

# Quantitative Imaging: Physics integrated and machine learning based models in MRI



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Mathematical  
Colloquium @  
Chinese University of  
Hong Kong

1. Preliminary on (quantitative) MRI
2. Mathematical understanding of MRF-based methods
3. Integrated physics-based method for qMRI
4. Using learning-informed physical models
  - 4.1 Some analytical aspects
  - 4.2 Application to qMRI

# Preliminary on (quantitative) MRI

# Magnetic resonance imaging

Three major steps in the current routine of MRI experiment:

- Aligning magnetic nuclear spins in an applied constant magnetic field  $B_0$
- Perturbing this alignment via radio frequency (RF) pulse  $B_1$
- Applying magnetic gradient field  $G$  to distinguish individual contributions

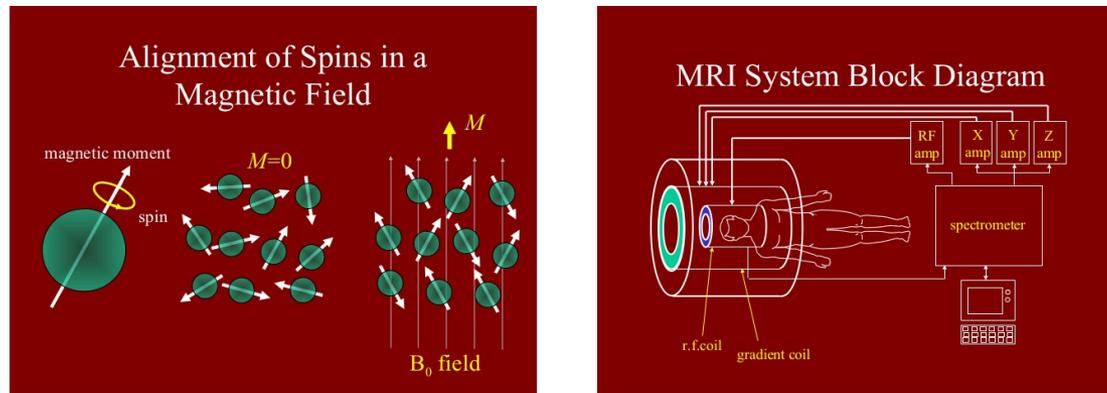


Abbildung: MRI diagram (Published in Health and Medicine)

„All models are wrong, but some are useful“  
George Box, 1976

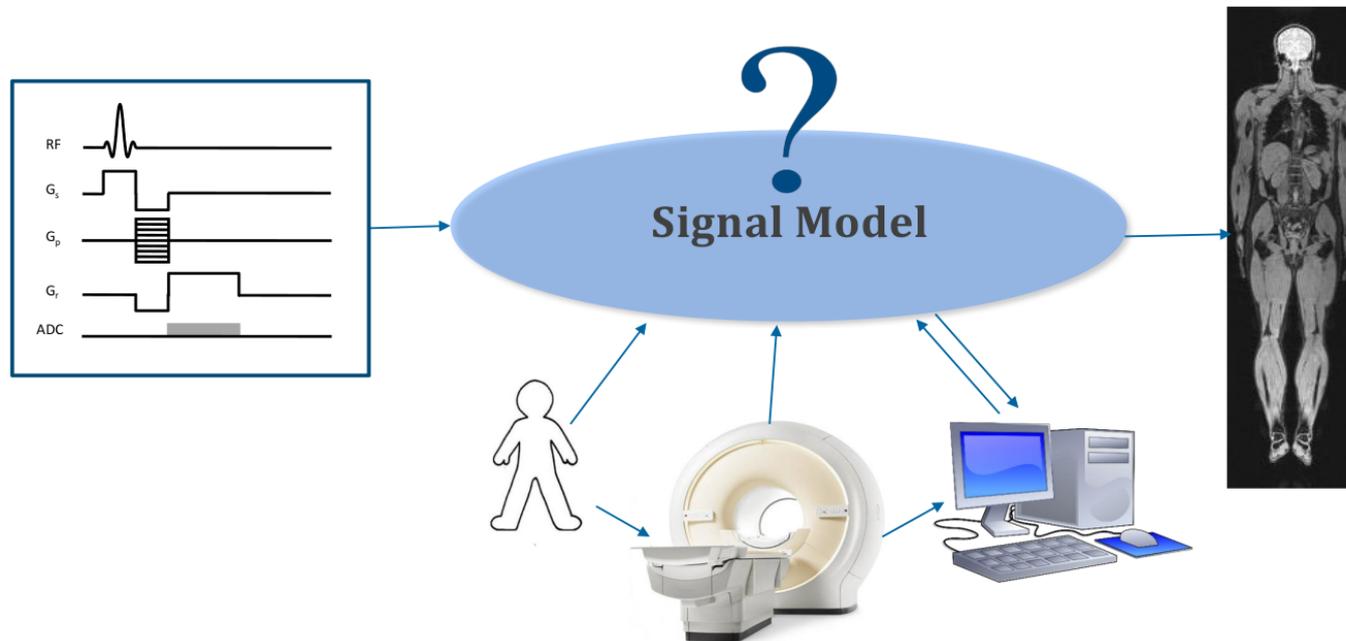


Abbildung: Courtesy of Dr. Mariya Doneva (Philips)

# Bloch equations and simulation of MRI data

- Bloch equations (physical law behind the nuclear magnetic resonance):

$$\frac{\partial m(\mathbf{x}, t)}{\partial t} = \gamma m(\mathbf{x}, t) \times B(\mathbf{x}, t) - \left( \frac{m_x(\mathbf{x}, t)}{T_2}, \frac{m_y(\mathbf{x}, t)}{T_2}, \frac{m_z(\mathbf{x}, t) - 1}{T_1} \right)^\top.$$

$\gamma$  is a known parameter,  $B = B_0 + B_1 + (0, 0, G \cdot \mathbf{x})$ .  $T_1$  and  $T_2$  are longitude and transverse relaxation times, respectively, tissue (space) dependent.

- Some phrases in MRI:

- Flip angles  $\alpha$ : Characterized by the RF pulses  $B_1$  field  $\alpha(t) = \gamma \int_0^t |B_1(s)| ds$ .
- Repetition time  $TR$ : The length of the time period from one pulse to the next pulse.

- Selecting a slice at  $z = z_0$

$$Y =: P\mathcal{F}(\rho T_{xy} m(\cdot, \cdot, z_0)).$$

$P$  denotes a subsampling operator,  $T_{xy} m := m_x + im_y$ , and  $\rho$  is proton density.

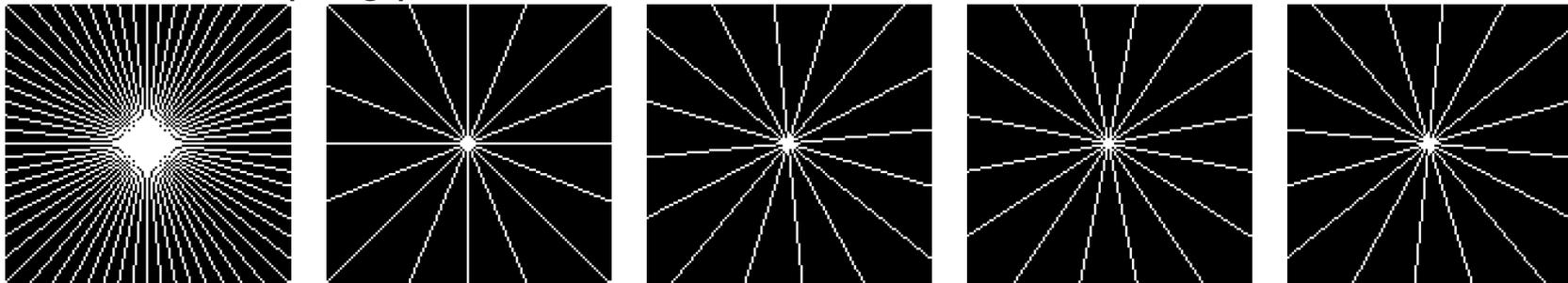
This is an idealized mathematical description, e.g., coil sensitivity are ignored.

