Sources of Error in Quantitative MRI (qMRI) Parameter Estimation

A Signal Processing Perspective

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Declaration of
Financial Interests or Relationships

Speaker Name: Joshua D. Trzasko, Ph.D.

General Electric holds a royalty-bearing license for MRI technologies developed by the speaker (JDT) and colleagues at Mayo Clinic.

Outline

- What is Quantitative MRI (qMRI)?
- qMRI: a Signal Processing Perspective
- Sources of Error in qMRI
  - Noise Model
  - Signal Model
  - Fitting Strategy
- Summary and Closing Remarks

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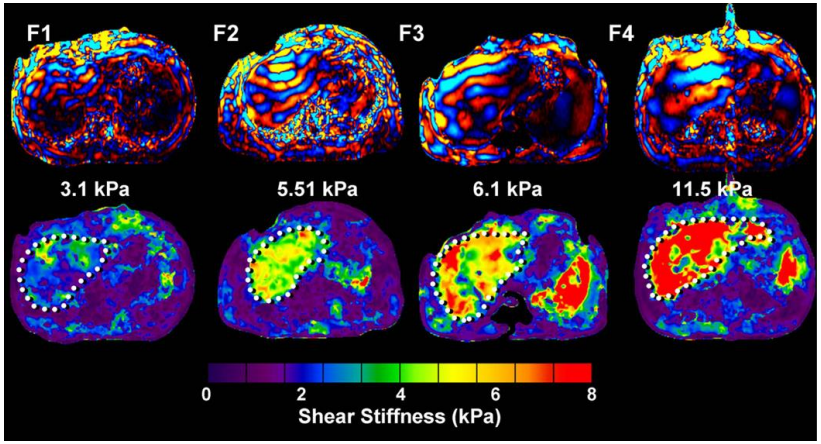
What is Quantitative MRI (qMRI)?

qMRI is any MRI application where the goal is to describe some property of the imaged object using meaningful physical or biological units.

Why is qMRI Clinically Important?

qMRI offers several key advantage over routine anatomical imaging:

- Simplified radiological interpretation
- Increased diagnostic confidence
- Improved detection and staging of disease, and monitoring of treatment
- Easier longitudinal and cross-sectional studies
- More efficient clinical workflows
- Potential for abbreviated exams



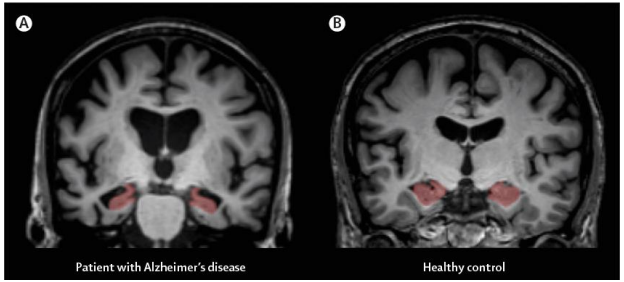
Example: Liver fibrosis staging via MR Elastography (MRE)

S. Venkatesh et al. JMRI 37.3 (2013): 544–555. PMC. Web. 18 Sept. 2018.

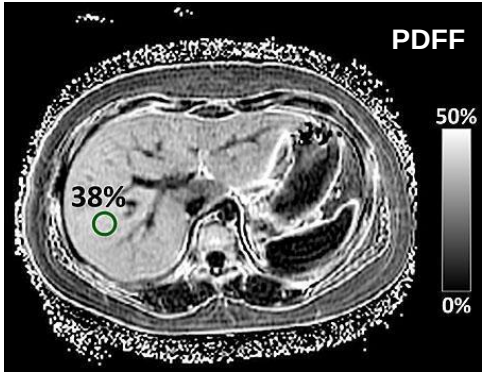
qMRI Categories

There are MANY different quantitative applications utilized both clinically and in research settings. These typically fall into one of two categories:

Structural



Physiological



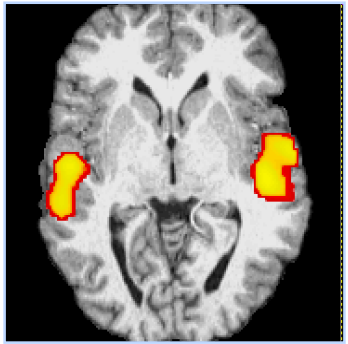
In this lecture, we'll focus exclusively on physiological qMRI

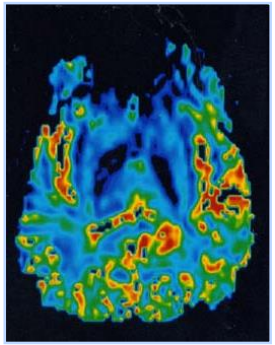
S. Teipel et al., *The Lancet. Neurology* 14 10 (2015): 1037-53.
J. Schwimmer et al. Hepatology 61.6 (2015): 1887-1895.

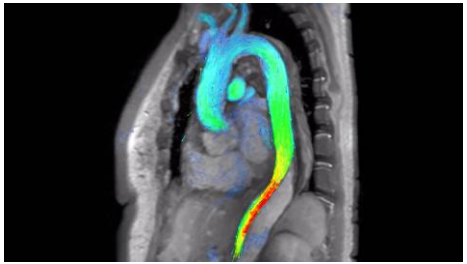
Example Physiological qMRI Applications

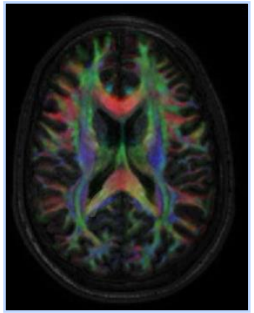
A non-inclusive list*:

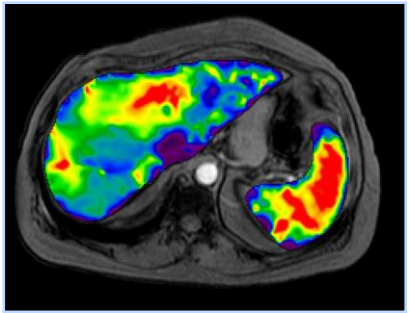
- Functional MRI (fMRI)
- Flow
- T1/T2 Mapping
- Pharmacokinetics
- Fat+Water Decomposition
- Elastography
- Diffusion
- Perfusion
- Thermometry
- Susceptibility Mapping (QSM)
- Metabolite Concentration











*apologies for unintentional omissions

How is qMRI Data Acquired?

