Klinikum rechts der Isar
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5181 A Generalized Formulation for Parameter Estimation in MR Signals of Multiple Chemical Species

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Declaration of Financial Interests or Relationships

Speaker Name: Maximilian N. Diefenbach

I have the following financial interest or relationship to disclose with regard to the subject matter of this presentation:

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Introduction

- **Quantitative MRI** makes extensive use of **parameter estimation techniques**

- Examples are:
  - Water–fat imaging [1]
  - T_2/T_2^* mapping [2, 3]
  - Magnetic-field mapping [4]
  - Myelin water imaging [5]

[1] Ma, JMRI 2008, 10.1002/jmri.21492; [2] Patten, Seminars in Musculoskeletal Radiology 2003, 10.1055/s-2004-815677; [3] Hesper, Skeletal Radiology 2014, 10.1007/s00256-014-1852-3; [4] Liu, MRM 2013, 10.1002/mrm.24272; [5] Sood, MRM 2016, 10.1002/mrm.26281;

Key Findings:

- A broad class of MR signal models (weighted sum of complex exponentials) can be mathematically described by four **“constraints matrices”**

- This allows for:
  - A **universal algorithm** to solve all models in the class
  - A **general** framework for **noise and bias analysis**

Signal models in water–fat imaging

- Single fat peak $$S(t_n) = (W + F\underline{e^{i\Delta\omega t_n})e^{i\omega t_n}e^{-R_2^* t_n}}$$
- Multiple fat peak $$S(t_n) = (W + F\sum_p \alpha_p \underline{e^{i\Delta\omega_p t_n})e^{i\omega t_n}e^{-R_2^* t_n}}$$
- Single R_2^* $$S(t_n) = (W + Fc_n\underline{)e^{i\omega t_n}e^{-R_2^* t_n}}$$
- Double R_2^* $$S(t_n) = (W\underline{e^{-R_{2,W}^*}} + Fc_n\underline{e^{-R_{2,F}^* t_n})e^{i\omega t_n}}$$
- Unconstrained phase $$W = \rho_w \underline{e^{i\phi_w}} \quad F = \rho_f \underline{e^{i\phi_f}}$$
- Constrained phase $$S(t_n) = (\rho_w + \rho_f c_n)\underline{e^{i\phi}e^{i\omega t_n}e^{-R_2^* t_n}}$$

General Form:

Sum

of

complex exponentials

[1] Ma, JMRI 2008, 10.1002/jmri.21492; [6] Hernando, MRM 2010, 10.1002/mrm.22455; [7] Reeder, MRM 2011, 10.1002/mrm.23016; [8] Bydder, MRM 2011, 10.1016/j.mri.2010.08.011;

Generalization

sum over M chemical species

angle in transverse plane after RF pulse

transverse relaxation rate

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

MR signal evolution

concentration

resonance frequency

NOTE: model unspecific!

Different chemical species can have equal or inter-dependent properties.

Matrix Formulation [9]: Combining Observations

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

discrete echo times $t \to t_n$

Define: 2 matrices, 1 vector

$$A_{N\times M} = \begin{pmatrix} e^{i(\omega_1+ir_1)t_1} & \dots & e^{i(\omega_M+ir_M)t_1} \\ \vdots & & \vdots \\ e^{i(\omega_1+ir_1)t_N} & \dots & e^{i(\omega_M+ir_M)t_N} \end{pmatrix}$$

$$P_{M\times M} = \begin{pmatrix} e^{i\phi_1} & & \\ & \ddots & \\ & & e^{i\phi_M} \end{pmatrix}$$

$$\vec{\varrho}_{M\times 1} = (\varrho_1, \dots, \varrho_M)^T$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

NOTE: still model unspecific!

[9] Yu, JMRI 2007, 10.1002/jmri.21090;

Model specification: inter-species parameter relations

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

The actual model is specified by fixing the inter-species parameter relation on the level of signal derivatives.

Example:

$$\frac{\partial S(t)}{\partial \varrho_l} = \delta_l e^{i\phi_l} e^{i\omega_l t} e^{-r_l t}$$

Model specification: inter-species parameter relations

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

The actual model is specified by fixing the inter-species parameter relation on the level of signal derivatives.

Example:

$$\frac{\partial S(t)}{\partial \varrho_l} = e^{i\phi_l} e^{i\omega_l t} e^{-r_l t}$$

but maybe:

$$\varrho_l = \alpha \varrho_m$$

Model specification: inter-species parameter relations

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

The actual model is specified by fixing the inter-species parameter relation on the level of signal derivatives.