# Subsampling patterns

Cartesian subsampling pattern

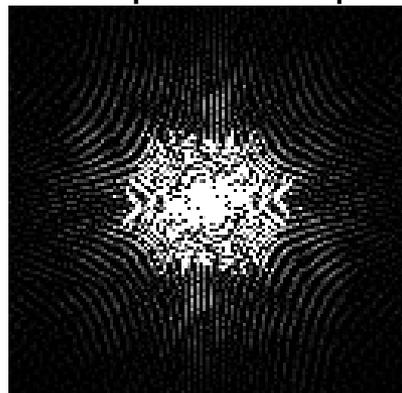


Radial subsampling pattern



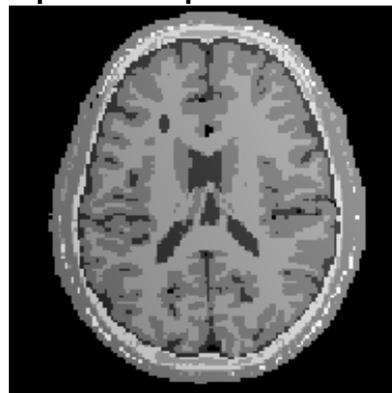
# Qualitative MRI v.s. Quantitative MRI

Example of K-space data



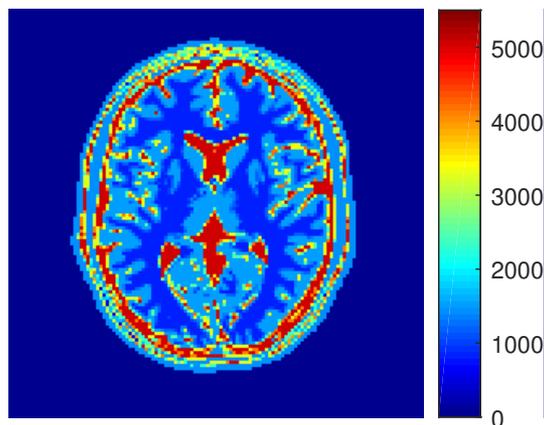
from under-sampled data

Example of qualitative MRI

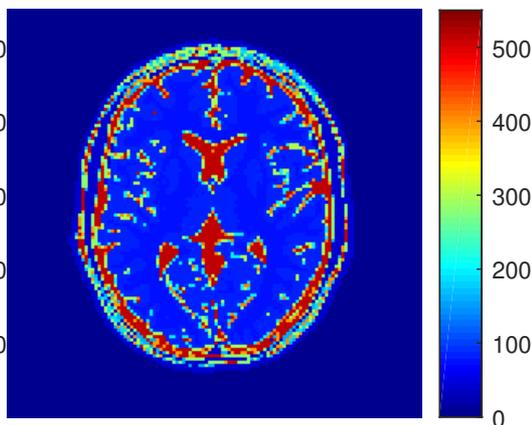


Example of quantitative MRI parameters ( $T_1$ ,  $T_2$ ,  $\rho$ )

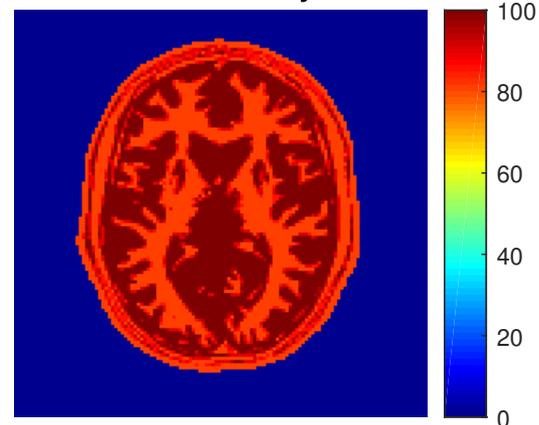
Ideal T1



Ideal T2

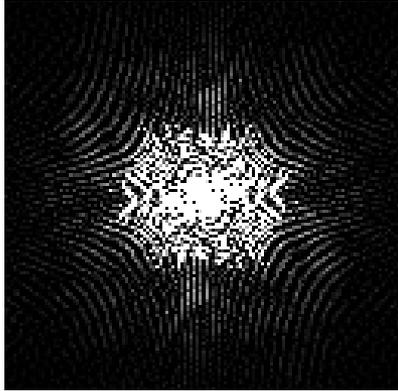


Ideal Density



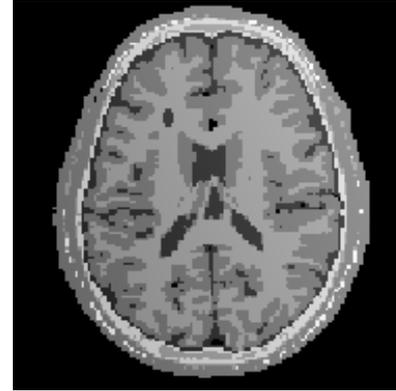
# Qualitative MRI v.s. Quantitative MRI

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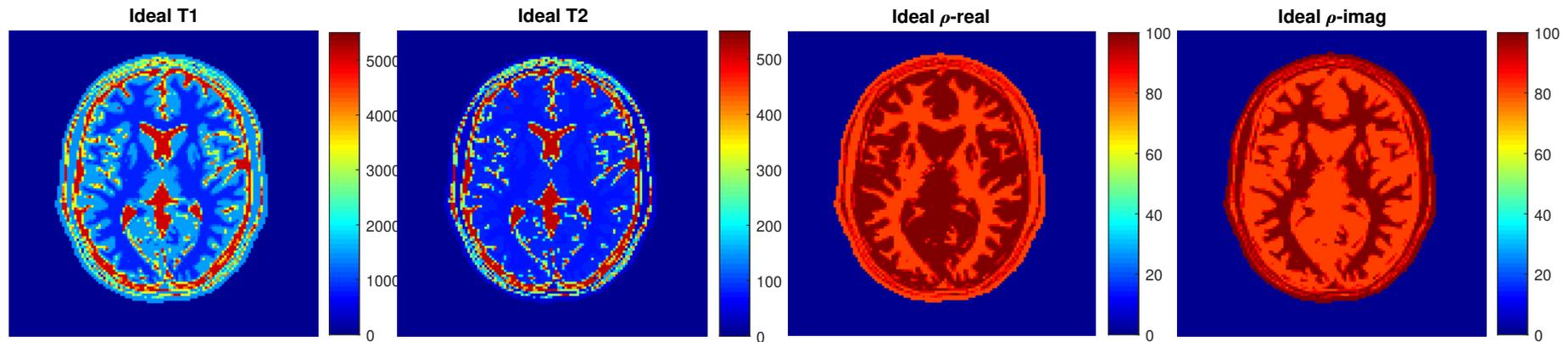


from under-sampled data

Example of qualitative MRI



Example of quantitative MRI parameters (contains coil-sensitivity error  $\hat{\rho} = \rho * C$ )



# Qualitative MRI v.s. Quantitative MRI

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## Qualitative MRI

- inverting under-sampled Fourier data, mature techniques
  - visualizing amplitude of magnetization for diagnosis
  - $T_1$ ,  $T_2$  or  $\rho$  weighted images by adjusting  $B_0$ ,  $B_1$
  - reconstruction can be done apart from the physics behind
- 

## Quantitative MRI

- techniques still in experimental stage
- precisely measure the magnetic and tissue parameters e.g.  $\theta = (T_1, T_2)^T$ , and  $\rho$
- imaging process is more time consuming
- physics (Bloch equations) explicitly entered into the reconstruction

# Mathematical understanding of MRF-based methods

# Magnetic resonance fingerprinting (MRF)

The working flow of the original MRF <sup>a</sup>:

- Create a dictionary  $\text{Dic}(C_{ad})$  of magnetizations  $m$ : Solve Bloch equations for a variety of  $T_1, T_2$ .  $C_{ad}$  restricts  $(T_1, T_2)$  to their natural range.
- Reconstruct  $X^* := (X^{(1)}, \dots, X^{(L)})$  magnetization from the data:

$$X^{(l)} \in \underset{X}{\text{argmin}} \|P^{(l)} \mathcal{F} X - Y^{(l)}\|_2^2, \quad l = 1, \dots, L.$$

Match the reconstructed magnetization to a dictionary element:

$$m^* \in \underset{m_{x,y} \in \text{Dic}(C_{ad})}{\text{argmin}} S(m_{x,y}, X^*) \text{ with } X^* = (X^{(1)}, \dots, X^{(L)}).$$

- Use look-up table to match  $(T_1, T_2)$  to  $m^*$ .

