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Published on: 01 Nov 2019 - Medical Physics (Med Phys)

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HYDRA: Hybrid Deep Magnetic Resonance Fingerprinting

Pingfan Song¹ Yonina C. Eldar² Gal Mazor³ Miguel R. D. Rodrigues⁴

Abstract

Purpose: Magnetic resonance fingerprinting (MRF) methods typically rely on dictionary matching to map the temporal MRF signals to quantitative tissue parameters. Such approaches suffer from inherent discretization errors, as well as high computational complexity as the dictionary size grows. To alleviate these issues, we propose a HYbrid Deep magnetic ResonAnce fingerprinting approach, referred to as HYDRA.

Methods: HYDRA involves two stages: a model-based signature restoration phase and a learning-based parameter restoration phase. Signal restoration is implemented using low-rank based de-aliasing techniques while parameter restoration is performed using a deep nonlocal residual convolutional neural network. The designed network is trained on synthesized MRF data simulated with the Bloch equations and fast imaging with steady state precession (FISP) sequences. In test mode, it takes a temporal MRF signal as input and produces the corresponding tissue parameters.

Results: We validated our approach on both synthetic data and anatomical data generated from a healthy subject. The results demonstrate that, in contrast to conventional dictionary-matching based MRF techniques, our approach significantly improves inference speed by eliminating the time-consuming dictionary matching operation, and alleviates discretization errors by outputting continuous-valued parameters. We further avoid the need to store a large dictionary, thus reducing memory requirements.

Conclusions: Our approach demonstrates advantages in terms of inference speed, accuracy and storage requirements over competing MRF methods.

Key words: Magnetic Resonance Fingerprinting, Quantitative Magnetic Resonance Imaging, Deep Learning, Nonlocal Residual Convolutional Neural Network, Self-attention

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:

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10.1002/mp.13727.

³⁰ This work was supported by the Royal Society International Exchange Scheme IE160348, by the European Union's Horizon

^{31 2020} grant ERC-BNYQ, by the Israel Science Foundation grant no. 335/14, by ICore: the Israeli Excellence Center 'Circle of

³² Light', by the Ministry of Science and Technology, Israel, by UCL Overseas Research Scholarship (UCL-ORS) and by China

³³ Scholarship Council (CSC) and by EPSRC grant EP/K033166/1.

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I. Introduction

Magnetic Resonance Fingerprinting (MRF)^{1,2,3,4,5,6,7,8} has emerged as a promising Quan-41 titative Magnetic Resonance Imaging (QMRI) approach, with the capability of providing 42 multiple tissue's intrinsic spin parameters simultaneously, such as the spin-lattice magnetic 43 relaxation time (T1) and the spin-spin magnetic relaxation time (T2). Based on the fact 44 that the response from each tissue with respect to a given pseudo-random pulse sequence is 45 unique, MRF exploits pseudo-randomized acquisition parameters to create unique temporal 46 signal signatures, analogous to a "fingerprint", for different tissues. A dictionary matching 47 operation is then performed to map an inquiry temporal signature to the best matching 48 entry in a precomputed dictionary, leading to multiple tissue parameters directly. 49

The temporal signatures are generated by varying the acquisition parameters of a 50 pseudo-random excitation pulse sequence, such as repetition time (TR), time of echo (TE), 51 and radio frequency flip angle (FA) over time. The dictionary is composed of a large number 52 of entries that are usually simulated by the Bloch equations given pseudo-random pulse se-53 quences. Each entry represents a unique temporal signature associated with a specific tissue 54 and its quantitative parameters, such as the T1 and T2 relaxation times. Thus, once the 55 best matching (i.e. most correlated) entry is found, it directly leads to multiple quantitative 56 parameters simultaneously via a lookup-table operation. 57

MRI physics and physiological constraints make the MR scanning procedure time-58 consuming. To shorten acquisition time, subsampling is commonly performed in k-space 59 (a.k.a conjugate Fourier transform domain) in order to reduce the number of samples and 60 accelerate imaging speed. However, such k-space subsampling results in temporal signatures 61 that are corrupted by aliasing, blurring and noise. This hampers the accuracy associated 62 with estimation of the tissue parameters using a dictionary matching procedure. In order 63 to alleviate the impact of such distortion and corruption, de-aliasing operations are often 64 exploited to restore cleaner signatures before performing signature-to-parameter mapping. 65 Therefore, MRF reconstruction usually involves two operations: signature restoration and 66 parameter restoration. 67

Inspired by the successful application of sparsity-driven image processing approaches in MRI reconstruction^{9,10,11,12}, several works^{3,4,5,6} suggest to incorporate prior knowledge such as sparsity and low-rank to attenuate distortion and corruption, improving the signature

I.. INTRODUCTION

restoration performance, during the initial MRF reconstruction stage. This is then followed 71 by a dictionary matching operation, performing mapping from purified temporal signatures 72 to tissue's quantitative parameters. However, such dictionary matching based signature-73 to-parameter mapping exhibits several drawbacks^{13,14}. Since the simulated dictionary and 74 lookup-table contain a finite number of elements, they can only cover a limited number 75 of discrete values for each type of tissue parameter. We refer to the difference between a 76 continuous-valued tissue parameter and its closest available discrete value on a lattice as the 77 discretization error. For example, a pair of dictionary and lookup-table that contain 101 78 elements will lead to a discretization error of maximum 25 ms if they cover the range of 0 ms 79 5000 ms with a fixed interval of 50 ms for a specific tissue parameter, e.g. T1. To reduce 80 the discretization error, a huge dictionary that is composed of a large number of entries is 81 needed to represent tissues with fine granularity over the entire value range of target tissue 82 parameters. However, storing a large dictionary becomes prohibitively memory-consuming, 83 as the dictionary size and density often increase exponentially with the number of tissue 84 parameters. Specifically, the number of entries in a dictionary will be P^s for s parameters 85 each containing P values, since every combination of these s parameters determines a specific 86 tissue which is characterized by a specific signature. For example, given T1, T2 relaxations, 87 i.e. s = 2, if each of them contains 1000 values, the dictionary will have 1000^2 entries. In addition, finding the best matching entry becomes computationally intense for a large 89 dictionary, considerably limiting the inference speed. 90

In this paper, we propose an alternative approach to dictionary matching based on deep 91 neural networks (a.k.a. deep learning)^{15,16}, which we refer to as HYDRA: HYbrid Deep mag-92 netic ResonAnce fingerprinting. The motivation derives from the fact that a well designed 93 and tuned deep neural network is capable of approximating complex functions, leading to 94 state-of-the-art results in a number of tasks such as image classification, super-resolution, 95 speech recognition, and more^{17,18,19,20,21,22,23}. Recent work^{13,14} proposed to exploit neural 96 networks to replace the dictionary and lookup-table used in conventional MRF reconstruction approaches. These proposed neural networks suffer from two limitations: First, these 98 approaches are based on neural network models containing only 3-layers, thus suffer from 99 limited capacity of capturing complex mapping functions. Second, these methods focused 100 exclusively on parameter restoration stage (the second stage in MRF reconstruction), but not 101 on signature restoration (the first stage in MRF reconstruction). Therefore, these techniques 102

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rely on fully-sampled data instead of typically available sub-sampled k-space data. 103

Different from Cohen et al.'s fully-connected feed-forward neural network¹³, and Hoppe 104 et al.'s vanilla convolutional neural network (CNN)¹⁴, the proposed HYDRA involves both 105 a signature restoration and a parameter restoration phase. Signature restoration is im-106 plemented using a low-rank based de-aliasing method adapted from Mazor et al.⁶ while 107 parameter restoration is implemented using a deep nonlocal residual convolutional neural 108 network developed for this purpose. Our key contributions with respect to prior work are: 109

HYDRA is, to the best of our knowledge, the first deep network approach to combine model-based de-aliasing and learning-based parameter mapping. HYDRA eliminates the requirement for the memory and time-consuming dictionary matching operation, thus significantly improving inference speed without compromising on reconstruction performance.

- A 1D nonlocal residual convolutional neural network is designed to capture the mappings from temporal MRF signals to tissue parameters. Owing to residual learning and a self-attention mechanism, our network is deeper and more sophisticated than competing network models. This allows to capture complex parameter mappings more effectively, and output continuous parameters to alleviate discretization issues. 119
 - The designed network is trained on synthesized MRF data simulated with the Bloch equations, but is still applicable to anatomical data. This contributes to eliminating the requirement for a large amount of real MRF data.

A low-rank based de-aliasing technique is developed in order to take advantage of temporal similarity for signature restoration.

The low-rank based signature restoration is organically combined with the learningbased parameter restoration to achieve fast and accurate MRF reconstruction. Such strategy enables HYDRA to handle both fully-sampled k-space data and more importantly sub-sampled k-space data.

