

3rd project details & figs

# Progress to date

- qMT optimization framework using qMRIILab
  - Tissue & Protocol wrapper classes
  - Jacobian(Tissue, Protocol) class for pre-calc/caching Jacobian.
    - SPGR qMT Jacobian calculated using qMRIILab's steady-state qMT signal simulator
  - Optimization(Jacobian) class for optimizing qMT sequence
- Evaluated improved B1 optimization metric
  - Solve  $\min \|\mathbf{J}_p \Delta p + \mathbf{J}_{B_1} \Delta B_1\|$  for  $\Delta p$  given  $\Delta B_1$
  - Tested by reproducing MRM simulations/sensitivity figure
- Evaluated qMT parameter-error from above metric calc for uniform protocols /w varying:
  - # of offset points
  - # of  $FA_{MT}$

# Progress to date

- Computed Jacobian for a full (312 pt) search-space qMT protocol
  - 26 offsets (300 Hz to 20 kHz)
  - 12  $FA_{MT}$  vals (150:50:700)
- Optimized qMT protocol using iterative procedure & CRLB
- Optimized qMT protocol for  $B_1$  insensitivity by:
  - Optimizing for  $\delta F_{B_1}$  only
  - Alternating between for CRLB and  $\delta F_{B_1}$  at every other iterations
  - Optimizing for CRLB but regularized by  $\delta F_{B_1}$ 
    - Found optimal lambda  $\approx 0.5$
- Preliminary no-noise simulations of errors in  $F$  due to  $B_1$  err = 5%
  - UK protocol ->  $\delta F \sim 1\text{-}2\%$
  - CRLB optimized ->  $\delta F \sim 0.5\%$
  - CRLB regularized by  $\delta F_{B_1}$  ->  $\delta F \sim 0.09\%$

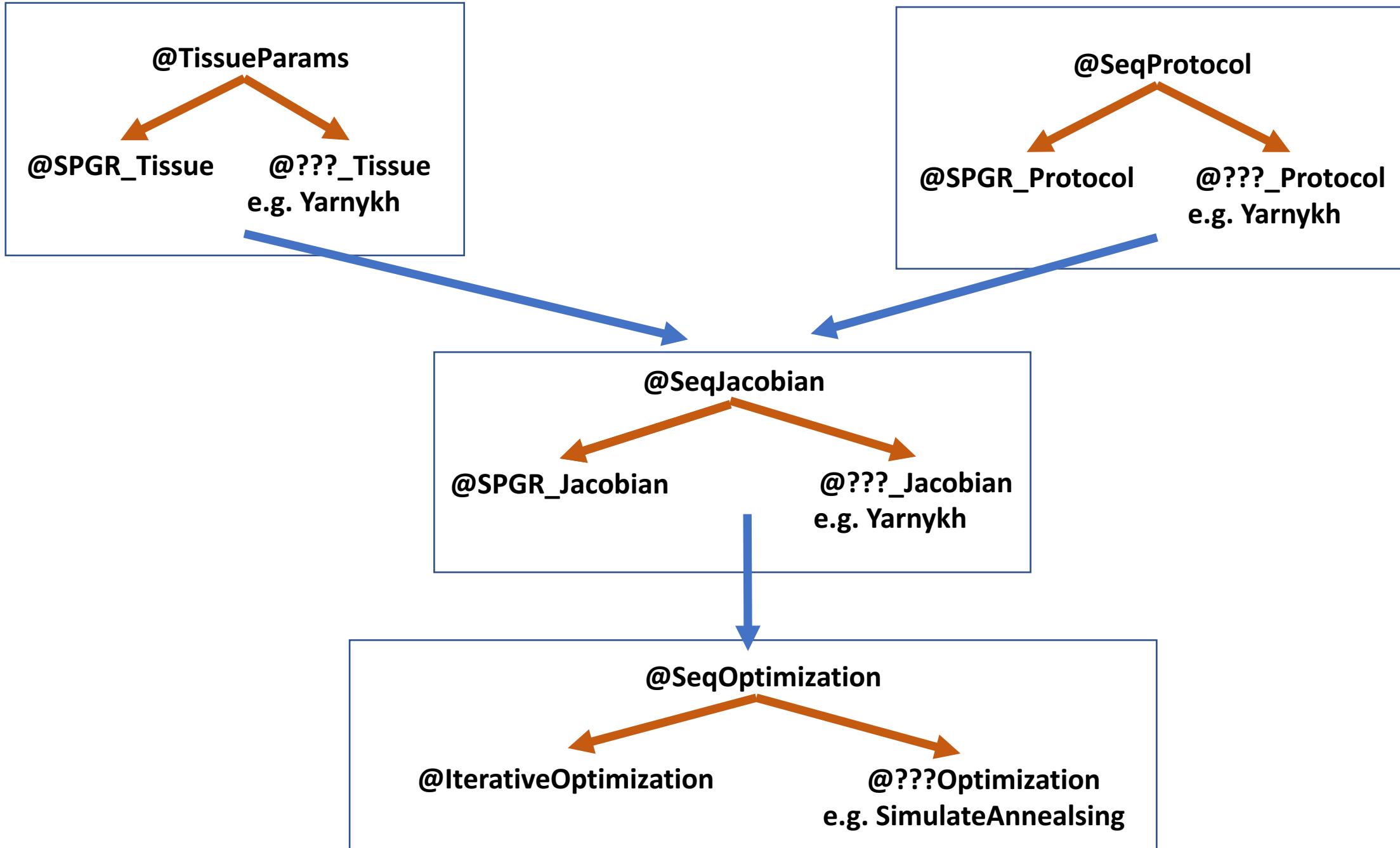
## To-Do (must)

- WM Monte-carlo simulations
  - 3 different 10 pt protocols
    - 2FA with log-uniform offsets
    - CRLB optimized ( $\lambda = 0$ )
    - CRLB regularized by  $B_1$  ( $\lambda = 0.5$ ,  $\delta F_{B_1}^{VFA}$ )
  - Generate 10,000 signal sets for each protocol, with rician noise added
    - 50, 100, 200 SNR for  $M_0$ ? More?
  - Fit Data
    - For  $\delta B_1 = 0, 1, 5, 10, 25 \%$ ?
    - Analysis? (means and std of fitted params, stat tests between methods?)

## To-Do (optional?)

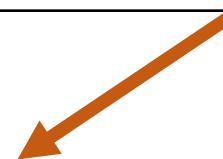
- Repeat Monte Carlo for other fixed tissues (e.g. GM & lesions)?
- Repeat Monte Carlo for gaussian-distributed tissue values?
- Repeat Monte Carlo for voxels with partial voluming?
- Repeat protocol optimization & Monte Carlo simulations for other qMT methods?
  - Ramani, Yarnikh
- Evaluate optimization for different regularization criteria?
  - e.g.  $T_1$  &  $B_0$ , or  $B_1$  for kf?

# Code overview



## **@TissueParams**

Public Properties	Public Methods
None	save(obj, fileName) load(obj, fileName) paramsArray = getParams(tissueKeys) paramValue = getParameter(paramKey)



## **@SPGR\_Tissue**

Public Properties	Public Methods
paramsKeys = {'F', 'kf', 'R1f', 'R1r', 'T2f', 'T2r'} fitParamsKeys = {'F', 'kf', 'R1f', 'T2f', 'T2r'}	<b>SPGR_Tissue(paramsValues)</b> <ul style="list-style-type: none"><li>• paramsValues: Array of values for paramsKeys</li></ul>

## @SeqProtocol

Public Properties	Public Methods
None	<p>save(obj, fileName) load(obj, fileName) prot = getProtocol()</p> <p><b>**Abstract**</b></p> <ul style="list-style-type: none"><li>• totalNumOfMeas = getNumberOfMeas()</li><li>• paramValue = getParameter(protKey)</li><li>• remove(indices)</li></ul>

## @SPGR\_Protocol

Public Properties	Public Methods
fitProtKeys = {'B1_IR', 'B1_VFA'} B1_value = 1.0	<p><b>SPGR_Protocol(fileName)</b></p> <ul style="list-style-type: none"><li>• fileName: qMRLab saved protocol *.mat string</li></ul> <p>totalNumOfMeas = getNumberOfMeas() paramValue = getParameter(protKey) remove(indices)</p>

## @SeqJacobian

Public Properties	Public Methods
None	<p>SeqJacobian(@SeqProtocol, @TissueParams)</p> <p>jacobianMatrix = getJacobian()</p> <p>*jacobianStruct = getJacobianStruct()</p> <p><b>computeOpts = compute(computeOpts)</b></p> <ul style="list-style-type: none"> <li>• computOpts: Struct with the following properties:           <ol style="list-style-type: none"> <li>1. mode: 'New', 'Resume', or 'Completed'</li> <li>2. paramsOfInterest: Cell array of strings of fitParamsKeys to calculate Jacobian.</li> <li>3. lineBuffer:</li> </ol> </li> </ul>

**@SPGR\_Protocol**



Public Properties	Public Methods
None	<b>SPGR_Jacobian(@SPGR_Protocol, @SPGR_Tissue)</b>

**\*jacobianStruct properties:**

- jacobianMatrix
- paramsKeys
- paramsVals
- protocol
- status
- completedLines
- signal
- d\_signal

## @SeqOptimization

Public Properties	Public Methods
None	<p>*Static*</p> <p>paramError = minimizeParamErrorBecauseOfMeasError(paramJacMat, measJacMat, measError)</p> <p>fisherInformationMatrix = calcFIM(jacobianMatrix)</p> <p>crlb = calcCRLB(jacobianMatrix)</p> 
	<p><b>@IterativeOptimization</b></p> <p>Public Properties</p> <p>metricSet = {'CRLB'};</p> <p><b>IterativeOptimization(@SeqJacobian, opts)</b></p> <ul style="list-style-type: none"><li>• opts: Struct with the following properties:<ol style="list-style-type: none"><li>1. fitParams: Cell array of strings of fitParamsKeys to include in optimization (cols of Jac.)</li><li>2. (optional) b1Params: Cell string of B1 params name for B1-sensitivity optimization)</li></ol></li></ul> <p><b>computeSingle(metricFlag)</b></p> <p>computeDoubleAlternate(metricFlags)</p> <p>computeRegularized(metricFlags, regularizationCoeff)</p> <p>rankedAcqPoints = getRankedAcqPoints()</p> <p>metricValsAcqPoints = getMetricValsAcqPoints()</p> <p>reguTermValsAcqPoints = getReguTermValsAcqPoints()</p> <p><b>[rankedAcqPoints_sorted, metricValsAcqPoints_sorted] = getSorted()</b></p> <p><b>[rankedAcqPoints_sorted, reguTermValsAcqPoints_sorted] = getSortedRegTerm()</b></p> <p><b>[rankedAcqPoints_sorted, protocol_sorted] = getSortedProtocol()</b></p>

# Theory Overview

# MRM Paper theory

$$\begin{pmatrix} S_{F,1} & S_{k_f,1} & S_{T_{2,f},1} & S_{T_{2,r},1} \\ S_{F,2} & S_{k_f,2} & S_{T_{2,f},2} & S_{T_{2,r},2} \\ \vdots & \vdots & \vdots & \vdots \\ S_{F,N} & S_{k_f,N} & S_{T_{2,f},N} & S_{T_{2,r},N} \end{pmatrix} \begin{pmatrix} \Delta F \\ \Delta k_f \\ \Delta T_{2f} \\ \Delta T_{2r} \end{pmatrix} = - \begin{pmatrix} S_{B_1,1} \\ S_{B_1,2} \\ \vdots \\ S_{B_1,N} \end{pmatrix} \Delta B_1$$