Example:

$$\varrho_l = \alpha \varrho_m$$

$$\frac{\partial S(t)}{\partial \varrho_l} = e^{i\phi_l} e^{i\omega_l t} e^{-r_l t} + \alpha e^{i\phi_m} e^{i\omega_m t} e^{-r_l m t}$$

Model specification: inter-species parameter relations

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + ir_m)t}$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

The actual model is specified by fixing the inter-species parameter relation on the level of signal derivatives.

Example: Generally, all inter-peak relations in the concentrations $\vec{\varrho}$ can be captured in binary indicator functions $I_a(b)$.

$$\frac{\partial S_n}{\partial \varrho_l} = \sum_m I_{\varrho_l}(\varrho_m) e^{i\phi_m} e^{i\omega_m t} e^{-r_m t} \qquad I_a(b) = \begin{cases} \alpha & \text{if} \quad a = b \\ 0 & \text{otherwise,} \end{cases}$$

… and similar for the other parameters

$$\frac{\partial S_n}{\partial \varrho_l} = \sum_m I_{\varrho_l}(\varrho_m) e^{i\phi_m} e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial \phi_l} = i \sum_m \varrho_m I_{\phi_l}(\phi_m) e^{i\phi_m} e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial \omega_l} = i t_n \sum_m \varrho_m e^{i\phi_m} I_{\omega_l}(\omega_m) e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial r_l} = -t_n \sum_m \varrho_m e^{i\phi_m} e^{i\omega_m t} I_{r_l}(r_m) e^{-r_m t}$$

NOTE: specifying the indicator functions $I_a(b)$ means specifying the signal model.

Model specification: Matrix Formulation

Indicator functions can be expressed by "constraints matrices"

$$\{C_\varrho, C_\phi, C_\omega, C_r\}$$

$$T = \mathrm{diag}(t_1, ..., t_N)$$

$$\frac{\partial S_n}{\partial \varrho_l} = \sum_m I_{\varrho_l}(\varrho_m) e^{i\phi_m} e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial \phi_l} = i \sum_m \varrho_m I_{\phi_l}(\phi_m) e^{i\phi_m} e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial \omega_l} = i t_n \sum_m \varrho_m e^{i\phi_m} I_{\omega_l}(\omega_m) e^{i\omega_m t} e^{-r_m t}$$

$$\frac{\partial S_n}{\partial r_l} = -t_n \sum_m \varrho_m e^{i\phi_m} e^{i\omega_m t} I_{r_l}(r_m) e^{-r_m t}$$

"single-observation" formulation

$$\frac{\partial \vec{S}}{\partial \vec{\varrho}} = AP C_\varrho$$

$$\frac{\partial \vec{S}}{\partial \vec{\phi}} = iAP \,\mathrm{diag}(\vec{\varrho}) C_\phi$$

$$\frac{\partial \vec{S}}{\partial \vec{\omega}} = iTAP \,\mathrm{diag}(\vec{\varrho}) C_\omega$$

$$\frac{\partial \vec{S}}{\partial \vec{r}} = -TAP \,\mathrm{diag}(\vec{\varrho}) C_r$$

matrix formulation

Recap: What happened so far…

1. *M*-species model generalization $$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

2. Matrix Formulation $$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

3. Derivatives $$\frac{\partial \vec{S}}{\partial \vec{\rho}}, \frac{\partial \vec{S}}{\partial \vec{\phi}}, \frac{\partial \vec{S}}{\partial \vec{\omega}}, \frac{\partial \vec{S}}{\partial \vec{r}}$$

4. Model Specification

$$APC_\varrho, iAP\,\mathrm{diag}(\vec{\varrho})C_\phi, iTAP\,\mathrm{diag}(\vec{\varrho})C_\omega, -TAP\,\mathrm{diag}(\vec{\varrho})C_r$$

Signal derivatives form Jacobian

$$J = \left[\frac{\partial \vec{S}}{\partial \vec{\rho}}, \frac{\partial \vec{S}}{\partial \vec{\phi}}, \frac{\partial \vec{S}}{\partial \vec{\omega}}, \frac{\partial \vec{S}}{\partial \vec{r}}\right]$$

$$= \left[APC_{\varrho}, iAP\,\mathrm{diag}(\vec{\varrho})C_{\phi}, iTAP\,\mathrm{diag}(\vec{\varrho})C_{\omega}, -TAP\,\mathrm{diag}(\vec{\varrho})C_{r}\right]$$