A series of numerical experiments are conducted to evaluate the proposed approach 129 on both synthetic and anatomical data. The results demonstrate improved inference 130 speed, accuracy and discretization errors over competing methods^{1,2,3,4,5,6,13,14}. 131

The rest of the paper is organized as follows. In Section II., we formulate the MRF 132 reconstruction problem, introduce related methods, and present our approach, involving the 133

(2)

use of a low-rank based signature restoration procedure together with a deep network for
parameter restoration. Section III. is devoted to experimental results, followed by a discussion
in Section IV. and a conclusion in Section V..

¹³⁷ II. Materials and Methods

138 II.A. The MRF Problem Formulation

¹³⁹ MRF data is composed of multiple frames sampled in k-space over time. A series of such ¹⁴⁰ frames are vectorized and then stacked together along the temporal dimension to construct ¹⁴¹ a measurement matrix $\mathbf{Y} \in \mathcal{C}^{Q \times L}$, where Q is the number of k-space samples in each frame, ¹⁴² and L is the number of frames. Due to k-space subsampling, every column vector $\mathbf{Y}_{:,i}$ ¹⁴³ represents a subsampled Fourier transform of a vectorized image frame $\mathbf{X}_{:,i}$:

$$\mathbf{Y} = [\mathbf{Y}_{:,1}, \cdots, \mathbf{Y}_{:,L}] = [F_u\{\mathbf{X}_{:,1}\}, \cdots, F_u\{\mathbf{X}_{:,L}\}],$$
(1)

where $F_u\{\cdot\}$ denotes a subsampled 2D Fourier transform.

Each column $\mathbf{X}_{:,i}$ represents a MR contrast acquired with RF sequence parameters:

 $\boldsymbol{\Theta}_{:i}^{TRE} = [TR^i, TE^i, FA^i]^T, \ i \in [1, L]$

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where TR^i and TE^i denote the repetition time and echo time, respectively, and FA^i denotes the flip angle of the RF pulse during sampling the *i*-th contrast. Every row $\mathbf{X}_{j,:}$ represents a temporal signature, i.e. temporal signal evolution of a specific tissue at the *j*-th image pixel. The signature depends on the tissue's relaxation times, such as T1 and T2, grouped as a row vector:

$$\Theta_{j,:}^{T12} = [T1^j, T2^j], \ j \in [1, N]$$
(3)

where, N denotes the number of pixels in each image frame. Note that, j is the spatial index while i is the temporal index throughout. Given RF sequence parameters Θ^{TRE} , and parameters $\Theta_{j,:}^{T12}$ of a specific tissue, its temporal signature $\mathbf{X}_{j,:}$ can be derived as:

$$\mathbf{X}_{j,:} = f(\mathbf{\Theta}_{j,:}^{T12}, \mathbf{\Theta}^{TRE})$$
(4)

where $f(\cdot)$ denotes the Bloch equations. This MR contrast matrix **X** is associated with the k-space measurements **Y** per column by the subsampled Fourier transform, and it is related to tissue parameters Θ^{T12} per row by the Bloch equations, as illustrated in Fig. 1.

II.. MATERIALS AND METHODS

page 5

Given RF sequence parameters Θ^{TRE} and k-space measurements Y, the goal of MRF reconstruction is to estimate the tissue parameters Θ^{T12} . Typically, the image stack X is first reconstructed from Y, referred to as signature restoration, and then mapped to tissue parameters Θ^{T12} via dictionary matching, referred to as parameter restoration^{1,2,3,4,5,6}. This process is illustrated in Fig. 2.

The dictionary is a collection of temporal signatures that are usually simulated by the Bloch equations for various typical tissues, given the pseudo-random RF pulse sequences and tissue parameters. Given an inquiry temporal signature, dictionary matching computes the inner product between the temporal signature with each dictionary entry, selecting the entry in the dictionary exhibiting the highest correlation with the inquiry one as the best matching signature. Once the best entry is found, it directly leads to multiple tissue parameters, such as T1, T2, simultaneously, via searching a lookup-table.

Let $\mathbf{LUT} \in \mathcal{R}^{K \times 2}$ denote a lookup-table composed of K tissues, each containing 2 parameters, i.e., T1 and T2 relaxation times¹. Let $\mathbf{D} \in \mathcal{C}^{K \times L}$ denote the corresponding dictionary simulated using Bloch equations given the RF sequence parameters Θ^{TRE} , formulated as $\mathbf{D}_{k,:} = f(\mathbf{LUT}_{k,:}, \Theta^{TRE})$. Since each temporal signature $\mathbf{D}_{k,:}$ is linked with the k-th tissue's parameters $\mathbf{LUT}_{k,:}$, the choice of a large dictionary size K can in principle provide enough granularity to capture a range of possible tissue values.

In conclusion, existing MRF reconstruction approaches involve two stages: signature restoration and parameter restoration, that can be succinctly written as

$$\boldsymbol{\Theta}_{j,:}^{T12} = g(h(\mathbf{Y})_{j,:} | \boldsymbol{\Theta}^{TRE}), \ j \in [1, N],$$

$$(5)$$

where the function $\mathbf{X} = h(\mathbf{Y})$ represents the signature restoration operation such as sparsity or low-rank based de-aliasing and denoising methods, whereas $g(\mathbf{X}_{j,:}|\mathbf{\Theta}^{TRE})$ denotes the parameter restoration operation, such as dictionary matching based methods^{1,2,3,4,5,6}.

Our approach aims to perform signature restoration via low-rank based de-aliasing and parameter restoration via a neural network in order to achieve improved MRF reconstruction performance. We highlight that our method only requires a simulated dictionary during network training. Once the network is trained, the dictionary is not needed anymore. In

¹Note that the off resonance parameter, which appeared in the original MRF paper¹, has been omitted here, since the sequence used in our experiments is derived from the FISP sequence, which is insensitive to off resonance effects^{2,6}.

Algorithm 1 Original MRF method¹ Input: A set of subsampled k-space images: Y A pre-simulated dictionary: D An appropriate lookup-table: LUT Output: Magnetic parameter maps: \hat{T}_1 , \hat{T}_2 Step 1. Restore signatures:

 $\widehat{\mathbf{X}}_{:,i} = F_u^H \{ \mathbf{Y}_{:,i} \}, \, \forall i$

Step 2. Restore parameters for every j via dictionary matching:

$$\widehat{k_j} = \arg\max_k \frac{\operatorname{\mathbf{Re}}\left\langle \mathbf{D}_{k,:}, \widehat{\mathbf{X}}_{j,:} \right\rangle}{\|\mathbf{D}_{k,:}\|_2^2} , \quad \widehat{T}_1^j, \widehat{T}_2^j = \operatorname{\mathbf{LUT}}(\widehat{k_j})$$

addition, our approach also eliminates a simulated dictionary for signature restoration, which is a key difference from FLOR^{5,6} during signature restoration.

¹⁹¹ II.B. Previous Methods

Dictionary Matching based MRF approaches. The original MRF reconstruction algorithm¹ is based on dictionary matching, as presented in Algorithm 1. It finds the best matching dictionary entry for the acquired temporal signature according to their inner product and then searches the lookup-table to obtain corresponding tissue parameters. Here, $F_u^H\{\cdot\}$ denotes the inverse Fourier transform operating on the zero filled k-space data where zeros are filled at the unknown frequencies and symbol $\mathbf{Re} \langle \mathbf{a}, \mathbf{b} \rangle$ represents the real part of the inner product of two vectors \mathbf{a} and \mathbf{b} .

Exploiting the nature of signals, by using appropriate prior knowledge, can often con-199 tribute to improved signal processing performance. In this spirit, later works suggested 200 to incorporate sparsity in MRF reconstruction to further improve performance, inspired 201 by successful applications of sparsity in MRI reconstruction^{9,10,11}. Davies et al.³ proposed 202 BLoch response recovery via Iterative Projection (BLIP) which exploits sparsity in the dic-203 tionary domain. BLIP consists of iterating between two main steps: (a) a gradient step 204 which enforces consistency with the measurements, based on the Projected Landweber Al-205 gorithm (PLA) generalized from the iterative hard thresholding method; (b) a projection 206 which matches each row of X to a single dictionary atom. Instead of exploiting sparsity in 207

II.. MATERIALS AND METHODS

the dictionary domain, Wang et al.⁴ suggested to leverage sparsity in the wavelet domain of 208 each imaging frame, $\mathbf{X}_{::i}$. They further replaced the Euclidean norm with the Mahalanobis 209 distance for dictionary matching. Considering that adjacent MR image frames along the 210 temporal dimension should exhibit high resemblance, Mazor et al.^{5,6} proposed a magnetic 211 resonance Fingerprint with LOw-Rank prior for reconstructing the image stack and quanti-212 tative parameters, referred to as FLOR, which achieved state-of-the-art performance. The 213 algorithm, described in Algorithm 2, relies on two priors: a low rank prior on the the matrix 214 **X**, and the fact that the rows of **X** lie in the column space of the dictionary **D**. 215

Algorithm 2 FLOR⁶

Input:

A set of subsampled k-space images: **Y**; A pre-simulated dictionary: **D**; An appropriate lookuptable: **LUT**; Parameters μ for gradient step and λ for regularization

Output:

Magnetic parameter maps: \widehat{T}_1 , \widehat{T}_2 Initialization: $\widehat{\mathbf{X}}^0 = 0$, $\mathbf{P} = \mathbf{D}^{\dagger}\mathbf{D}$, where \mathbf{D}^{\dagger} is the pseudo-inverse of \mathbf{D} . Step 1. Restore signatures via iterating until convergence:

• Gradient step for every *i*:

$$\widehat{\mathbf{Z}}_{:,i}^{t+1} = \widehat{\mathbf{X}}_{:,i}^t - \mu F_u^H \{ F_u \{ \widehat{\mathbf{X}}_{:,i}^t \} - \mathbf{Y}_{:,i} \}$$
(6)

where the superscript t represents the index of iterations.