$$S_{p_k,i} \equiv \frac{\partial M_i}{\partial p_k}$$

$$\mathbf{S}_p \Delta p = - \mathbf{S}_{B_1} \Delta B_1$$

$$\hat{\mathbf{S}}_p \cdot \hat{\mathbf{S}}_{B_1}$$

# Updated approach

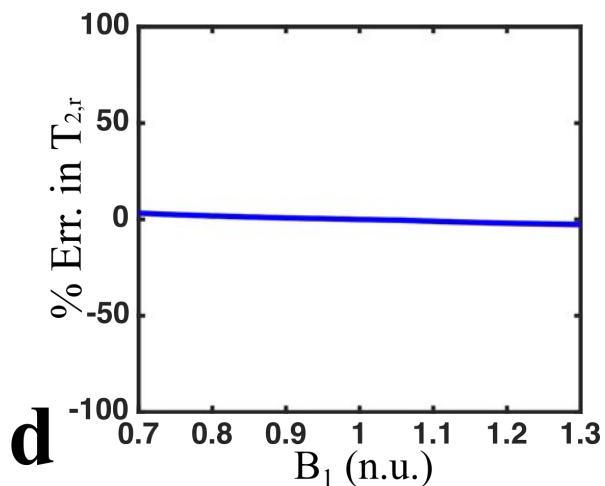
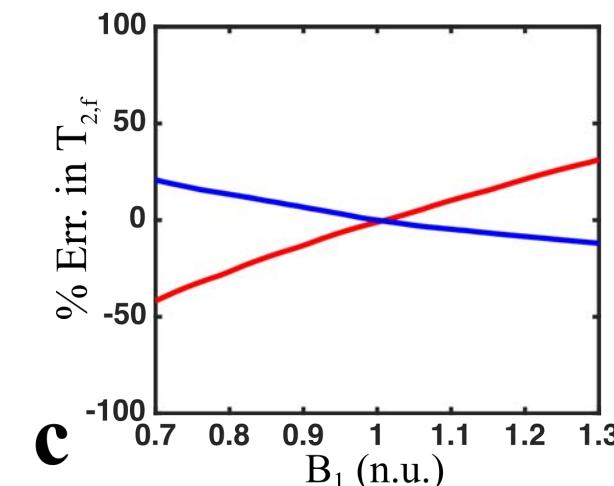
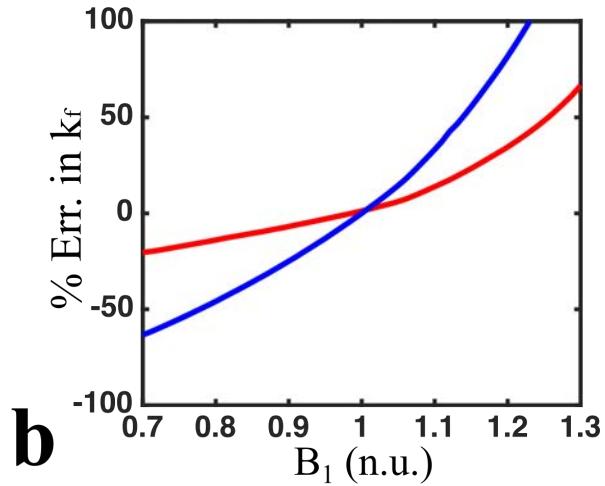
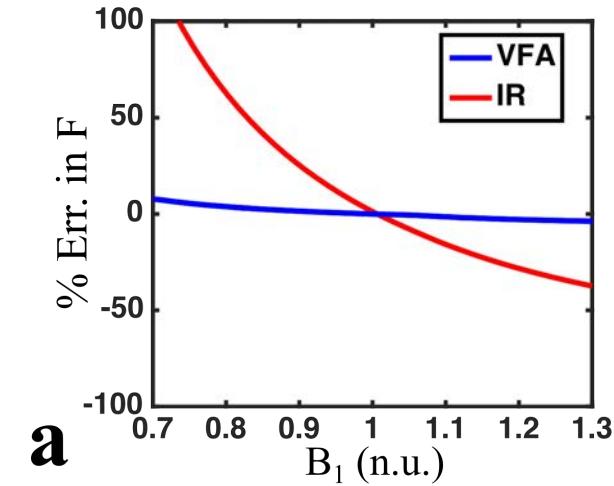
$$\begin{pmatrix} S_{F,1} & S_{k_f,1} & S_{T_{2,f},1} & S_{T_{2,r},1} \\ S_{F,2} & S_{k_f,2} & S_{T_{2,f},2} & S_{T_{2,r},2} \\ \vdots & \vdots & \vdots & \vdots \\ S_{F,N} & S_{k_f,N} & S_{T_{2,f},N} & S_{T_{2,r},N} \end{pmatrix} \begin{pmatrix} \Delta F \\ \Delta k_f \\ \Delta T_{2f} \\ \Delta T_{2r} \end{pmatrix} = - \begin{pmatrix} S_{B_1,1} \\ S_{B_1,2} \\ \vdots \\ S_{B_1,N} \end{pmatrix} \Delta B_1$$

$$\mathbf{J}_p \Delta p = -\mathbf{J}_{B_1} \Delta B_1$$

$$\|\mathbf{J}_p \Delta p + \mathbf{J}_{B_1} \Delta B_1\| = 0$$

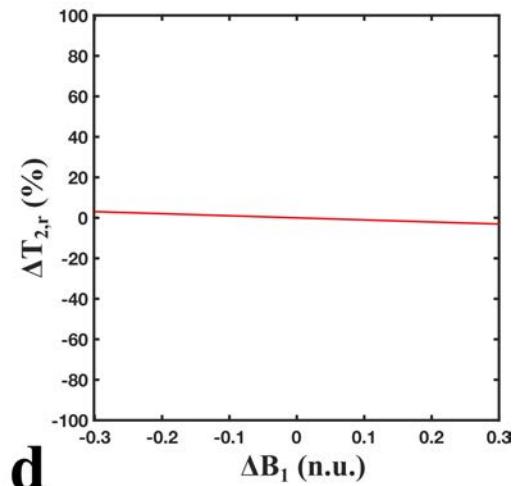
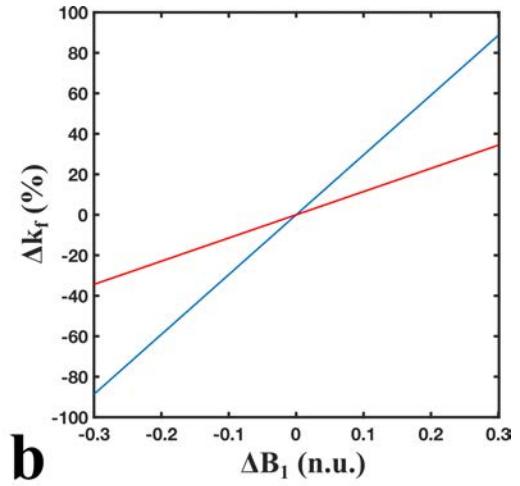
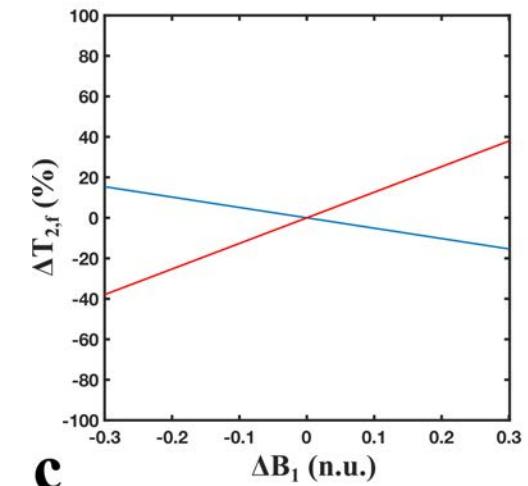
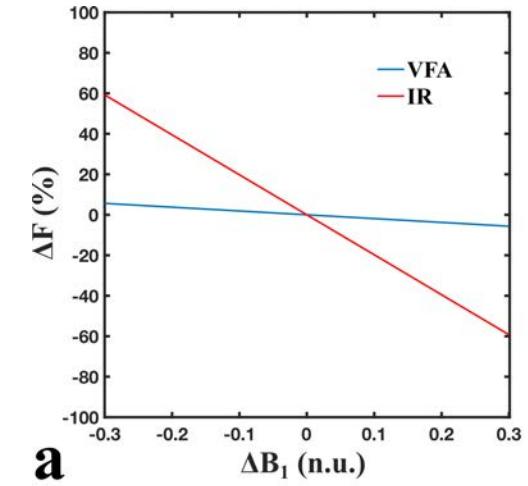
Solve  $\min \|\mathbf{J}_p \Delta p + \mathbf{J}_{B_1} \Delta B_1\|$  for  $\Delta p$  given  $\Delta B_1$

# Parameter fitting error in simulations



MRM Paper

$$\Delta p : \min \| J_p \Delta p + J_{B_1} \Delta B_1 \|$$



Current Work

$\Delta p$  for uniform protocols /w varying FA and  
#offsets?

# WM tissue parameter values

- $F = 0.15$  n.u.
- $k_f = 4.0 \text{ s}^{-1}$
- $T_{1,f} = 900 \text{ ms}$
- $R_{1,r} = 1 \text{ s}$
- $T_{2,f} = 30 \text{ ms}$
- $T_{2,r} = 12 \mu\text{s}$

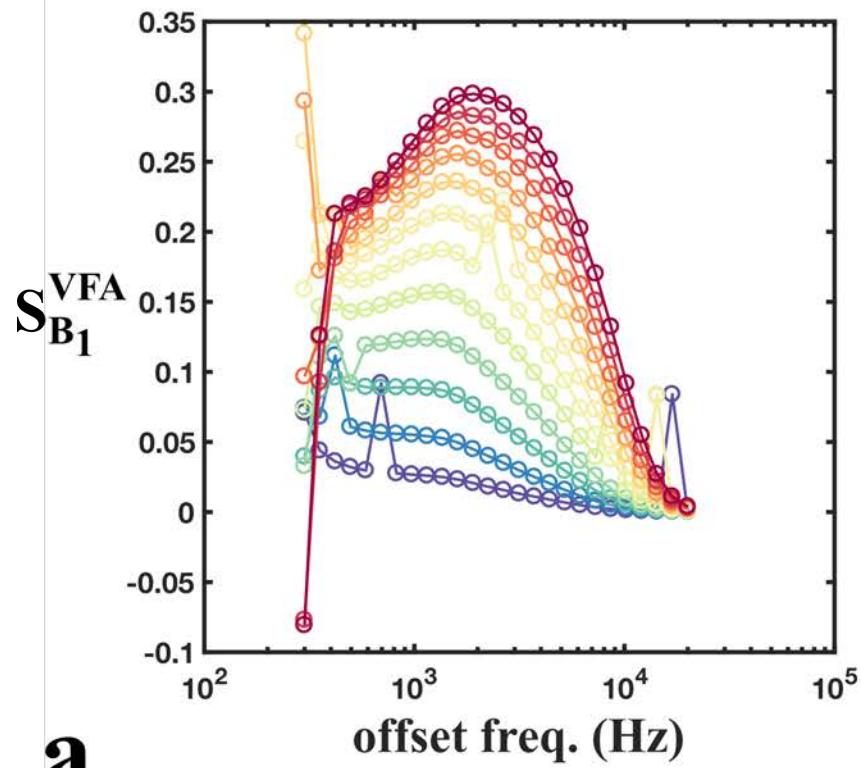
# Protocol definitions

- Single FA
  - 150
  - 400
  - 650
- 2FA
  - (150, 400)
  - (150, 650)
  - (400, 650)
- 3FA
  - (150, 400, 650)
- Offset values
  - [300 Hz, 20 kHz]
  - uniform-logarithmically spaced
  - Total # of points ranging from 8 to 30
    - Single FA, 8:2:30 offsets
    - 2FA, 4:1:15 offsets
    - 3FA, 3:1:10 FA