$X^*$  might be non-unique and not optimal for under-sampled data!

<sup>a</sup>D. Ma et al. Magnetic resonance fingerprinting, Nature, **495**(187) (2013)

# Other dictionary-based methods

The BLIP algorithm <sup>a</sup> applies projected gradient descent (also called projected Landweber iteration) to approximate the following optimization problem:

$$\begin{aligned} \min_X \quad & \|P\mathcal{F}X - Y\|^2, \\ \text{subject to } & X \in \mathbb{R}^+ \text{Dic}(C_{ad}). \end{aligned} \tag{BLIP}$$

- BLIP gives better reconstruction of the magnetization in MRF.
- From a geometric point of view,  $\text{Dic}(C_{ad})$  is a high dimensional manifold.
- The Bloch manifold is nonconvex with respect to  $\theta = (T_1, T_2)^\top$ , and the projection is ill-posed.
- Fineness of dictionary matters to the accuracy.

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<sup>a</sup>M. Davies et al. A compressive sensing framework for magnetic resonance fingerprinting, SIAM J. Imag. Sciences, 7(4) (2014)

# Other dictionary-based methods

The FLOR algorithm<sup>a</sup> uses a low rank penalty for the representation of the magnetization in the dictionary:

$$\min_X \|PF X - Y\|^2 + \lambda \text{Rank}(X), \quad (\text{FLOR})$$

subject to  $X \in \mathbb{R}^+ \text{Dic}(C_{ad})$ .

- $X$  is a vector spanned by only a few elements from  $\text{Dic}(C_{ad})$ .
- FLOR further optimizes the reconstructing and matching steps in MRF.
- Produces better results than BLIP in radial sub-sampling.
- Algorithm does not work well in Cartesian cases.
- Fineness of dictionary still matters.

<sup>a</sup>G. Mazor, L. Weizman, A. Tal, Y.C. Eldar. Low-rank magnetic resonance fingerprinting, *Medical Physics*, **45**(9), 2018

# qMRI interpreted as coupled inverse problems

Dictionary based methods mostly approach qMRI problem from the following aspect:  
Solving two coupled (nonlinear) operator equations

$$PF(\rho m) = g,$$

and

$$\mathcal{B}(\theta) = m.$$

We have the following type of stability estimate<sup>a</sup>:

## Theorem

Let  $m, m^\delta \in \text{Dic}(C_{ad})$ , if  $\|m - m^\delta\| \leq \delta$  for some positive  $\delta > 0$ , then there exist constant  $C$

$$\|\theta - \theta^\delta\| \leq C\delta.$$

<sup>a</sup>G. Dong, M. Hintermüller, K. Papafitsoros. Quantitative magnetic resonance imaging: From fingerprinting to integrated physics-based models, SIAM J. Imag. Sciences, Vol. 12, No. 2, pp. 927–971, 2019.

# Integrated physics-based method for qMRI

# Integrated physics-based method for qMRI

- Integrate the two inverse problems into a single non-linear operator equation<sup>a</sup>:

$$Q(\rho, \theta) = g,$$

where

$$Q(\rho, \theta) := P\mathcal{F}(\rho T_{x,y}m(\theta)) \quad \text{and} \quad [\rho(\mathbf{r}); \theta(\mathbf{r})] \in \mathcal{C}_{ad} := [\mathbb{R}^+; C_{ad}] \quad \text{for all } \mathbf{r} \in \Omega.$$

- Time continuous function  $m(\theta)$  practically replaced by **discrete dynamics**  $M(\theta)$  e.g. Inversion Recovery balanced Steady-State Free Precession.
- Some important properties are proven:
  - $M : [L^\infty(\Omega)]^2 \rightarrow [L^2(\Omega)]^3$  is Fréchet differentiable.
  - $M(C_{ad})$  is a non-convex set.
  - $Q : [L^\infty(\Omega)]^3 \rightarrow [L^2(K)]^3$  is Fréchet differentiable.

<sup>a</sup>G. Dong, M. Hintermüller, K. Papafitsoros. Quantitative magnetic resonance imaging: From fingerprinting to integrated physics-based models, SIAM J. Imag. Sciences, Vol. 12, No. 2, pp. 927–971, 2019.

# Time discrete Bloch dynamics

In practice, discrete dynamic sequences  $M = (M_l)_{l=1}^L$  (e.g. Inversion Recovery balanced Steady-State Free Precession flip angle sequence patterns)

$$\begin{cases} M_l = E_1(TR_l, \theta) R_{\phi_l} R_x(\alpha_l) R_{\phi_l}^\top M_{l-1} + E_2(TR_l, \theta) M_e, \\ M_e = (0, 0, 1)^\top, \\ M_0 = -M_e = (0, 0, -1)^\top. \end{cases}$$

where

$$E_1(TR_l, \theta) = \begin{pmatrix} e^{-\frac{TR_l}{T_2}} & 0 & 0 \\ 0 & e^{-\frac{TR_l}{T_2}} & 0 \\ 0 & 0 & e^{-\frac{TR_l}{T_1}} \end{pmatrix}, \quad E_2(TR_l, \theta) = \left(1 - e^{-\frac{TR_l}{T_1}}\right)$$
$$R_{\phi_\ell} = \begin{pmatrix} \cos(\phi_\ell) & \sin(\phi_\ell) & 0 \\ -\sin(\phi_\ell) & \cos(\phi_\ell) & 0 \\ 0 & 0 & 1 \end{pmatrix} \text{ and } R_x(\alpha_\ell) = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos(\alpha_\ell) & \sin(\alpha_\ell) \\ 0 & -\sin(\alpha_\ell) & \cos(\alpha_\ell) \end{pmatrix}.$$

$M_l$  has a closed form:

$$M_l = \left( \prod_{k=1}^l E_1(TR_k, \theta) R(\alpha_k) \right) M_0 + E_2(TR_l, \theta) M_e + \sum_{k=1}^{l-1} \left( E_2(TR_k, \theta) \prod_{j=k+1}^l E_1(TR_j, \theta) R(\alpha_j) \right) M_e.$$

# Gauss-Newton iteration

- Denote  $u = (T_1, T_2, \rho)^\top$ . Consider first order Taylor expansion:

$$Q(u_{n+1}) \simeq Q(u_n) + Q'(u_n)(u_{n+1} - u_n) = g,$$

suggests a projected Gauss-Newton iteration:

$$\begin{aligned} g_n &= g - Q(u_n) + Q'(u_n)u_n, \\ v_{n+1} &= (Q')^\dagger(u_n)g_n := ((Q'(u_n))^\top Q'(u_n))^{-1} (Q'(u_n))^\top g_n, \\ u_{n+1} &= P_{\tilde{C}_{ad}} v_{n+1}. \end{aligned}$$

$$\text{where } (P_{\tilde{C}_{ad}} v)_p(r) = \begin{cases} \underline{C}_p & \text{for } v_p(r) \leq \underline{C}_p \\ v_p(r) & \text{for } \underline{C}_p < v_p(r) < \overline{C}_p \\ \overline{C}_p & \text{for } \overline{C}_p \leq v_p(r) \end{cases}$$

Converge superlinearly for proper initial values, **but sensitive to noise.**

# A Levenberg-Marquardt method

- An estimation for  $u, h \in [L^\infty(\Omega)]^3$ , and  $Q : [L^\infty(\Omega)]^3 \rightarrow ([L^2(K)]^2)^L$ :

$$\|Q(u+h) - Q(u) - Q'(u)h\|_{([L^2(K)]^2)^L} = o(\|h\|_{[L^2(\Omega)]^3}).$$

- L-M is a kind of regularization for the case of noisy and under-sampled data.