• Project onto the dictionary subspace:

$$[\mathbf{U}, \mathbf{S}, \mathbf{V}] = \operatorname{svd}(\widehat{\mathbf{Z}}^{t+1}\mathbf{P})$$
(7)

where svd denotes the singular-value decomposition operation, and $\mathbf{S} = diag(\{\sigma_j\})$ is a rectangular diagonal matrix with singular values $\{\sigma_j\}$ on its diagonal.

• Soft-threshold the non-zero singular values with $\lambda \mu$ and reconstruct signatures $\widehat{\mathbf{X}}^{t+1}$:

$$\sigma'_{j} = \max\{\sigma_{j} - \lambda \mu, 0\}, \quad \widehat{\mathbf{X}}^{t+1} = \mathbf{U}\mathbf{S}'\mathbf{V}^{H}$$
(8)

where $\mathbf{S}' = diag(\{\sigma'_i\}).$

Step 2. Restore parameters for every j via dictionary matching:

$$\widehat{k_j} = \arg\max_k \frac{\operatorname{\mathbf{Re}}\left\langle \mathbf{D}_{k,:}, \widehat{\mathbf{X}}_{j,:} \right\rangle}{\|\mathbf{D}_{k,:}\|_2^2} , \quad \widehat{T}_1^j, \widehat{T}_2^j = \operatorname{\mathbf{LUT}}(\widehat{k_j})$$

216 Learning-based MRF approaches. The above techniques all use dictionary matching

II.. MATERIALS AND METHODS

to perform mapping from temporal signatures to tissue parameters. Therefore, these meth-217 ods suffer from drawbacks such as discretization error, slow inference speed and memory-218 consuming storage. In order to alleviate these issues, recent works^{13,14} propose to exploit 219 neural networks to replace dictionaries and lookup-tables used in conventional MRF recon-220 struction approaches. Cohen et al. suggest a fully-connected feed-forward neural network 221 $(FNN)^{13}$. Since the input layer of the FNN is fully connected with the input temporal 222 signature, the number of neurons in the input layer corresponds to the length of the input 223 temporal signature. This makes the network structure less flexible, as a FNN network trained 224 on temporal signatures with a certain length is not applicable to temporal signatures with 225 a different length. In addition, the fully-connected structure results in rapid increase in the 226 number of parameters along with the growth of depth, making the network more suscepti-227 ble to overfitting. Hoppe et al.¹⁴ propose a 3-layer vanilla CNN for parameter restoration. 228 Both¹³ and¹⁴ focus exclusively on learning the signature-to-parameter mapping from a pair 229 of dictionary and lookup-table simulated using the Bloch equations. During the validation, 230 they assume that clean temporal signatures are available as input into the trained networks. 231 However, since temporal signatures obtained from k-space subsampled MRF data are al-232 ways contaminated by aliasing and noise, their approaches, when applied directly in such 233 k-space subsampling situations, suffer from heavy artifacts introduced during the signature 234 restoration phase, leading to poor performance. 235

²³⁶ II.C. Proposed Methods

The proposed hybrid deep magnetic resonance fingerprinting (HYDRA) approach, summarized in Algorithm 3, consists of two stages: signature restoration and parameter restoration, (see also (5)). As illustrated in Fig. 3, a low-rank based de-aliasing method is used to restore signatures, and then a 1D nonlocal residual convolutional neural network is used to map each restored signature to corresponding tissue parameters.

In particular, given Θ^{TRE} and k-space samples \mathbf{Y} , in our proposed approach, the function $\mathbf{X} = h(\mathbf{Y})$ in (5) represents a signature restoration operation using low-rank based de-aliasing techniques without requiring a dictionary. The function $\Theta_{j,:}^{T12} = g(\mathbf{X}_{j,:}|\Theta^{TRE})$ in (5) represents a parameter restoration operation that exploits a trained neural network to map each restored signature $\mathbf{X}_{j,:}$ to corresponding tissue parameters $\Theta_{j,:}^{T12}$ directly. In the subsequent sections, we provide a detailed description of both stages of our technique.

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II.C.1. Low-rank based signature restoration

Since MRF data consists of multiple frames exhibiting temporal similarity, the imaging contrasts matrix X is typically a low-rank matrix⁶. Therefore, $h(\cdot)$ leverages a low-rank prior for denoising and de-aliasing, formulated as

$$h(\mathbf{Y}) = \arg\min_{\mathbf{X}} \quad \frac{1}{2} \sum_{i} \|\mathbf{Y}_{:,i} - F_u\{\mathbf{X}_{:,i}\}\|_2^2$$

s.t. $\operatorname{rank}(\mathbf{X}) < r$ (9)

where the parameter r is the rank of the matrix, a fixed pre-chosen parameter. Since typically r is not known in advance, we consider a relaxed regularized version:

$$h(\mathbf{Y}) = \arg \min_{\mathbf{X}} \frac{1}{2} \sum_{i} \|\mathbf{Y}_{:,i} - F_u \{\mathbf{X}_{:,i}\}\|_2^2 + \lambda \|\mathbf{X}\|_*$$
(10)

where $\|\mathbf{X}\|_{*}$ denotes the nuclear norm²⁴ of \mathbf{X} , defined as the sum of the singular values of X, and λ is the Lagrangian multiplier manually selected for balancing data fidelity and the rank. Problem (10) can be solved using the incremental subgradient proximal method²⁵, similar as to FLOR⁶. The procedure for solving (5) is shown in Algorithm 3.

One of differences from FLOR⁶ is the fact that we removed the operation of project-260 ing the temporal signal onto a dictionary. This allows to eliminate the requirement for a 261 simulated dictionary in the signature restoration stage, which also alleviates the memory 262 consumption issue. In addition, the computational complexity is reduced by $N \cdot L^2$ floating-263 point operations in each iteration, where L is the dimension of a dictionary element, and N 264 is the number of pixels in each image frame. On the other hand, the gained benefits are at 265 the price of requiring more iterations to converge. Another difference from FLOR⁶ is that 266 we exploit a network, instead of dictionary matching, for signature-to-parameter mapping. 267

²⁶⁸ II.C.2. Learning-based parameter restoration

Once the imaging contrasts matrix \mathbf{X} is recovered from the k-space samples \mathbf{Y} , each temporal signature $\mathbf{X}_{j,:}$ is input into the trained network for parameter restoration, formulated as:

$$\boldsymbol{\Theta}_{j,:}^{T12} = g(\mathbf{X}_{j,:} | \boldsymbol{\Theta}^{TRE}), \ j \in [1, N]$$
(11)

where $g(\cdot)$ denotes the trained network, Θ^{TRE} denotes the fixed RF sequence parameters. We next describe the network structure, training and testing procedures.

274 Network structure.

Algorithm 3 Proposed MRF reconstruction approach: HYDRA Input: A set of subsampled k-space images: Y

The trained network: g

Parameters μ for gradient step and λ for regularization

Output: Magnetic parameter maps \hat{T}_1, \hat{T}_2

Initialization: $\widehat{\mathbf{X}}^0 = 0$

Step 1. Restore signatures via iterating until convergence:

- Gradient step for every i, the same as (6).
- Perform SVD:

$$[\mathbf{U}, \mathbf{S}, \mathbf{V}] = \operatorname{svd}(\widehat{\mathbf{Z}}^{t+1})$$

• Soft-threshold the non-zero singular values $\{\sigma_j\}$ of **S** with parameter $\lambda \mu$ and reconstruct signatures $\widehat{\mathbf{X}}^{t+1}$, the same as (8).

Step 2. Restore parameters for every j via the trained network:

$$\widehat{T}_1^j, \widehat{T}_2^j = g(\widehat{\mathbf{X}}_{j,:})$$

The proposed network has a 1D nonlocal residual CNN architecture with short-cuts for residual learning and nonlocal operations for achieving a self-attention mechanism. As illustrated in Fig. 3, it starts with two 1D convolutional layers before connecting with 4 residual / non-local operation blocks, and finally ends with a global-average-pooling layer followed by a fully-connected layer. Every residual block is followed by a non-local operation block. Four such blocks are interspersed with each other.

