Quantifying exchange using optimized small-tip fast recovery (STFR) sequences

Naveen Murthy, Jeffrey A. Fessler, Nicole Sieberlich

University of Michigan

MRI Workshop on Acquisition and Reconstruction

September 9, 2021

Motivation: Mapping exchange

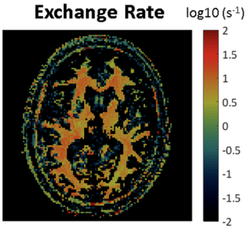


Figure: 2-D exchange map from MRF-X[1]

- Exchange captures inter-compartmental interactions (exchange of water + electrolytes)

[1] Hamilton, Jesse, et al. "MR fingerprinting with chemical exchange (MRF-X) for in vivo multi-compartment relaxation and exchange rate mapping." ISMRM 2016.

[2] Harkins, Kevin D., et al. "Effect of intercompartmental water exchange on the apparent myelin water fraction in multiexponential T2 measurements of rat spinal cord." MRM 67.3 (2012): 793-800.

Motivation: Mapping exchange

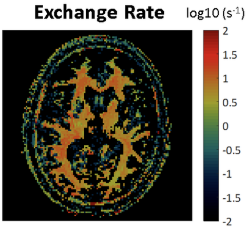


Figure: 2-D exchange map from MRF-X[1]

- Exchange captures inter-compartmental interactions (exchange of water + electrolytes)
- Exchange can be a useful clinical biomarker[2]

---

[1] Hamilton, Jesse, et al. "MR fingerprinting with chemical exchange (MRF-X) for in vivo multi-compartment relaxation and exchange rate mapping." ISMRM 2016.

[2] Harkins, Kevin D., et al. "Effect of intercompartmental water exchange on the apparent myelin water fraction in multiexponential T2 measurements of rat spinal cord." MRM 67.3 (2012): 793-800.

Motivation: Mapping exchange

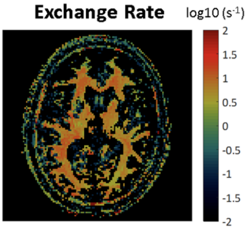


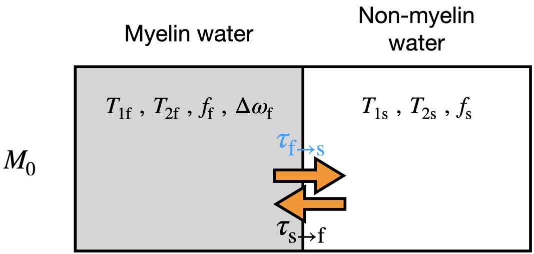
Figure: 2-D exchange map from MRF-X[1]

- Exchange captures inter-compartmental interactions (exchange of water + electrolytes)
- Exchange can be a useful clinical biomarker[2]
- Hard to estimate exchange *in vivo* currently

[1] Hamilton, Jesse, et al. "MR fingerprinting with chemical exchange (MRF-X) for in vivo multi-compartment relaxation and exchange rate mapping." ISMRM 2016.

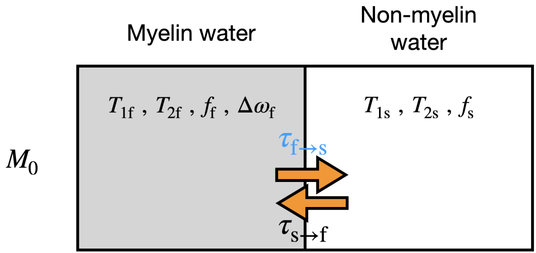
[2] Harkins, Kevin D., et al. "Effect of intercompartmental water exchange on the apparent myelin water fraction in multiexponential T2 measurements of rat spinal cord." MRM 67.3 (2012): 793-800.