Key steps of the algorithm (Note now in Hilbert space  $([L^2(\Omega)]^3)$ ):

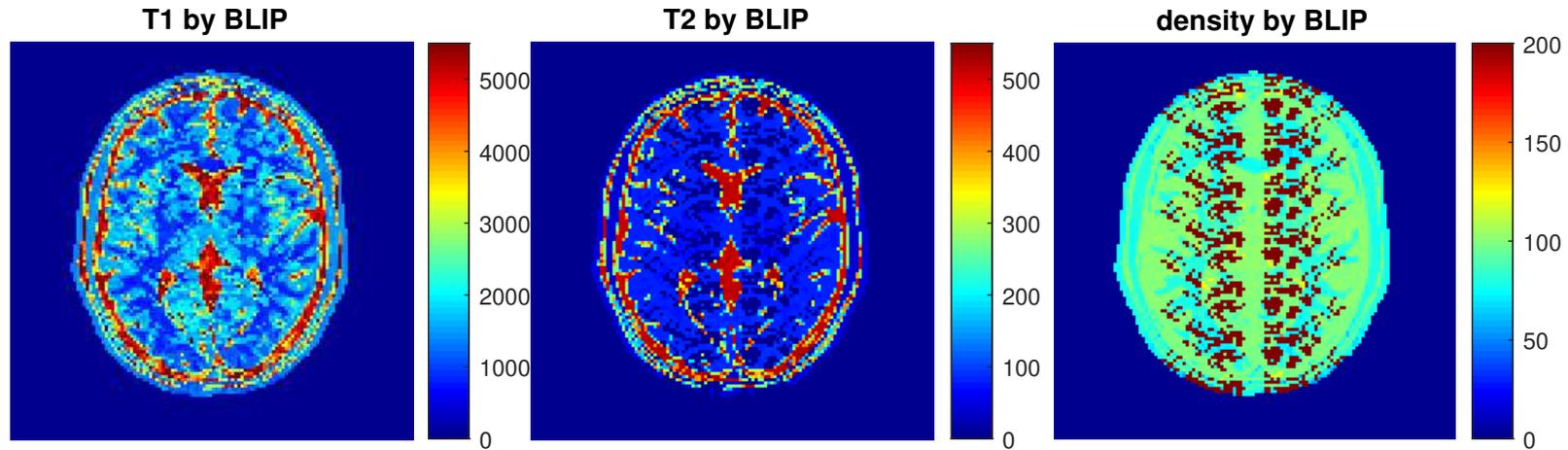
- Initialization: using BLIP algorithm with a coarse dictionary.
- A projected Levenberg-Marquardt iteration:

$$\begin{aligned}\tilde{g}_n^\delta &= g^\delta - Q(u_n) \\ h_n^\delta &= \operatorname{argmin}_h \|Q'(u_n)h - \tilde{g}_n^\delta\|_{([L^2(K)]^2)^L}^2 + \lambda_n \|h\|_{[L^2(\Omega)]^3}^2 \\ u_{n+1} &= P_{\tilde{\mathcal{C}}_{ad}}(u_n + h_n^\delta)\end{aligned}$$

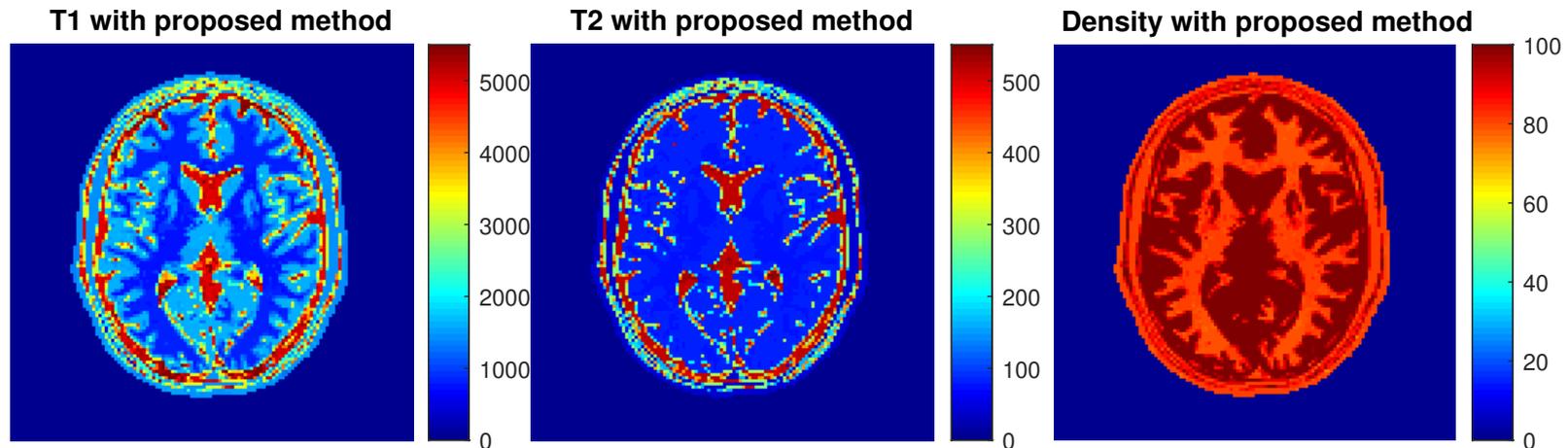
with updated parameter  $\lambda_n = \max\{\lambda_0 \beta^n, \mu_n\}$ , where  $\beta \in (0, 1)$ , and  $\mu_n \geq 0$ .