Each residual block contains a max-pooling layer with stride 2, two convolution layers and a shortcut that enforces the network to learn the residual content. The filter size is set to be equal to 21 throughout convolutional layers. The number of channels, a.k.a feature maps, in the first two convolutional layers is set to 16 and then is doubled in subsequent four residual blocks until 128 in the final residual block. The size of feature maps in the next block halves in contrast with the previous one due to max-pooling. In this way, we gradually reduce temporal resolution while extract more features to increase content information.

Inspired by the self-attention scheme and nonlocal neural networks^{26,27}, non-local operations are incorporated into the designed network to achieve the attention mechanism, in order to capture long-range dependencies with fewer layers. In contrast to the progressive behavior of convolutional operations that process one local neighborhood at a time, the non-

II.. MATERIALS AND METHODS

local operations compute the response at a position as a weighted sum of the features at all
positions in the feature maps. Formally, the nonlocal operation is formulated as²⁷:

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$$\mathbf{y}_i = \frac{1}{C(\mathbf{x})} \sum_{\forall j} f(\mathbf{x}_i, \mathbf{x}_j) g(\mathbf{x}_j) \,. \tag{12}$$

Here, i is the index of an output position and j is the index that enumerates all possible 295 temporal positions, \mathbf{x} is the input temporal signal or its features and \mathbf{y} is the output signal 296 of the same size as x. A pairwise function f computes a scalar between i and all j to 297 represent the affinity relationship of these two positions. The unary function q computes a 298 representation of the input signal at position j. The response is normalized by a factor $C(\mathbf{x})$. 299 There exists a few instantiations for function f and q. For simplicity, the unary function 300 g is chosen as a linear embedding: $g(\mathbf{x}_j) = \mathbf{W}_g(\mathbf{x}_j)$, where \mathbf{W}_g is a weight matrix to be 301 learned. Regarding the affinity matrix f, we adopt the embedded Gaussian to compute 302 similarity in an embedding space, which is formulated as: $f(\mathbf{x}_i, \mathbf{x}_j) = e^{\theta(\mathbf{x}_i)^\top \phi(\mathbf{x}_j)}$. Here, 303 $\theta(\mathbf{x}_i) = \mathbf{W}_{\theta} \mathbf{x}_i$ and $\phi(\mathbf{x}_j) = \mathbf{W}_{\phi} \mathbf{x}_j$ are two learned embeddings. The normalization factor is 304 set as $C(\mathbf{x}) = \sum_{\forall j} f(\mathbf{x}_i, \mathbf{x}_j)$. For a given $i, \frac{1}{C(\mathbf{x})} f(\mathbf{x}_i, \mathbf{x}_j)$ becomes the softmax computation 305 along the dimension j, which leads to $\mathbf{y} = softmax(\mathbf{x}^{\top}\mathbf{W}_{\theta}^{\top}\mathbf{W}_{\phi}\mathbf{x})g(\mathbf{x})$, which is the self-306 attention form 26 . 307

The non-local behavior in (12) is due to the fact that all positions (j) are considered in the operation. As a comparison, a convolutional operation sums up the weighted input in a local neighborhood²⁷. It implies that the non-local operation directly captures long-range dependencies in the temporal dimension via computing interactions between any two points, regardless of their positional distance. In this way, the network is able to extract global features and take advantage of the full receptive field in each layer.

The global-average-pooling layer is used to average each feature map in order to integrate 314 information in every channel for improved robustness to corrupted input data. This global-315 average-pooling layer also reduces the number of parameters significantly, thus lessening the 316 computation cost as well as preventing over-fitting. The last fully-connected layer outputs 317 estimated parameters – T1 and T2 relaxation times. The designed network contains around 318 0.27 million parameters. The weights are initialized using He-normal-distribution²⁸. The 319 max-norm kernel constraint²⁹ is exploited to regularize the weight matrix directly in order to 320 prevent over-fitting. The designed network can also be adapted for various MRF sequences, 321 such as the original MRF sequence – inversion-recovery balanced steady state free-precession 322

II.. MATERIALS AND METHODS

(IR-bSSFP) sequence, that depends also on the intrinsic df parameter. It is possible to adjust
the number of outputs to adapt to more parameters, such as proton density, B0.

To summarize, our network is motivated and inspired by recent successful applications 325 of convolutional neural networks and variants. Convolutional neural networks have been 326 proved to be a powerful model to capture useful features from signals and images. By 327 introducing convolution, local receptive field and weight sharing design, a CNN is capable 328 of taking advantage of local spatial coherence and translation invariance characteristics in 329 the input signal, thus become especially well suited to extract relevant information at a low 330 computational $\cot^{17,18,19,20,21,22}$. On the other hand, the residual network architecture^{18,19} 331 provides an effective way to design and train a deeper model, since it alleviates the gradient 332 vanishing or exploding problems by propagating gradients throughout the model via short-333 cuts, a.k.a skip connections. By leveraging non-local operation based attention mechanism, 334 neural networks are endowed with capability of extracting global features and capturing 335 long-range dependencies. 336

337 Network training.

The designed network is trained on a synthesized dictionary **D** and corresponding lookup-table **LUT** to learn the signature-to-parameter mappings $\mathbf{LUT}_{k,:} = g(\mathbf{D}_{k,:}|\Theta^{TRE})$.

The training dataset is synthesized as follows. First, we determine the range of tissue 340 parameters. For example, one may set T1 relaxation times to cover a range of [1, 5000] ms 341 and T2 relaxation times to cover a range of [1, 2000] ms with an increment of 10 ms for both. 342 Thus, the T1 and T2 values constitute a grid with dimension 500×200 , in which each point 343 represents a specific combination of T1 and T2 values, and hence characterizes a specific 344 tissue. Points corresponding to T1 < T2 have been excluded as such combinations have no 345 physical meaning. All the valid points are stacked together to generate a lookup-table. For 346 instance, the above setting for T1 and T2 leads to a lookup-table of dimension 80100×2 . 347 The RF pulse sequences used in our work are fast imaging with steady state precession 348 (FISP) pulse sequences with parameters that have been used in previous publications in the 349 field of MRF^{2,6,8}. Given the lookup-table and RF pulse sequences, dictionary entries can be 350 synthesized by solving the Bloch equations using the extended phase graph formalism^{30,31}. 351

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When the training dataset is ready, the dictionary entries are used as input signals and

II.. MATERIALS AND METHODS

corresponding lookup-table entries serve as the groundtruth. All the dictionary entries are 353 input into the designed network batch by batch which outputs estimated parameters. The 354 root mean square errors (RMSE) of the outputs are calculated with respect to corresponding 355 groundtruth. The resulting RMSE loss is then backpropagated from the output layer to the 356 first layer to update the weights and bias by using Adam³² as the optimization algorithm. 357 More training details are provided in the subsequent experiment section. Once the training 358 procedure is completed, given an inquiry signal evolution $\mathbf{X}_{j,:}$, it is able to map such a time 359 sequence directly to corresponding tissue parameters, as formulated in (11), implying that 360 no dictionary or lookup-table are required during the inference. Since we only need to store 361 the trained network which is a compact model, it consumes less memory than storing the 362 dictionary and lookup-table. 363

We emphasize that even though the network is trained on a grid of tissue values, it is expected to capture the mapping function from temporal signatures to tissue parameters. Thus the trained network is capable of outputting tissue values not existing in the grid of training values. Detailed results can be found in Fig. 7 and Table 2. This feature is favorable, as it implies that well designed and trained networks have an ability to overcome discretization issues. The overall procedures for solving (10) and (11) are shown in Algorithm 370 3.

³⁷¹ III. Experimental Results

In this section, we conduct a series of experiments to evaluate our approach, comparing it with other state-of-the-art MRF methods 1,3,6,13,14 .

The experiments are categorized into a few types: training, testing on synthetic data, 374 testing on anatomical data using variable density Gaussian sampling patterns and spiral 375 sampling patterns at different sampling ratios and number of time frames, as described in 376 Table 1. For the network training, synthesized temporal signatures, i.e. simulated dictionary 377 entries of **D** shown as Fig. 4, are used as input signals and corresponding parameter values 378 in the lookup-table **LUT** serve as the groundtruth. The proposed network is trained to 379 capture the signature-to-parameter mappings. For testing on synthetic data, synthesized 380 temporal signatures in X are used as input signals and corresponding parameter values in 381 $\Theta^{T_{12}}$ serve as the groundtruth. The aim is to test the parameter restoration performance 382

III.. EXPERIMENTAL RESULTS

only. For testing on anatomical data, the k-space measurements \mathbf{Y} which are derived from the Fourier transform (for Gaussian patterns) or non-uniform FFT (for spiral trajectories)³³ of \mathbf{X} , are used as input and corresponding parameter values in Θ^{T12} serve as reference. When there is no k-space subsampling, the aim is to test the parameter restoration performance only. When there exists k-space subsampling, the aim is to test the overall performance, including both signature restoration and parameter restoration. More detailed descriptions are provided in each subsection.