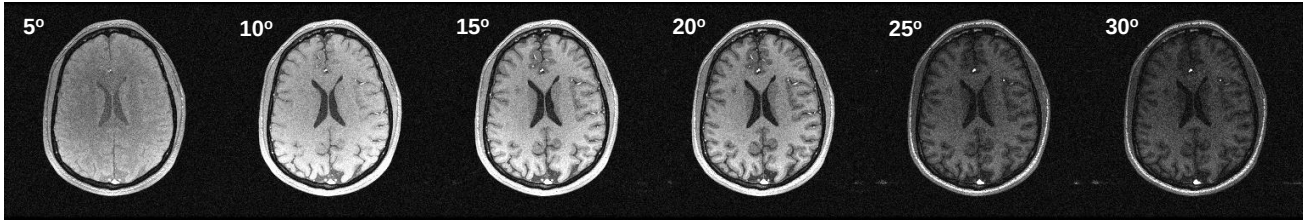
Due to a variety of physical (e.g., receiver gains) and physiological factors (e.g., patient motion), MR image intensity values are not intrinsically quantitative….

However, we typically have (via physics) a solid understanding of the causal factors of an image's appearance; e.g., in spoiled gradient echo (SPGR) MRI, a pixels intensity is modeled as:

$$f = m_0 \frac{\sin(\alpha B_1^+)\left(1 - \exp\left(-\frac{TR}{T1}\right)\right)}{1 - \cos(\alpha B_1^+)\exp\left(-\frac{TR}{T1}\right)}$$

Arbitrary Scaling Factor (∝ PD)

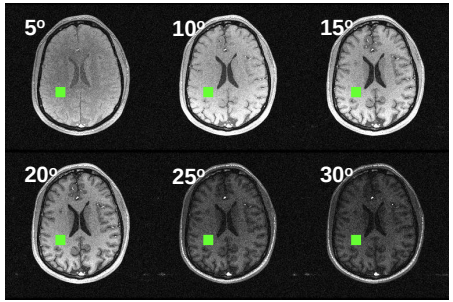
By repeating a scan with different acquisition parameters (e.g., flip angle), the individual contributions of underlying variables (e.g., T1) are revealed:

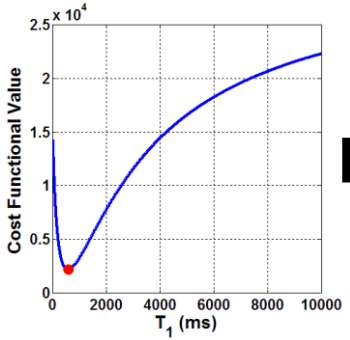


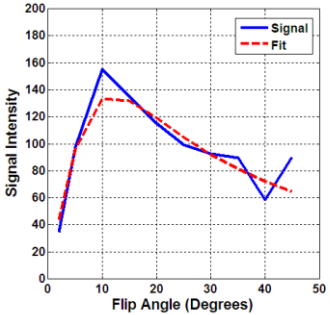
How is qMRI Data Processed?

qMRI data is typically processed by:

1. Forming a signal model
2. Identify known vs. unknown variables
3. Defining a fitting strategy
4. Evaluating performance







$$g[t] = m_0 \frac{\sin(\alpha[t]B_1^+)\left(1-\exp\left(-\frac{TR}{T1}\right)\right)}{1-\cos(\alpha[t]B_1^+)\exp\left(-\frac{TR}{T1}\right)} + n[t]$$

$$\widehat{T1} = \arg\min_{T1,m_0}\left\{\sum_{t=1}^{T}\left|m_0\frac{\sin(\alpha[t]B_1^+)\left(1-\exp\left(-\frac{TR}{T1}\right)\right)}{1-\cos(\alpha[t]B_1^+)\exp\left(-\frac{TR}{T1}\right)} - g[t]\right|^2\right\}$$

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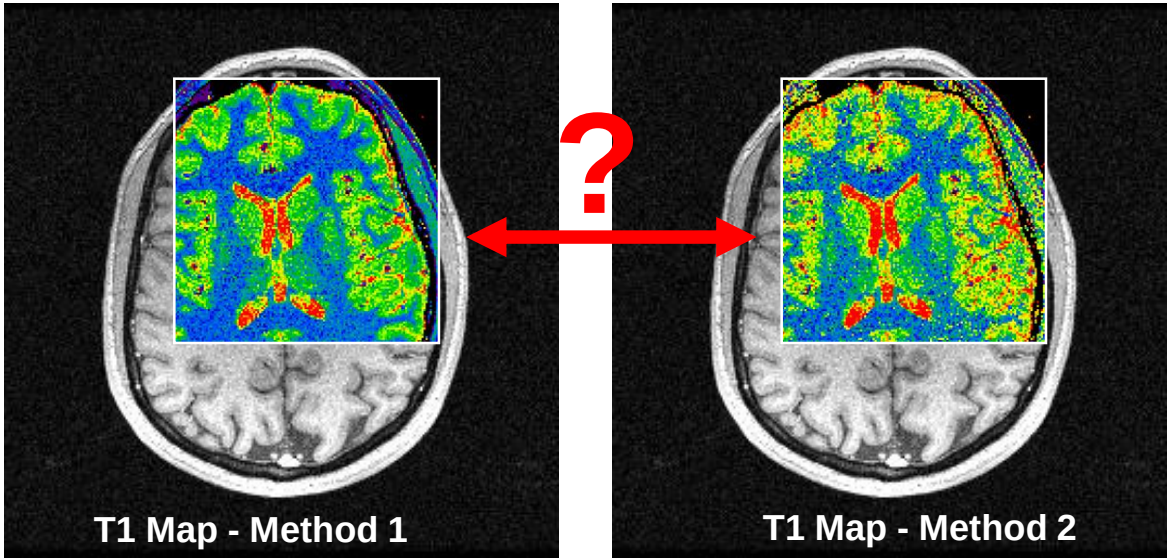
The Challenge of Being Quantitative

Acquisition settings aside, there will be different ways in which parameters can be estimated from qMRI data sets – how do we know which is the “best”?

