Advances in Quantitative MRI: Acquisition, Estimation, and Application

Gopal Nataraj

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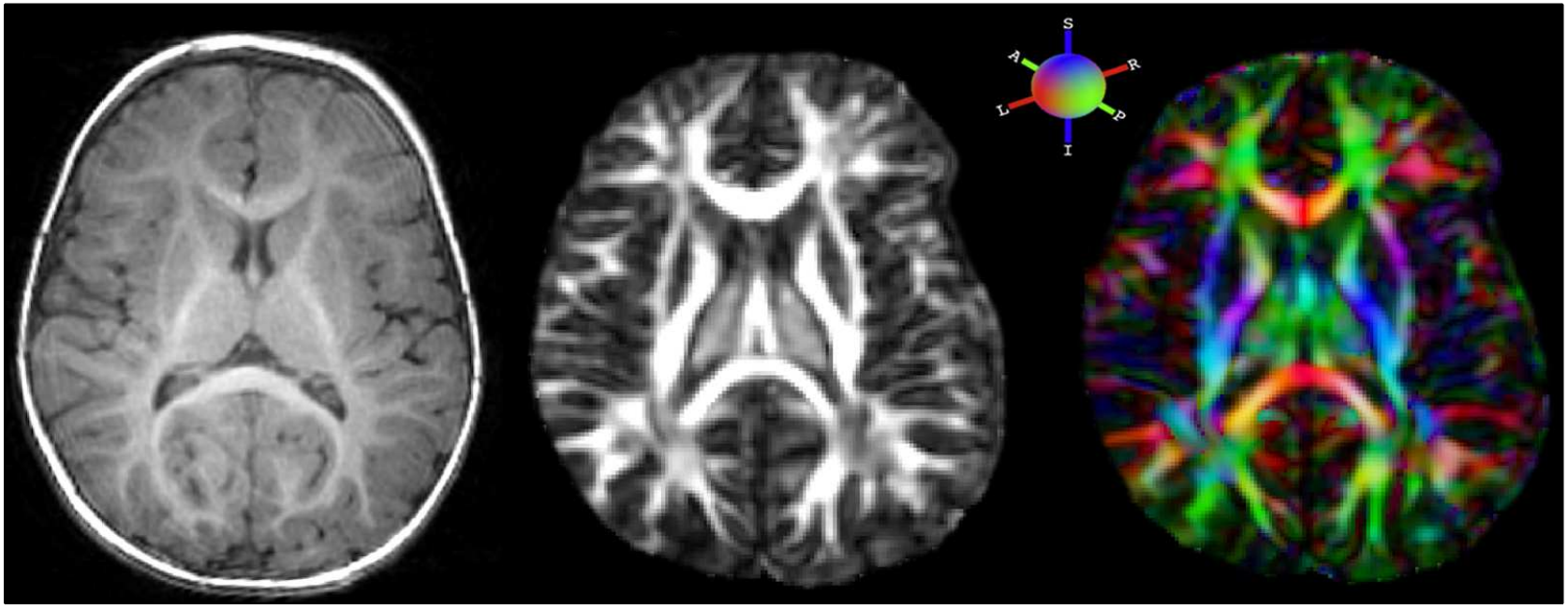
Dept. of Electrical Engineering and Computer Science
University of Michigan

Example: flow imaging

qualitative quantitative[1]

[1] figure borrowed from [Hope et al., 2013]