³⁹⁰ III.A. Training

As mentioned in Section II.C.2., the designed network is trained on a pair of synthesized dictionary **D** and lookup-table **LUT**, simulated using Bloch equations and FISP pulse sequences^{2,6}.

The FISP pulse sequence used in our experiments was designed with parameters $\Theta_{:,i}^{TRE} = [TR^i, TE^i, FA^i]^T, i \in [1, L]$ that have been used in previous publications in the field of MRF^{2,6,8}. The echo time TE^i was constant of 2ms. The repetition time TR^i was randomly varied in the range of 11.5 - 14.5 ms with a Perlin noise pattern. All the flip angles $FA^i, i \in [1, L]$ constituted a sinusoidal variation in the range of 0 - 70 degrees to ensure smoothly varying transient state of the magnetization, as shown in Figure 5.

For the range of tissue parameters, T1 relaxation times are set to cover a range of 400 [1, 5000] ms and T2 relaxation times to cover a range of [1, 2000] ms with an increment 401 of 10 ms for both. Such parameter ranges cover the relaxation time values that can be 402 commonly found in a brain scan³⁴. All the valid combinations of T1 and T2 values are 403 stacked together, generating a lookup-table LUT of dimension $K \times 2$ where K = 80100. 404 Given the lookup-table and RF pulse sequences, dictionary entries are synthesized by solving 405 the Bloch equations using the extended phase graph formalism, leading to a dictionary of 406 dimension $K \times L$ where L = 200 or 1000 is the number of time frames. 407

When the training dataset is ready, the dictionary entries are used as input signals and corresponding lookup-table entries serve as the groundtruth to train the designed network, as mentioned in Section II.C.2.. The model was trained for 50 epochs. It takes around 30 seconds for running one epoch on average, thus around 25 minutes for completing 50 epochs, on a NVIDIA GeForce GTX 1080 Ti GPU. In each training epoch, 20% of the training

III.. EXPERIMENTAL RESULTS

samples are separated aside for validation dataset. The learning rate decays from 1e-2 to 1e-6 every 10 epochs. Each batch was experimentally set to contain 256 time-sequences in order to balance the convergence rate and weights updating rate well. For comparison purposes, we also implemented Hoppe et al.'s CNN referring to¹⁴, and Cohen et al.'s FNN referring to¹³ with the same structure and parameters as specified in their papers. Then we use the same GPU and training dataset to train their networks with specified learning rate and number of epochs until convergence.

We adopt a few widely used metrics, such as root mean square error (RMSE), signalto-noise ratio (SNR) and peak signal-to-noise ratio (PSNR) to evaluate the image quality quantitatively. The definitions of RMSE, SNR and PSNR are given as follows:

$$RMSE = \sqrt{\frac{\|\mathbf{X} - \widehat{\mathbf{X}}\|_F^2}{N}},$$
(13)

$$SNR = 20 \log_{10} \frac{\|\mathbf{X}\|_F^2}{RMSE}, \qquad (14)$$

$$PSNR = 20 \log_{10} \frac{PeakVal}{RMSE}, \qquad (15)$$

where matrices **X** and $\widehat{\mathbf{X}}$ denote the ground truth signal and its reconstructed version, respectively, N denotes the total number of elements in the signal and $\|\cdot\|_F$ denotes the Frobenius norm. PeakVal stands for the pixel peak value in an image, e.g., 1 for a normalized signal.

⁴²⁴ III.B. Testing on synthetic dataset

In this subsection, we evaluate the performance of HYDRA on a synthetic testing dataset. 425 The procedures of constructing a synthetic testing dataset is similar to the construction of 426 the training dataset: 500 different T1 values are randomly selected from 1 - 5000 ms, while 427 200 different T2 values are randomly selected from 1 - 2000 ms, using random permutation 428 based on uniformly distributed pseudorandom numbers. All the valid combinations from 429 the selected T1 and T2 values are stacked together, generating a parameter matrix Θ^{T12} 430 of dimension 80000×2 with N = 80000. The RF pulse sequences are the same as in the 431 training stage. Given the parameter matrix and RF pulse sequences, input signal signatures 432 are synthesized by solving the Bloch equations using the extended phase graph formalism, 433 leading to a signature matrix **X** of dimension $N \times L = 80000 \times 200$, with each row representing 434

III.. EXPERIMENTAL RESULTS

a temporal signature corresponding to a specific combination of T1 and T2 values. The signature matrix **X** and parameter matrix Θ^{T12} constitute the synthetic testing dataset, with **X** as input and Θ^{T12} as the groundtruth.

We input the synthetic testing signatures \mathbf{X} into Hoppe et al.'s CNN¹⁴, Cohen et al.'s 438 FNN¹³, and the network of HYDRA to compare the outputs with groundtruth T1 and T2 439 values in Θ^{T12} . We also compare with dictionary matching methods^{1,2,3,4,5,6} which exploit 440 the same dictionary **D** and lookup-table **LUT** to find the best matching entry for each sig-441 nature in \mathbf{X} and then estimate parameter values by searching the lookup-table. As shown 442 in Table 2, Table 3, Fig. 6 and Fig. 7, the estimated parameter values using the proposed 443 network obtained outstanding agreement with the groundtruth, yielding higher PSNR, SNR 444 and smaller RMSE than the dictionary matching method^{1,2,3,4,5,6}, as well as competing net-445 works^{13,14}. 446

In particular, to illustrate in detail how well neural networks tackle the discretization 447 issue inherent to dictionary matching, we show the testing performance on continuous-valued 448 T1, T2 parameters which have small intervals, e.g. 0.5ms, that is 20 times smaller than the 449 training grid intervals 10ms, between neighboring values in Table 3. Since these values and 450 their corresponding MRF signatures do not exist in the training dictionary and lookup-table². 451 the dictionary matching methods report a T1 and T2 value – the closest discretized value 452 present in the dictionary – that can be quite distinct from the groundtruth. In contrast, the 453 various neural network approaches can potentially learn an underlying mapping from the 454 temporal signatures to the respective T1 and T2 values, leading to estimate that are much 455 closer to the groundtruth. Interestingly, our approach outperforms previous networks^{13,14} 456 as shown in Table 3 and Fig. 6. Evidently, neural networks demonstrate much better ro-457 bustness to discretization issues, leading to improved parameter restoration in comparison 458 to dictionary based methods. 459

Another impressive advantage of HYDRA is the fast inference speed. HYDRA takes only
8.2 s to complete the mapping operation for eighty thousand temporal signatures, that is,
53× faster than dictionary matching. Furthermore, the inference speed of HYDRA is subject
to the network topology. That is, once the network structure is fixed, the complexity is fixed.

² As mentioned in the experiment setting in section 5.1, in the training dataset, T1 relaxation times are set to cover a range of [1, 5000] ms and T2 relaxation times to cover a range of [1, 2000] ms with an increment of 10 ms for both, that is, T1 values = $\{1, 11, 21, \dots, 4991\}$, and T2 values = $\{1, 11, 21, \dots, 1991\}$.

In contrast, the complexity of dictionary matching is limited by the dictionary density. This implies that our advantage will be more prominent in comparison with competing techniques using a dictionary with higher density.

467 III.C. Testing on anatomical dataset

In this subsection, we evaluate our approach on an anatomical testing dataset. We construct 468 the dataset from brain scans that were acquired with GE Signa 3T HDXT scanner from a 469 healthy subject.³ Since there are no groundtruth parameter values for the T1 and T2 param-470 eter maps, we obtain gold standard data by acquiring Fast Imaging Employing Steady-state 471 Acquisition (FIESTA) and Spoiled Gradient Recalled Acquisition in Steady State (SPGR) 472 images, at 4 different flip angles $(3^{\circ}, 5^{\circ}, 12^{\circ} \text{ and } 20^{\circ})$, and implementing corrections³⁵ fol-473 lowed by DESPOT1 and DESPOT2³⁶ algorithms. The constructed gold standard T1, T2 474 parameter maps have a dimension of 128×128 for each map, accordingly leading to a pa-475 rameter matrix Θ^{T12} of size 16384×2 by stacking vectorized T1, T2 maps together. Based 476 on the parameter matrix Θ^{T12} and pre-defined RF pulse sequences, we generate temporal 477 signatures using Bloch equations, the same mechanism as generating the synthetic testing 478 dataset, leading to a signature matrix **X** of dimension $N \times L = 16384 \times 200$. The signature 479 matrix **X** and parameter matrix Θ^{T12} constitute the anatomical testing dataset, with **X** as 480 input and Θ^{T12} as the gold standard reference. 481

⁴⁸² Note that, since the gold standard T1, T2 maps exhibit spatial structures in the image ⁴⁸³ domain, the resulting signature matrix **X** can be regarded as a stack of L = 200 vectorized ⁴⁸⁴ image frames, where each frame exhibits specific spatial structures. Therefore, it makes ⁴⁸⁵ sense to perform Fourier transform and k-space subsampling for each column of **X** to get ⁴⁸⁶ k-space measurements **Y**. This is the key difference between the anatomical dataset and the ⁴⁸⁷ synthetic dataset.