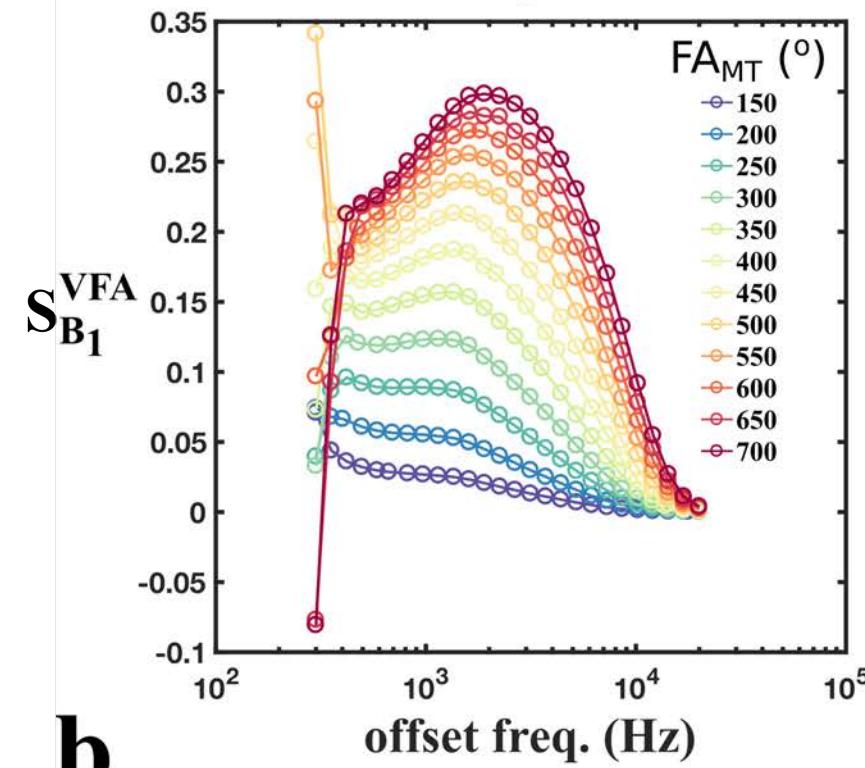
# Protocol pre-processing

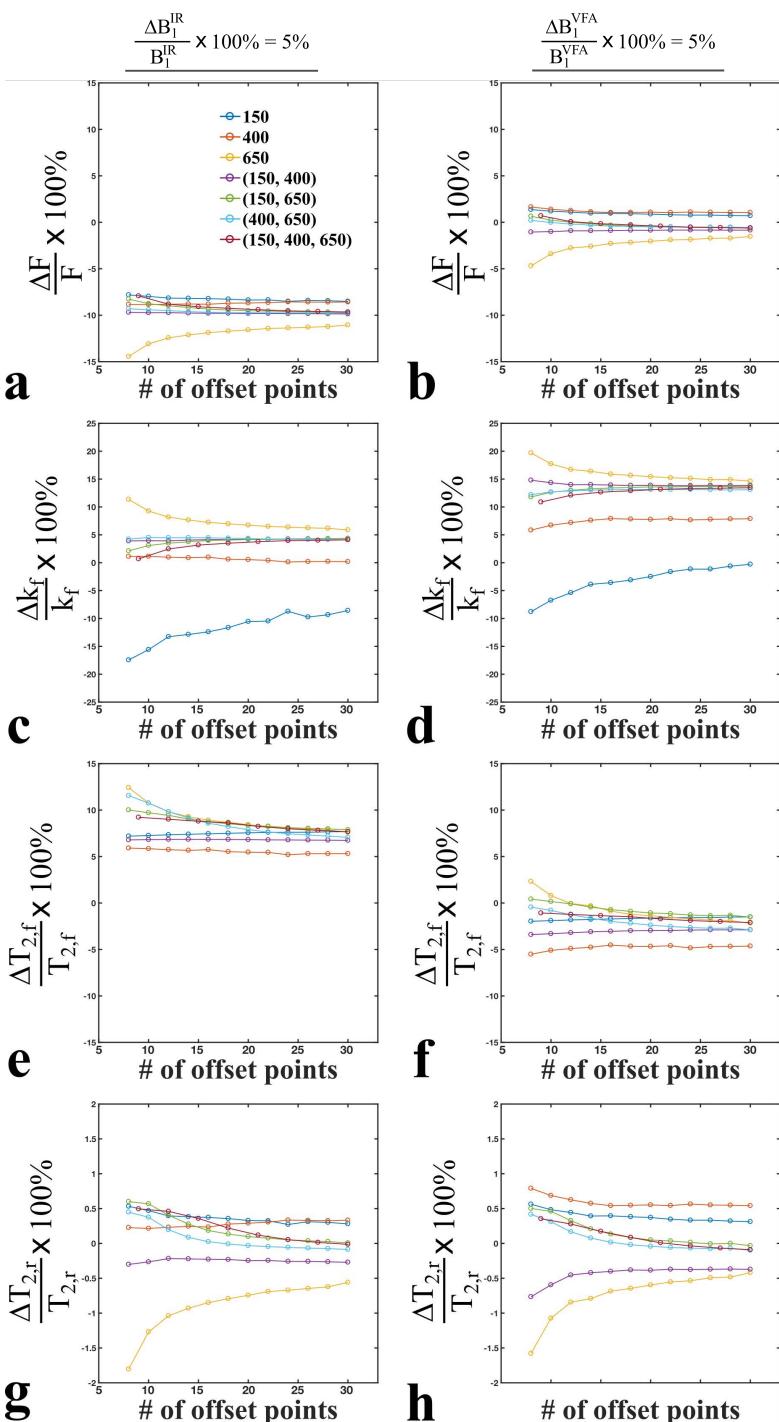
- Calculate higher « protocol resolution » Sf cache, then set-up each protocol using that Sf cache.
- Some protocol points (<5%) produced erroneous/outlier (non-continuous) Jacobian element values
  - Wonky/sensitive steady-state signal convergence?
- Identified all such point in the higher « protocol resolution » set, and if an outlier point was present in a studied protocol, change it to the nearest neighbour from high res.

with outliers

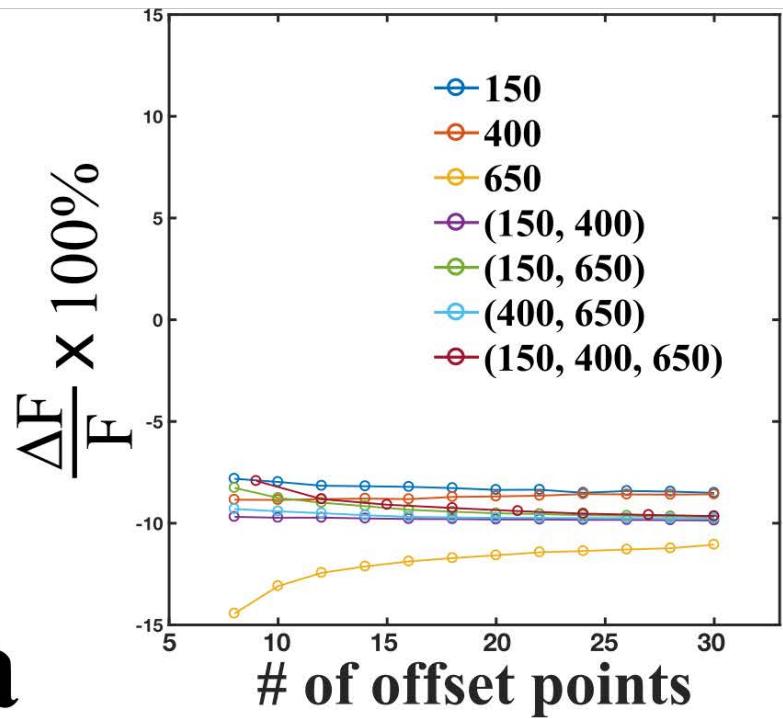


nearest-neighbour corr.

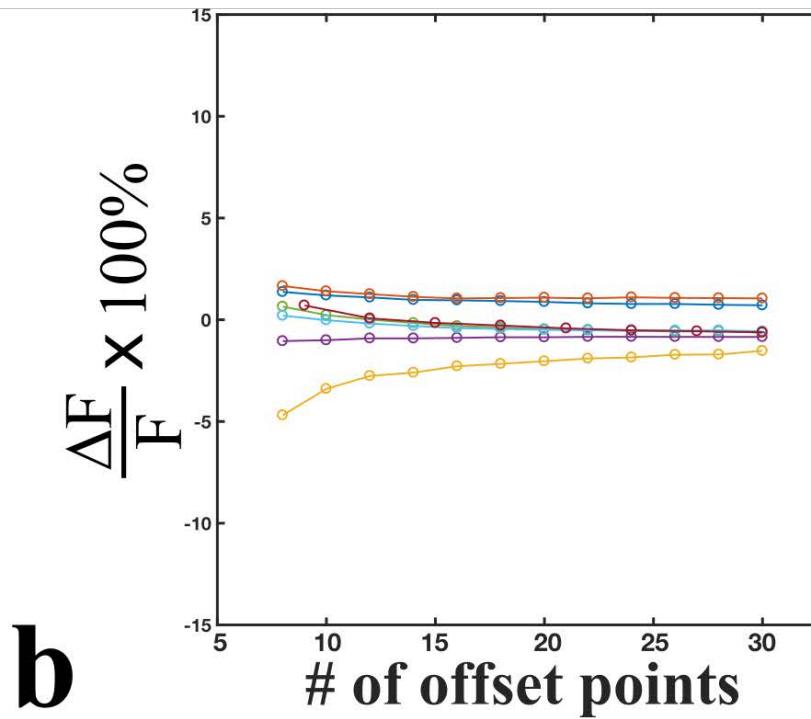


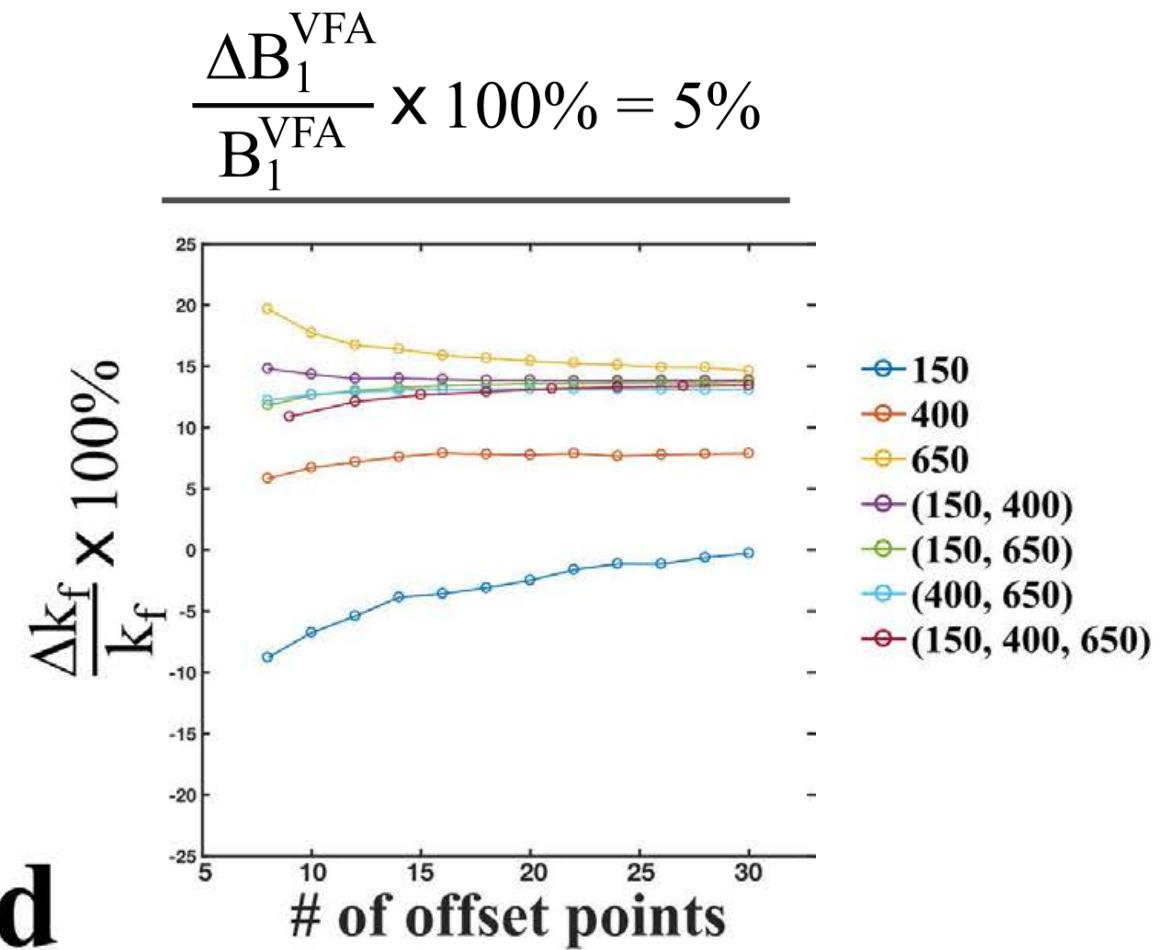
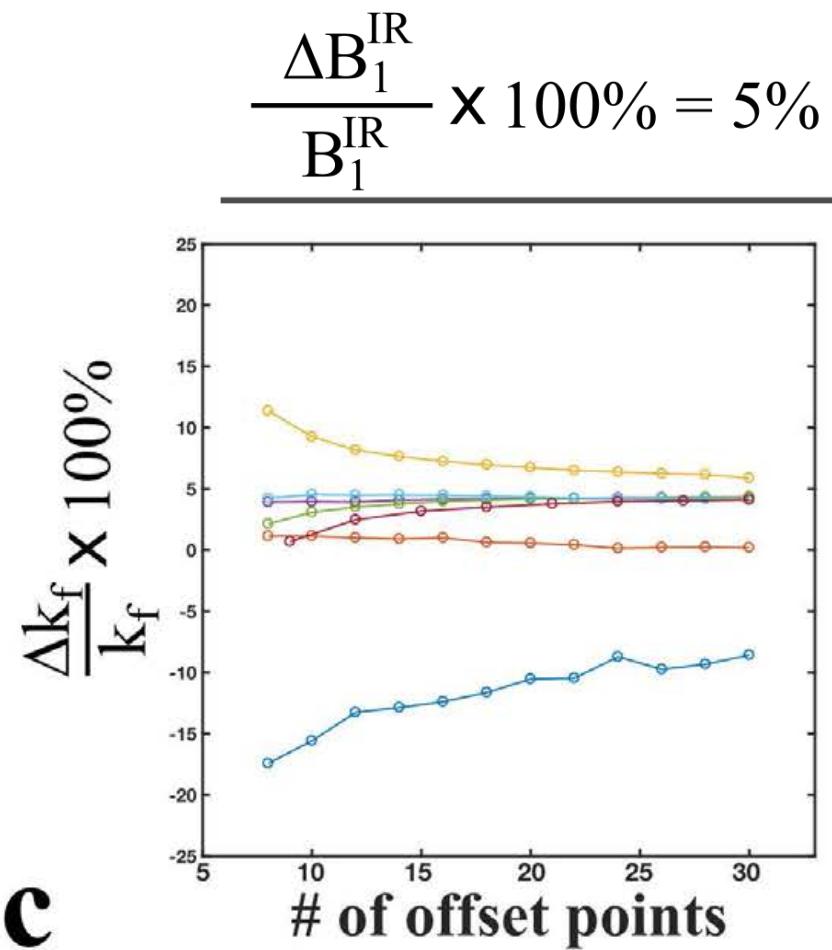