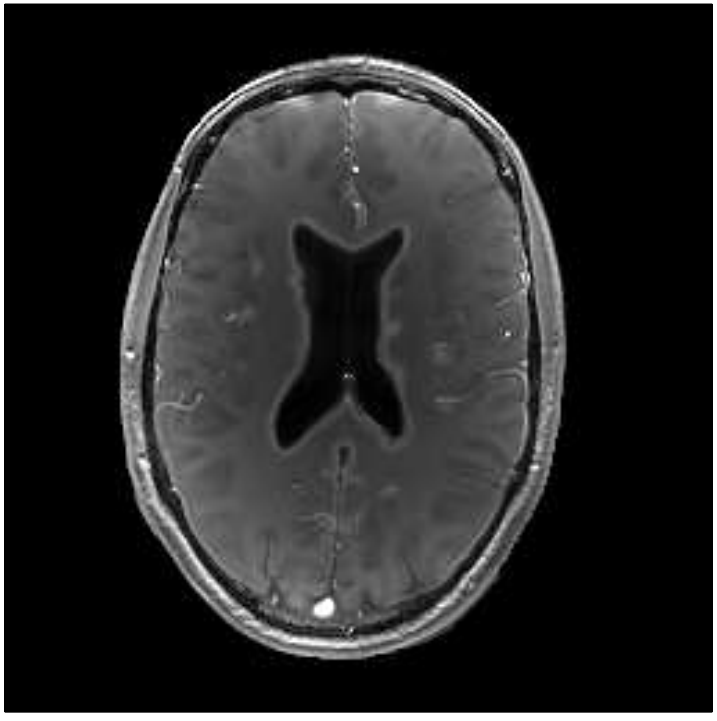
Example: diffusion imaging



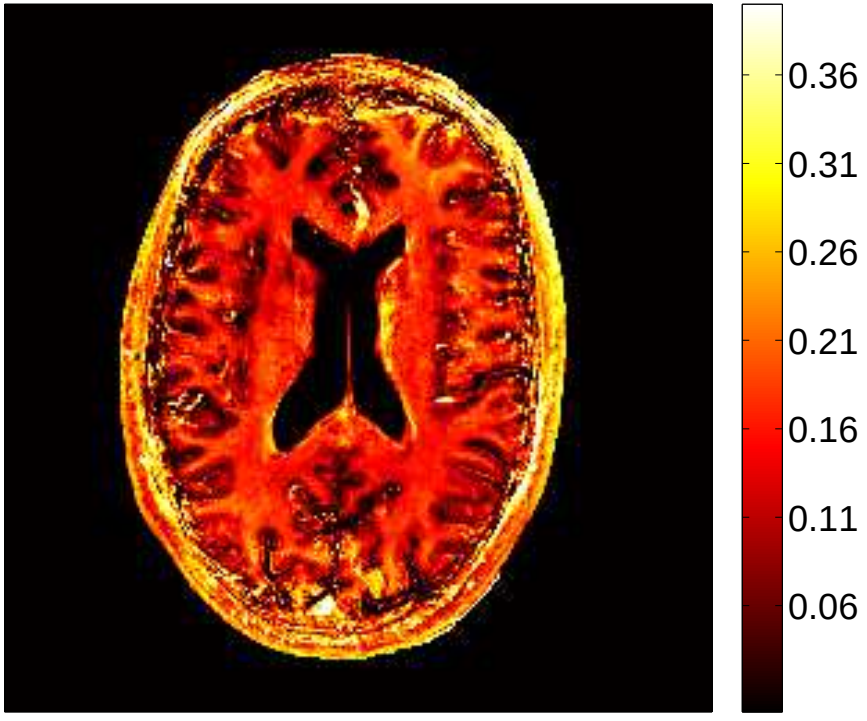
qualitative fractional anisotropy (FA) directional FA[2]

[2] figure borrowed from www.diffusion-imaging.com

Example: myelin water imaging



qualitative



fast-relaxing fraction[3]

[3] figure adapted from [Nataraj et al., 2017a]

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Challenge: rapidly vs. accurately often competing goals

- more accurate models typically depend on more markers
- precisely estimating more markers usually requires longer scans and more computation

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Signal Model

After reconstruction, single voxel y_d in dth image modeled as

$$y_d = s_d(\mathbf{x}; \boldsymbol{\nu}, \mathbf{p}_d) + \epsilon_d \tag{1}$$

- $\mathbf{x} \in \mathbb{R}^L$ unknown parameters
- $\boldsymbol{\nu} \in \mathbb{R}^K$ "known" parameters
- $\mathbf{p}_d \in \mathbb{R}^A$ acquisition parameters
- $s_d : \mathbb{R}^{L+K+A} \mapsto \mathbb{C}$ dth signal model
- $\epsilon_d \in \mathbb{C}$ noise $\sim \mathbb{C}\mathcal{N}\left(0, \sigma_d^2\right)$

Signal Model

A *scan profile* is a set of D scans that produces at each voxel a measurement vector $\mathbf{y} := [y_1, \ldots, y_D]^\mathsf{T}$ modeled as