The generalized Jacobian, describes signal changes depending on parameters and echo times. This allows for model unspecific…

parameter mapping

noise & bias analysis (experimental design) parameter mapping

Model split in linear and nonlinear parameters

$$\vec{S} = A(\vec{\omega}, \vec{r})\ \underbrace{P(\vec{\phi})\vec{\varrho}}_{\vec{\rho}} \equiv A\vec{\rho} = S(\beta)$$

$$\beta = \left(\vec{\varrho}, \vec{\phi}, \vec{\omega}, \vec{r}\right)^T$$

- Matrices depend on nonlinear parameters β_{nonlin}
- Vectors depend on linear parameters β_{lin}

[10] Golub, Inverse Problems, 19(2), 1–26., 10.1088/0266-5611/19/2/201;

parameter mapping

Parameter mapping based on generalized Jacobian

Variable Projection Method (VARPRO) [10]

Voxel-based iterative minimization (least-squares) [11]

$$J = \left[\frac{\partial \vec{S}}{\partial \vec{\rho}}, \frac{\partial \vec{S}}{\partial \vec{\phi}}, \frac{\partial \vec{S}}{\partial \vec{\omega}}, \frac{\partial \vec{S}}{\partial \vec{r}}\right]$$

$$= [APC_\varrho, iAP\,\mathrm{diag}(\vec{\varrho})C_\phi, iTAP\,\mathrm{diag}(\vec{\varrho})C_\omega, -TAP\,\mathrm{diag}(\vec{\varrho})C_r]$$

Require: $\beta^{(0)}_{\text{nonlin}}$

while residual $> \epsilon$ **do**

1. compute linear parameters
2. compute nonlinear parameters
3. compute residual

end while

[10] Golub, Inverse Problems, 19(2), 1–26., 10.1088/0266-5611/19/2/201; [11] Hernando, MRM 2008, 10.1002/mrm.21522;

noise analysis

Statistical analysis based on generalized Jacobian

$$\vec{S} = A\vec{\rho} + \vec{n}$$

$$\vec{n} \in \mathcal{N}(\mu,\sigma) + i\mathcal{N}(\mu,\sigma)$$

Likelihood function $$P \sim \exp\left(\frac{1}{2\sigma^2}\left|\vec{S} - A\vec{\rho}\right|^2\right)$$

Fisher Matrix $$F_{kl} = E\left[\frac{\partial}{\partial\beta_k}\frac{\partial}{\partial\beta_l}\ln P\right]$$

$$\boxed{F = \frac{1}{\sigma^2}J^\dagger J}$$

The Fisher matrix is the starting point for statistical analysis.

Cramér–Rao Analysis:

$$\sigma_{kl}^2 \geq (F^{-1})_{kl}$$

Cramér–Rao lower bound

("Alphabetic") Optimal Design (echo time selection):

- A-optimality
- D-optimality
- G-optimality
- V-optimality

[12] Pineda, MRM 2005, 10.1002/mrm.20623; [13] Kay, S. M., Statistical signal processing, Volume I: Estimation Theory (1993), ISBN: 978-0133457117;
[15] Chernof, Sequential analysis and optimal design (1989), ISBN: 0-89871-006-5; [16] Montgomery, D. C., Design and analysis of experiments (2012), ISBN: 978-1-118-14692-7;

Recap: The generalized Jacobian allows for…

Generalized Jacobian

$$J = [APC_\varrho, iAP\,\mathrm{diag}(\vec{\varrho})C_\phi, iTAP\,\mathrm{diag}(\vec{\varrho})C_\omega, -TAP\,\mathrm{diag}(\vec{\varrho})C_r]$$

parameter mapping

$$\Delta\beta_{\mathrm{nonlin}} = J^+(\vec{S} - A\beta_{\mathrm{lin}})$$

noise & bias analysis

$$F = \frac{1}{\sigma^2} J^\dagger J$$

How do constraints matrices look like?