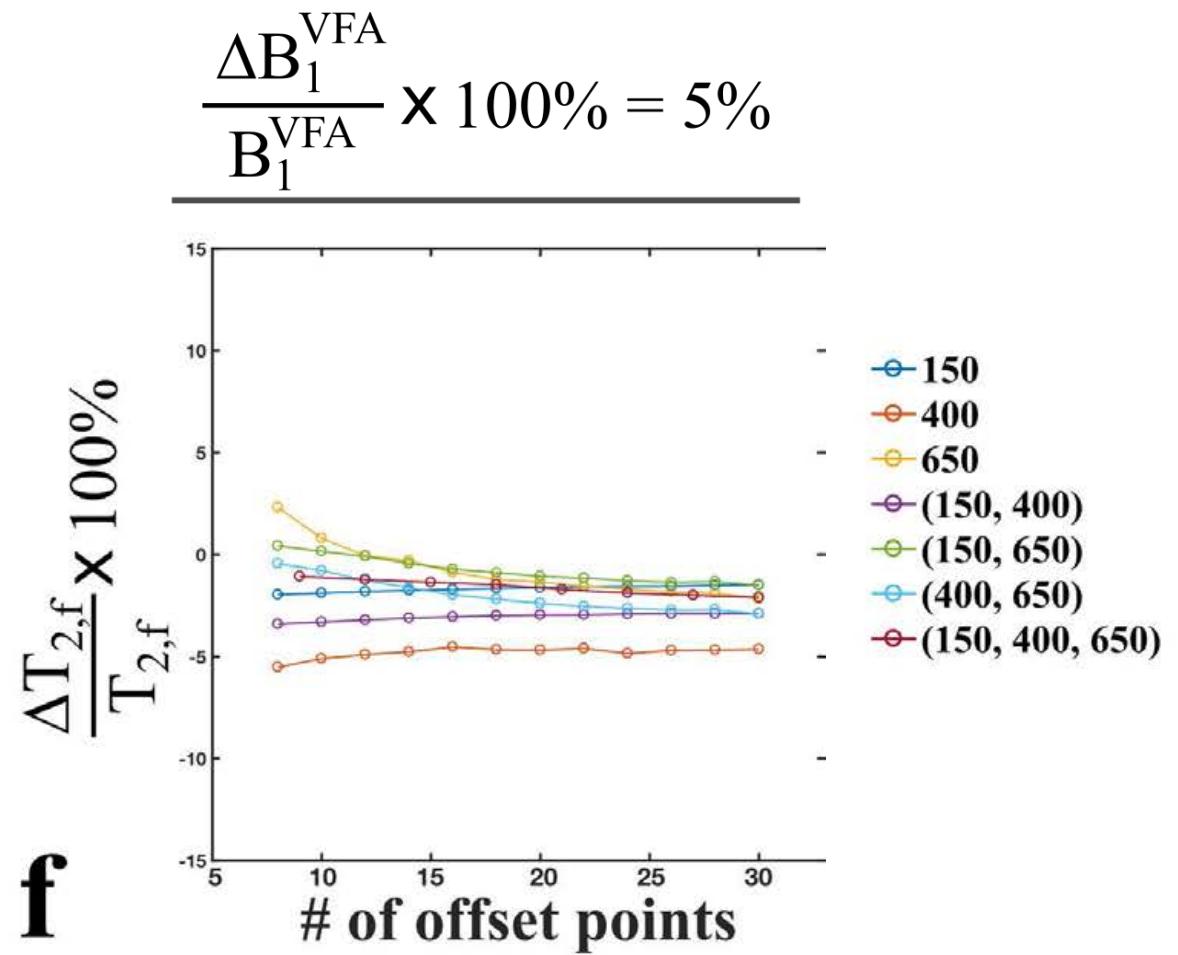
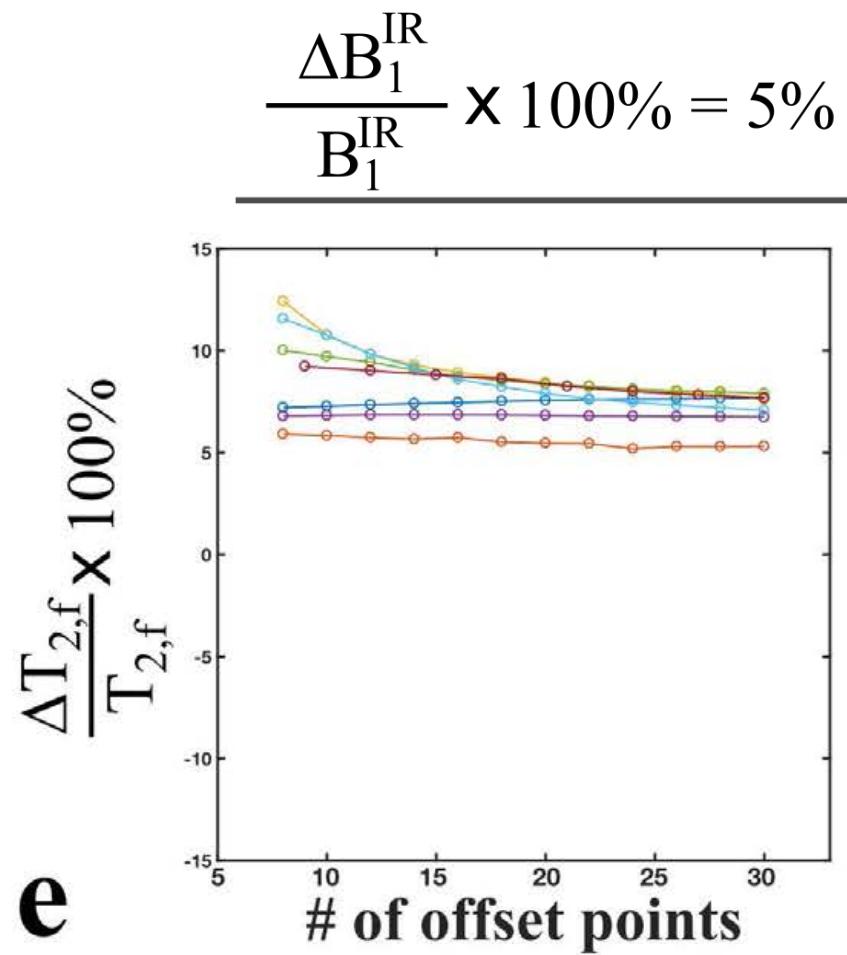
$$\frac{\Delta B_1^{\text{IR}}}{B_1^{\text{IR}}} \times 100\% = 5\%$$



$$\frac{\Delta B_1^{\text{VFA}}}{B_1^{\text{VFA}}} \times 100\% = 5\%$$

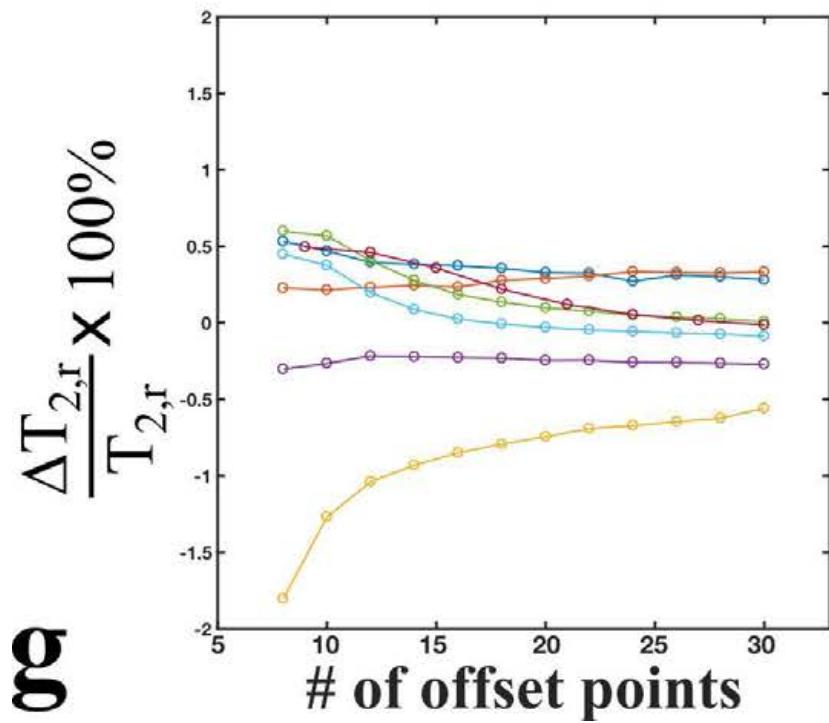






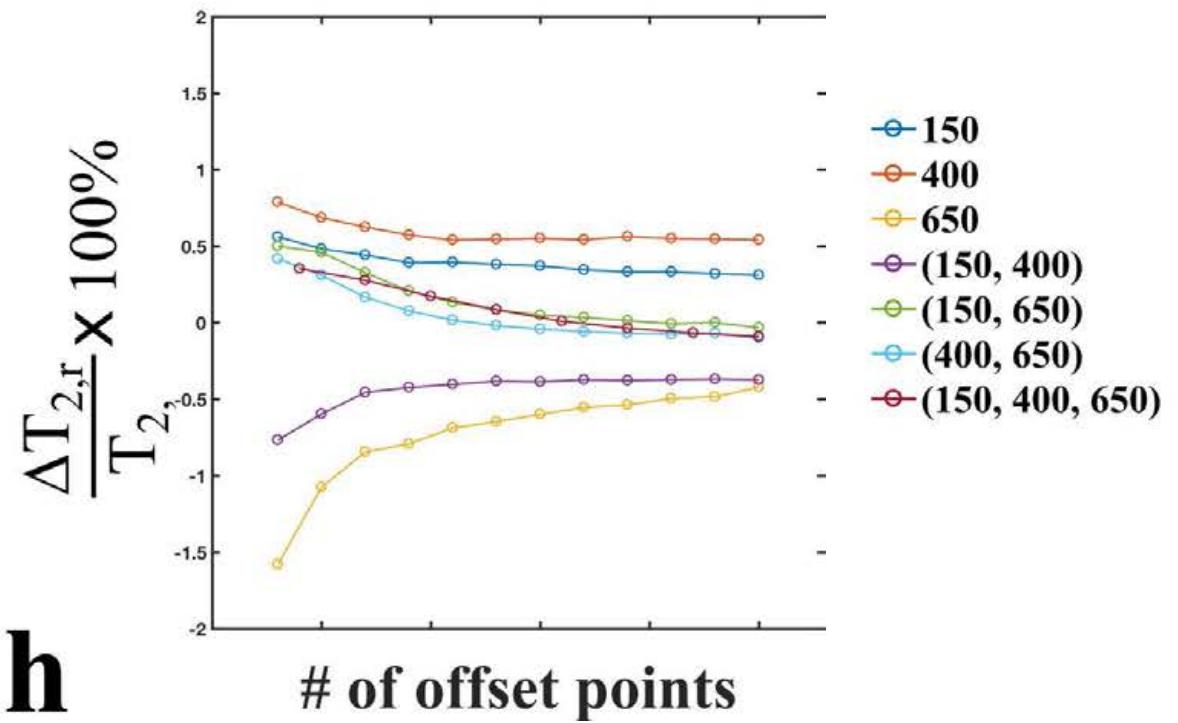
$$\frac{\Delta B_1^{\text{IR}}}{B_1^{\text{IR}}} \times 100\% = 5\%$$


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$$\frac{\Delta B_1^{\text{VFA}}}{B_1^{\text{VFA}}} \times 100\% = 5\%$$


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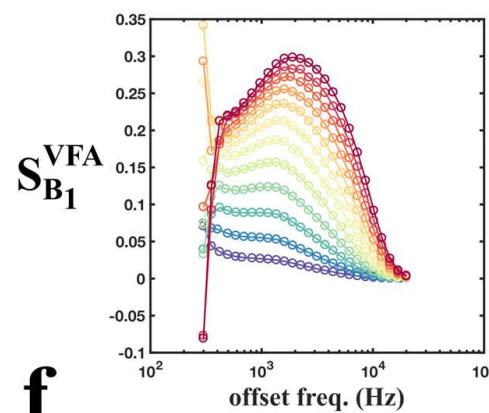
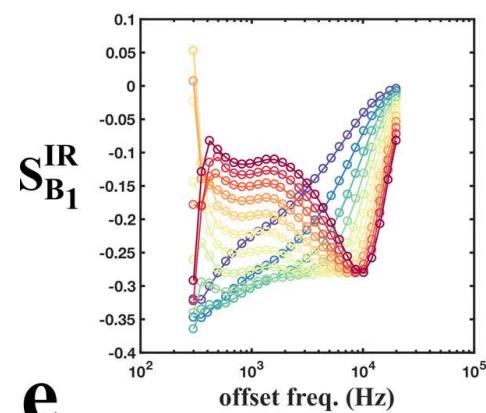
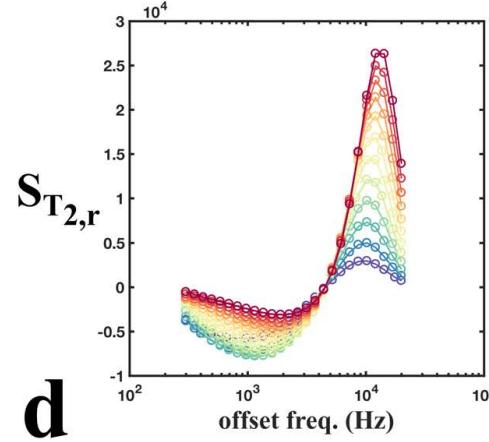
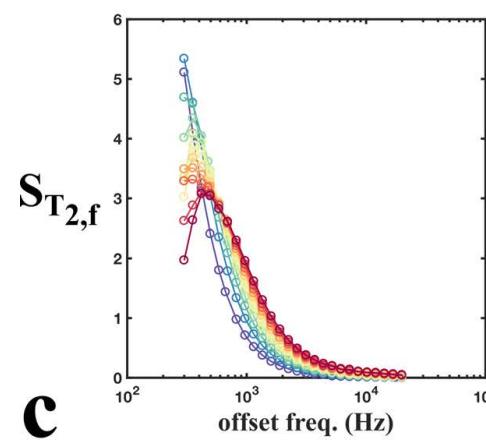
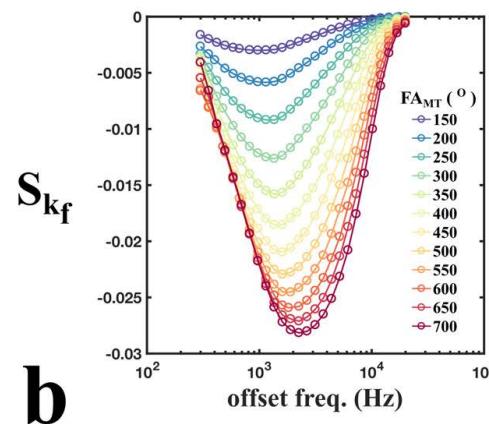
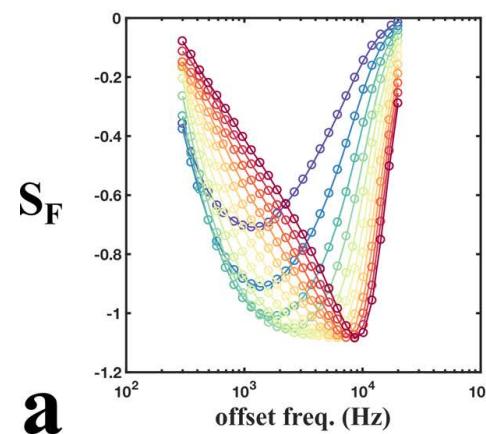