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- $\mathbf{s} : \mathbb{R}^{L+K+AD} \mapsto \mathbb{C}^D$ vector signal model
- $\boldsymbol{\epsilon} \sim \mathbb{C}\mathcal{N}(\mathbf{0}_D, \boldsymbol{\Sigma})$ noise, with $\boldsymbol{\Sigma} := \mathrm{diag}\left(\sigma_1^2, \ldots, \sigma_D^2\right)$

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Task: design $\mathbf{P}$ to enable precise unbiased estimation of $\mathbf{x}$

Towards an Objective Function

When $\mathbf{s}$ is analytic in $\mathbf{x}$ (as is typical),

Fisher information characterizes unbiased estimator precision:

$$\mathbf{F}(\mathbf{x};\boldsymbol{\nu},\mathbf{P}) := (\nabla_{\mathbf{x}}\mathbf{s}(\mathbf{x};\boldsymbol{\nu},\mathbf{P}))^{\mathsf{H}}\boldsymbol{\Sigma}^{-1}\nabla_{\mathbf{x}}\mathbf{s}(\mathbf{x};\boldsymbol{\nu},\mathbf{P}). \tag{2}$$

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When $\mathbf{F}$ is invertible, Cramér-Rao Bound (CRB) [Cramér, 1946] ensures covariance of unbiased estimates $\widehat{\mathbf{x}}$ of $\mathbf{x}$ satisfy

$$\operatorname{cov}\widehat{\mathbf{x}};\boldsymbol{\nu},\mathbf{P} \succeq \mathbf{F}^{-1}(\mathbf{x};\boldsymbol{\nu},\mathbf{P}). \tag{3}$$

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or (equivalently for Gaussian data) at sufficiently high SNR.
Idea: choose $\mathbf{P}$ such that imprecision matrix $\mathbf{F}^{-1}$ "small"

Scan Design

Idea: choose $\mathbf{P}$ to minimize the objective

$$\Psi(\mathbf{x};\boldsymbol{\nu},\mathbf{P}) = \mathrm{tr}\Big(\mathbf{W}\mathbf{F}^{-1}(\mathbf{x};\boldsymbol{\nu},\mathbf{P})\mathbf{W}^{\mathsf{T}}\Big), \tag{4}$$

where $\mathbf{W} \in \mathbb{R}^{L\times L}$ is a pre-selected diagonal matrix of weights.

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Two problems considered:

- min-max scan design [Nataraj et al., 2017b]

$$\check{\mathbf{P}} \in \left\{ \arg \min_{\mathbf{P}\in\mathbb{P}} \max_{\substack{\mathbf{x}\in\mathbb{X}^{\mathrm{t}} \\ \boldsymbol{\nu}\in\mathbb{N}^{\mathrm{t}}}} \Psi(\mathbf{x};\boldsymbol{\nu},\mathbf{P}) \right\} \tag{5}$$

  where $\mathbb{X}^{\mathrm{t}} \subseteq \mathbb{R}^{L}$ and $\mathbb{N}^{\mathrm{t}} \subseteq \mathbb{R}^{K}$ are "tight" ranges of interest and $\mathbb{P}$ is defined by acquisition/timing constraints

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- Consider scan profiles consisting of two fast pulse sequences
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  - Dual-Echo Steady-State (DESS) [Redpath and Jones, 1988]

Detailed Example Study

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- Consider scan profiles consisting of two fast pulse sequences
  - Spoiled Gradient-Recalled Echo (SPGR) [Zur et al., 1991]
  - Dual-Echo Steady-State (DESS) [Redpath and Jones, 1988]
- For each scan profile feasible under total time constraint:
  1. Let $\mathbf{s}$ model corresponding single-component signal
     - $\mathbf{x} \leftarrow [m_0, T_1, T_2]^{\mathsf{T}}$, where m_0 is a scale factor
     - $\boldsymbol{\nu} \leftarrow$ flip angle variation
     - $\mathbf{P} \leftarrow$ nominal flip angles, repetition times
  2. Optimize $\mathbf{P}$ subject to flip angle, sequence timing constraints
     - $\mathbf{W} \leftarrow \mathrm{diag}(0, 0.1, 1)$ emphasizes T_1, T_2 est roughly equally
     - $\mathbb{X}^{\mathrm{t}}$ chosen to focus on WM/GM at 3T field strength
     - $\mathbb{N}^{\mathrm{t}}$ chosen to allow 10% flip angle variation