Examples for constraints matrices of several signal models:

- Simple magnetic-field mapping [4]
- Multi-peak fat spectrum [17]
- Phase constrained models [8]
- Fat unsaturation and chain length mapping [18]

[4] Liu, MRM 2013, 10.1002/mrm.24272; [17] Yu, MRM 2008, 10.1002/mrm.21737; [8] Bydder, MRM 2011, 10.1016/j.mri.2010.08.011; [18] Berglund, MRM 2012, 10.1002/mrm.24196; [5] Sood, MRM 2016, 10.1002/mrm.26281;

Examples of constraints matrices

Simple magnetic-field mapping [4]:

$$S(t) = \varrho e^{i\phi} e^{i\omega t} e^{-R_2^* t}$$

$$C_\varrho = C_\phi = C_\omega = C_r = [1, 0, \cdots, 0]^T$$

NOTE:
One “matrix” for each “parameter type”.

[4] Liu, MRM 2013, 10.1002/mrm.24272;

Examples of constraints matrices

WFI signal model with multi-peak fat spectrum (single R_2^*) [17]:

$$S(t_n) = (W + F\sum_{p=1}^{P}\alpha_p e^{i\Delta\omega_p t_n})e^{i\omega t}e^{-R_2^* t_n} \qquad \sum_{p=1}^{P}\alpha_p = 1$$

$$C_\varrho = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ 0 & \alpha_1 & \cdots & 0 \\ 0 & \alpha_2 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 0 & \alpha_P & \cdots & 0 \end{pmatrix} \quad C_\phi = \begin{pmatrix} 1 & 0 & 0 & \cdots & 0 \\ 0 & 1 & 0 & \cdots & 0 \\ 0 & 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & & \vdots \\ 0 & 1 & 0 & \cdots & 0 \end{pmatrix} \quad C_\omega = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 1 & 0 & \cdots & 0 \end{pmatrix} \quad C_r = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 1 & 0 & \cdots & 0 \end{pmatrix}$$

NOTE:

- All constraints matrices are of size M x M with M = P+1
- Diagonal elements correspond to unknowns of the model
- Lower triangular columns correspond to constrained parameters

[17] Yu, MRM 2008, 10.1002/mrm.21737;

Examples of constraints matrices

WFI signal model with multi-peak fat spectrum (double R_2^*) [7]:

$$S(t_n) = \left(W e^{-R^*_{2,W} t_n} + F e^{-R^*_{2,F} t_n} \sum_{p=1}^{P} \alpha_p e^{i\Delta\omega_p t_n} \right) e^{i\omega t_n} \qquad \sum_{p=1}^{P} \alpha_p = 1$$

$\{C_\varrho, C_\phi, C_\omega\}$ as in single-R_2^* model.

$$C_r = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 1 & 0 & \cdots & 0 \end{pmatrix} \longrightarrow C_r = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ 0 & 1 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 0 & 1 & \cdots & 0 \end{pmatrix}$$

Single R_2^* Double R_2^*

[7] Reeder, MRM 2011, 10.1002/mrm.23016;

Examples of constraints matrices

WFI signal model with constrained phase [8]:

$$S(t_n) = \left(\varrho_W e^{-R^*_{2,W} t_n} + \varrho_F e^{-R^*_{2,F} t_n} \sum_{p=1}^{P} \alpha_p e^{i\Delta\omega_p t_n} \right) e^{i\phi} e^{i\omega t_n} \qquad \sum_{p=1}^{P} \alpha_p = 1$$

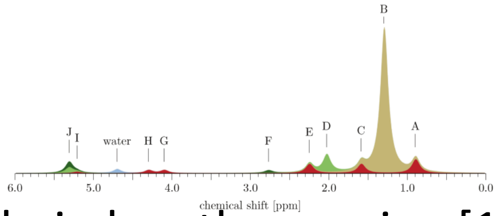
$\{C_\varrho, C_\omega, C_r\}$ as in unconstrained-phase model.

$$C_\phi = \begin{pmatrix} 1 & 0 & 0 & \cdots & 0 \\ 0 & 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & & \vdots \\ 0 & 1 & 0 & \cdots & 0 \end{pmatrix} \longrightarrow C_\phi = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 1 & 0 & \cdots & 0 \end{pmatrix}$$

Unconstrained phase Constrained phase

[8] Bydder, MRM 2011, 10.1016/j.mri.2010.08.011;

