







# Diffusion-Weighted Imaging with Learned Nonlinear Latent Space Modeling and Self-Supervised Reconstruction (DeepDWI)

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Abstract—The code is publicly available at: https://github.com/ZhengguoTan/DeepDWI.

Index Terms— Diffusion-weighted imaging, Image reconstruction, Generative AI, Latent space, Self-supervised learning

#### I. INTRODUCTION

IGH-dimensional magnetic resonance imaging (HD-MRI) has been an emerging and flourishing field, which has achieved substantial improvements in terms of spatiotemporal fidelity. Instead of the conventional two-dimensional static single-contrast-weighted imaging, HD-MRI acquires and reconstructs multi-dimensional information. For instance, Brown et al. [1] proposed magnetic resonance spectroscopic imaging (MRSI), which uses multiple readout gradients to acquire multiple echo images for the computation of spatially resolved metabolic distribution. Le BiHan et al. [2] and Merboldt et al. [3] proposed diffusion-weighted imaging (DWI), which utilizes spatially and angularly varying diffusion encoding gradients in combination with fast echo-planar imaging (EPI) readouts [4] to obtain multi-contrast diffusionweighted images as a probe into tissue microstructure. Ma et al. [5] proposed magnetic resonance fingerprinting (MRF)

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which consists of a  $T_1$ - and  $T_2$ -prepared pseudo-randomized sequence to acquire time-resolved transient-state images and a Bloch-equation-based dictionary matching algorithm [6] for simultaneous quantitative  $T_1$  and  $T_2$  mapping.

HD-MRI, however, conventionally requires long scan time. Advances in parallel imaging [7]–[11] and compressed sensing [12]–[14] have enabled accelerated acquisition for HD-MRI. In particular, the low-rank modeling and regularization [15] has been a powerful tool in reducing the dimensionality of high-dimensional data, which enables accelerated acquisition and high spatiotemporal-resolution reconstruction. Usually, singular value decomposition (SVD) is used to learn a truncated temporal basis function from a large-scale physics-informed dictionary [16]–[18]. The temporal basis function is then integrated with the MRI forward model, i.e. the sensitivity encoding operator [10], for joint reconstruction of the corresponding spatial basis images. In addition, low-rank regularization can be employed in the joint reconstruction [19].

Beyond the low-rank technique, advanced neural networks, e.g. autoencoder [20], have been explored for HD-MRI reconstruction and proven to supply more accurate representations of high-dimensional data than SVD. Lam et al. [21] and Mani et al. [22] proposed to first learn a denoising autoencoder (DAE) model from a physics-informed simulated dictionary and then incorporate the learned DAE model as a regularizer in the alternating direction method of multipliers (ADMM) [23] unrolling reconstruction. Pioneered by Gregor and LeCun [24], algorithm unrolling enables the use of learned deep prior as regularization and faster inference than iterative reconstruction with hand-crafted regularization functions [25]. Algorithm unrolling has been introduced to accelerated MRI reconstruction and employed in various scenarios: supervised learning with fully sampled reference images [26], [27], selfsupervised learning with only undersampled data available for training [28], [29].

Deep neural networks are capable of learning not only regularization functions, but also MR-physics forward operators. Zhu et al. [30] proposed the automated transform by manifold approximation (AUTOMAP), which learns the mapping between the sensor and the image domain for data-driven supervised image reconstruction. Liu et al. [31] proposed the reference-free  $T_1$  parameter maps extraction (RELAX) self-supervised deep learning reconstruction, which learns the mapping from  $T_1$  parameter maps to undersampled multi-coil multi-contrast k-space data. Arefeen et al. [32] proposed to

replace the conventional SVD-based linear subspace modeling [16] by the latent decoder model within DAE for improved  $T_2$ -weighted image reconstruction.

Several challenges exist when adopting deep learning to DWI reconstruction. First, the capability of DAE to learn diffusion MRI models is open to questions. DAE is composed of sequential fully connected layers with nonlinear activation functions. This simple architecture may fail to learn complicated functions. DWI signal is such an example. The standard diffusion tensor model [33] consists of six tensor elements, and forms DWI signals based on the multiplication of exponential functions. Second, it is rather difficult to acquire fully-sampled data for the training of a regularization functional. On the one side, fully sampled DWI requires a longer echo train in EPI, which not only elongates the scan time but also increases off-resonance-induced geometric distortion. On the other side, there exists a wide range of diffusion acquisition modes, thereby requiring a larger dataset than the two-dimensional imaging scenario.