# Numerical results on qMRI–Cartesian subsampling case

## Solution of BLIP algorithm

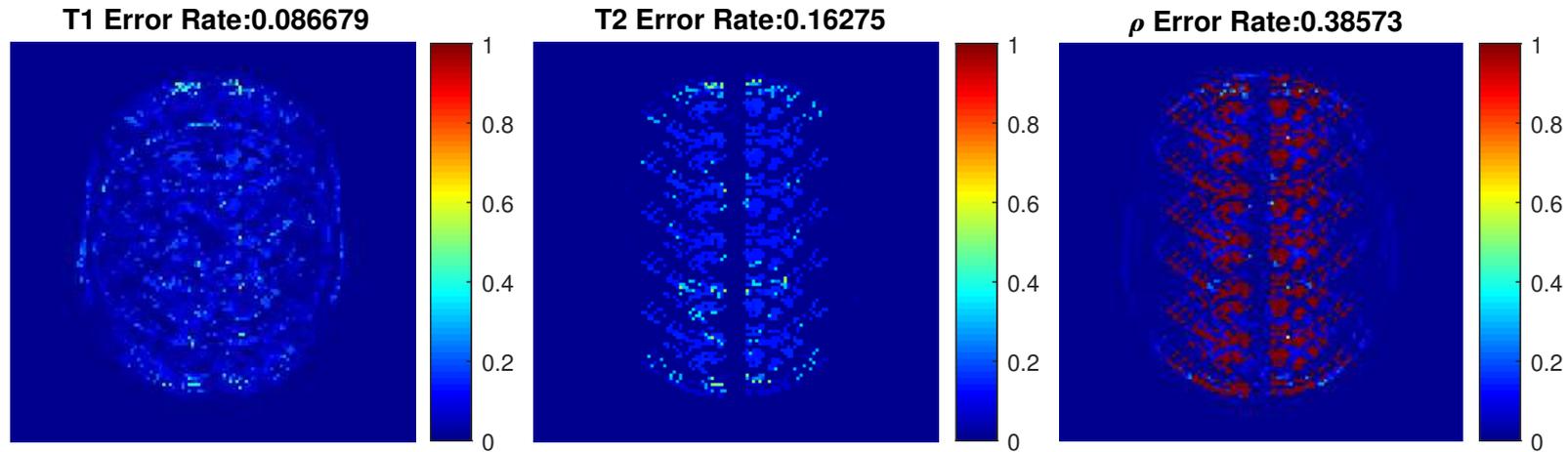


## Solution of proposed method

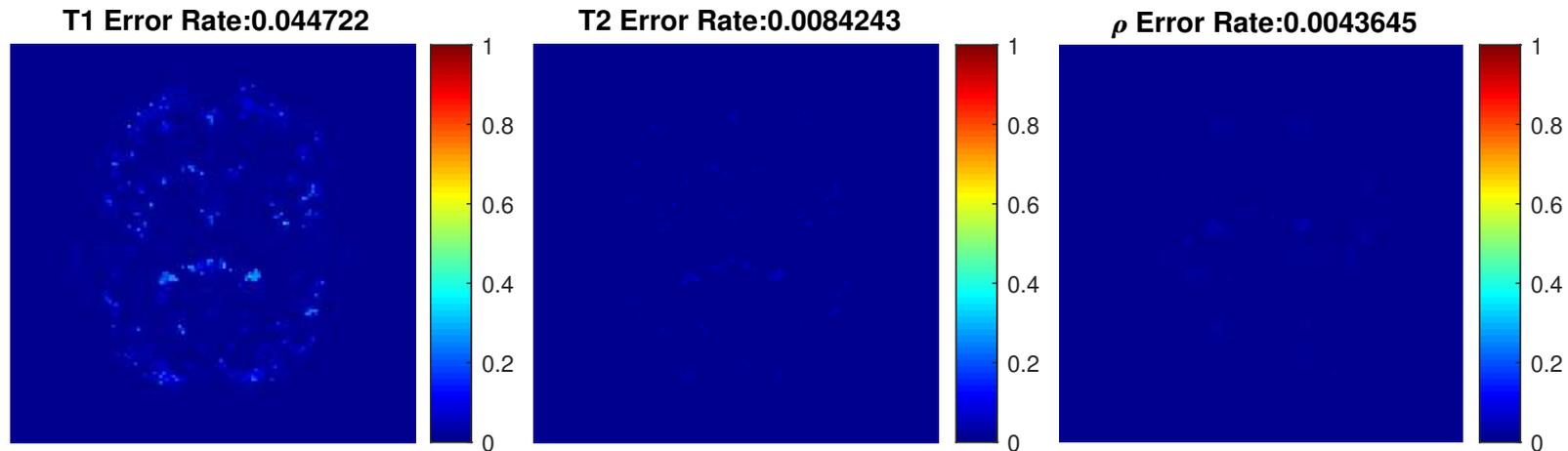


# Numerical results on qMRI–Cartesian subsampling case

## Relative error map from BLIP algorithm

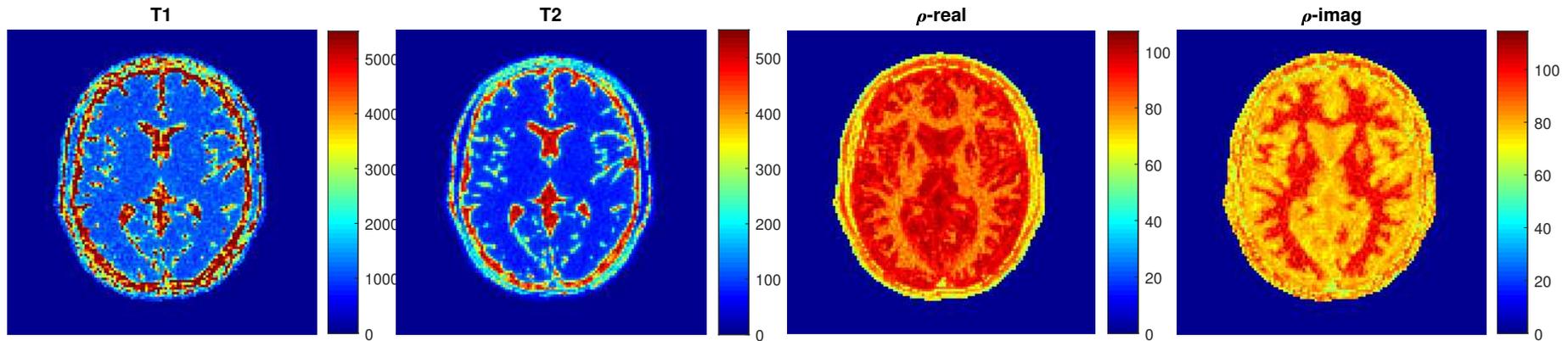


## Relative error map from proposed method

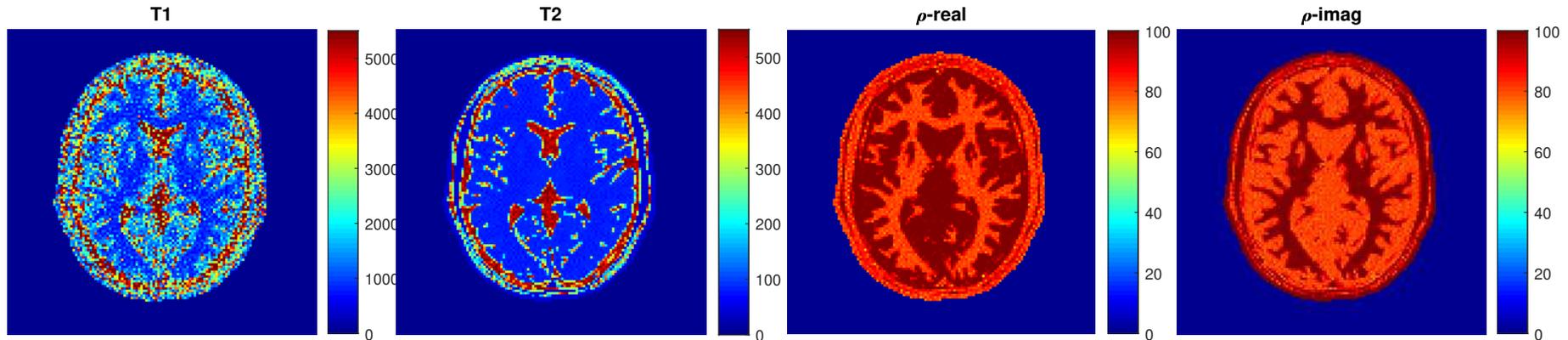


# Numerical results on qMRI–Radial subsampling case

## Solution of FLOR algorithm

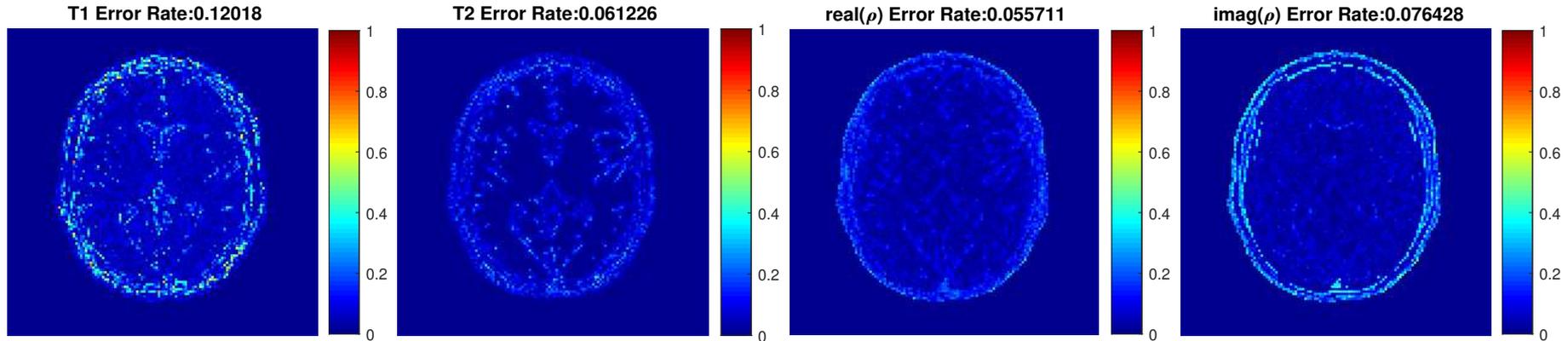


## Solution of proposed method

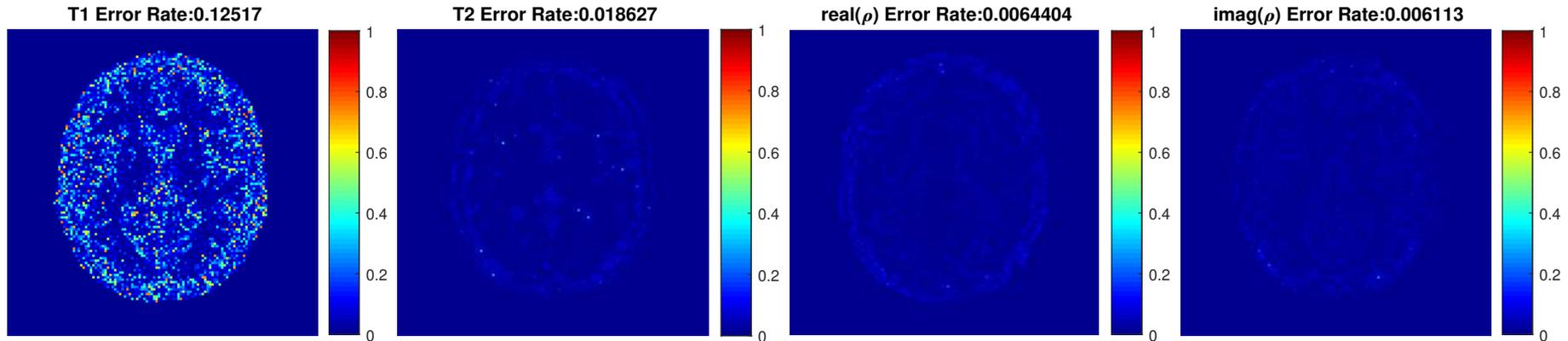


# Numerical results on qMRI–Radial subsampling case

## Relative error map from FLOR algorithm



## Relative error map from proposed method



# Using learning-informed physical models

- A general physics-based inverse (imaging) problem:

$$Ay = g, \quad \text{given } g \in H$$

$$\text{where } e(y, u) = 0 \text{ for } (y, u) \in Y \times U \text{ and } u \in \mathcal{C}_{ad}$$

Let  $y = \Pi(u)$  be an explicit representation of  $e(y, u) = 0$  (e.g., solution map of Bloch equations,  $u = \theta = (T_1, T_2, \rho)$ ).