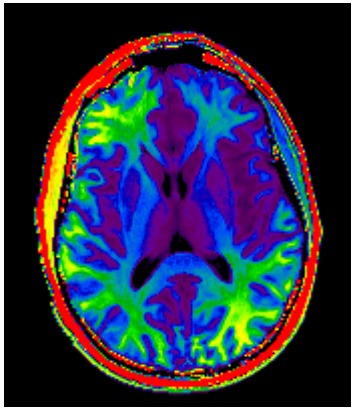


To fully answer this question, we must first understand why different methods yield (sometimes significantly) different results.

Sources of Error in qMRI Data Processing

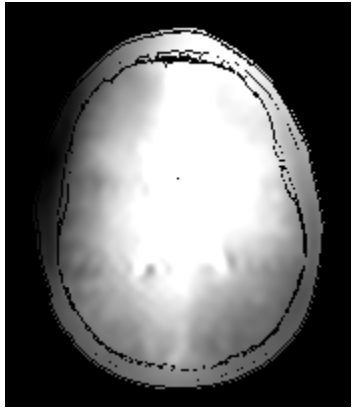
qMRI processing methods each rely on different assumptions about the data and/or fitting method. If these assumptions are violated, errors will form in the parameter estimates. Common error sources include:

1. Incomplete/inaccurate noise model
2. Incomplete/inaccurate signal model
3. Unstable fitting strategy
4. Insufficient data diversity*

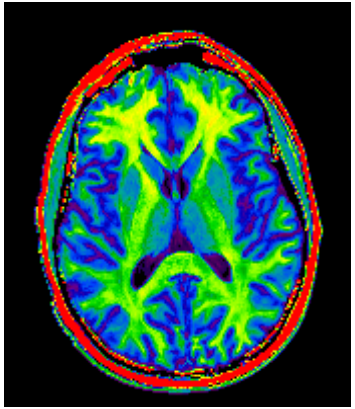


R1 Map (w/o B1+ Correction)

VS



B1+ Map

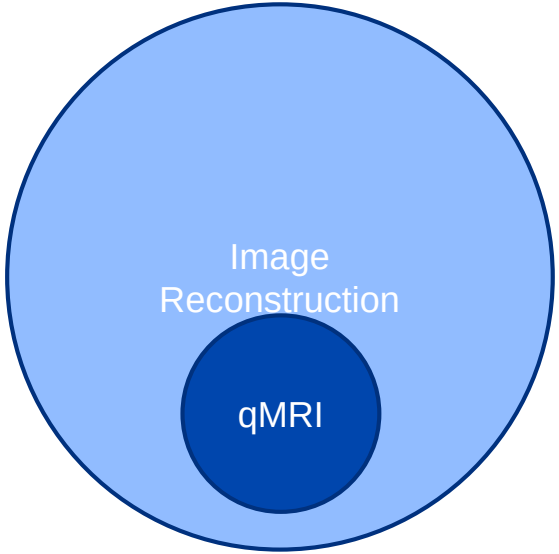


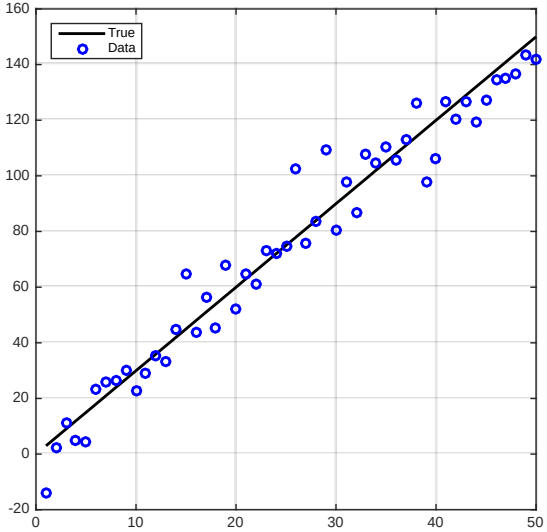
R1 Map (w/ B1+ Correction)

*Will not be covered in detail here

qMRI Processing is a Model Fitting Problem

qMRI parameter estimation – like image reconstruction and artifact correction – is fundamentally a parametric <u>model fitting problem</u>. As such, established <u>statistical signal processing</u> tools can be used to both develop and rigorously characterize/optimize qMRI method performance.





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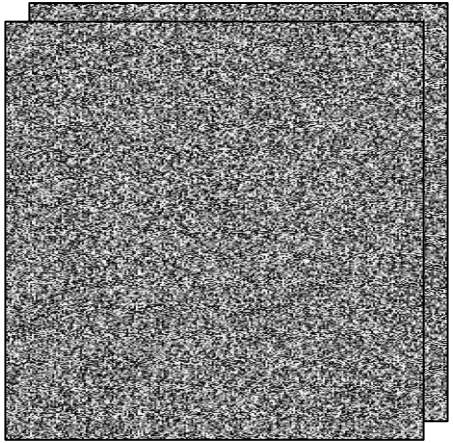
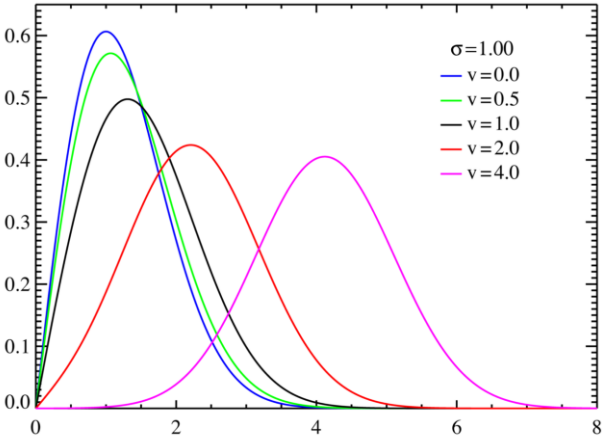
Noise in MRI

All MRI data – whether raw or reconstructed – contains “noise”, or random fluctuations from thermal interactions in our bodies and scanner electronics.