To overcome these challenges, we aim to develop a generalized DWI reconstruction framework with learned nonlinear latent space modeling and self-supervised reconstruction, dubbed DeepDWI.

#### II. RELATED WORK

## A. Variational Autoencoder (VAE)

Autoencoders (AEs) are neural network type trained in an unsupervised manner. They utilize two smaller networks an encoder and a decoder, connected through a latent space. The trained encoder acts as a dimensionality reducer, producing a compact sparse representation of the data in the latent space. The decoder is trained to reconstruction the input data from the encoder produced latent representation. Because the the standard AE training scheme does not constrain the latent space in any way, the network has problems to generalize. The Variational Autoencoder (VAE) was first introduced by Kingma and Welling [34] and uses the principle of variational inference. By that the VAE is forced to learn the probability distributions of the latent variables and a second term is added to the loss function of the network, the result of the Kullbeck Leibler Divergence, which describes how much the learned latent distributions diverge from the real distributions by that regularizing the reconstruction training. The latent space in VAE is not consisting of simple neurons but resambles distributions of the latent activations and samples from these. The sampling operation is not backpropagateable, however, so the network makes use of the reparameterization trick the VAE learns a mean and a variance for each latent variable and these are used to scale the drawn samples from a gaussian distribution (mean=0, variance=1). In Figure 1 (A) the used VAE model is shown.

# B. Multi-Band Multi-Shot DWI Acquisition & Modeling

Figure 1 (B) illustrates the joint k-q-slice forward forward operator for multi-band multi-shot DWI acquisition [35]. This operator can be understood as an extended sensitivity encoding

(SENSE) operator [10], which maps the multi-slice multi-diffusion-weighted images  $(\tilde{\mathbf{x}})$  to their corresponding k-space,

$$\mathcal{A}(\tilde{\mathbf{x}}) = \mathbf{P} \mathbf{\Sigma} \mathbf{\Theta} \mathbf{F} \mathbf{S} \mathbf{\Phi} \tilde{\mathbf{x}} \tag{1}$$

Here, the images  $\tilde{\mathbf{x}}$  are point-wise multiplied with the precomputed shot-to-shot phase variation maps  $(\Phi)$  and coil sensitivity maps  $(\mathbf{S})$ . The output images are then converted to k-space via two-dimensional fast Fourier transform  $(\mathbf{F})$ , point-wise multiplied with the multi-band phases  $(\Theta)$ , summed along the slice dimension  $(\Sigma)$ , and then multiplied by the undersampling mask  $(\mathbf{P})$ .

With the operator A, the inverse problem in DWI reads,

$$\underset{\tilde{\mathbf{x}}}{\operatorname{argmin}} \|\mathbf{y} - \mathcal{A}(\tilde{\mathbf{x}})\|_{2}^{2} + \lambda \mathcal{R}(\tilde{\mathbf{x}})$$
 (2)

where  $\mathbf{y}$  is the measured k-space data. The first term in Equation (2) presents data consistency, and the second term presents the regularization function  $\mathcal{R}(\tilde{x})$  with the regularization strength  $\lambda$ . When using the Tikhonov regularization, i.e.  $\mathcal{R}(\tilde{\mathbf{x}}) = \|\tilde{\mathbf{x}}\|_2^2$ , Equation (2) can be solved via the conjugate gradient (CG) method.

# C. Algorithm Unrolling for Image Reconstruction

Similar to conventional optimization algorithms, algorithm unrolling requires iterative procedures to solve Equation (2). In MRI image reconstruction, two algorithm unrolling approaches have been proposed. The first one is known as the variational network (VarNet) [26], whose update rule reads

$$\begin{cases}
\mathbf{z}^{(k)} = \tilde{\mathbf{x}}^{(k)} - \lambda \cdot \mathcal{A}^{H} \left( \mathcal{A}(\tilde{\mathbf{x}}^{(k)}) - \mathbf{y} \right) \\
\tilde{\mathbf{x}}^{(k+1)} = \mathbf{z}^{(k)} - \mathcal{N}_{\theta}^{(k)} (\mathbf{z}^{(k)})
\end{cases}$$
(3)

with k being the iteration step. To learn the parameters  $\theta$  and the gradient step size  $\lambda$ , the loss function in VarNet is given

$$\underset{(\theta^{(1)}, \dots, \theta^{(K)}, \lambda)}{\operatorname{argmin}} \mathcal{L}(\mathbf{x}_{\text{ref}}, \tilde{\mathbf{x}}^{(K)}) = \left\| \tilde{\mathbf{x}}^{(K)} - \mathbf{x}_{\text{ref}} \right\|_{2}^{2}$$
(4

where  $\tilde{\mathbf{x}}^{(K)}$  is the estimate after K iterations, and  $\mathbf{x}_{\text{ref}}$  denotes fully-sampled reference images. Here, the neural network parameters  $\theta$  differ among iterations.