- We study the following generic problem:

$$\begin{aligned} & \underset{(y,u) \in (Y \times U)}{\text{minimize}} && \frac{1}{2} \|Ay - g^\delta\|_H^2 + \frac{\alpha}{2} \|u\|_U^2, \\ & \text{subject to} && e(y, u) = 0, \\ & && u \in \mathcal{C}_{ad}. \end{aligned}$$

<sup>1</sup>G. Dong, M. Hintermüller, K. Papafitsoros. Optimization with learning-informed differential equation constraints and its applications, ESAIM: Control, Optimisation and Calculus of Variations, 2021.

# Optimization with (learning-informed) physics-constraints <sup>1</sup>

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$$\begin{aligned} & \underset{u}{\text{minimize}} && \frac{1}{2} \|A\Pi(u) - g^\delta\|_H^2 + \frac{\alpha}{2} \|u\|_U^2 =: \mathcal{J}(u), \\ & \text{subject to} && u \in \mathcal{C}_{ad}. \end{aligned}$$

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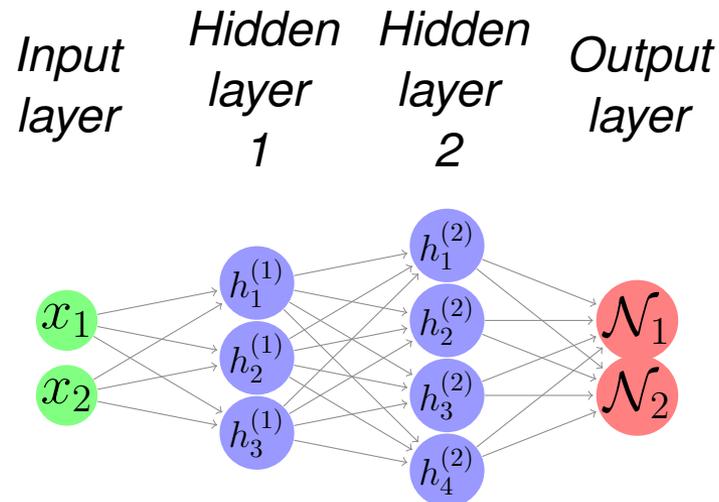
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- We study the following generic problem:

$$\begin{aligned} & \underset{u}{\text{minimize}} && \frac{1}{2} \|A\Pi_{\mathcal{N}}(u) - g\|_H^2 + \frac{\alpha}{2} \|u\|_U^2 =: \mathcal{J}_{\mathcal{N}}(u), \\ & \text{subject to} && u \in \mathcal{C}_{ad}. \end{aligned}$$

<sup>1</sup>G. Dong, M. Hintermüller, K. Papafitsoros. Optimization with learning-informed differential equation constraints and its applications, ESAIM: Control, Optimisation and Calculus of Variations, 2021.

# Artificial Neural Network



*A fully connected multi-layer feedforward ANN.*

*From one layer to the next: connected by affine mapping and activation function*

$$\mathbf{h} = \sigma(\mathbf{z}) = \sigma(W\mathbf{x} + \mathbf{b}).$$

# Universal approximation theorem for ANNs<sup>2</sup>

*ANNs have been very successful approximators for functions  $f : \Omega \rightarrow \mathbb{R}^n$ , defined on bounded  $\Omega \subset \mathbb{R}^m$ .*

## Theorem (function value approximation)

*A standard multi-layer feedforward network with a continuous activation function can uniformly approximate any continuous function to any degree of accuracy if and only if its activation function is not a polynomial.*

## Theorem (derivative approximation)

*There exists a neural network which can approximate both the function value and the derivatives of  $f$  uniformly to any degree of accuracy if the activation function is continuously differentiable and is not a polynomial.*

<sup>2</sup>Pinkus, Approximation theory of the MLP model in neural networks. Acta Numerica, 1999.

# Activation functions of ANNs

Examples of *smooth* activation functions:

- *Sigmoid: e.g., tansig* ( $\sigma(z) = \frac{e^z - e^{-z}}{e^z + e^{-z}}$ ), *logsig* ( $\sigma(z) = \frac{1}{1 + e^{-z}}$ ), *arctan* ( $\sigma(z) = \arctan(z)$ ), *etc.*
- *Probability functions: e.g., softmax* ( $\sigma_i(z) = \frac{e^{-z_i}}{\sum_j e^{-z_j}}$ )

Examples of *nonsmooth* activation functions:

- *ReLU: Rectified Linear Unit* ( $\sigma(z) = \max(0, z)$ )

**Important:** Choosing *smooth* vs. *nonsmooth* activation functions should respect prior information on to be approximated object and has numerous implications in optimization.

# Remark on neural network approximation

NNs approximate an objective  $f$  in different settings

Examples

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1.  $f : \Omega \subset \mathbb{R}^m \rightarrow \mathbb{R}^n$ , with finite  $m$  and  $n$   
Universal approximation theorem

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2.  $f : \mathcal{K} \subset \mathcal{B}_1 \rightarrow \mathbb{R}^n$ , where  $\mathcal{B}_1$  is some Banach space  
Under-development (mostly convolutionary NNs)

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3.  $f : \Omega \subset \mathbb{R}^m \rightarrow \mathcal{B}_2$ , where  $\mathcal{B}_2$  is some Banach space  
Under-development (many different methods)

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4.  $f : \mathcal{K} \subset \mathcal{B}_1 \rightarrow \mathcal{B}_2$ ,  $(\mathcal{B}_k)_{k=1}^2$  can be infinite dimensional  
Under-development (very few still)

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- (Generalized) Regression

- (Image) Classification

- Solving (partial) differential equations

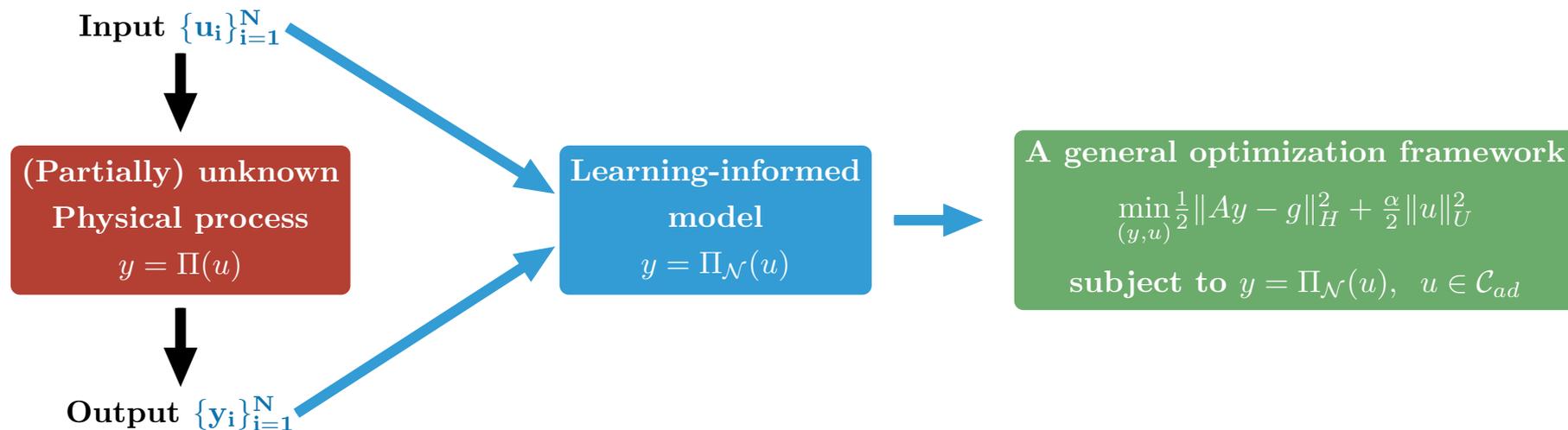
- Operator learning

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Except for case 1, mathematical understanding of cases 2–4 still mostly in progress.