Two pool exchanging model



$\Delta\omega_f$: Myelin-specific frequency shift

Two pool exchanging model

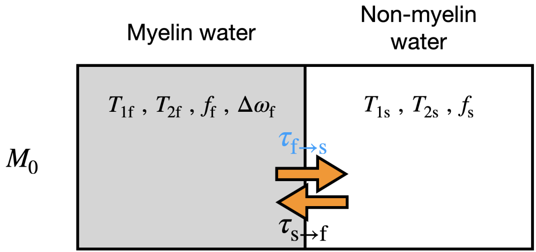


Objectives

- Obtain a scan design that is able to estimate exchange with high precision
- Quantify exchange rates using an appropriate estimator

$\Delta\omega_f$: Myelin-specific frequency shift

Two pool exchanging model



Setup

- $f_\mathrm{f} + f_\mathrm{s} = 1$
- Well-mixed: $f_\mathrm{f}/f_s = \tau_{\mathrm{f}\to\mathrm{s}}/\tau_{\mathrm{s}\to\mathrm{f}}$
- 8 unknowns: $(M_0, f_\mathrm{f}, T_{1\mathrm{f}}, T_{1\mathrm{s}}, T_{2\mathrm{f}}, T_{2\mathrm{s}}, \tau_{\mathrm{f}\to\mathrm{s}}, \Delta\omega_\mathrm{f})$

$\Delta\omega_\mathrm{f}$: Myelin-specific frequency shift

High-level overview

Scan design

- Cramer-Rao Bound (CRB) based optimization (weighted wrt exchange)
- Pulse sequence: Small-tip Fast Recovery (STFR) sequence[3]

[3] Sun, Hao, et al. "Steady-state functional MRI using spoiled small-tip fast recovery imaging." *Magnetic resonance in medicine* 73.2 (2015): 536-543.

High-level overview

Scan design

- Cramer-Rao Bound (CRB) based optimization (weighted wrt exchange)
- Pulse sequence: Small-tip Fast Recovery (STFR) sequence[3]

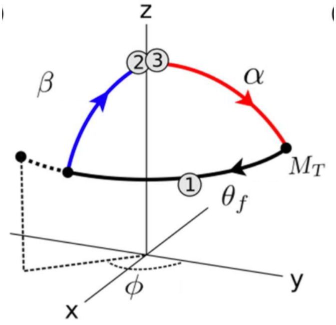
Estimation

- Parameter Estimation via Regression with Kernels (PERK)[4]
- Fast dictionary-free parameter estimation method
- Lifts measurements to a higher-dimensional space followed by kernel regression

[3] Sun, Hao, et al. “Steady-state functional MRI using spoiled small-tip fast recovery imaging.” *Magnetic resonance in medicine* 73.2 (2015): 536-543.

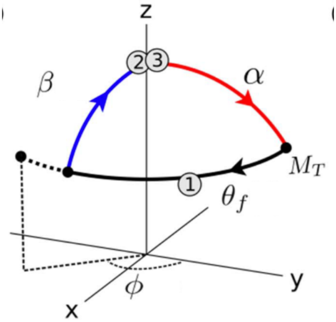
[4] Nataraj, Gopal, et al. “Dictionary-free MRI PERK: Parameter estimation via regression with kernels.” *IEEE transactions on medical imaging* 37.9 (2018): 2103-2114.

Small-tip Fast Recovery (STFR)



- Goal: Design a set of D STFR scans.

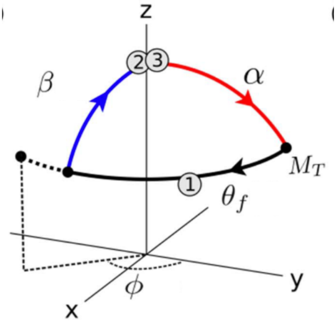
Small-tip Fast Recovery (STFR)



- Goal: Design a set of D STFR scans.
- Scan parameters: $(T_{\text{free}}, T_{\text{g}}, \alpha, \beta, \phi, T_{\text{E}})_d$,

  where $d = 1, 2, \ldots D$.

Small-tip Fast Recovery (STFR)



- Goal: Design a set of D STFR scans.
- Scan parameters:
  $(T_{\mathrm{free}}, T_{\mathrm{g}}, \alpha, \beta, \phi, T_{\mathrm{E}})_d,$

  where $d = 1, 2, \ldots D$.