Scan Profile Comparison

(#SPGR, #DESS) Profiles	$(2,1)$	$(1,1)$	$(0,2)$
SPGR nom. flip (deg)	(15, 5)	15	–
DESS nom. flip (deg)	30	10	(35, 10)
SPGR rep. times (ms)	(12.2, 12.2)	13.9	–
DESS rep. times (ms)	17.5	28.0	(24.4, 17.5)
optimal max cost	4.0	4.9	**3.5**

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Main finding: 2 DESS sequences can yield T_1, T_2 WM/GM estimates that are at least as precise as T_1, T_2 estimates from SPGR/DESS scan profiles, under this competitive time constraint.

Experimental Setup

Candidate $(2,1)$, $(1,1)$, $(0,2)$ SPGR/DESS scan profiles

- Prescribed optimized nominal flip angles, repetition times
- Used $256 \times 256 \times 8$ 3D matrix over $24 \times 24 \times 4$cm FOV
- Required **1m37s** scan time for each profile

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- Four inversion recovery (IR) scans for T_1 estimation
- Four spin-echo (SE) scans for T_2 estimation
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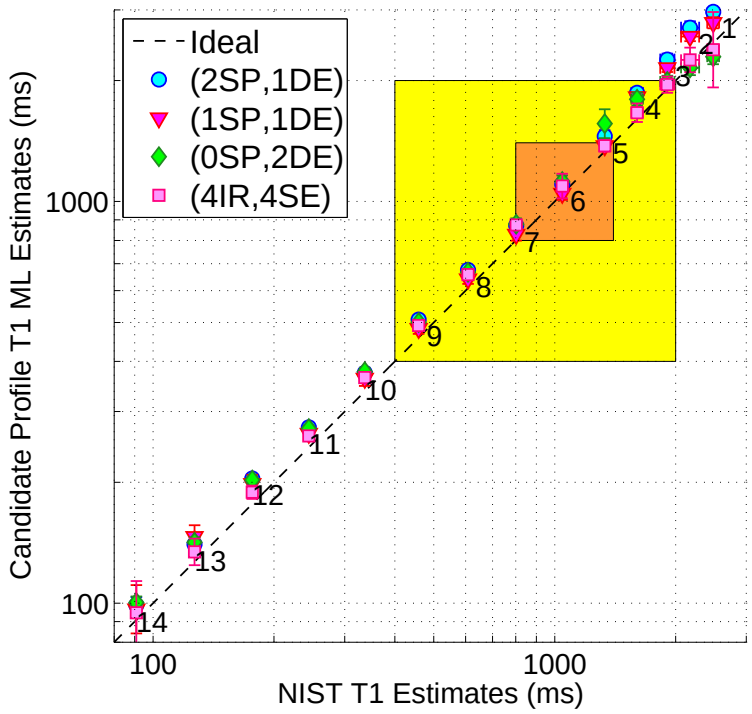
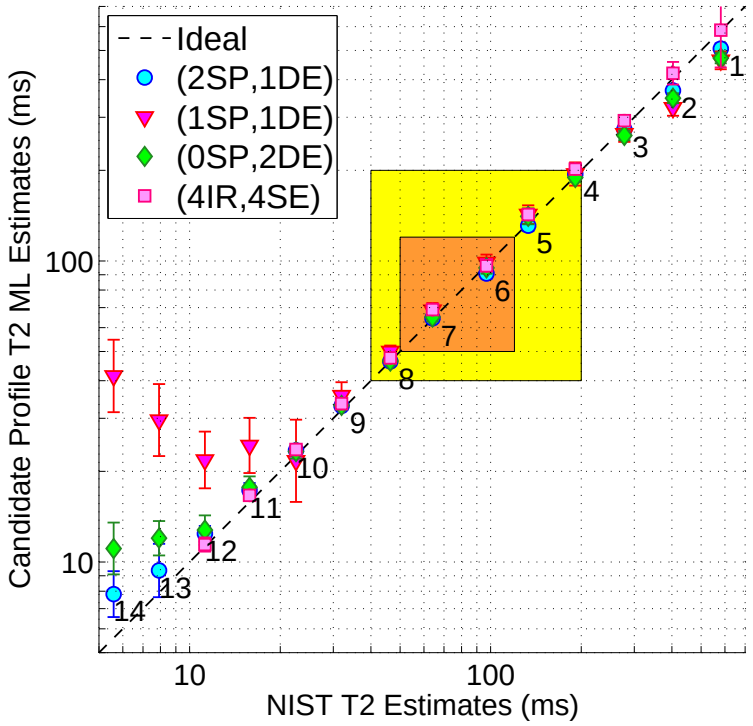
Bloch-Siegert (BS) acquisition for separate flip angle calibration