# Data visualization ideas

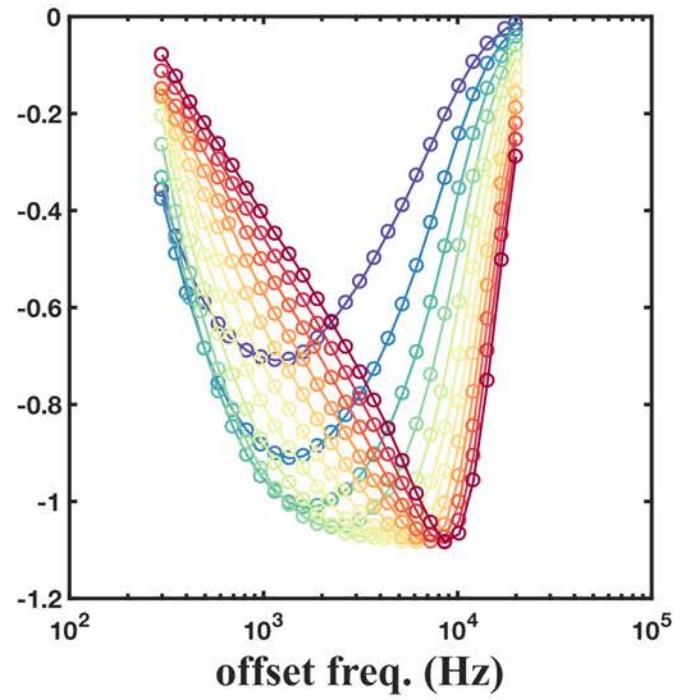
- $\frac{\Delta F}{\Delta B_1^{\text{VFA}}}$  instead?

# Jacobian/Sensitivity plots

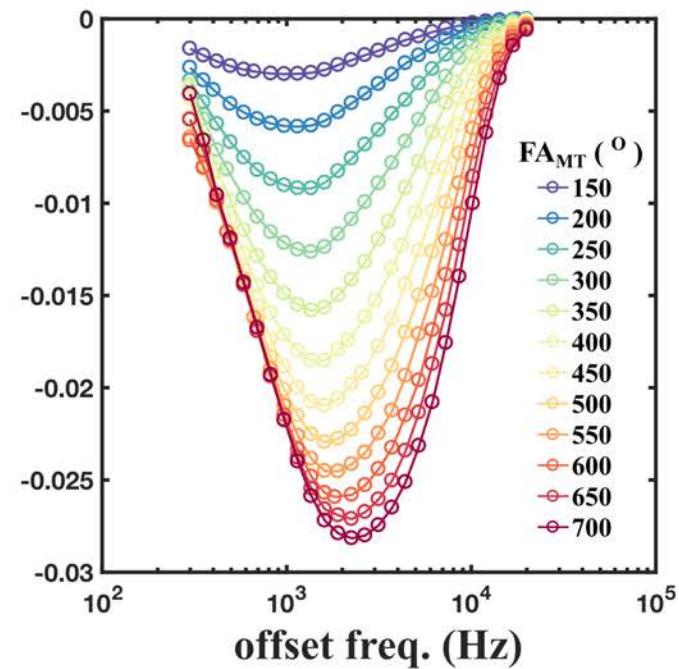
- Pre-calculated/cached the Jacobian for the following protocol:
  - TR = 25 ms
  - 12 FA<sub>MT</sub> (150:50:700 deg)
  - 26 offsets (300 Hz to 20 kHz)

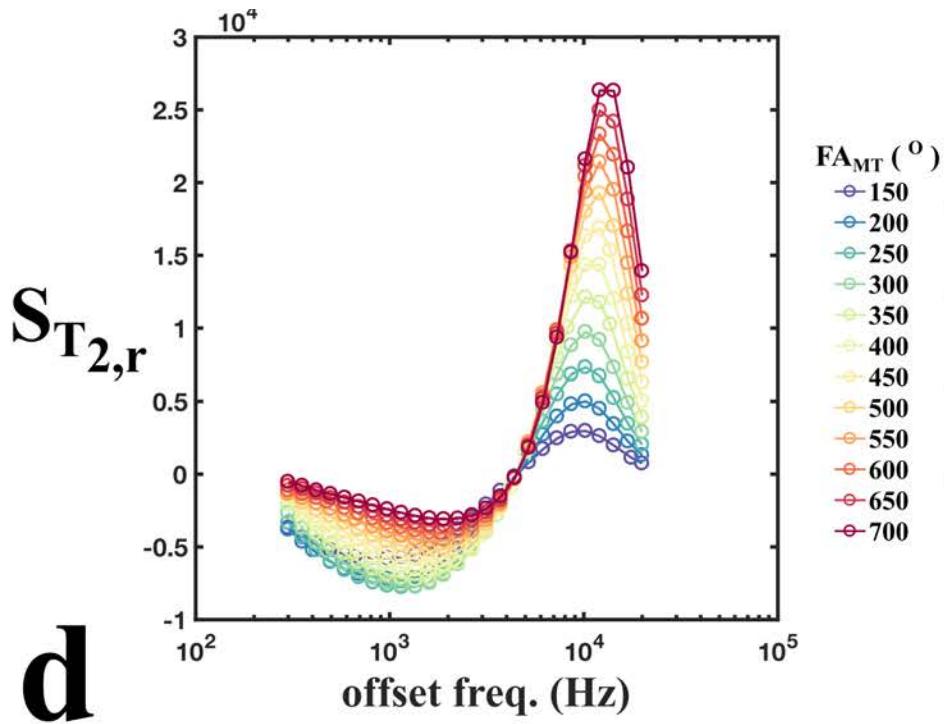
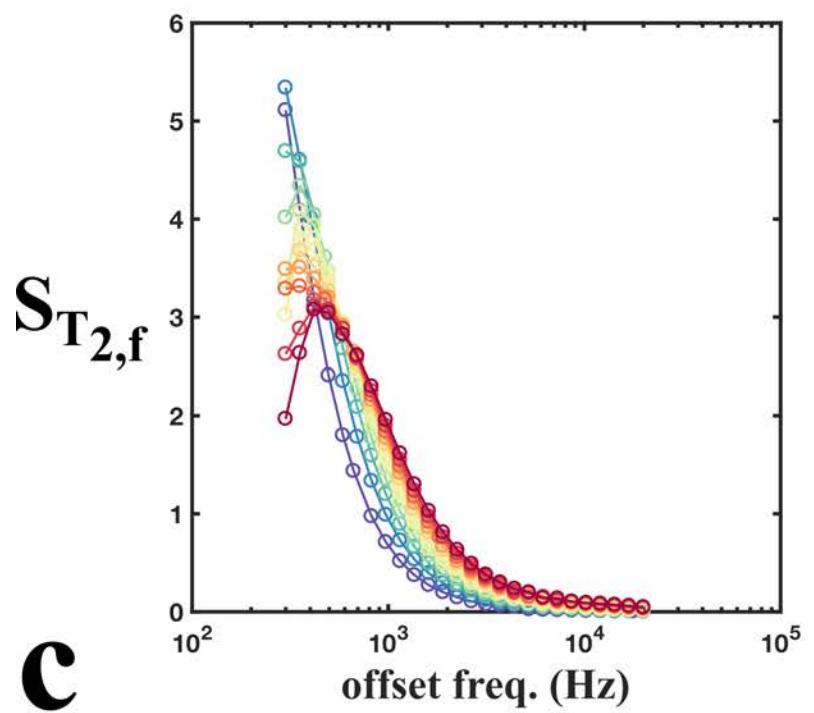