Noise in raw MRI data is proper complex AWGN*. However, this is generally no longer true once data has been processed; e.g., computing a magnitude:



AWGN (Real, Imag)



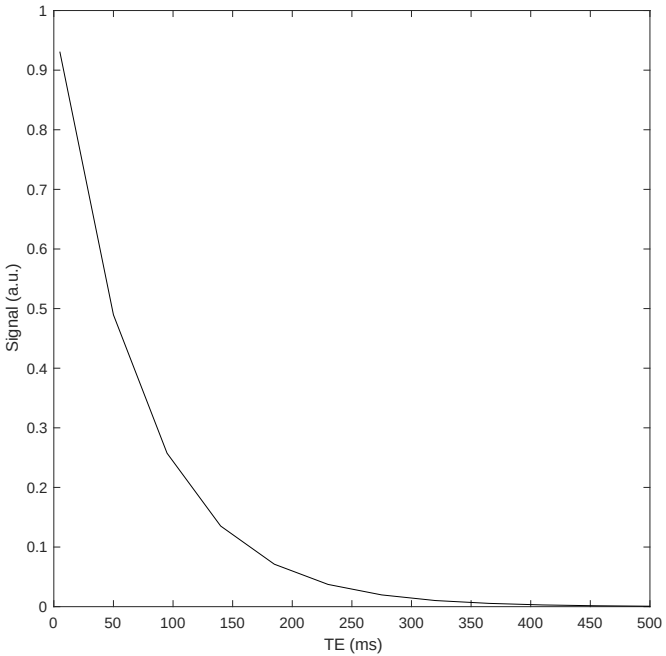
Rician

Inaccurate noise modeling (e.g., ignoring it) is one of the greatest sources of error in qMRI parameter estimation.

*Phased array data may be correlated across the channel dimension

Example: T2 Mapping

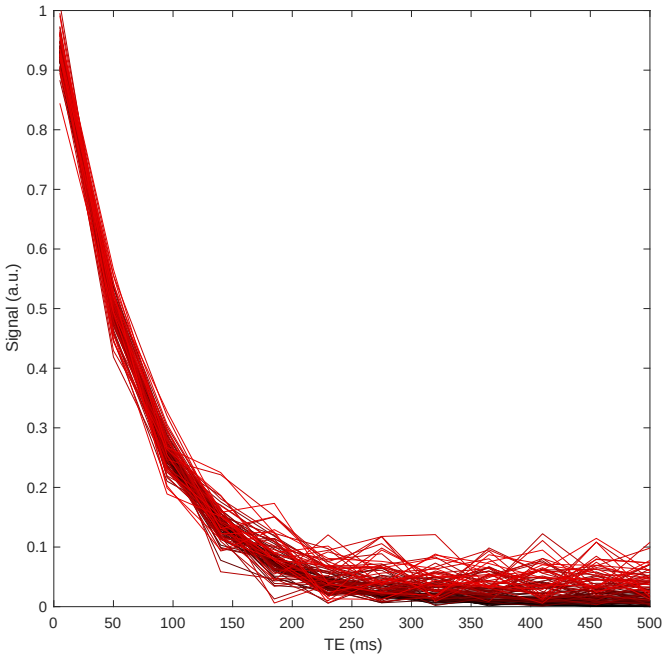
T2 mapping is often considered one of the “easiest” qMRI applications – but is this just a case of “ignorance is bliss”? Consider the following decay curve:




```
m0 = 1;
TE = linspace(5,500,12)'*1e-3; %ms
T2 = 70e-3; % ms
g0 = m0*exp(-TE/T2);
```

Example: T2 Mapping

Now let's add some complex AWGN and compute the signal's magnitude. Repeat this 1000x at 1000 different noise levels.



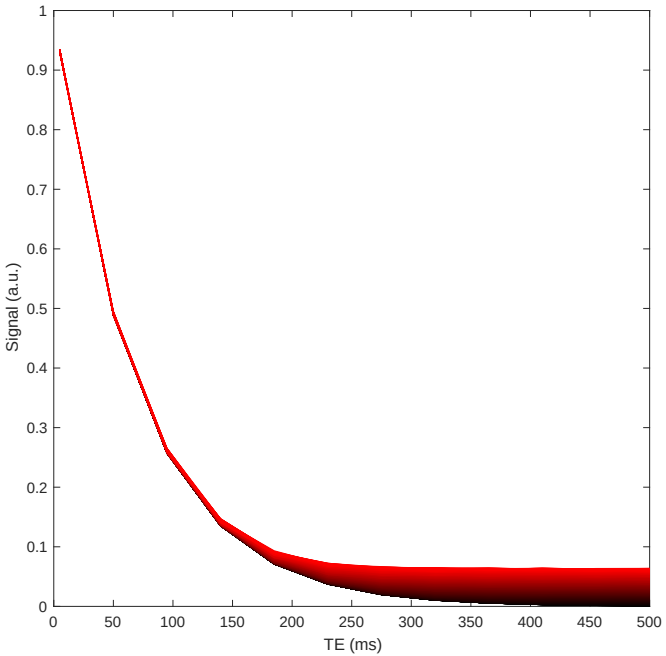

```
m0 = 1;
TE = linspace(5,500,12)'*1e-3; %ms
T2 = 70e-3; % ms
g0 = m0*exp(-TE/T2);

T = 1000; Ns = 1000; Nt = length(TE);
sigma = linspace(1e-4,0.05,Ns)';
X.raw = zeros([Nt Ns T]);
for s=1:Ns
    for t=1:T
        X.raw(:,s,t) = g0 +
                sigma(s)*(randn([Nt 1]) +
                1i*randn([Nt 1]));
    end
end
X.mag = abs(X.raw);
```