We first explore the case with full k-space sampling in order to evaluate the parameter restoration performance of HYDRA. Then, we consider situations with k-space subsampling in order to evaluate both the signature restoration and the parameter restoration performance of HYDRA.

³The experiment procedures involving human subjects described in this paper were approved by the Institutional Review Board of Tel-Aviv Sourasky Medical Center, Israel.

⁴⁹² III.C.1. Full k-space sampling

In the first case, the fully-sampled k-space measurements **Y**, derived from the Fourier trans-493 form of X, are used as input to obtain the estimated Θ^{T12} . This is equivalent to inputting X 494 into the network of HYDRA, or performing dictionary matching based on X directly, since 495 the inverse Fourier transform of the fully-sampled measurements Y is exactly the same as 496 X. The aim is to test the parameter restoration performance only. In the experiment, cor-497 responding parameter values in $\Theta^{T_{12}}$ serve as the gold standard reference. For comparison, 498 dictionary matching methods 1,2,3,4,5,6 exploit the same dictionary **D** and lookup-table **LUT** 499 as in our training stage to find the best matching entry and estimate parameter values for 500 each signature in \mathbf{X} . 501

Visual and quantitative results are shown in Fig. 8, Fig. 9 and Table 4. It can be 502 seen that our basic version of HYDRA outperforms dictionary matching^{1,2,3,4,5,6}, vielding 503 better visual and quantitative performance, e.g., 7.9 dB SNR gains for T2 mapping. The 504 RMSE of T2 mapping is also reduced to 2.498 from 6.252, accordingly. Our nonlocal version 505 of HYDRA achieves even better performance, leading to 10 dB SNR gains with RMSE 506 as small as 1.86. This is owing to the advantage that the trained network is a powerful 507 function approximator, which is able to output well-estimated parameter values based on 508 learnt mapping functions, even though these values do not exist in the training dictionary 509 and lookup-table. In contrast, dictionary matching only matches signatures to discrete 510 parameters existing in the training dataset. In other words, if there are no exact matching 511 dictionary element and parameter values for an inquiry MRF signature, it will find adjacent 512 values as approximations, thus introducing discretization error. On the other hand, the 513 advantage of HYDRA over dictionary matching on T1 mapping is not as significant as on 514 T2 mapping quantitatively. But the visual improvements are evident. A similar trend 515 is observed when comparing our network with competing networks such as Hoppe et al.'s 516 CNN^{14} and Cohen et al.'s FNN¹³. In addition, HYDRA takes around 2 s to accomplish the 517 mapping for 16384 signatures, $40 \times$ faster than dictionary matching^{1,2,3,4,5,6}. 518

⁵¹⁹ III.C.2. k-space subsampling using Gaussian patterns

In k-space subsampling situations, the developed low-rank based de-aliasing method is applied to restore the signature matrix \mathbf{X} from the measurements matrix \mathbf{Y} . Then, the re-

constructed X is used as input into the network for parameter mapping to obtain the cor-522 responding tissue parameter values. In the experiments, the sub-sampling factor β is set to 523 be 70% and 15%. For $\beta = 15\%$, 15% k-space data is acquired by a series of 2D random 524 Gaussian sampling patterns, shown in Fig. 10, leading to a k-space measurement matrix Y 525 of size $Q \times L = 2458 \times 200$. Similarly, $\beta = 70\%$ gives rise to a k-space measurement matrix 526 **Y** of size $Q \times L = 11469 \times 200$. A larger λ enforces lower rank for the restored signature 527 matrix X to strengthen the de-aliasing effect, while a smaller λ encourages X to have a sub-528 sampled Fourier transform that approximates the k-space measurements matrix Y better. 529 Therefore, we tried a range of values from 1 to 20 for λ and experimentally select the best 530 one $\lambda = 5$. Since the low-rank based signature restoration involves gradient descent steps, a 531 larger step size μ accelerates gradient descent speed, but tends to result in oscillation or even 532 divergence, while a smaller μ leads to a slower convergence. We experimentally find that 533 $\mu = 1$ gives a good balance. The same k-space measurements Y are also used by dictionary-534 matching based methods^{1,3,6} for comparison, and the same signature restoration approach 535 is used to convert Y onto X for learning based methods^{13,14}. The aim is to evaluate the 536 overall performance on both signature restoration and parameter restoration. 537

Quantitative performance is shown in Table 5. Note that the advantage of learning-538 based methods over dictionary matching degrades when the subsampling factor increases. 539 This is due to the fact that the restored signatures from highly subsampled k-space data 540 exhibit deviations and distortions, thus leading to poorer input for the trained networks. In 541 spite of this, the proposed approach outperforms the dictionary matching based methods^{1,3} 542 with significant gains, and also yields better or comparable performance as the state-of-the-543 art methods FLOR⁶, CNN¹⁴ and FNN¹³. In addition, it takes around 23s for low-rank based 544 signature restoration and less than 3s for network based parameter restoration. Thus, the 545 total time cost is around 26s, almost $4.8 \times$ faster than FLOR⁶. Furthermore, the speed of 546 our method is $60 \times$ faster than FLOR⁶ for parameter restoration. 547

We compared the performance with/without nonlocal operations in our developed network. The results in Table 4 and 5 show that the proposed network with nonlocal operations based self-attention scheme outperforms the basic counterpart. In particular, the nonlocal version achieves 6 dB gains in terms of SNR over the basic version for T2 mapping. Such significant improvement demonstrates the benefits of capturing long-range dependencies and global features using the nonlocal operation based attention scheme.

III.. EXPERIMENTAL RESULTS

We also investigated the performance with respect to the number of time frames. In 554 particular, we increased L from 200 to 1000 and kept other experiment settings the same as 555 before. The quantitative results are shown in Table 6. It is noticed that given more time 556 frames, all the methods show better performance. Moreover, the performance of learning-557 based methods, including CNN¹⁴, FNN¹³ and HYDRA, improve more than model-based 558 techniques^{1,3,6}. In particular, our approach outperforms competing algorithms quantitatively 559 in terms of PSRN, SNR, and RMSE, as well as demonstrates visual advantage, as shown in 560 Figure 11 and Figure 12. 561

² III.C.3. k-space subsampling using spiral trajectories

We carried out additional experiments with widely used non-Cartesian sampling patterns – 563 variable density spiral trajectories^{6,37}. A set of spiral trajectories used in the experiments are 564 shown in Figure 13. They have FOV of 24 and rotation angle difference of 7.5 degrees between 565 any two adjacent spirals to spread out the alias artifacts. Given such spiral trajectories, 566 data were subsampled to acquire 1488 k-space samples in each time frame, leading to a 567 subsampling ratio of 9% which is defined by the number of acquired samples in the k-space 568 domain divided by the number of pixels in a frame. This setting closely matches the original 569 MRF paper¹ where each single spiral trajectory samples 1450 k-space points (leading to a 570 subsampling ratio around 9%) and any two adjacent spiral trajectories have a rotation angle 571 of 7.5 degrees. 572

In the case of spiral subsampling, during the signature restoration, SParse Uniform Re-573 Sampling (SPURS) algorithm³⁸ was exploited to implement nonuniform Fourier transform 574 between k-space domain and image domain, as SPURS has proved to achieve smaller approx-575 imation errors while maintaining low computational cost comparing with other resampling 576 methods, such as nonuniform-FFT algorithm³³ and regularized Block Uniform ReSampling 577 (rBURS)³⁹. In the experiments, 1000 density variable spiral trajectories were used for k-space 578 subsampling, leading to 1000 time frames. The quantitative and qualitative reconstruction 579 results demonstrate that HYDRA outperforms competing methods with smaller estimation 580 errors, as shown in Table 7, Figure 15 and Figure 14. 581