Hypothesis

Optimized STFR sequences are sensitive to $\Delta\omega_{\mathrm{f}}$, which might lead to more precise exchange estimates.

$\Delta\omega_{\mathrm{f}}$: Myelin-specific frequency shift

Scan design

Setup:

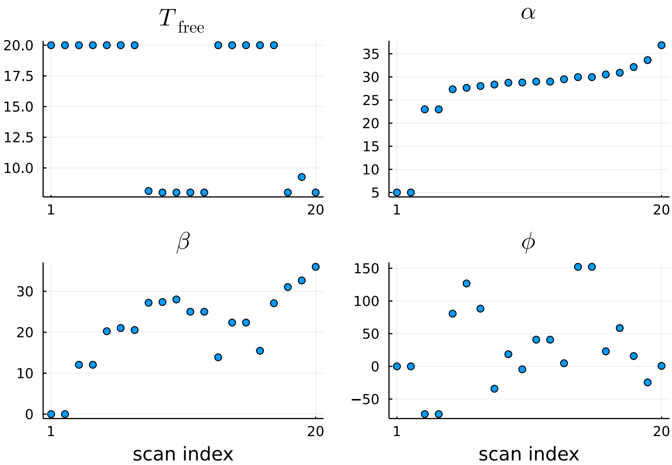
- D = 20 scans
- max FA = 40°, range of T_{free} = 8-20ms

Scan design

Setup:

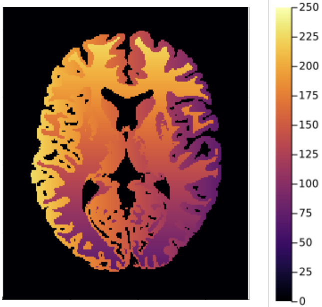
- D = 20 scans
- max FA = 40°, range of T_{free} = 8-20ms
- B0 and B1+ maps are computed through separate SPGR and Bloch-Siegert scans
- Total scan time: $\sim$21mins for 10 slices

Optimized STFR design



- Coeff. of variation is **20%** for exchange estimation in WM (vs. 93% for initial design).

Simulations



(a) Exchange map - ground truth (in ms) [5]

Parameter	White Matter	Gray Matter
M_0	0.77	0.86
f_f	0.15	0.03
$T_{1,f}$ (ms)	400	500
$T_{1,s}$ (ms)	832	1331
$T_{2,f}$ (ms)	20	20
$T_{2,s}$ (ms)	80	80
$\Delta\omega_f$ (Hz)	15	5
$\Delta\omega$ (Hz)	Varies	Varies
κ	Varies	Varies

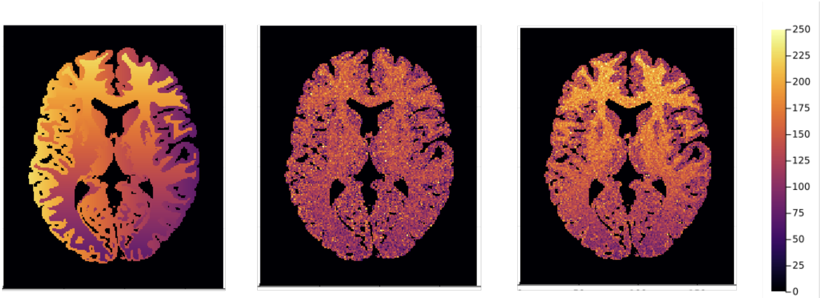
(b) Nominal values for WM and GM at 3T [6]

---

[6] Collins, D. Louis, et al. "Design and construction of a realistic digital brain phantom." *IEEE TMI* 1998.

[7] Whitaker, Steven T., et al. "Myelin water fraction estimation using small-tip fast recovery MRI." *MRM* 2020.