*Only a subset of instances visualized

Example: T2 Mapping

Compute the mean across trials. Observe that as noise increases, the exponential (erroneously) appears to decay more slowly – this is <u>noise bias</u>.




```
m0 = 1;
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T = 1000; Ns = 1000; Nt = length(TE);
sigma = linspace(1e-4,0.05,Ns)';
X.raw = zeros([Nt Ns T]);
for s=1:Ns
    for t=1:T
        X.raw(:,s,t) = g0 +
                sigma(s)*(randn([Nt 1]) +
                1i*randn([Nt 1]));
    end
end
X.mag = abs(X.raw);

Y = mean(Y,3);
```
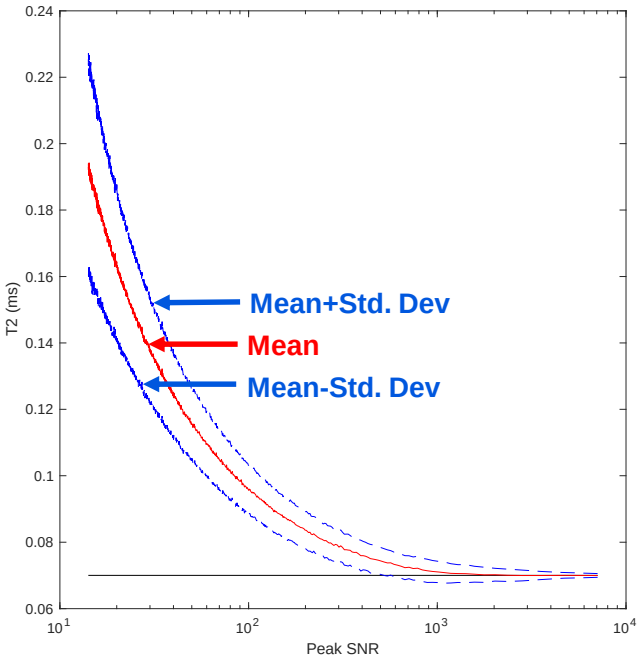

Example: T2 Mapping

Monte Carlo simulation can also be used to reveal the bias-variance behavior of specific estimators; e.g., linearized method-of-moments for T2 estimation:



$$g[t] = me^{-TE[t]/T2} + n[t]$$

$$\mathbf{E}\big[g[t]\big] = me^{-TE[t]/T2}$$

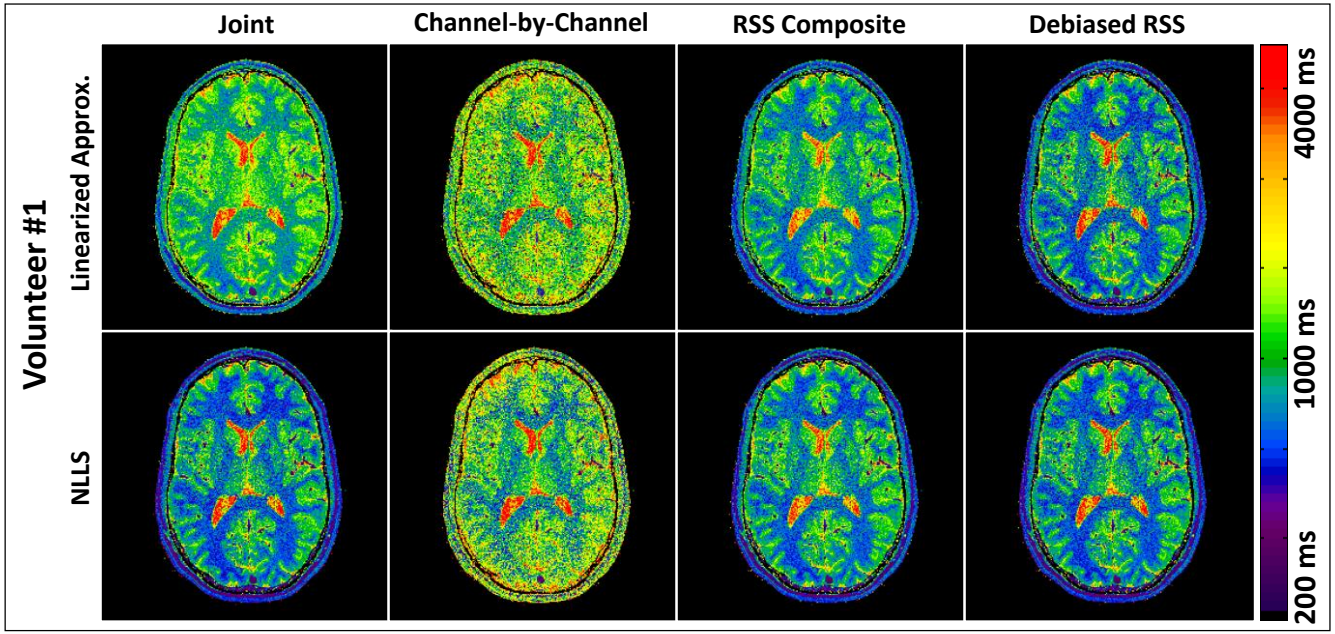
$$\ln(|\mathbf{E}[g[t]|]) = \ln(|m|) - TE[t]/T2$$

$$\begin{bmatrix} \ln\big(|\mathbf{E}\big[g[1]\big]|\big) \\ \vdots \\ \ln(\mathbf{E}[|g[T]|]) \end{bmatrix} = \begin{bmatrix} 1 & -TE[1] \\ \vdots & \vdots \\ 1 & -TE[T] \end{bmatrix} \begin{bmatrix} \ln(|m|) \\ 1/T2 \end{bmatrix}$$

$$T2 \approx \left(\delta_2^T \begin{bmatrix} 1 & -TE[1] \\ \vdots & \vdots \\ 1 & -TE[T] \end{bmatrix}^{\dagger} \begin{bmatrix} \ln\big(|\mathbf{E}\big[g[1]\big]|\big) \\ \vdots \\ \ln\big(|\mathbf{E}\big[g[T]\big]|\big) \end{bmatrix} \right)^{-1}$$

Noise Affects Every Method Differently

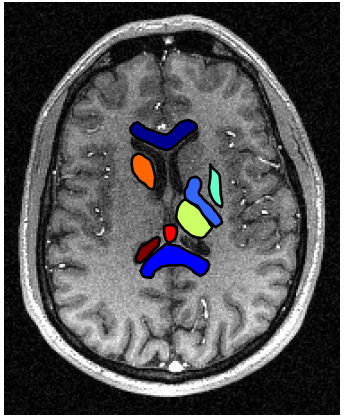
Below are the results of 8 different T1 mapping variants applied to the same (complex) multi-channel VFA-SPGR data set – note how performance varies.