The second algorithm unrolling in MRI is known as Modelbased deep learning architecture for inverse problems (MoDL) [27], which tends to learn a denoising neural network, and redefines Equation (2) as

$$\underset{\tilde{\mathbf{x}}}{\operatorname{argmin}} \|\mathbf{y} - \mathcal{A}(\tilde{\mathbf{x}})\|_{2}^{2} + \lambda \|\tilde{\mathbf{x}} - \mathcal{D}_{\omega}(\tilde{\mathbf{x}})\|_{2}^{2}$$
 (5)

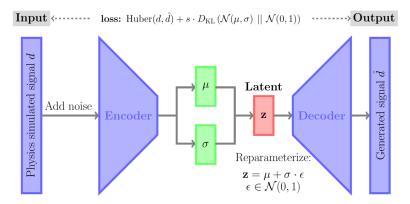
Instead of the VarNet update rule in Equation (3), MoDL employs the alternating minimization scheme,

$$\begin{cases} \mathbf{z}^{(k)} = \mathcal{D}_{\omega}(\tilde{\mathbf{x}}^{(k)}) \\ \tilde{\mathbf{x}}^{(k+1)} = \underset{\mathbf{x}}{\operatorname{argmin}} \|\mathbf{y} - \mathcal{A}(\mathbf{x})\|_{2}^{2} + \lambda \|\mathbf{x} - \mathbf{z}^{(k)}\|_{2}^{2} \end{cases}$$
(6)

where the second minimization problem is solved by CG. MoDL shares weights among iterations, and thus the loss function reduces to only one set of model parameters. Both VarNet and MoDL require reference images, and thus fall into the category of supervised learning.

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### (A) Variational autoencoder



(B) Joint k-q-slice forward operator for multi-band multi-shot DWI acquisition

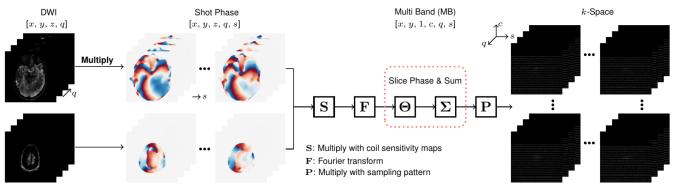


Fig. 1. (A) The architecture of a variational autoencoder. (B) An illustration of the joint k-q-slice forward operator for multi-band multi-shot DWI acquisition. [x, y, z, q] denotes the shape of input DWI  $(\tilde{\mathbf{x}})$ , with x and y as the image size, z as the number of slices, and q as the number of diffusion encodings. The operator outputs multi-dimensional k-space with the shape [x, y, 1, c, q, s], with c as the number of receiver coils, s as the number of shots.

In practice, it is challenging to acquire fully-sampled reference images. To enable deep neural network training without fully sampled reference data, Yaman et al. [28] proposed self-supervised learning via data undersampling (SSDU). In SSDU, the undersampled data is partitioned into two disjoint sets, one for the data-consistency term, and another for the loss function calculation. Thus, the sampling mask **P** splits,

$$\mathbf{P} = \Theta \cup \Lambda \tag{7}$$

SSDU follows the alternating update scheme in MoDL, and such a splitting leads to two modifications in training. First, the k-space data and the forward model in Equation (6) is masked as  $\mathbf{y}_{\Theta}$  and  $\mathcal{A}_{\Theta}$ , respectively. Second, the loss function is computed in k-space,

$$\underset{(\theta,\lambda)}{\operatorname{argmin}} \mathcal{L}(\mathbf{y}_{\Lambda}, \mathcal{A}_{\Lambda}(\tilde{\mathbf{x}}^{(K)})) \tag{8}$$

where a normalized  $\ell_1$ - $\ell_2$  loss is used [28]. Further, Yaman et al. [29] proposed subject-specific zero-shot learning, where one single scan data is partitioned into three disjoint sets, two used to enforce data consistency and to update loss, and the last served as self-validation to allow for early stopping.