- Acquired 2 BS-shifted 3D SPGR scans in 1m40s total
- Used for T_1, T_2 est from both candidate and reference profiles

Phantom Accuracy Results



(a) $\widehat{T}_1^{\mathrm{ML}}$ Estimates



(b) $\widehat{T}_2^{\mathrm{ML}}$ Estimates

Compared against NIST NMR measurements [Keenan et al., 2016]

Phantom Precision Results

- Repeated each profile 10 times
- Estimated T_1, T_2 std dev of typical voxel across repetitions

Phantom Precision Results

	(2, 1)	(1, 1)	(0, 2)
V5 $\widehat{\sigma}_{\widehat{T}_1^{\mathrm{ML}}}$	50 ± 12	$40 \pm 10.$	39 ± 9.4
V6 $\widehat{\sigma}_{\widehat{T}_1^{\mathrm{ML}}}$	70 ± 18	60 ± 15	60 ± 16
V7 $\widehat{\sigma}_{\widehat{T}_1^{\mathrm{ML}}}$	60 ± 13	50 ± 13	50 ± 13
V5 $\widehat{\sigma}_{\widehat{T}_2^{\mathrm{ML}}}$	2.6 ± 0.63	6 ± 1.4	3.5 ± 0.84
V6 $\widehat{\sigma}_{\widehat{T}_2^{\mathrm{ML}}}$	1.9 ± 0.46	5 ± 1.1	2.3 ± 0.54
V7 $\widehat{\sigma}_{\widehat{T}_2^{\mathrm{ML}}}$	1.4 ± 0.34	3.4 ± 0.80	1.5 ± 0.35
$\sqrt{\text{opt max cost}}$ estimate	8.9 ± 1.8	11 ± 2.6	$\mathbf{8.3 \pm 2.1}$

Table 1: Pooled sample standard deviations $\pm$ pooled standard errors of sample standard deviations (ms), from optimized SPGR/DESS profiles.

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Similar trends across profiles of empirical vs. theoretical std dev!