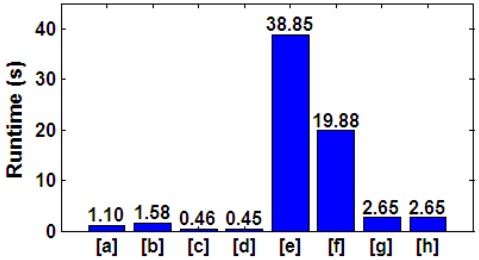


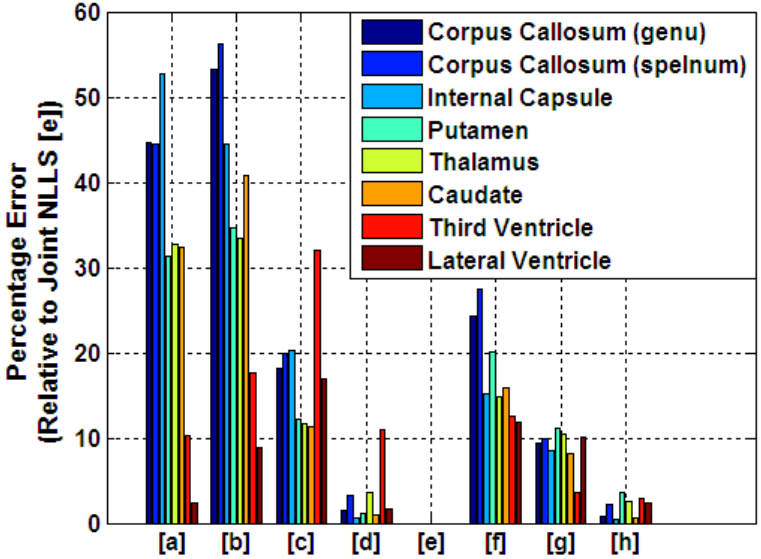
Trzasko et al. MRM 69(6):1787-1794, 2013.

Making Informed Tradeoffs

Joint nonlinear least squares (NLLS) fitting is expected to yield the lowest MSE results for this application – how do the other methods perform relatively?







[a] Linearized Approx. – Joint
[b] Linearized Approx. – Channel-by-Channel
[c] Linearized Approx. – RSS Composite
[d] Linearized Approx. – Debiased RSS Composite
[e] NLLS – Joint
[f] NLLS – Channel-by-Channel
[g] NLLS – RSS Composite
[h] NLLS – Debiased RSS Composite

Trzasko et al. MRM 69(6):1787-1794, 2013.

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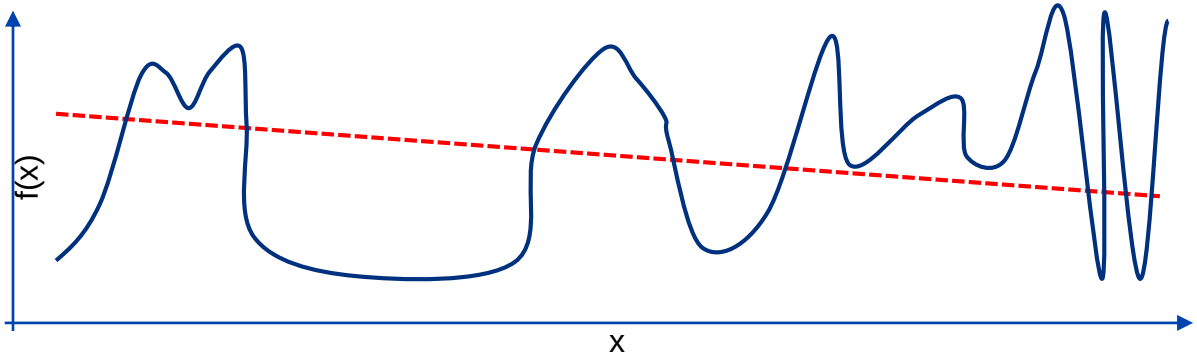
Model Mismatch

Mismatch between the data generating mechanism and the model presumed during data fitting is another key source of error in parameter estimates. In qMRI, mismatch is typically due to use of an oversimplified model.



$$g[t] = f(\theta)[t] + n[t]$$

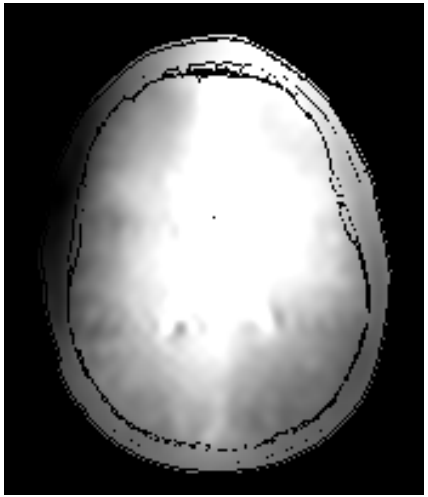
$$res = \sum_{t=1}^{T} |f(\theta)[t] - g[t]|^2 = \sum_{t=1}^{T} |n[t]|^2$$

Model Mismatch

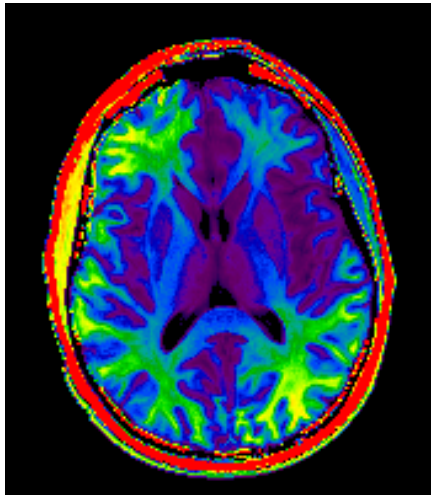
$$res = \sum_{t=1}^{T} |h(\theta)[t] - g[t]|^2 = \sum_{t=1}^{T} |(f(\theta)[t] - h(\theta)[t]) + n[t]|^2$$

Example: Variable Flip Angle T1/R1 Mapping

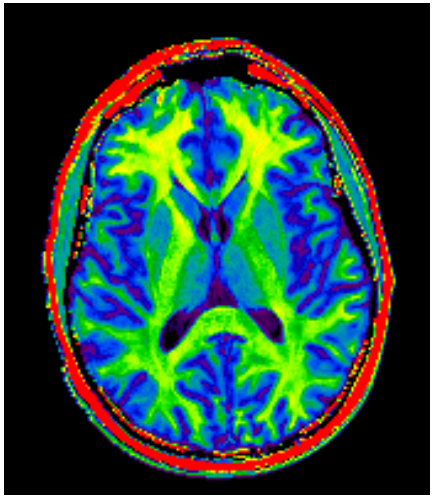
It is well-known that RF transmit (B1+) is not spatially uniform, especially at high field. If this reality is ignored during model fitting (e.g., universal flip angle), model-data mismatch will cause erroneous T1/R1 values to be generated.