III.. EXPERIMENTAL RESULTS

IV. Discussion

⁵⁸³ IV.A. Relation to previous works

Our low-rank based signature restoration method is adapted from FLOR⁶ by removing the 584 operation of projecting the temporal signal onto a dictionary. Thus, the signature restoration 585 does not require a simulated dictionary, and saves computational cost. Although recent 586 works^{13,14} exploit neural networks to perform parameter mapping, replacing dictionaries and 587 lookup-tables used in conventional MRF reconstruction approaches, our technique is different 588 from these methods^{13,14}. We design a deep nonlocal residual CNN for capturing signature-to-589 parameter mapping which is organically combined with low-rank based de-aliasing techniques 590 for signature restoration. In this way, our algorithm can bypass some of the issues associated 591 with other techniques: (1) The input dimension issue. The proposed approach can ingest 592 temporal signatures with different lengths without the need to change the structure of the 593 network. This is due to the fact that we rely on convolutional neural networks (CNNs) 594 rather than fully-connected neural networks (FNNs) such as the model used in¹³. (2) The 595 k-space subsampling issue. The proposed approach involves a hybrid of a neural network 596 with a low-rank based de-aliasing approach. Thus it is able to deal with correlations both 597 over time and space via exploiting low-rank regularization and convolution operation. This 598 enables our work to handle k-space subsampling situations. (3) The complex mappings 599 issue. By exploiting a residual network structure, our method can be successfully extended 600 to deeper levels and thus obtain a better capacity to learn complex signature-to-parameter 601 mapping functions. (4) Distortion and corruption issue. Due to the subsampling in k-space, 602 the restored temporal signatures suffer from local distortion and corruption. Such deviation 603 may lead to performance degeneration in the second stage. By incorporating non-local 604 operations in the network design, our method is able to capture global features and find 605 most relevant components for inference, thereby reducing interference of local distortion and 606 corruption. 607

⁶⁰⁸ IV.B. Computational complexity

HYDRA involves two main stages: the low-rank based signature restoration stage and the network based parameter restoration stage. Even though the time cost for parameter restoration is longer than previous methods^{13,14}, the time cost in the this stage is only a small fraction of the total time consumption, as the computational complexity is dominated by

IV.. DISCUSSION

⁶¹³ the signature restoration stage. In other words, the computational burden of HYDRA lies
⁶¹⁴ in the SVD calculation in the first stage. Hence, fast SVD methods can be employed to
⁶¹⁵ dramatically improve the efficiency of signature restoration.

⁶¹⁶ IV.C. Model storage requirements

Regarding the storage requirement (in double precision), HYDRA needs only 2.1 megabytes to store the network with 0.5 million parameters, while it requires 108 megabytes to store a simulated dictionary of size 80100×200 and 551 megabytes for size 80100×1000 . Note that the dictionary volume will grow exponentially with the number of parameters, but the space required for storing a network is not strictly limited by the dictionary density once the topology of the network is fixed, thus significantly alleviating the storage burden inherent to the exponential growth of multi-dimensional dictionaries.

₆₂₄ IV.D. Impact of providing continuous T1/T2 values

Providing continuous T1/T2 values is an advantage of neural network based parameter mapping over dictionary matching. This property may find promising applications in some 626 practical scenarios, for exampling, monitoring sensitive changing of pathology condition 627 over time, such as multiple sclerosis 40,41 , stroke 42 , and treatment responses 43,44 , where the 628 differences in T1 and T2 values between healthy and diseased tissues or between disease 629 stages could be very small⁴⁵. On the other hand, to fulfil this potential of network based 630 MRF techniques, prerequisites on the accuracy and precision of MRI measurements are 631 needed. Taking T1/T2 quantification as an example, even for the inversion recovery spin 632 echo (IR-SE) / multiple single-echo spin echo MRI sequences which are considered as the 633 gold standard for T1/T2 quantification, there exist variations of 2% - 9% on the measured 634 relaxation times⁴⁵. Such anatomical measurement uncertainties and model imperfections 635 may weaken the advantage and clinical impact of providing continuous T1/T2 values using 636 network based MRF techniques to some extent. Therefore, improving the accuracy of gold 637 standard approaches in the future would contribute to making the most of the potential of 638 neural networks in the MRF domain. 639

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V. Conclusion

We proposed a hybrid deep MRF approach which combines low-rank based signature restoration with learning-based parameter restoration. In our approach, a low-rank based dealiasing method is used to restore clean signatures from subsampled k-space measurements. Then, a 1D deep nonlocal residual CNN is developed for efficient signature-to-parameter mapping, replacing the time-consuming dictionary matching operation in conventional MRF techniques. Our approach demonstrates advantages in terms of inference speed, accuracy and storage requirements over competing MRF methods as no dictionary is needed for recovery.

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V.. CONCLUSION

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Figure 1: Relationship between key variables. The MR contrast matrix \mathbf{X} is associated with the k-space measurements \mathbf{Y} per column by the subsampled Fourier transform. It is related to tissue parameters $\boldsymbol{\Theta}^{T12}$ per row by the Bloch equations. Given $\boldsymbol{\Theta}^{TRE}$ and \mathbf{Y} , the image stack \mathbf{X} is commonly first reconstructed from \mathbf{Y} , referred to as signature restoration, and then mapped to tissue parameters $\boldsymbol{\Theta}^{T12}$ via dictionary matching, referred to as parameter restoration.



Figure 2: Parameter restoration using dictionary matching. Given an inquiry temporal signature, dictionary matching computes its inner product with each dictionary entry, and selects the most correlated one with the highest inner product as the best matching signature. Once the best matching entry is found, it directly leads to multiple tissue parameters, such as T1, T2, simultaneously, via searching a lookup-table.



Figure 3: Diagram of the proposed MRF reconstruction approach. During the training stage, synthesized dictionary entries are used as training signatures to train the designed 1D nonlocal residual CNN until the outputs approximate parameter values in **LUT** well. In this way, the network captures the signature-to-parameter mapping. During the testing stage, a low-rank based algorithm is used to restore the image stack, a matrix containing signatures in rows, from k-space measurements. Then the restored signatures are input into the trained network to obtain corresponding tissue parameters directly.

Experiment	Settings
	Input: D , size $K \times L = 80100 \times 200$.
Training	Groundtruth: LUT , size 80100×2 .
	k-space subsampling factor β : not available.
Testing on synthetic data	Input: X , size $N \times L = 80000 \times 200$.
	Groundtruth: Θ^{T12} , size 80000×2 .
	k-space subsampling factor β : not available.
Testing on	Input: Y , size $Q \times L = 16384\beta \times 200$ or $16384\beta \times 1000$.
resting on	Reference: Θ^{T12} , size $N \times 2 = 16384 \times 2$.
anatomical data	k-space subsampling factor β : 70%, 15% using Gaussian patterns.
Testing on	Input: Y , size $Q \times L = 16384\beta \times 1000$.
resting on	Reference: $\mathbf{\Theta}^{T12}$, size $N \times 2 = 16384 \times 2$.
anatomical data	k-space subsampling factor β : 9% using spiral trajectories.

Table 1: Brief description of experiment types and settings.



Figure 4: Synthetic MRF temporal signatures with 200 time frames. (a) Temporal signatures corresponding to parameter values $\{(T1, T2)\}\ ms = \{(800,40),(800,60),(800,80),(800,100)\}\ ms.$ (2) Temporal signatures corresponding to parameter values $\{(T1, T2)\}\ ms = \{(400,80),(600,80),(800,80),(1000,80)\}\ ms.$



Figure 5: FISP pulse sequence parameters. All the flip angles (FA) constituted a sinusoidal variation in the range of 0 - 70 degrees to ensure smoothly varying transient state of the magnetization. The repetition time (TR) was randomly varied in the range of 11.5 - 14.5 ms with a Perlin noise pattern.

Table 2:	Testing on	synthetic	dataset.	Comparing	parameter	$\operatorname{restoration}$	performance,	in
terms of	PSNR, SNF	R, RMSE a	and correl	ation coeffic	ient.			

	Dict. Match.	CNN ¹⁴	FNN ¹³	Proposed
	T1 / T2	T1 / T2	T1 / T2	T1 / T2
PSNR (dB)	$59.15 \ / \ 52.31$	$62.96 \ / \ 49.64$	$58.97 \ / \ 54.96$	79.30 / 72.99
SNR (dB)	$55.23 \; / \; 47.15$	$59.05 \ / \ 44.49$	$55.06 \ / \ 49.81$	${\bf 75.38}~/~{\bf 67.83}$
RMSE (ms)	$5.515 \; / \; 4.847$	$3.554\ /\ 6.591$	$5.63 \; / \; 3.57$	0.542 ~/~ 0.448
CorrCoef	$1.00\ /\ 1.00$	$1.00 \ / \ 1.00$	$1.00 \ / \ 1.00$	$1.00 \ / \ 1.00$
time cost (s)	464.10	2.87	1.58	8.2