Examples of constraints matrices



Complex signal model for fat unsaturation and chain length mapping [18]:

$$S(t_n) = (W + a_{F_1}F_1 + a_{F_2}F_2 + a_{F_3}F_3 + a_{F_4}F_4)\, e^{(i\omega - R_2^*)t_n}$$

$$\begin{aligned} a_{F_1} &= 9a_A + 6a_C + 6a_E + 2a_G + 2a_H + a_I \\ a_{F_2} &= 2a_B \\ a_{F_3} &= 4a_D + 2a_J \\ a_{F_4} &= 2a_F + 2a_J \end{aligned}$$

$$a_m \equiv a_m(t) = e^{i\omega_m t}$$

$\{C_\phi, C_\omega, C_r\}$ as in unconstrained-phase single-R_2^* model.

$$C_\varrho = \begin{bmatrix} 1 &&&&&&&&&& \\ & 1 &&&&&&&&& \\ & 0 & 1 &&&&&&&& \\ & 2/3 && 0 &&&&&&& \\ & 0 &&& 1 &&&&&& \\ & 2/3 &&& 0 & 0 &&&&& \\ & 0 &&& 0 && 1 &&&& \\ & 2/9 &&& 0 && 0 & 0 &&& \\ & 2/9 &&& 0 && 0 && 0 && \\ & 1/9 &&& 0 && 0 &&& 0 & \\ & 0 &&& 1/2 && 1 &&&& 0 \end{bmatrix}$$

[18] Berglund, MRM 2012, 10.1002/mrm.24196; Figure taken from [18]

Application

Comparison of standard WFI model with and without frequency shift [19]

$$S(t_n) = (W + F\sum_{p=1}^{P}\alpha_p e^{i\Delta\omega_p t_n})e^{i\omega t}e^{-R_2^* t_n}$$

$\{C_\varrho, C_\phi, C_r\}$ as before.

$$C_\omega = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 \\ \vdots & \vdots & & \vdots \\ 1 & 0 & \cdots & 0 \end{pmatrix}$$

(standard) single-R_2^*

$$S(t_n) = (W + F\sum_{p=1}^{P}\alpha_p e^{i(\Delta\omega_p \boxed{+x})t_n})e^{i\omega t}e^{-R_2^* t_n}$$

$\{C_\varrho, C_\phi, C_r\}$ as in single-R_2^* model.

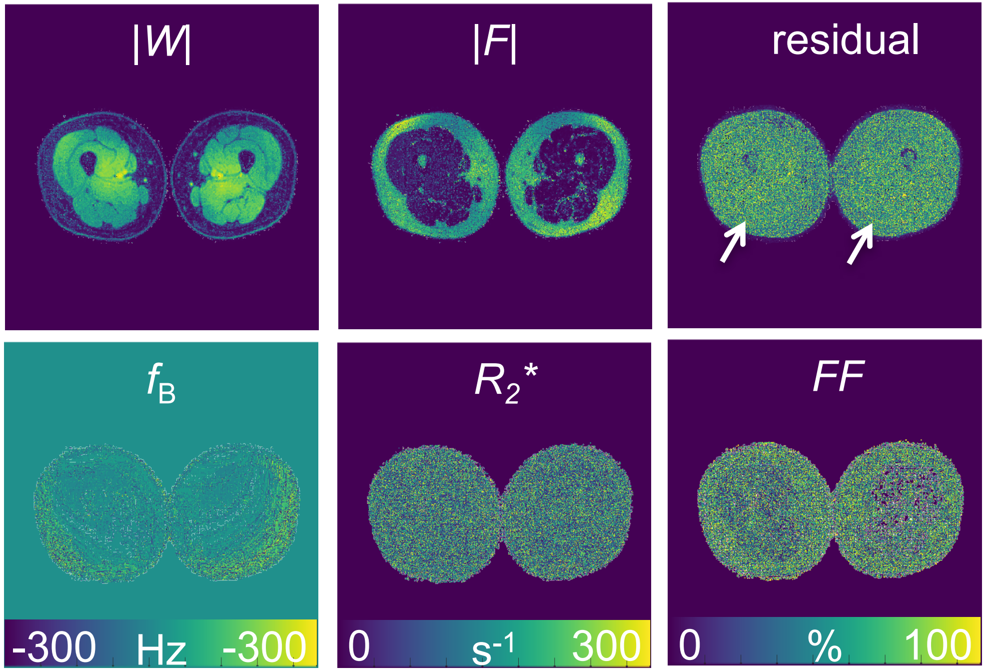
$$C_\omega = \begin{pmatrix} 1 & 0 & 0 & \cdots & 0 \\ 0 & 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & & \vdots \\ 0 & 1 & 0 & \cdots & 0 \end{pmatrix}$$

