(0, M^c).
\]

7.2 More Details of Experiments

For all volumes of training data, we drop the first and last five slices to avoid training the model with noise-only data as [Chung et al., 2021] did. For testing, we randomly select 6 volumes from the validation set and dropped the first and last 5 slices from each volume for both PD and PDFS. The model architectures used in experiments stems from U-Net [Ronneberger et al., 2015] and is added by time embedding modules and self-attention layers. We train the model with batch size of 48 for 35k steps in MC-DDPM experiments. About \( \alpha_t \) and \( \beta_t \), we first use the "cosine" schedule which is also used in [Dhariwal and Nichol, 2021], and then multiply \( \beta_t \) by 0.5. The details can be seen in our code. All code was implemented in PyTorch [Paszke et al., 2019].

7.3 More Experimental Results

We list more quantitative metrics, including NMSE and MSE, for both volumes and slices in Table 2 and Table 3. More reconstruction results are shown in Fig. 5, Fig. 6, Fig. 7, and Fig. 8.
Figure 5: Reconstruction results of $4 \times$ on PD. The "mean" and "std" (range is set $[0, 1]$) are computed by 20 samples generated by proposed method. We also list five samples. Yellow numbers indicate PSNR and SSIM, respectively.
Figure 6: Reconstruction results of $8 \times$ on PD. The "mean" and "std" (range is set [0, 1]) are computed by 20 samples generated by proposed method. We also list five samples. Yellow numbers indicate PSNR and SSIM, respectively.
Figure 7: Reconstruction results of 4× on PDFS. The "mean" and "std" (range is set [0, 1]) are computed by 20 samples generated by proposed method. We also list five samples. Yellow numbers indicate PSNR and SSIM, respectively.
Figure 8: Reconstruction results of 8× on PDFS. The "mean" and "std" (range is set [0, 1]) are computed by 20 samples generated by proposed method. We also list five samples. Yellow numbers indicate PSNR and SSIM, respectively.