B_1^+ Map



R_1 Map – w/o correction

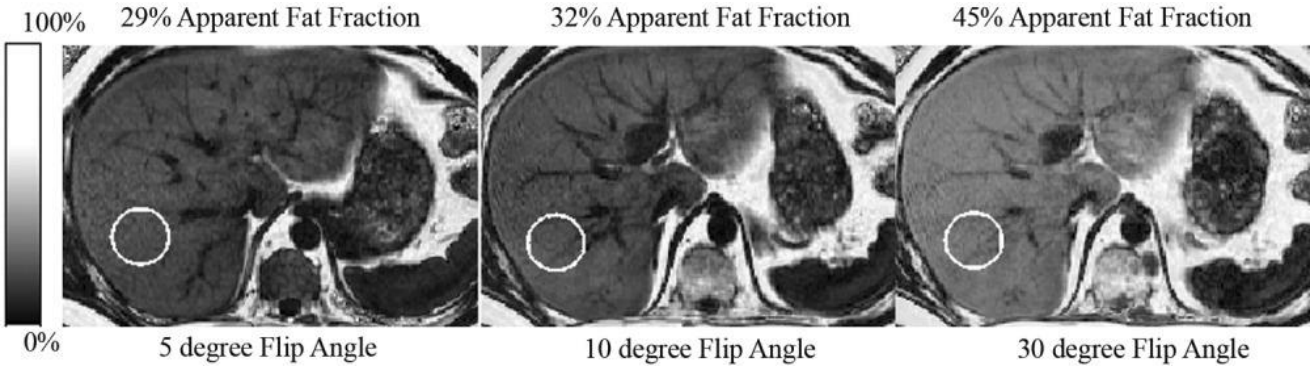


R_1 Map – w/ correction

Cheng and Wright. MRM 55:566–574, 2006
Trzasko et al., in preparation

Example: Fat+Water Imaging

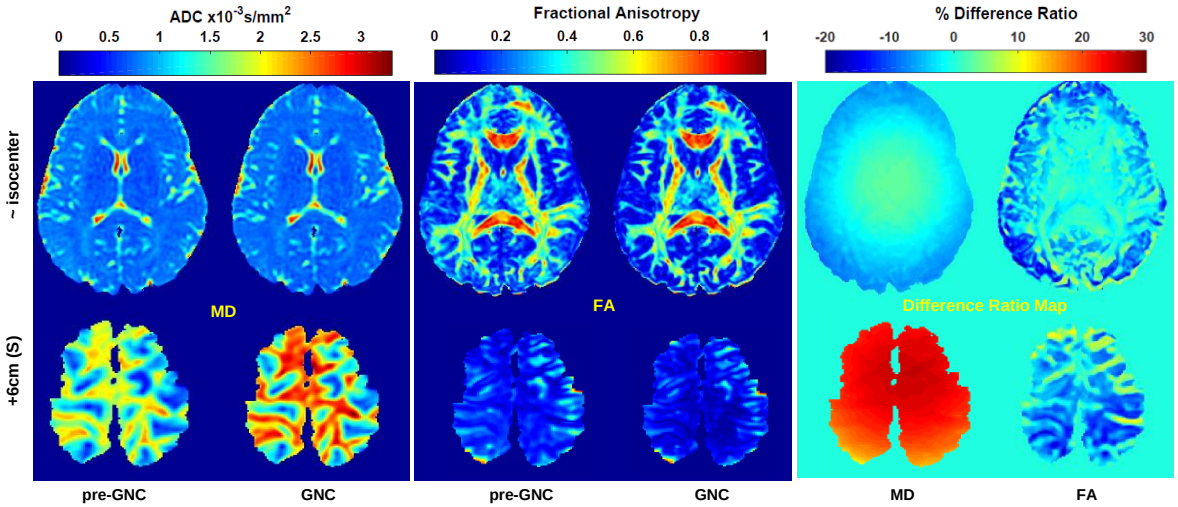
It is well known that accurate estimation of water+fat from multi-echo GRE data requires fitting with a model that includes off-resonance and R2*. However, ignoring T1, tissue temperature, and concomitant fields can also cause model mismatch and error generation in parameter estimates.



Liu et al., MRM 58(2):354-364, 2007
Hernando et al., MRM 72 (2), 464-470, 2014
Colgan et al., MRM 78 (2), 730-738, 2017

Example: Diffusion Imaging

Gradient nonlinearity is typically associated with geometric image distortion. However, it also causes gradient-based motion encoding strength (i.e., b-values) to spatially vary. If this is not accounted for during model fitting, diffusion parameters will exhibit spatially-varying errors.



Beyond diffusion, gradient nonlinearity affects every motion encoding-based scheme, including flow and elastography.

Tao et al, JMRI, in press
Tan et al., MRM 38(2):448-53, 2013
Bammer et al., MRM 50(3):560-9, 2003

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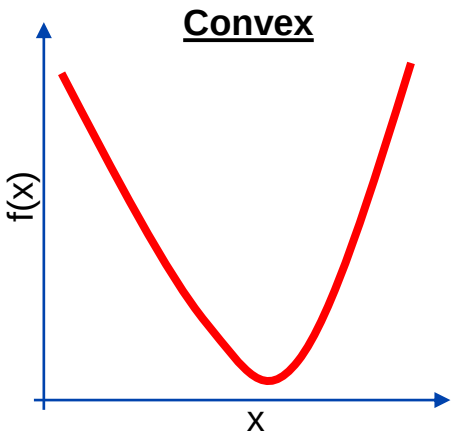
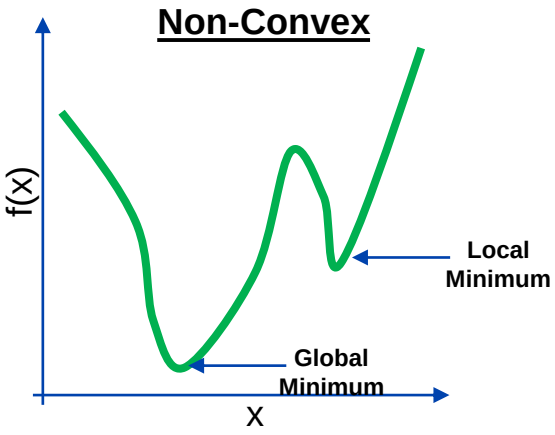
Can My Algorithm Really Cause Errors?