Results

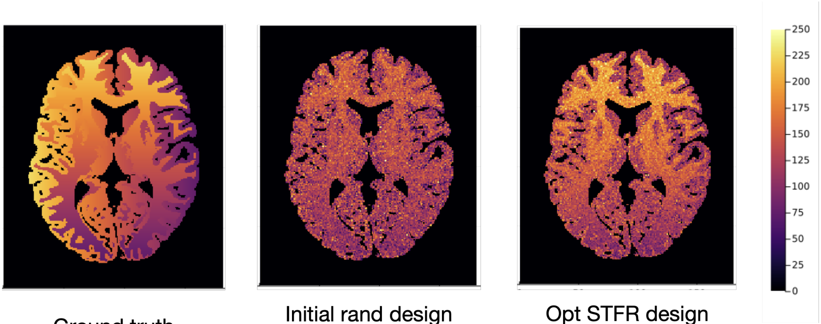


Ground truth

Initial rand design
(RMSE in WM: 38ms)

Opt STFR design
(RMSE in WM: **23ms**)

Results



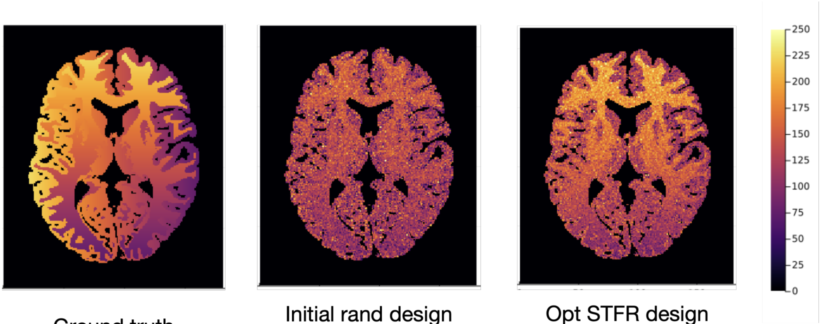
Ground truth

Initial rand design
(RMSE in WM: 38ms)

Opt STFR design
(RMSE in WM: **23ms**)

- Opt STFR design has an RMSE of **15%** in WM (vs. 25% for initial design).

Results



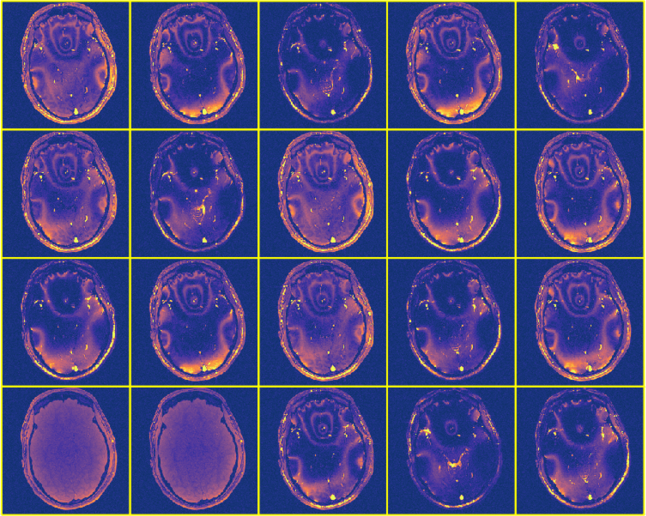
Ground truth

Initial rand design
(RMSE in WM: 38ms)

Opt STFR design
(RMSE in WM: **23ms**)

- Opt STFR design has an RMSE of **15%** in WM (vs. 25% for initial design).
- Performs as worse as a mean estimator in GM (caveat: very little myelin content in GM)

Invivo data (in progress)



Acknowledgements for data: Melissa Haskell

Conclusions

Conclusions:

- Obtained an optimized STFR design that has $\sim$**20%** coefficient of variation for estimating exchange in WM.
- Optimized design performs better in WM than a random design (by $\sim$**10%**); does as worse as a mean estimator in GM.

Conclusions

Conclusions:

- Obtained an optimized STFR design that has $\sim$**20%** coefficient of variation for estimating exchange in WM.
- Optimized design performs better in WM than a random design (by $\sim$**10%**); does as worse as a mean estimator in GM.

Next steps:

- Investigate the performance of the estimator in the presence of off-resonance.
- Investigate how the opt design does for invivo data; compare with other state-of-the-art methods.