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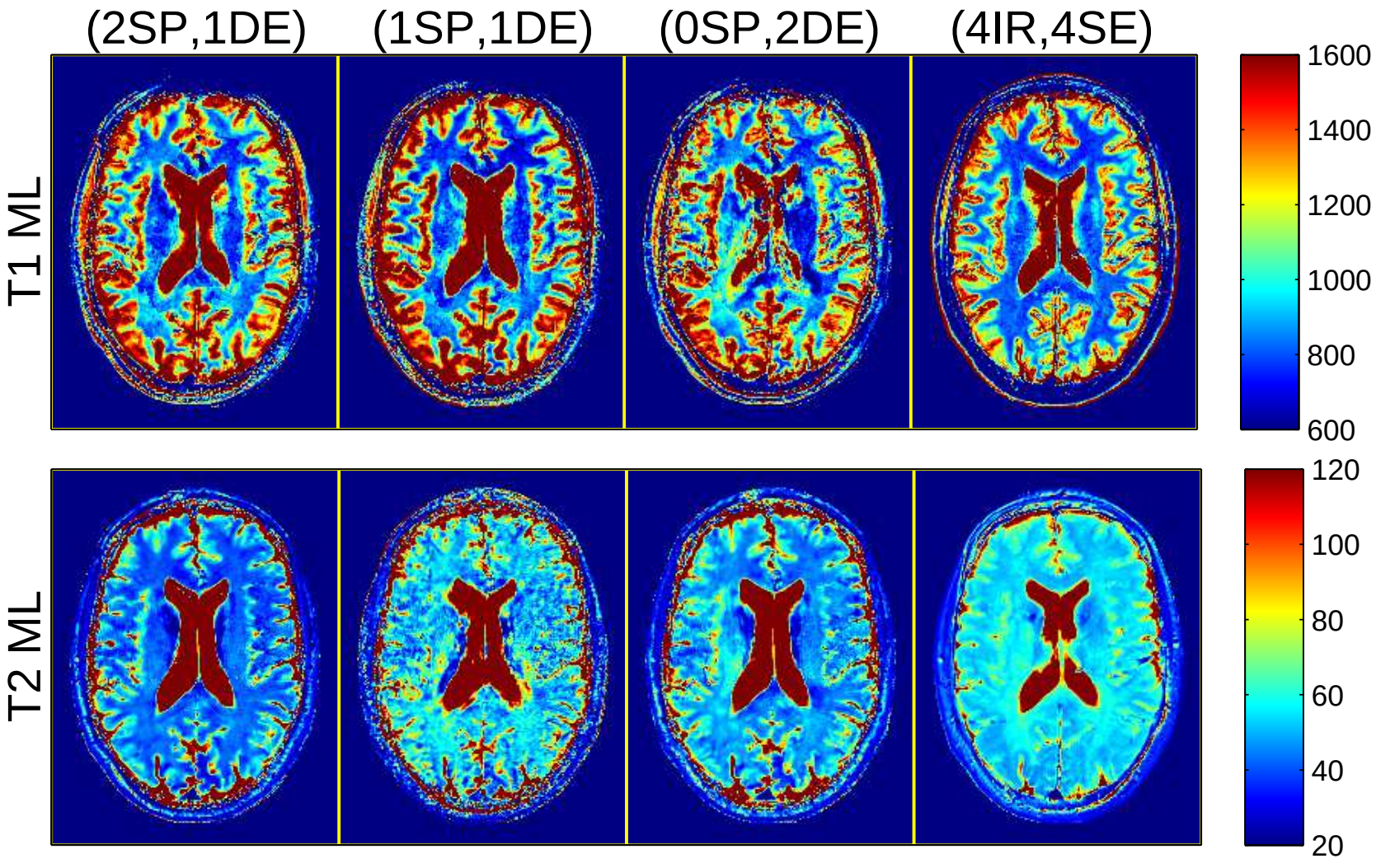

Figure 1: Colorbar ranges in ms.

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How to address in vivo model mismatch?

- More accurate *in vivo* signal models
- More scalable parameter estimation

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References i


Cramér, H. (1946).
Mathematical methods of statistics.
Princeton Univ. Press, Princeton.


Hope, M. D., Wrenn, S. J., and Dyverfeldt, P. (2013).
Clinical applications of aortic 4d flow imaging.
Curr. Cardiovasc. Imag. Rep., 6(2):128–39.


Keenan, K. E., Stupic, K. F., Boss, M. A., Russek, S. E., Chenevert, T. L., Prasad, P. V., Reddick, W. E., Cecil, K. M., Zheng, J., Hu, P., and Jackson, E. F. (2016).
Multi-site, multi-vendor comparison of T1 measurement using ISMRM/NIST system phantom.
In *Proc. Intl. Soc. Mag. Res. Med.*, page 3290.

References ii


Nataraj, G., Nielsen, J.-F., and Fessler, J. A. (2017a).
Myelin water fraction estimation from optimized steady-state sequences using kernel ridge regression.
In *Proc. Intl. Soc. Mag. Res. Med.*, page 5076.


Nataraj, G., Nielsen, J.-F., and Fessler, J. A. (2017b).
Optimizing MR scan design for model-based T1, T2 estimation from steady-state sequences.
IEEE Trans. Med. Imag., 36(2):467–77.


Redpath, T. W. and Jones, R. A. (1988).
FADE-A new fast imaging sequence.
Mag. Res. Med., 6(2):224–34.


Zur, Y., Wood, M. L., and Neuringer, L. J. (1991).
Spoiling of transverse magnetization in steady-state sequences.
Mag. Res. Med., 21(2):251–63.