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		T1 Est	imation		T1 E	rrors		
Truth	D.M.	14	13	Ours	D.M.	14	13	Ours
1005.0	1001.0	1002.9	1009.3	1004.8	-4.0	-2.1	4.3	-0.2
1005.5	1001.0	1003.3	1010.0	1005.3	-4.5	-2.3	4.5	-0.2
1006.0	1011.0	1003.6	1010.6	1005.8	5.0	-2.4	4.6	-0.2
1006.5	1011.0	1004.1	1011.2	1006.3	4.5	-2.5	4.7	-0.2
1007.0	1011.0	1004.5	1011.8	1006.8	4.0	-2.5	4.8	-0.3
RMSE	-	-	-	-	4.4	2.3	4.6	0.2
		T2 Est	imation			T2 E	rrors	
Truth	D.M.	14	13	Ours	D.M.	14	13	Ours
505.0	501.0	513.6	504.3	505.2	-4.0	8.6	-0.7	0.2
505.5	511.0	514.1	504.8	505.7	5.5	8.6	-0.7	0.2
	F01 0	F147	505 2	506.2	-5.0	86	-0.7	0.2
506.0	501.0	514.7	000.0	000.2	-0.0	0.0	-0.1	0.2
$\begin{array}{c} 506.0 \\ 506.5 \end{array}$	$\begin{array}{c} 501.0\\ 511.0\end{array}$	514.7 515.2	505.5 505.9	506.2 506.8	4.5	8.7	-0.6	0.2
$506.0 \\ 506.5 \\ 507.0$	$501.0 \\ 511.0 \\ 511.0$	514.7 515.2 515.7	505.3 505.9 506.4	506.2 506.8 507.3	4.5 4.0	8.7 8.7	-0.6 -0.6	$\begin{array}{c} 0.2\\ 0.3\\ 0.3\end{array}$



Figure 6: Testing on synthetic dataset involving detailed T1 / T2 examples that are not on the training grid and their intervals are much smaller than the training grid intervals. Dictionary matching finds best adjacent values from the dictionary, i.e. 1001, 1011 for T1, and 501, 511 for T2. In contrast, owing to the captured mapping functions, neural networks output continuous values. Proposed HYDRA leads to the smallest deviations and bias.

Table 4: Testing on anatomical dataset with full k-space sampling. Comparing parameter restoration performance, in terms of PSNR, SNR, RMSE and correlation coefficient.

-	,				
	Dict. Match.	$\rm CNN^{14}$	FNN ¹³	Proposed basic	Proposed nonlocal
	T1 / T2				
PSNR (dB)	56.64 / 52.04	54.06 / 49.88	$54.53 \ / \ 54.36$	56.59 / 60.01	$56.47 \ / \ 62.56$
SNR (dB)	42.20 / 27.81	$39.63 \ / \ 25.66$	40.09 / 30.07	$42.15 \ / \ 35.76$	$42.03 \ / \ 38.32$
RMSE (ms)	$6.623 \ / \ 6.252$	$8.912 \ / \ 8.015$	$8.45 \ / \ 4.78$	$6.661 \ / \ 2.498$	$6.76\ /\ 1.86$
CorrCoef	$1.00 \ / \ 1.00$	$1.00 \ / \ 1.00$	1.00 / 1.00	$1.00 \ / \ 1.00$	$1.00 \ / \ 1.00$
time cost (s)	84.56	0.69	0.41	1.6	2.1

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Figure 7: Testing on the synthetic dataset for comparing parameter restoration performance. Subfig. (a) - (d) show the results using dictionary matching 1,2,3,4,5,6 , FNN¹³, CNN¹⁴ and HYDRA. In each subfigure, the left figure compares the estimated T1 or T2 values (marked with red dot) with groundtruth values (marked with blue line), and the right figure shows the deviations of the estimation from the groundtruth. Parameter mapping performance of HYDRA is much better than competing methods, in the entire value range of T1 and T2 parameters, resulting in smaller deviations.

Table 5: Testing on anatomical dataset with k-space subsampling ratio 70% and 15% using Gaussian patterns and 200 time frames.

		k-space subsampling factor $\beta = 70\%$								
		Ma et al. ¹ BLIP ³		FLOR ⁶	CNN ¹⁴	FNN ¹³	Prop	oosed		
							basic	nonlocal		
Γ	PSNR (dB)	$23.69 \ / \ 38.17$	45.67 / 47.84	$50.11 \ / \ 50.85$	49.71 / 45.48	50.15 / 51.08	$50.79 \ / \ 51.59$	49.87 / 57.57		
	SNR (dB)	$8.73 \ / \ 13.84$	31.28 / 23.49	35.67 / 26.48	35.26 / 21.19	35.70 / 26.67	$36.34 \ / \ 27.19$	35.42 / 33.30		
	RMSE (ms)	$294.32 \ / \ 30.87$	$23.42 \ / \ 10.14$	14.01 / 7.17	14.71 / 13.31	$13.99 \ / \ 6.98$	$12.99 \ / \ 6.57$	14.44 / 3.31		
)	time cost (s)	72.88	75.70	85.35	23.72	23.53	24.85	26.3		
T		k-space subsampling factor $\beta = 15\%$								
		Ma et al. ¹ BLIP ³ FLOR ⁶			CNN ¹⁴	FNN ¹³	Prop	oosed		
							basic	nonlocal		
Г	PSNR (dB)	$27.94 \ / \ 32.84$	$35.45 \ / \ 39.25$	44.95 / 46.11	43.74 / 35.98	45.03 / 45.90	45.23 / 44.44	45.39 / 51.32		
	SNR (dB)	13.50 / 8.61	$20.99 \ / \ 14.58$	30.51 / 21.89	29.23 / 12.26	30.58 / 21.32	$30.76 \ / \ 19.78$	30.91 / 26.99		
1	RMSE (ms)	$180.3 \ / \ 57.03$	$76.01 \ / \ 27.25$	$25.46 \ / \ 12.37$	$29.27 \ / \ 39.73$	25.21 / 12.68	$24.65 \ / \ 15.00$	$24.20 \ / \ 6.79$		
Ľ.	time cost (s)	106	112.8	121.7	24.54	24.36	25.67	27.31		



Figure 8: Testing on the anatomical dataset with full k-space sampling for comparing parameter restoration performance. Subfig. (a) - (d) show the results using dictionary matching^{1,2,3,4,5,6}, FNN¹³, CNN¹⁴ and HYDRA. Each subfigure shows the deviations of the estimation from the reference. Parameter mapping performance using HYDRA outperforms competing methods significantly, resulting in smaller deviations. The performance is also verified by quantitative metrics, as shown in Table 4.

Table 6: Testing on anatomical dataset with k-space subsampling ratio 15% using Gaussian patterns and 1000 time frames.

	Ma et al. ¹	BLIP ³	FLOR ⁶	$\rm CNN^{14}$	FNN ¹³	Proposed
PSNR (dB)	$27.53 \ / \ 33.28$	$35.50 \ / \ 39.10$	50.90 / 50.04	41.96 / 39.21	52.62 / 49.86	$52.32 \ / \ 52.79$
SNR (dB)	$13.09 \ / \ 9.05$	21.06 / 14.87	$36.44 \ / \ 25.65$	$27.44 \ / \ 15.05$	38.17 / 25.43	37.86 / 28.35
RMSE (ms)	$189.09\ /\ 54.21$	$75.53 \ / \ 27.74$	$12.83 \ / \ 7.87$	$35.91 \ / \ 27.37$	$10.52 \;/\; 8.04$	$10.89 \ / \ 5.74$

Table 7: Testing on anatomical dataset with k-space subsampling ratio 9% using spiral trajectories and 1000 time frames.

	Ma et al. ¹	BLIP ³	FLOR ⁶	CNN ¹⁴	FNN ¹³	Proposed
PSNR (dB)	$26.66 \ / \ 30.44$	$29.35 \ / \ 39.47$	39.32 / 44.60	35.68 / 27.74	40.26 / 44.70	41.45 / 45.41
SNR (dB)	$12.22 \ / \ 6.21$	$15.03 \ / \ 15.22$	24.88 / 20.38	$21.45 \ / \ 4.48$	$25.84 \ / \ 20.30$	27.02 / 21.04
RMSE (ms)	$209.01\ /\ 75.18$	$153.37\ /\ 26.57$	$48.67 \ / \ 14.72$	$73.96\ /\ 102.57$	$43.65 \ / \ 14.55$	$38.08 \ / \ 13.41$

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page 34





T1/T2 Reference SNR = 42.20/27.81 dB SNR = 39.63/25.66 dB SNR = 40.09/30.07 dB SNR = 42.03/38.32 dBFigure 9: Visual results of testing on anatomical dataset with full k-space sampling for comparing parameter restoration performance. Top two rows correspond to T1 maps and residual errors while bottom two rows correspond to T2 maps and residual errors. Proposed HYDRA results in comparable performance for T1 mapping and yields much better performance for T2 mapping, obtaining 10dB higher SNR gains than competing dictionary-matching based methods^{1,2,3,4,5,6}. HYDRA also outperforms previous networks, such as CNN by Hoppe et al.¹⁴ and FNN by Cohen et al.¹³.



Figure 10: A series of Gaussian patterns used for k-space subsampling.



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HYDRA

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Figure 15: Visual results of testing on anatomical dataset with k-space subsampling factor 9% using spiral trajectories with L = 1000. Comparison between BLIP³, FLOR⁶, CNN by Hoppe et al.¹⁴, FNN by Cohen et al.¹³ and HYDRA.



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