III. METHODS

IV. RESULTS

- A. VAE enables robust & accurate learning of DWI signal
- B. Zero-shot learning enables motion-robust DWI
- C. Zero-shot learning: model generalization
- D. VAE modeling with zero-shot learning reconstruction

V. DISCUSSION

VI. CONCLUSION

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## REFERENCES

- T. R. Brown, B. M. Kincaid, and K. Uğurbil, "NMR chemical shift imaging in three dimensions," *Proc. Natl. Acad. Sci. USA*, vol. 79, pp. 3532–3526, 1982.
- [2] D. Le Bihan, E. Breton, D. Lallemand, P. Grenier, E. Cabanis, and M. Laval-Jeantet, "MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders," *Radiology*, vol. 161, pp. 401–407, 1986.
- [3] K.-D. Merboldt, W. Hanicke, and J. Frahm, "Self-diffusion NMR imaging using stimulated echoes," *J. Magn. Reson.*, vol. 64, pp. 479– 486, 1985.
- [4] P. Mansfield, "Multi-planar image formation using NMR spin echoes," J Phys C, vol. 10, pp. 55–58, 1977.
- [5] D. Ma, V. Gulani, N. Seiberlich, K. Liu, J. L. Sunshine, J. L. Duerk, and M. A. Griswold, "Magnetic resonance fingerprinting," *Nature*, vol. 495, pp. 187–192, 2013.

- [6] M. Doneva, P. Börnert, H. Eggers, C. Stehning, J. Sénégas, and A. Mertins, "Compressed sensing for magnetic resonance parameter mapping," *Magn. Reson. Med.*, vol. 64, pp. 1114–1120, 2010.
- [7] P. B. Roemer, W. A. Edelstein, C. E. Hayes, S. P. Souza, and O. M. Mueller, "The NMR phased array," *Magn. Reson. Med.*, vol. 16, pp. 192–225, 1990.
- [8] D. K. Sodickson and W. J. Manning, "Simultaneous acquisition of spatial harmonics (SMASH): Fast imaging with radiofrequency coil arrays," *Magn. Reson. Med.*, vol. 38, pp. 591–603, 1997.
- [9] K. P. Pruessmann, M. Weiger, M. B. Scheidegger, and P. Boesiger, "SENSE: Sensitivity encoding for fast MRI," *Magn. Reson. Med.*, vol. 42, pp. 952–962, 1999.
- [10] K. P. Pruessmann, M. Weiger, P. Börnert, and P. Boesiger, "Adcances in sensitivity encoding with arbitrary k-space trajectories," *Magn. Reson. Med.*, vol. 46, pp. 638–651, 2001.
- [11] M. A. Griswold, P. M. Jakob, R. M. Heidemann, M. Nittka, V. Jellus, J. Wang, B. Kiefer, and A. Haase, "Generalized autocalibrating partially parallel acquisitions (GRAPPA)," *Magn. Reson. Med.*, vol. 47, pp. 1202– 1210, 2002.
- [12] M. Lustig, D. Donoho, and J. M. Pauly, "Sparse MRI: The application of compressed sensing for rapid MR imaging," *Magn. Reson. Med.*, vol. 58, pp. 1182–1195, 2007.
- [13] K. T. Block, M. Uecker, and J. Frahm, "Undersampled radial MRI with multiple coils. Iterative image reconstruction using a total variation constraint," *Magn. Reson. Med.*, vol. 57, pp. 1186–1098, 2007.
- [14] Z.-P. Liang, "Spatiotemporal imaging with partially separable functions," in 4th IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'4), 2007, pp. 988–991.
- [15] J.-F. Cai, E. J. Candès, and Z. Shen, "A singular value thresholding algorithm for matrix completion," SIAM. J. Optim., vol. 20, pp. 1956– 1982, 2010.
- [16] C. Huang, C. G. Graff, E. W. Clarkson, A. Bilgin, and M. I. Altbach, "T<sub>2</sub> mapping from highly undersampled data by reconstruction of principal component coefficient maps using compressed sensing," Magn. Reson. Med., vol. 67, pp. 1355–1366, 2012.
- [17] F. Lam and Z.-P. Liang, "A subspace approach to high-resolution spectroscopic imaging," Magn. Reson. Med., vol. 71, pp. 1349–1357, 2014
- [18] D. F. McGivney, E. Pierre, D. Ma, Y. Jiang, H. Saybasili, V. Gulani, and M. A. Griswold, "SVD compression for magnetic resonance finger-printing in the time domain," *IEEE Trans. Med. Imaging*, vol. 33, pp. 2311–2322, 2014.
- [19] J. I. Tamir, M. Uecker, W. Chen, P. Lai, M. T. Alley, S. S. Vasanawala, and M. Lustig, "T<sub>2</sub> shuffling: Sharp, multicontrast, volumetric fast spin-echo imaging," *Magn. Reson. Med.*, vol. 77, pp. 180–195, 2017.
- [20] G. E. Hinton and R. R. Salakhutdinov, "Reducing the dimensionality of data with neural networks," *Science*, vol. 313, pp. 504–507, 2006.
- [21] F. Lam, Y. Li, and X. Peng, "Constrained magnetic resonance spectroscopic imaging by learning nonlinear low-dimensional models," *IEEE Trans. Med. Imaging*, vol. 39, pp. 545–555, 2019.
- [22] M. Mani, V. A. Magnotta, and M. Jacob, "qModeL: A plug-and-play model-based reconstruction for highly accelerated multi-shot diffusion MRI using learned priors," *Magn. Reson. Med.*, vol. 86, pp. 835–851, 2021.
- [23] S. Boyd, N. Parikh, E. Chu, B. Peleato, and J. Eckstein, "Distributed optimization and statistical learning via the alternating direction method of multipliers," *Foundations and Trends in Machine Learning*, vol. 3, pp. 1–122, 2010.
- [24] K. Gregor and Y. LeCun, "Learning fast approximations of sparse coding," in 27th International Conference on Machine Learning (ICML'27), 2010, pp. 399–406.
- [25] V. Monga, Y. Li, and Y. C. Eldar, "Algorithm Unrolling: Interpretable, Efficient Deep Learning for Signal and Image Processing," *IEEE Signal Processing Magazine*, vol. 38, pp. 18–44, 2021.
- [26] K. Hammernik, T. Klatzer, E. Kobler, M. P. Recht, D. K. Sodickson, T. Pock, and F. Knoll, "Learning a variational network for reconstruction of accelerated MRI data," *Magn. Reson. Med.*, vol. 79, pp. 3055–3071, 2018
- [27] H. K. Aggarwal, M. P. Mani, and M. Jacob, "MoDL: Model-based deep learning architecture for inverse problems," *IEEE Trans. Med. Imaging*, vol. 38, pp. 394–405, 2018.
- [28] B. Yaman, S. A. H. Hosseini, S. Moeller, J. Ellermann, K. Uğurbil, and M. Akçakaya, "Self-supervised learning of physics-guided reconstruction neural networks without fully sampled reference data," *Magn. Reson. Med.*, vol. 84, pp. 3172–3191, 2020.