Yes! Many qMRI fitting problems require minimization of non-convex cost functions that contain spurious local minima, whose results may violate data and/or prior assumptions (e.g., phase wrap ≠ smooth).

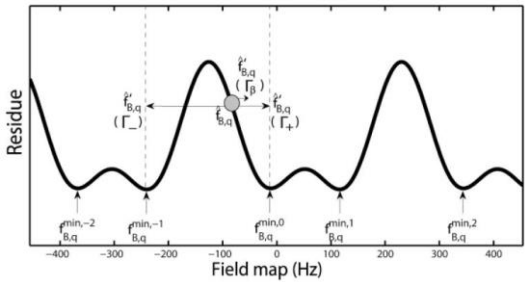


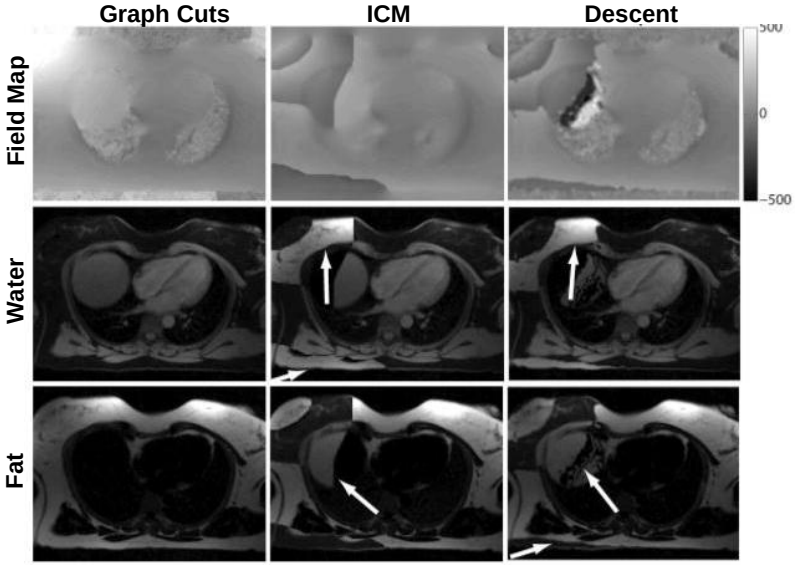


In lieu of using general-purpose numerical solvers, qMRI model fitting performance can often be improved by developing/applying custom solvers designed specifically for the target (mathematical) class of problem.

Example: Fat+Water Imaging

In fat+water imaging, “swaps” occur if the model fitting algorithm cannot robustly manage cost periodicity or local minima in the ∆B0 estimate. Few algorithms are capable of performing robustly in this scenario – an exception being iterated graph cuts (for binary Markov random fields (MRF)).

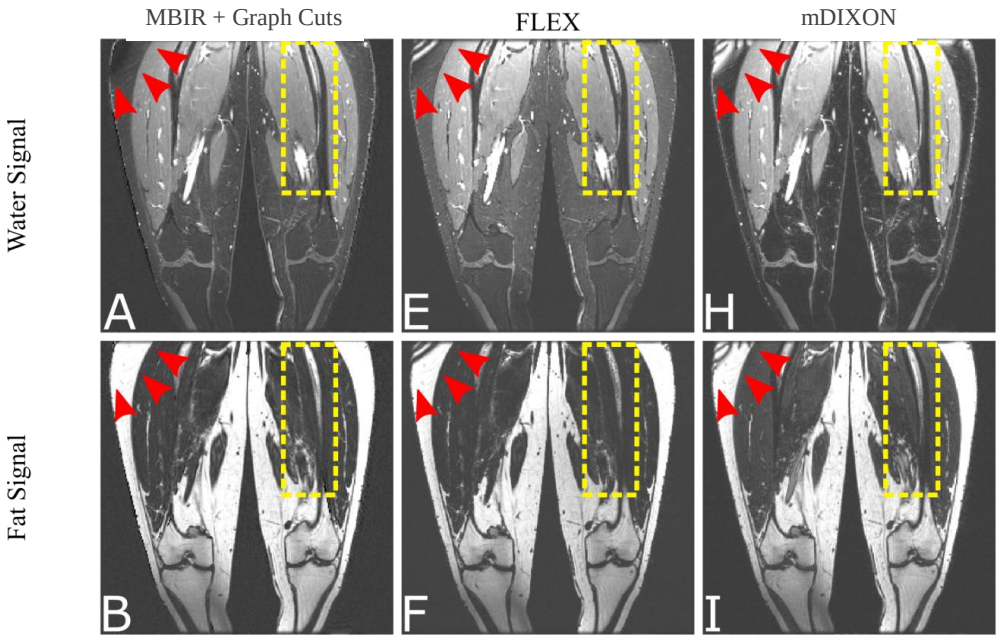




Hernando et al. MRM 63(1): 79-90, 2010

Example: Fat+Water Imaging

Researchers often rely on vendor-provided qMRI solutions for their studies – always be cognizant of all parts of the tools you adopt, include the fitting algorithms used under-the-hood.



Stinson et al. MRM, 78(6):2203–2215, 2017

Summary

In this lecture we:

- Defined and overviewed qMRI
- Discussed how qMRI processing is fundamentally a parametric model fitting problem
- Introduced statistical signal processing tools that are useful for qMRI applications
- Defined and demonstrated several independent sources error in qMRI processing
- Described modern signal processing tools for mitigating qMRI error

Closing Remarks

Hopefully you now have an appreciation for the many potential sources of error in qMRI parameter estimation, and the tools that can be used to both characterize and mitigate them.

Whether you're revisiting an old qMRI methods or checking out a new one, approach all with the same rigor and scrutiny.

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