**a**

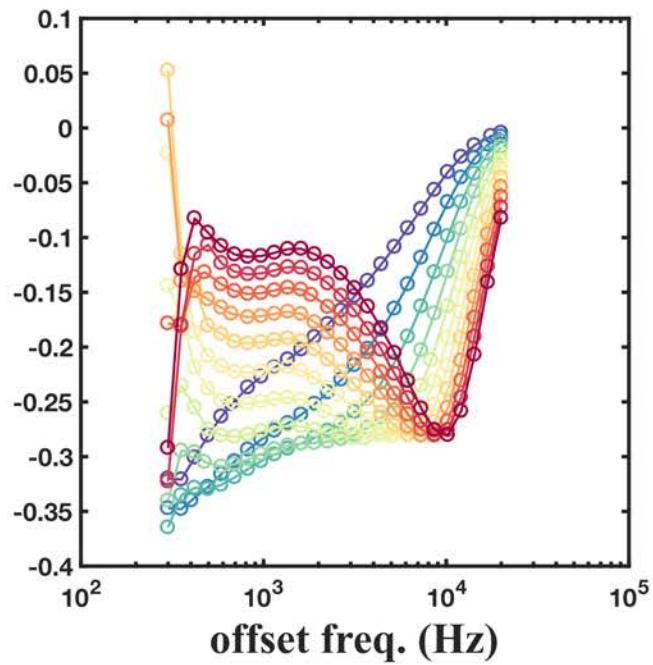


**b**

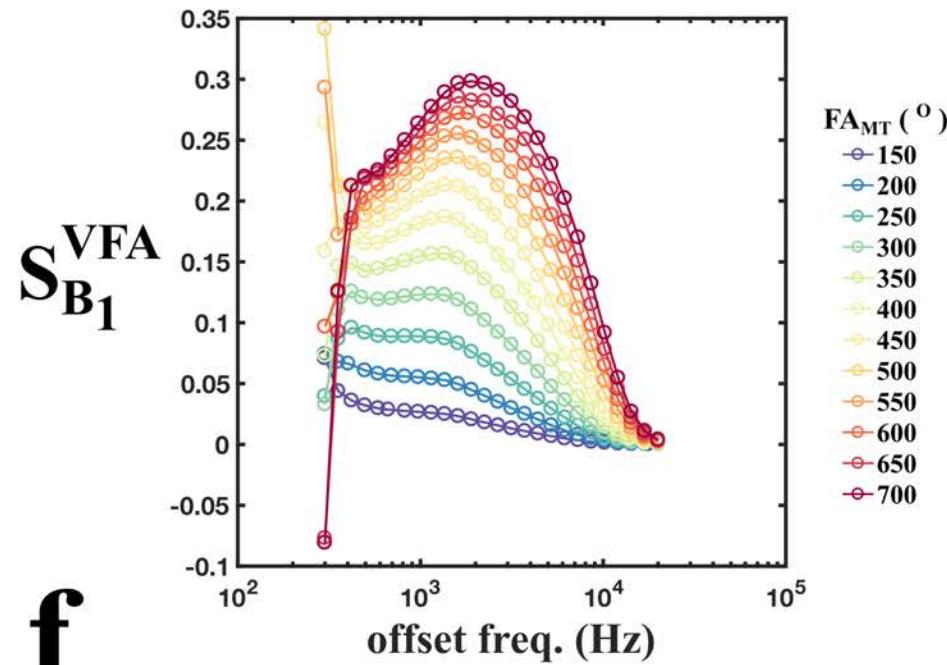




**e**  $S_{B_1}^{IR}$



**f**



# Iterative CRLB Optimization

Cercignani's Fisher Information/Cramer-Rao  
Lower Bound equations

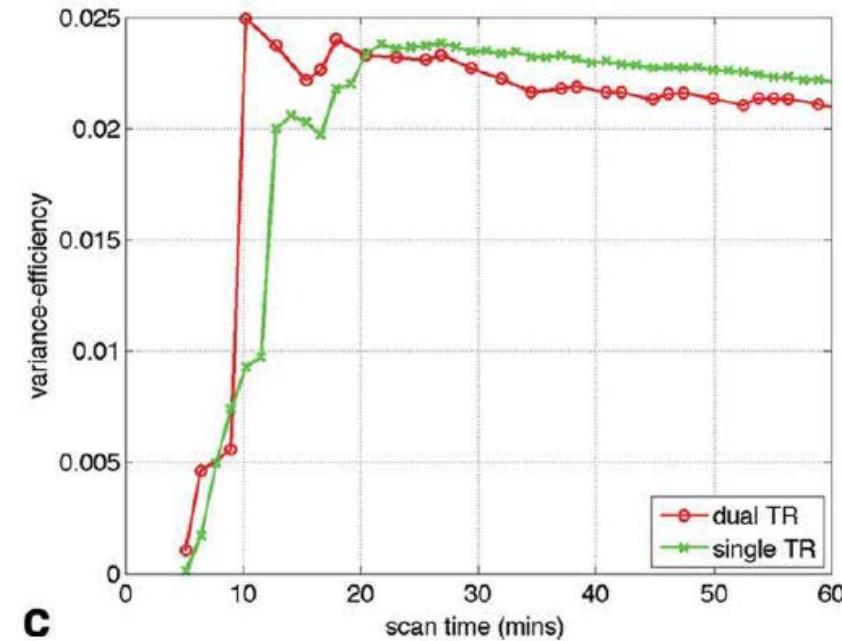
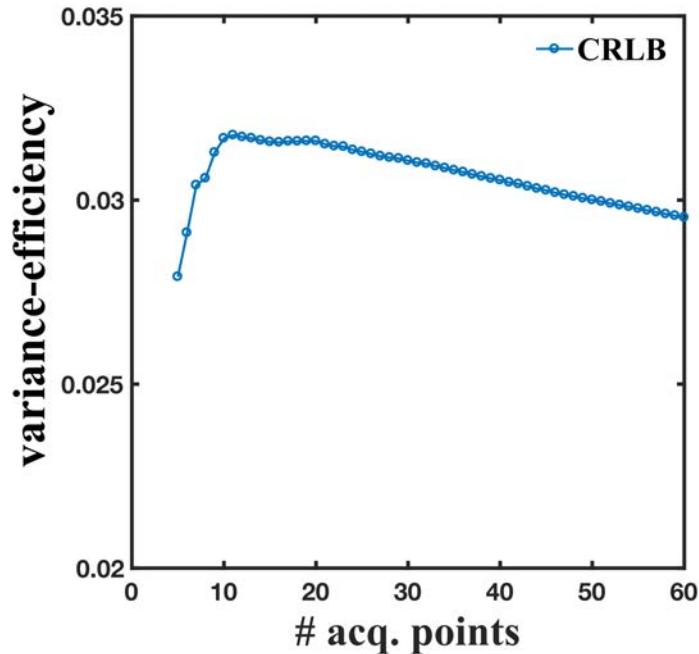
$$J_{ij} = \frac{1}{\sigma^2} \sum_{n=1}^N \frac{\partial S(p_1, \dots, p_Q; \mathbf{x}_n)}{\partial p_i} \frac{\partial S(p_1, \dots, p_Q; \mathbf{x}_n)}{\partial p_j}$$

$$V = \sum_{i=1}^Q p_i^{-2} [\mathbf{J}^{-1}]_{ii}$$

$$\min \frac{V_{n-1}}{V_n}$$

, considering all n-1 protocol combinations

# Iterative CRLB Optimization; comparison with Ives



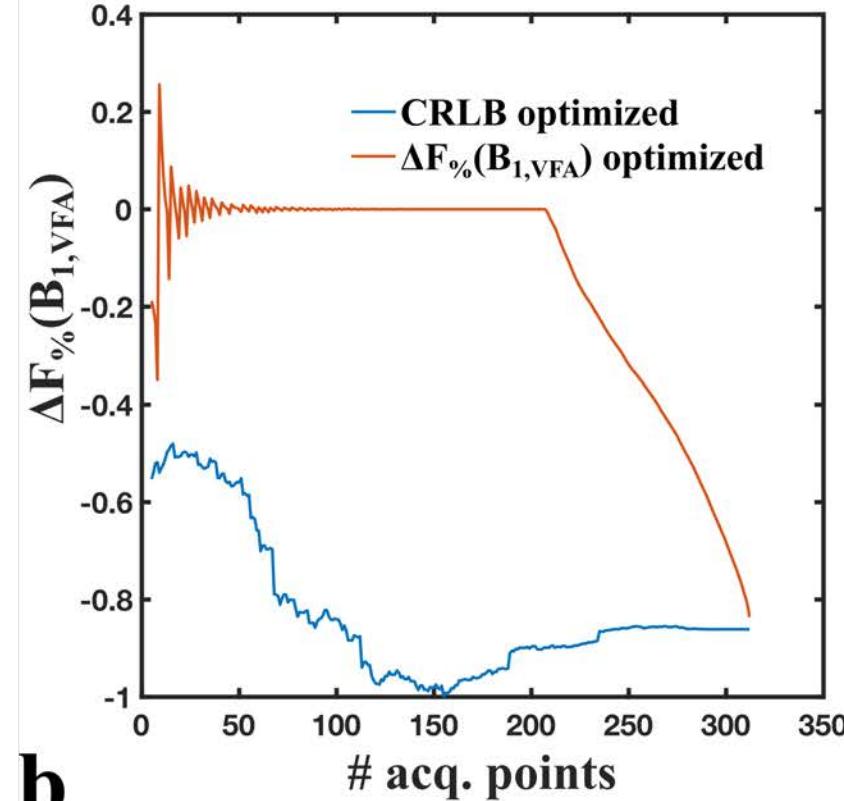
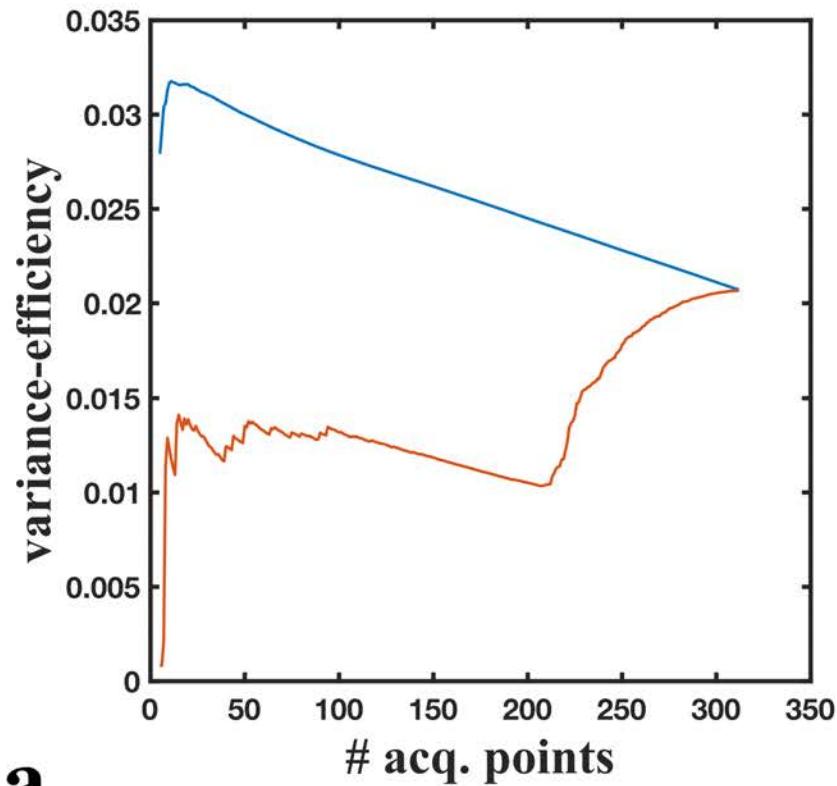
$$* \text{ variance-efficiency} = \frac{1}{\sqrt{V * n}}$$

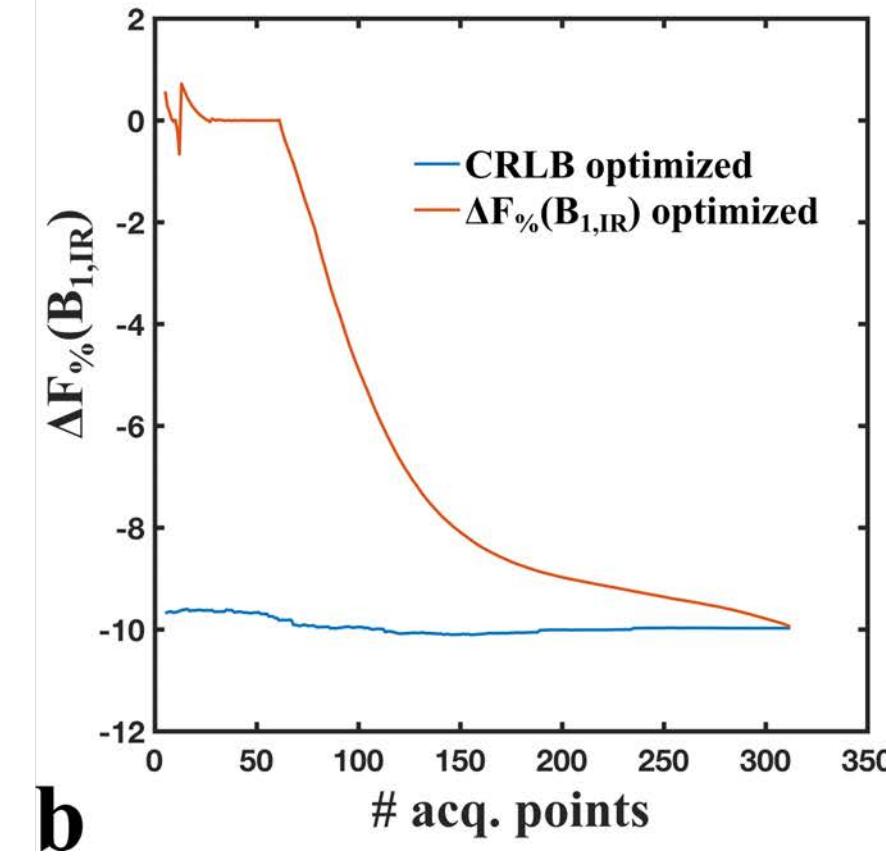
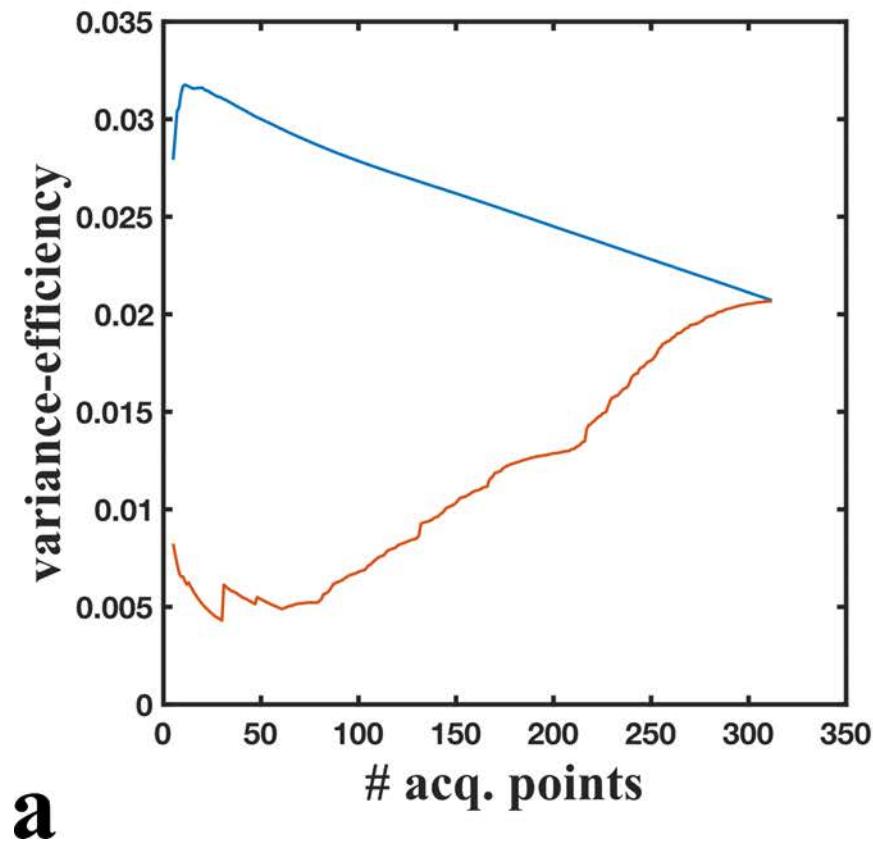
# Single Optimization

$$\min \frac{V_{n-1}}{V_n}$$

vs

$$\min |\Delta F|_{n-1}, \text{ from } \min \|\mathbf{J}_{p,n-1} x + \mathbf{J}_{B_1} \Delta B_1\| \text{ for } \Delta B_1 = 5\%$$





# Single Optimization

$$\min \frac{V_{n-1}}{V_n}$$

vs

$$\min |\Delta F|_{n-1}, \text{ from } \min \|\mathbf{J}_{p,n-1} x + \mathbf{J}_{B_1} \Delta B_1\| \text{ for } \Delta B_1 = 5\%$$