**Main difficulty:** Compactness condition problematic.

# A diagram of the proposed general framework



## Fundamental questions:

- Conditions for well-posedness of learned physical model and universal approximation property of  $\Pi_{\mathcal{N}} \sim \Pi$ .
- Approximation properties of optimizers associated to learning-informed models vs. those related to original physics-based models.

# Some analytical aspects

# Existence of solutions

Denote  $Q := A\Pi$  (or  $A\Pi_{\mathcal{N}}$ ) the reduced operator.

## Theorem

*Suppose that  $Q$  is weakly-weakly sequentially closed, i.e., if  $u_n \xrightarrow{U} u$  and  $Q(u_n) \xrightarrow{H} \bar{g}$ , then  $\bar{g} = Q(u)$ . Then the optimization problem admits a solution  $\bar{u} \in U$ .*

*In the special case when  $\mathcal{C}_{ad}$  is a bounded set of a subspace  $\hat{U}$  compactly embedded into  $U$ , then strong-weak sequential closedness of  $Q$  is sufficient to guarantee existence of a solution.*

- *In many PDE models, regularity of the resp. solution helps the weak-weak sequential closedness condition of the control-to-state map to be satisfied.*
- *While in imaging applications (inverse problems, more generally) regularization usually plays a role similar to  $\hat{U}$ .*

# Convergence under operator perturbations

Let  $Q_n := A\Pi_{\mathcal{N}_n}$  be the reduced learning-informed operators.

## Theorem

Let  $Q$  and  $Q_n$  for  $n \in \mathbb{N}$  be weakly sequentially closed operators, and

$$\sup_{u \in \mathcal{C}_{ad}} \|Q(u) - Q_n(u)\|_H \leq \epsilon_n, \quad \text{for } \epsilon_n \downarrow 0.$$

Suppose  $(u_n)_{n \in \mathbb{N}}$  is a sequence of minimizers associated to the optimization problems with reduced operator  $Q_n$  for all  $n \in \mathbb{N}$ .

Then, there is the strong convergence (up to a sub-sequence)

$$u_n \rightarrow \bar{u} \text{ in } U, \quad \text{and} \quad Q_n(u_n) \rightarrow Q(\bar{u}) \text{ in } H, \quad \text{as } n \rightarrow \infty,$$

where  $\bar{u}$  is a minimizer of the original optimization problem.

# Convergence rates

Denote  $L_0$  and  $L_1$  the Lipschitz constants associated to  $Q$  and  $Q'$ , respectively, where  $Q'$  is the Fréchet derivative of  $Q$ , and  $\eta_n := \|Q' - Q'_n\|_{\mathcal{L}(U,H)}$ .

## Theorem

*Under smallness of  $L_0, L_1$ , the solutions  $u_n$  converge to  $\bar{u}$  at the following rate*

$$\|u_n - \bar{u}\|_U = \mathcal{O}(L_0 \epsilon_n + \|Q(\bar{u}) - g\|_H \eta_n).$$

## Theorem (when $\mathcal{J}'(\bar{u}) = 0$ )

*Suppose the Lipschitz constant  $L_1$  satisfies*

$$L_1 \|Q(\bar{u}) - g\|_H < \alpha.$$

*If  $\mathcal{J}'(\bar{u}) = 0$ , then for sufficiently large  $n \in \mathbb{N}$  we have the following error bound*

$$\|u_n - \bar{u}\|_U = \mathcal{O}\left(\sqrt{\epsilon_n^2 + 2 \|Q(\bar{u}) - g\|_H^2}\right).$$

# Application to qMRI

qMRI fits the general optimization framework:

$$\underset{(y,u)}{\text{minimize}} \quad \frac{1}{2} \|P\mathcal{F}(y) - g^\delta\|_H^2 + \frac{\alpha}{2} \|u\|_U^2,$$

subject to

$$\frac{\partial y}{\partial t}(t) = y(t) \times \gamma B(t) - \left( \frac{y_1(t)}{T_2}, \frac{y_2(t)}{T_2}, \frac{y_3(t) - \rho m_e}{T_1} \right), \quad t = t_1, \dots, t_L,$$

$$y(0) = \rho m_0,$$

$$u \in \mathcal{C}_{ad}.$$

- The goal is to estimate the physical parameters  $u = (\rho, T_1, T_2)$

qMRI fits the general optimization framework:

$$\underset{(y,u)}{\text{minimize}} \quad \frac{1}{2} \|P\mathcal{F}(y) - g^\delta\|_H^2 + \frac{\alpha}{2} \|u\|_U^2,$$

subject to

$$\begin{aligned} y &= \mathcal{N}(u), \\ u &\in \mathcal{C}_{ad}. \end{aligned}$$

- The goal is to estimate the physical parameters  $u = (\rho, T_1, T_2)$
- ANNs  $\mathcal{N}$  approximate the parameter-to-solution map (Nemytskii type):

$$(\rho, T_1, T_2) \mapsto (y_{t_1}, \dots, y_{t_L})$$

# Universal approximation of learning-informed Bloch operator

Both  $\Pi$  and  $\Pi_{\mathcal{N}} = \mathcal{N}$  are operators of Nemytskii type in the qMRI case.

## Theorem

*The operator  $\Pi : \mathcal{C}_{ad} \subset [L^\infty(\Omega)^+]^3 \rightarrow [(L^\infty(\Omega))^3]^L$  is Lipschitz continuous, and Fréchet differentiable with locally Lipschitz derivative.*

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## Theorem

*Let  $u = (T_1, T_2, \rho)^\top \in \mathcal{C}_{ad}$ . Then for arbitrary small  $\epsilon > 0$  and  $\epsilon_1 > 0$ , there always exist neural network approximations so that*

$$\|\Pi_{\mathcal{N}}(u) - \Pi(u)\|_{[L^\infty(\Omega)^3]^L} \leq \epsilon,$$

*and*

$$\|\Pi'_{\mathcal{N}}(u) - \Pi'(u)\|_{\mathcal{L}([L^2(\Omega)]^3, [L^\infty(\Omega)^3]^L)} \leq \epsilon_1,$$

*are satisfied.*

# A sequential quadratic programming (SQP) algorithm

Define

$$\mathcal{J}_{\mathcal{N}}(u) := \frac{1}{2} \|P\mathcal{F}(\mathcal{N}(u)) - g^\delta\|_H^2 + \frac{\alpha}{2} \|u\|_U^2.$$

The derivative  $\mathcal{J}'_{\mathcal{N}}(u)$  has an explicit form

$$(\rho(\mathcal{N}'(T_1, T_2))^*, \mathcal{N}(T_1, T_2))^\top \mathcal{F}^*(\mathcal{F}(\rho\mathcal{N}'(T_1, T_2)) - g) + \alpha(\text{Id} - \Delta)(T_1, T_2, \rho)^\top.$$