- [29] B. Yaman, S. A. H. Hosseini, and M. Akçakaya, "Zero-shot self-supervised learning for MRI reconstruction," in 10th International Conference on Learning Representations (ICLR'10), 2022.
- [30] B. Zhu, J. Z. Liu, S. F. Cauley, B. R. Rosen, and M. S. Rosen, "Image reconstruction by domain-transform manifold learning," *Nature*, vol. 555, pp. 487–492, 2018.
- [31] F. Liu, R. Kijowski, G. E. Fakhri, and L. Feng, "Magnetic resonance parameter mapping using model-guided self-supervised deep learning," *Magn. Reson. Med.*, vol. 85, pp. 3211–3226, 2021.
- [32] Y. Arefeen, J. Xu, M. Zhang, Z. Dong, F. Wang, J. White, B. Bilgic, and E. Adalsteinsson, "Latent signal models: Learning compact representations of signal evolution for improved time-resolved, multi-contrast MRI," Magn. Reson. Med., vol. 90, pp. 483–501, 2023.
- [33] P. J. Basser, J. Mattiello, and D. Le Bihan, "MR diffusion tensor spectroscopy and imaging," *Biophys. J.*, vol. 66, pp. 259–267, 1994.
- [34] D. P. Kingma and M. Welling, "Auto-encoding variational bayes," in 2nd International Conference on Learning Representations (ICLR'2), 2014.
- [35] Z. Tan, P. A. Liebig, R. M. Heidemann, F. B. Laun, and F. Knoll, "Accelerated diffusion-weighted magnetic resonance imaging at 7 T: Joint reconstruction for shift-encoded navigator-based interleaved echo planar imaging (JETS-NAViEPI)," *Imaging Neuroscience*, vol. 2, pp. 1– 15, 2024.