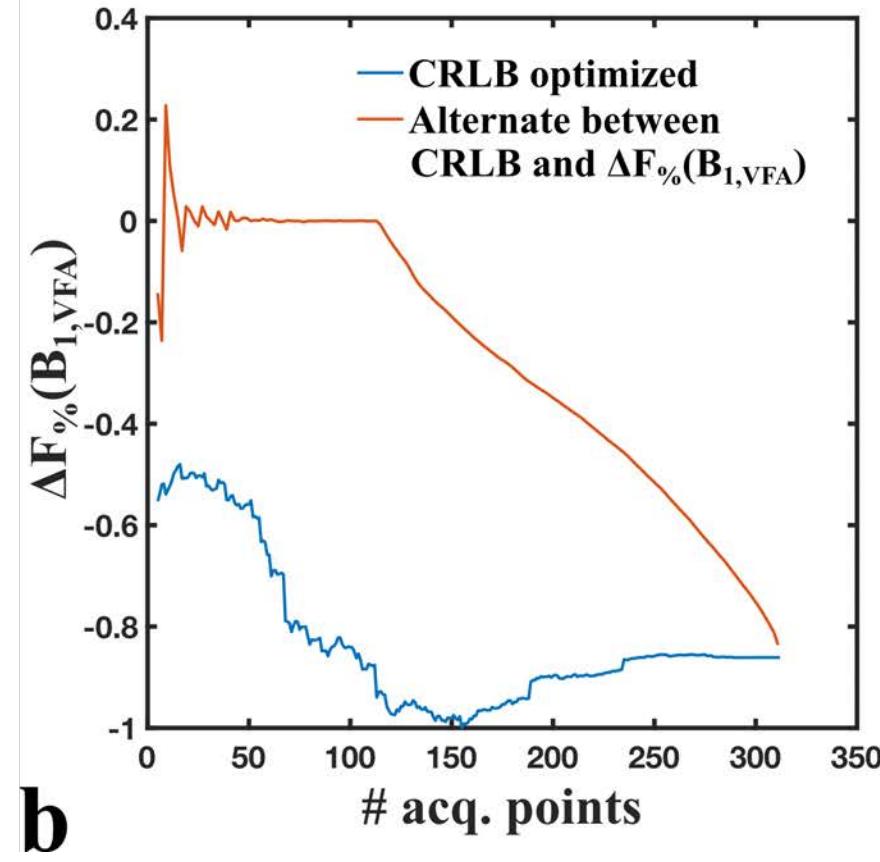
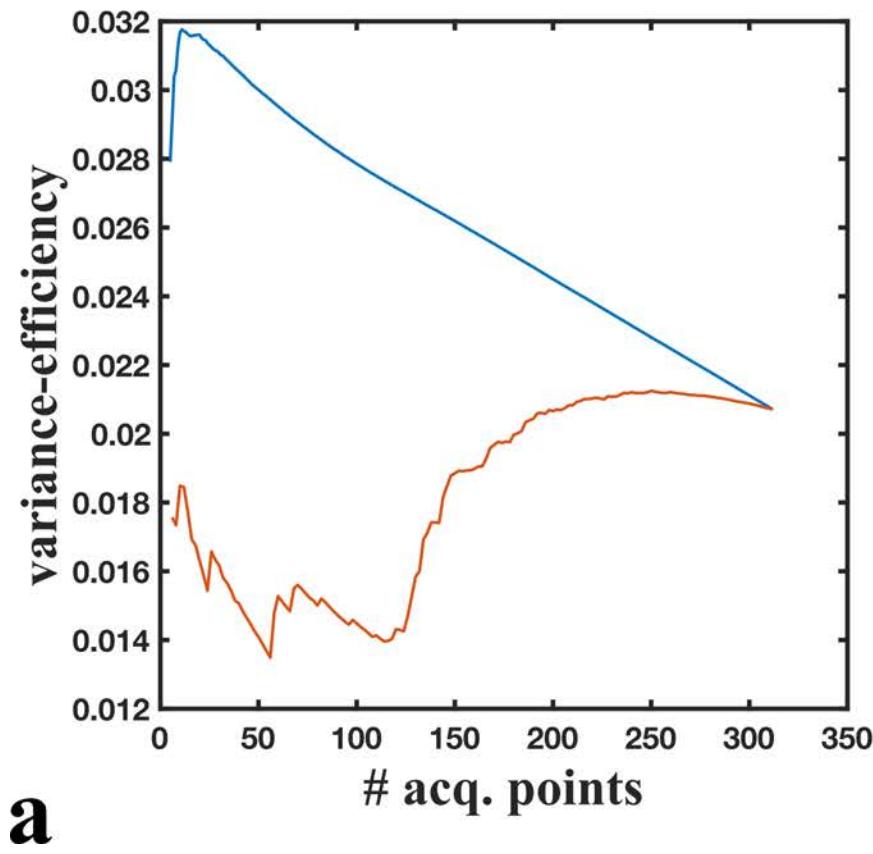
# Alternating Optimization

odd n-1

$$\min \frac{V_{n-1}}{V_n}$$

even n-1

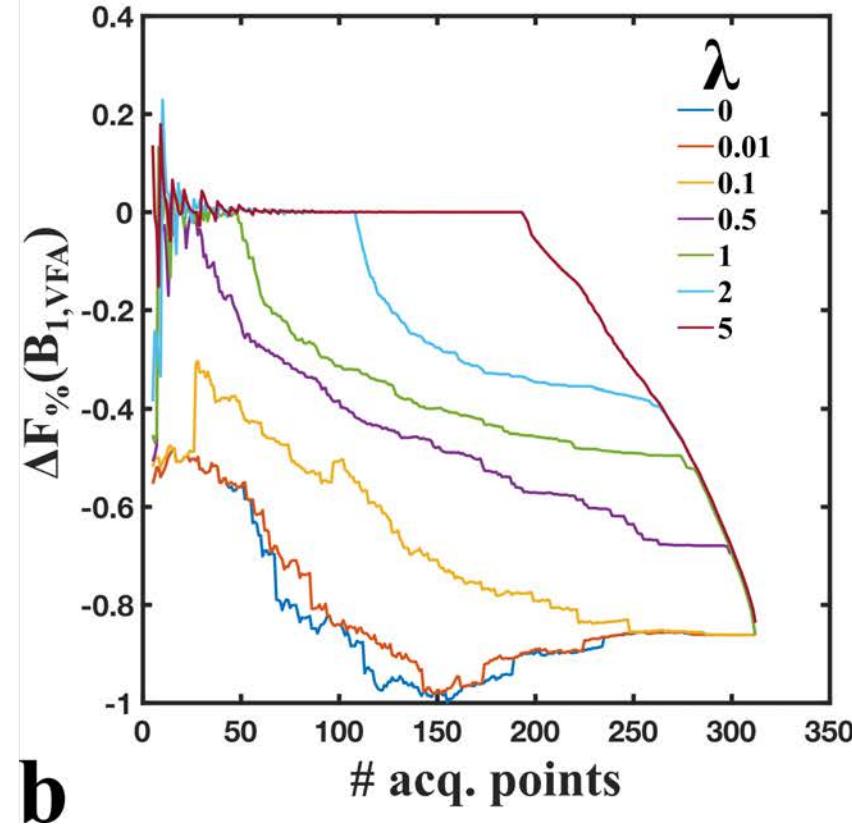
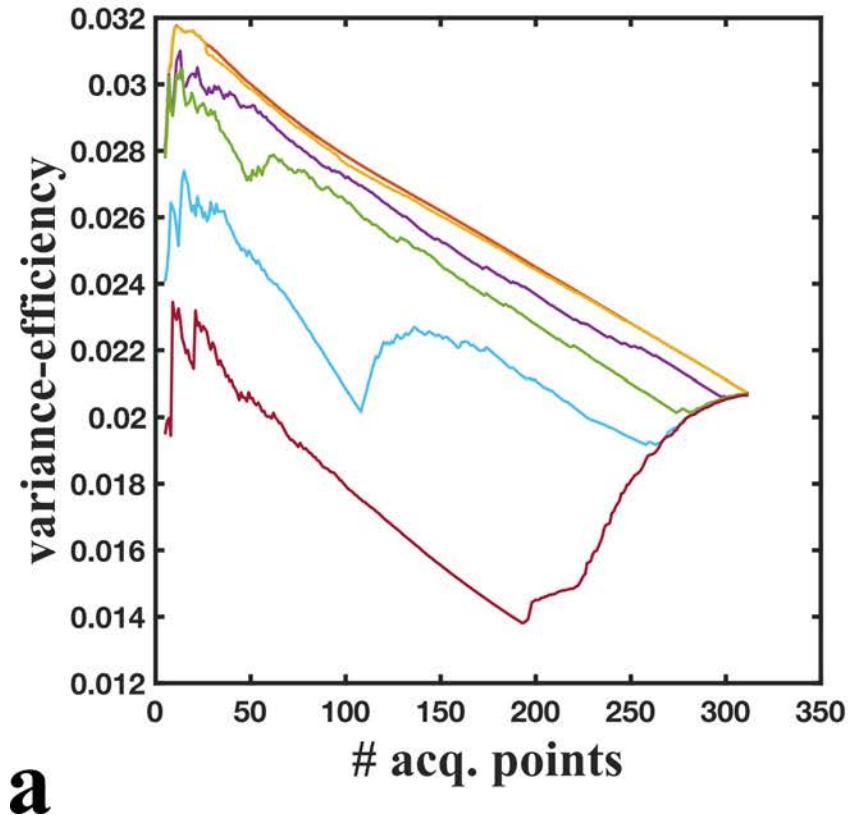
$$\min |\Delta F|_{n-1}, \text{ from } \min \|\mathbf{J}_{p,n-1} \mathbf{x} + \mathbf{J}_{B_1} \Delta B_1\| \text{ for } \Delta B_1 = 5\%$$

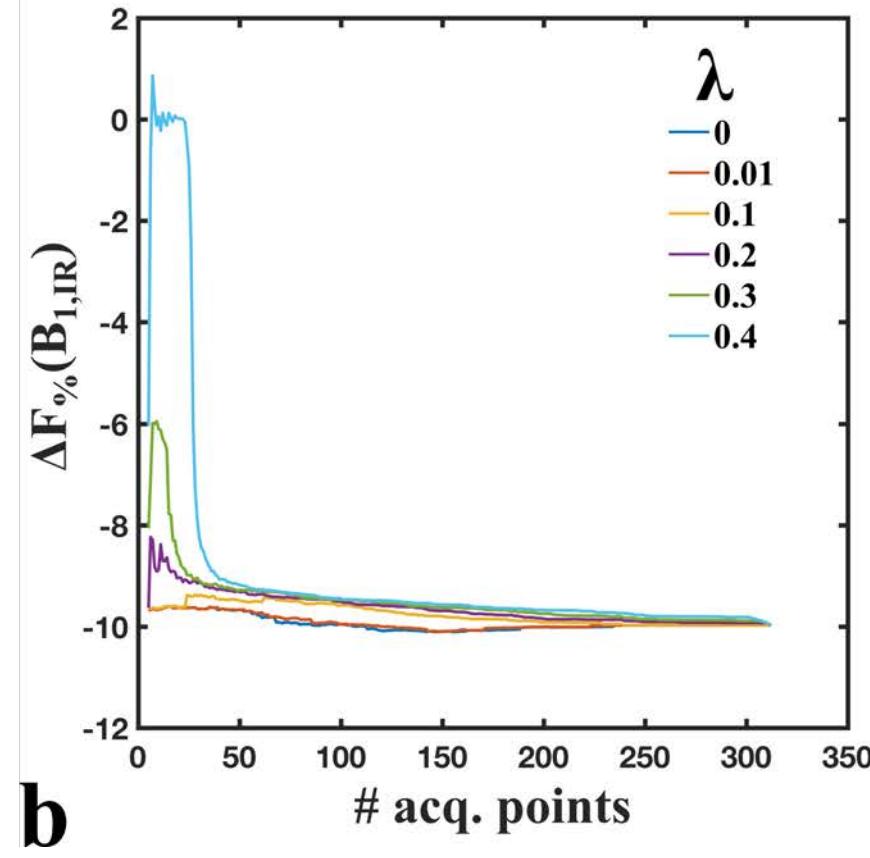
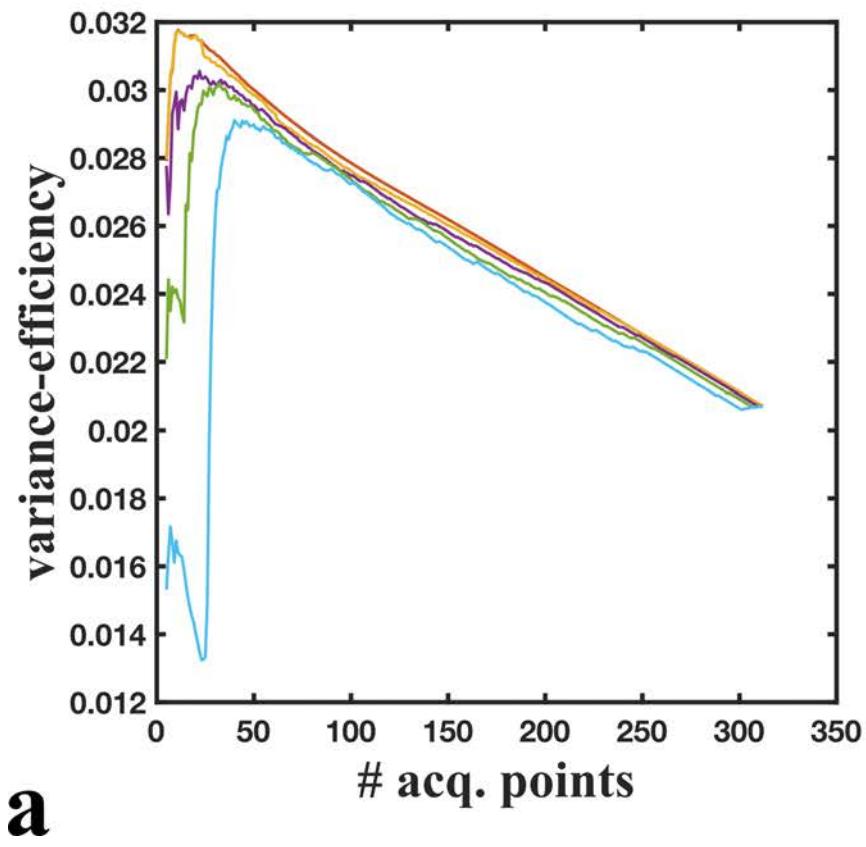