Every QP-step solves

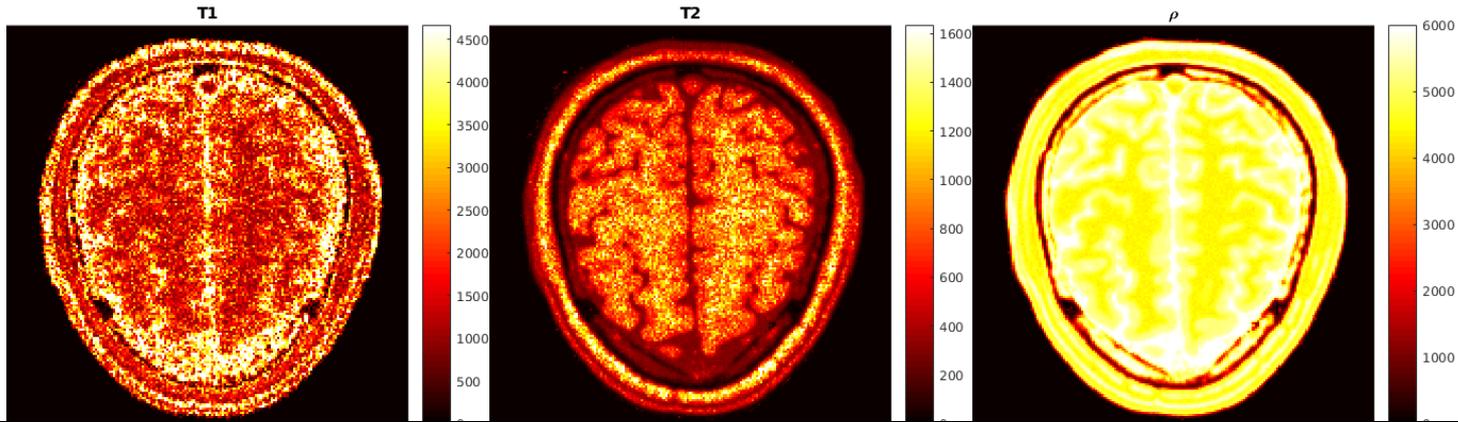
$$\begin{aligned} & \text{minimize} \quad \langle \mathcal{J}'_{\mathcal{N}}(u_k), h \rangle_{U^*, U} + \frac{1}{2} \langle H_k(u_k)h, h \rangle_{U^*, U} \quad \text{over } h \in U \\ & \text{s.t.} \quad u_k + h \in \mathcal{C}_{ad}, \end{aligned}$$

where  $H_k(u_k)$  is a pos.-def. approx. of the Hessian of  $\mathcal{J}_{\mathcal{N}}$  at  $u_k \in \mathcal{C}_{ad}$ :

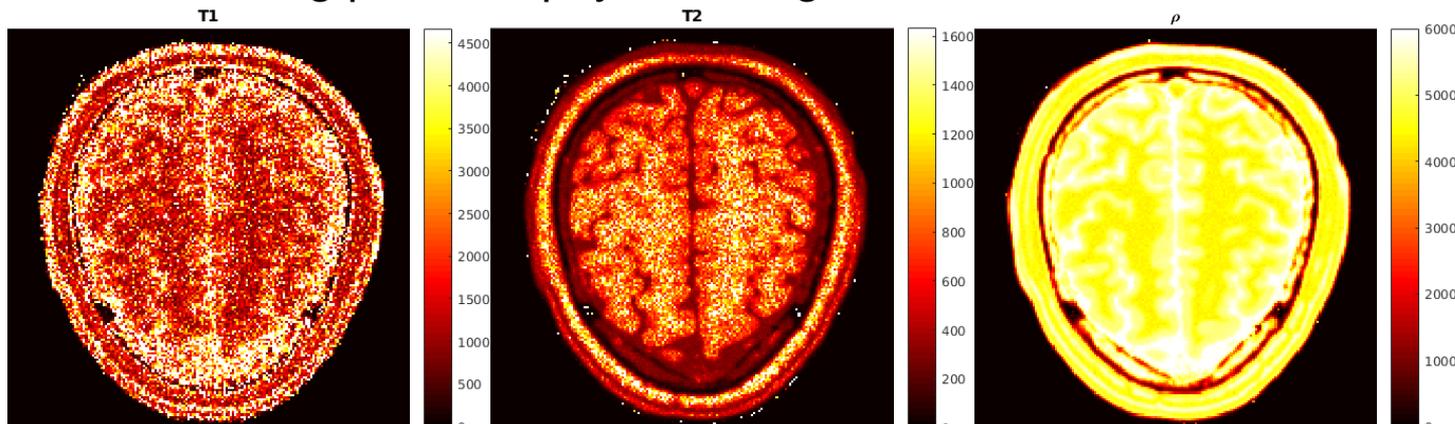
$$(\rho(\mathcal{N}'(T_1, T_2))^*, \mathcal{N}(T_1, T_2))^\top \mathcal{F}^* \mathcal{F}(\rho(\mathcal{N}'(T_1, T_2)), \mathcal{N}(T_1, T_2)) + \alpha(\text{Id} - \Delta).$$

# Numerical results on synthetic data

## Solutions using the proposed learning-informed method

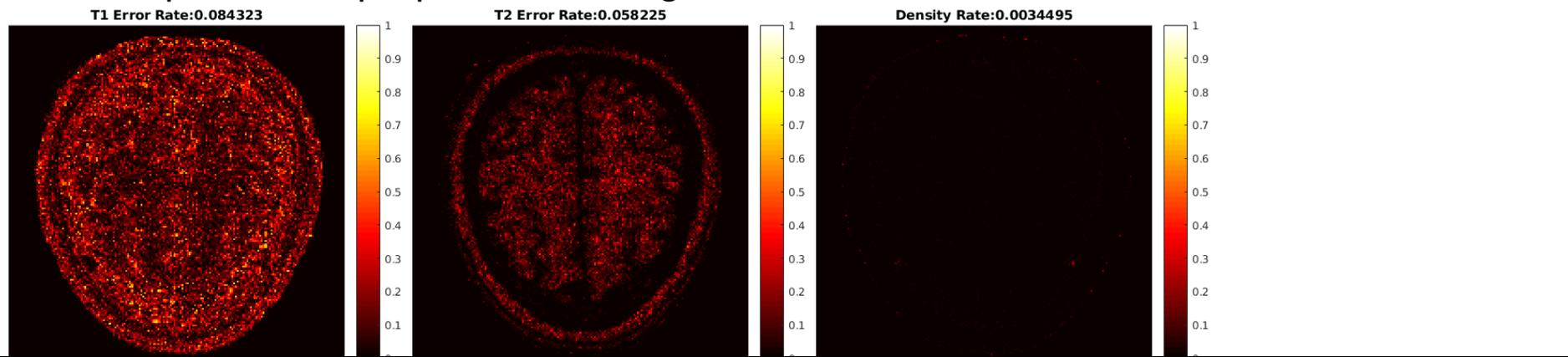


## Solutions using previous physics-integrated method

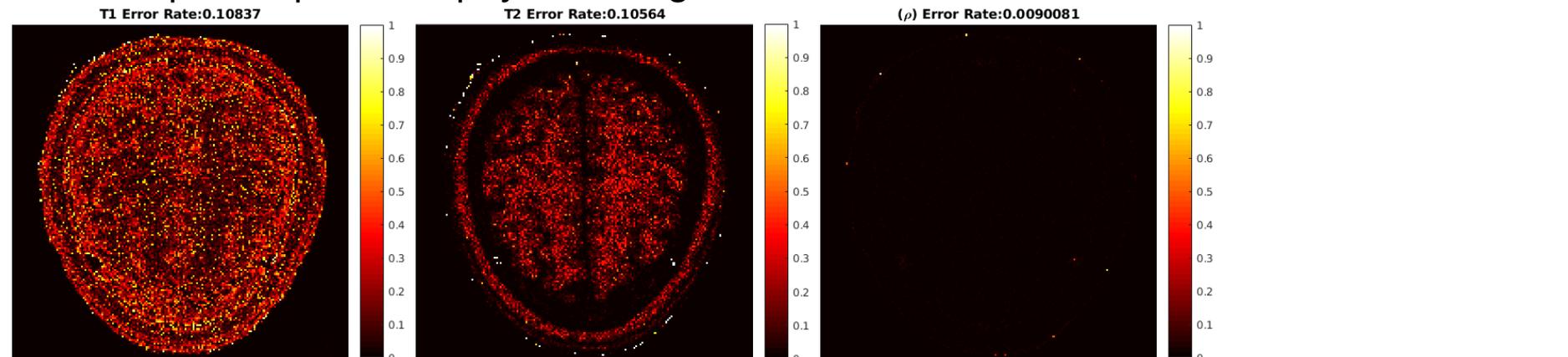


# Numerical results on synthetic data

## Error map from the proposed learning-informed method



## Error map from previous physics-integrated method



# Summary

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- Mathematical understanding of MRF type methods for qMRI.
- Integrated physics-based model for qMRI.
- Learning-informed model for explicit representations of physical operators.
- Mathematical analysis for the proposed methods and robust numerical algorithms.

Thank you for your attention!