# Regularized Optimization

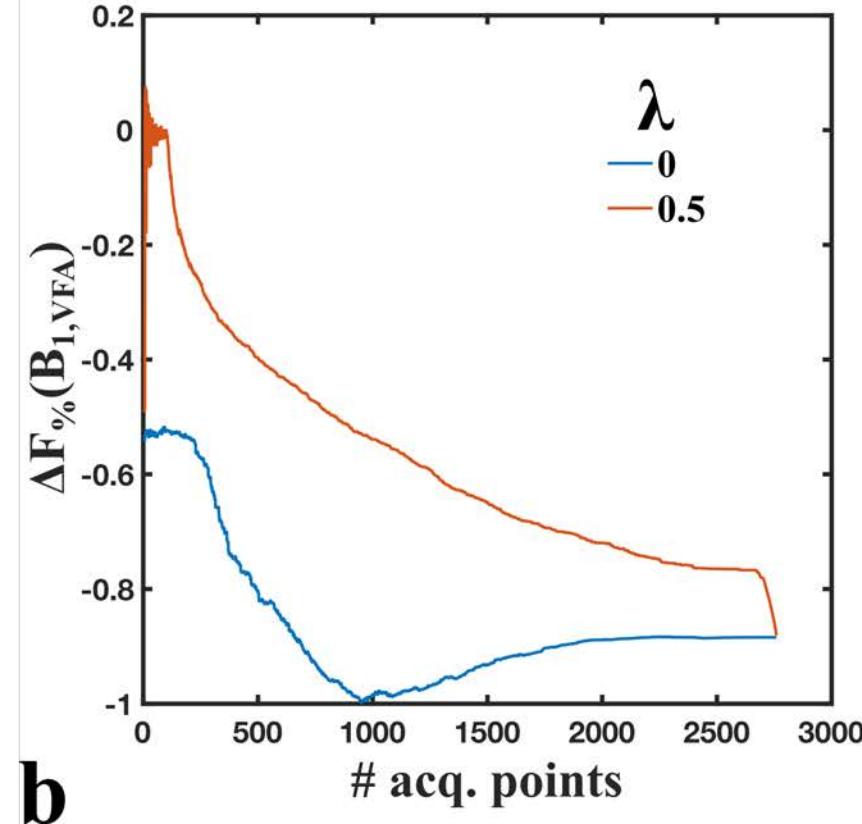
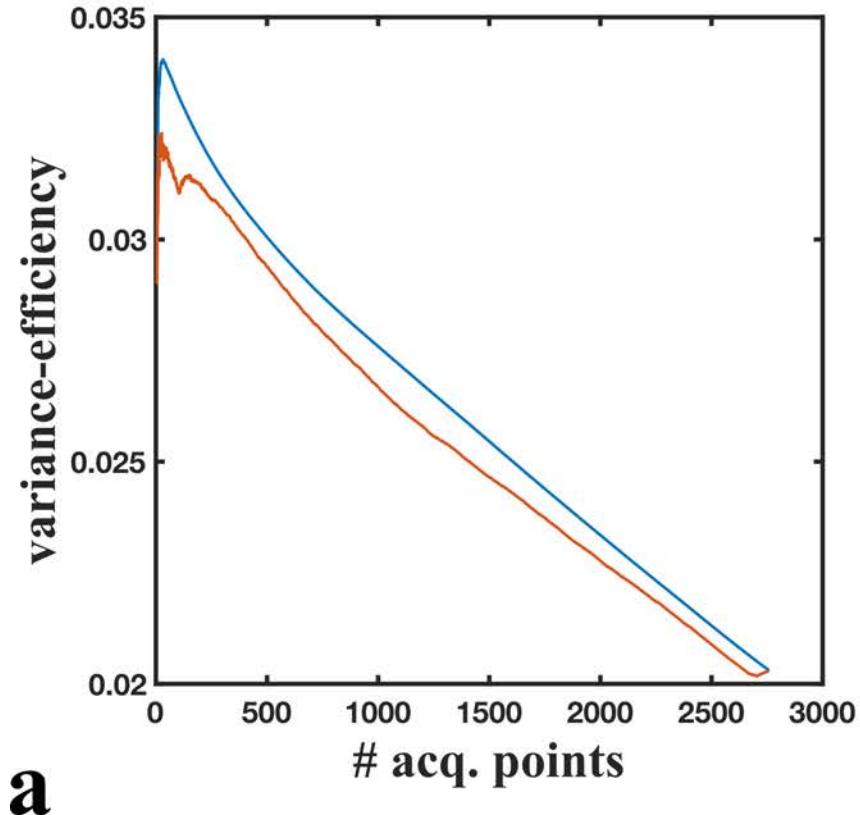
$$\min \frac{V_{n-1}}{V_n} + \lambda |\Delta F|_{n-1}$$

for a given  $\lambda$ , and  $\Delta B_1 = 5\%$

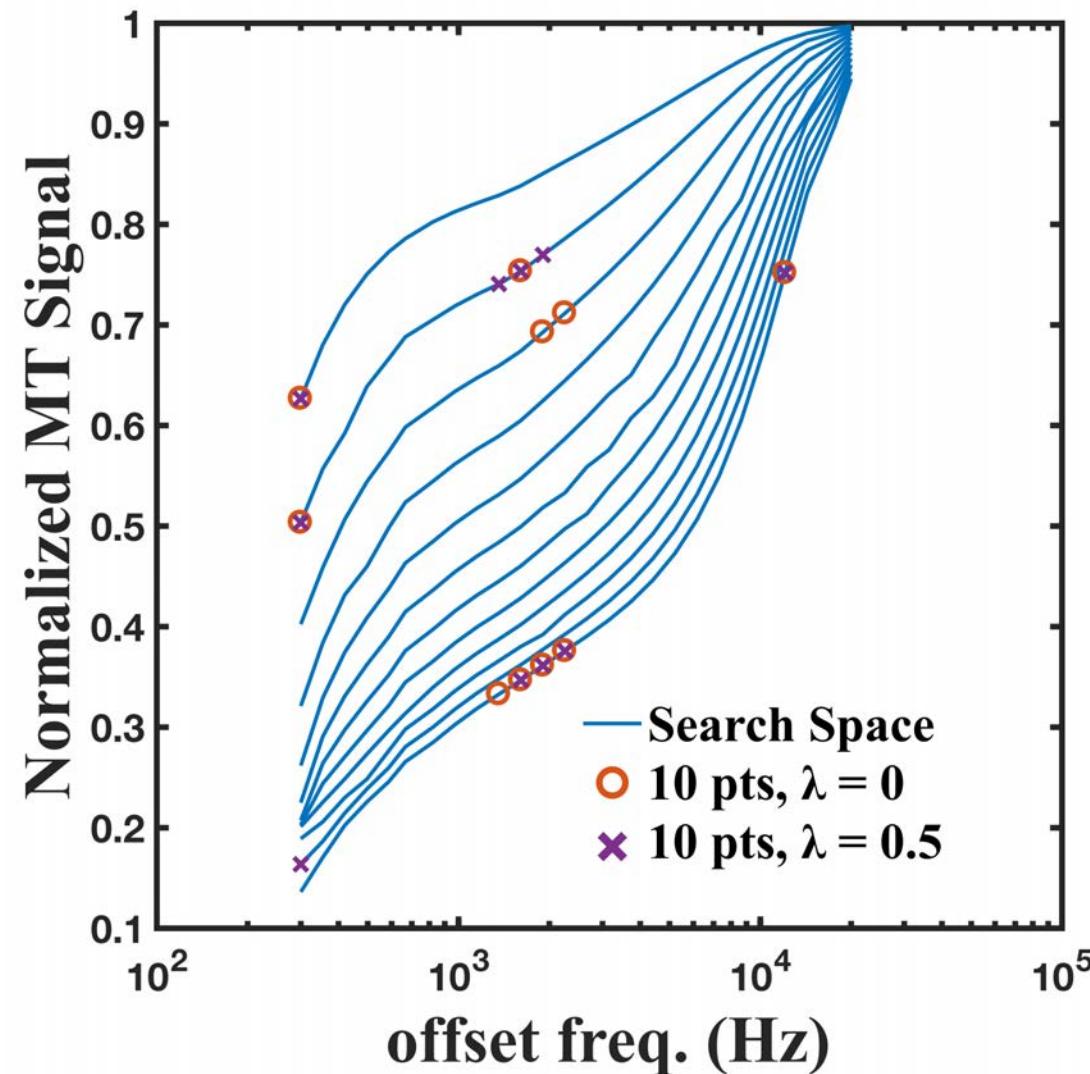




# **~2900 pt protocol**



**~300 pt protocol**



# No-noise fitting simulations

- (sidenote, using previous MRM paper's tissue values (e.g.  $F = 0.122$ ) and 10 point uniform protocol
  - 5% error in  $B_1$  lead to 1.86% error in fitted  $F$ , assuming VFA T1

$$10 \text{ pt Protocol: } \min \frac{V_{n-1}}{V_n}$$

B1err = 0

Field	Value
F	0.1518
kf	3.9373
kr	25.9454
R1f	1.1098
R1r	1
T2f	0.0313
T2r	1.1993e-05
resnorm	3.6333e-07
fields	<i>8x1 cell</i>
computed	1
Mask	1
Time	0.8567
Protocol	<i>1x1 struct</i>
FitOpt	<i>1x1 struct</i>

IR T1

Field	Value
F	0.1382
kf	4.1142
kr	29.7701
R1f	1.1085
R1r	1
T2f	0.0337
T2r	1.1989e-05
resnorm	9.6206e-07
fields	<i>8x1 cell</i>
computed	1
Mask	1
Time	0.9482
Protocol	<i>1x1 struct</i>
FitOpt	<i>1x1 struct</i>

% error in F = 8.9%

B1err = 5%

VFA T1

Field	Value
F	0.1510
kf	4.5062
kr	29.8406
R1f	1.2400
R1r	1
T2f	0.0308
T2r	1.1988e-05
resnorm	5.9021e-07
fields	<i>8x1 cell</i>
computed	1
Mask	1
Time	0.9571
Protocol	<i>1x1 struct</i>
FitOpt	<i>1x1 struct</i>

% error in F = 0.49%

10 pt Protocol:  $\min \frac{V_{n-1}}{V_n} + 0.5|\Delta F|_{n-1}$ , s. t.  $\Delta B_1^{VFA} = 5\%$

B1err = 0

Field	Value
F	0.1517
kf	3.9354
kr	25.9347
R1f	1.1098
R1r	1
T2f	0.0311
T2r	1.1991e-05
resnorm	2.5609e-06
fields	8x1 cell
computed	1
Mask	1
Time	2.2663
Protocol	1x1 struct
FitOpt	1x1 struct

IR T1

Field	Value
F	0.1391
kf	4.0734
kr	29.2923
R1f	1.1086
R1r	1
T2f	0.0340
T2r	1.2015e-05
resnorm	1.0430e-04
fields	8x1 cell
computed	1
Mask	1
Time	1.4556
Protocol	1x1 struct
FitOpt	1x1 struct

B1err = 5%

VFA T1

Field	Value
F	0.1519
kf	4.4654
kr	29.4022
R1f	1.2402
R1r	1
T2f	0.0311
T2r	1.2011e-05
resnorm	7.0947e-05
fields	8x1 cell
computed	1
Mask	1
Time	1.4351
Protocol	1x1 struct
FitOpt	1x1 struct

% error in F = 8.4%

% error in F = 0.09%

## To-Do (must)

- WM Monte-carlo simulations
  - 3 different 10 pt protocols
    - 2FA with log-uniform offsets
    - CRLB optimized ( $\lambda = 0$ )
    - CRLB regularized by  $B_1$  ( $\lambda = 0.5$ ,  $\delta F_{B_1}^{VFA}$ )
  - Generate 10,000 signal sets for each protocol, with rician noise added
    - 50, 100, 200 SNR for  $M_0$ ? More?
  - Fit Data
    - For  $\delta B_1 = 0, 1, 5, 10, 25 \%$ ?
    - Analysis? (means and std of fitted params, stat tests between methods?)

## To-Do (optional?)

- Repeat Monte Carlo for other fixed tissues (e.g. GM & lesions)?
- Repeat Monte Carlo for gaussian-distributed tissue values?
- Repeat Monte Carlo for voxels with partial voluming?
- Repeat protocol optimization & Monte Carlo simulations for other qMT methods?
  - Ramani, Yarnikh
- Evaluate optimization for different regularization criteria?
  - e.g.  $T_1$  &  $B_0$ , or  $B_1$  for kf?