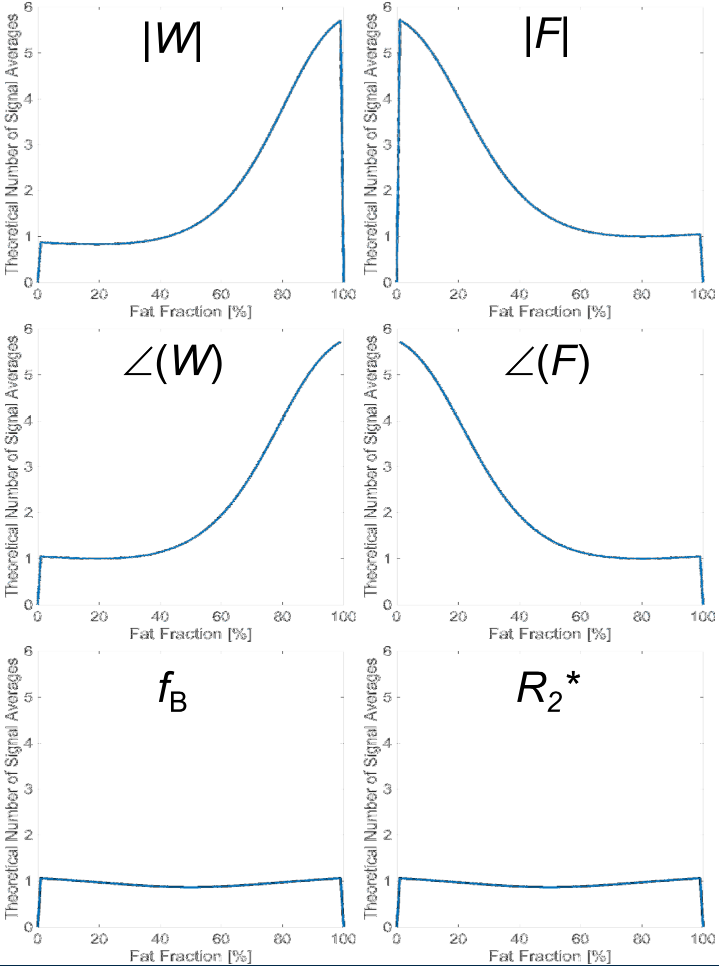
Single-R_2^* with frequency shift

[19] Karampinos, MRM 2012, 10.1002/mrm.24157;

Application

Parameter maps & Cramér Rao analysis for (standard) single-R_2^* water–fat model [12]

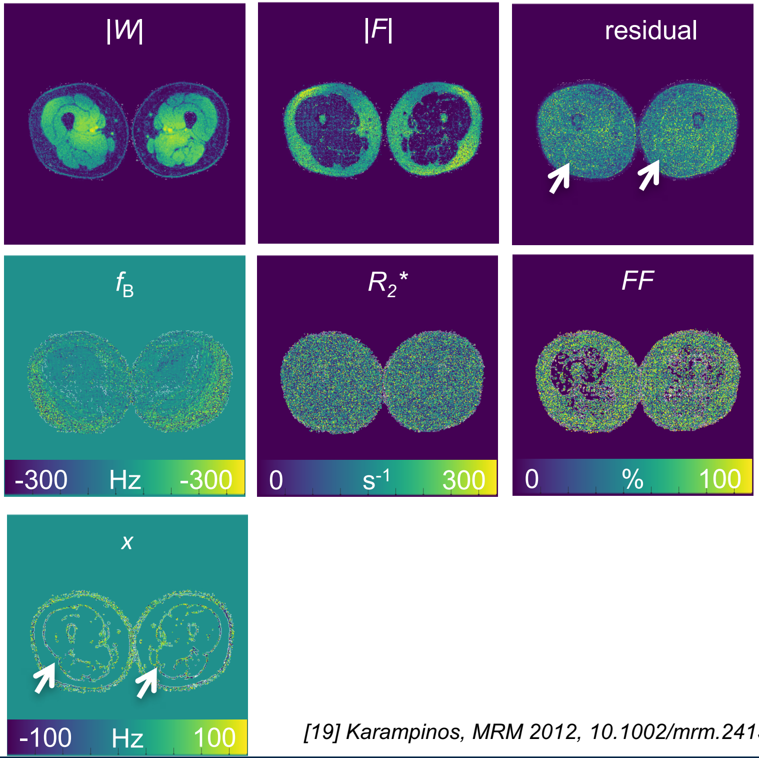


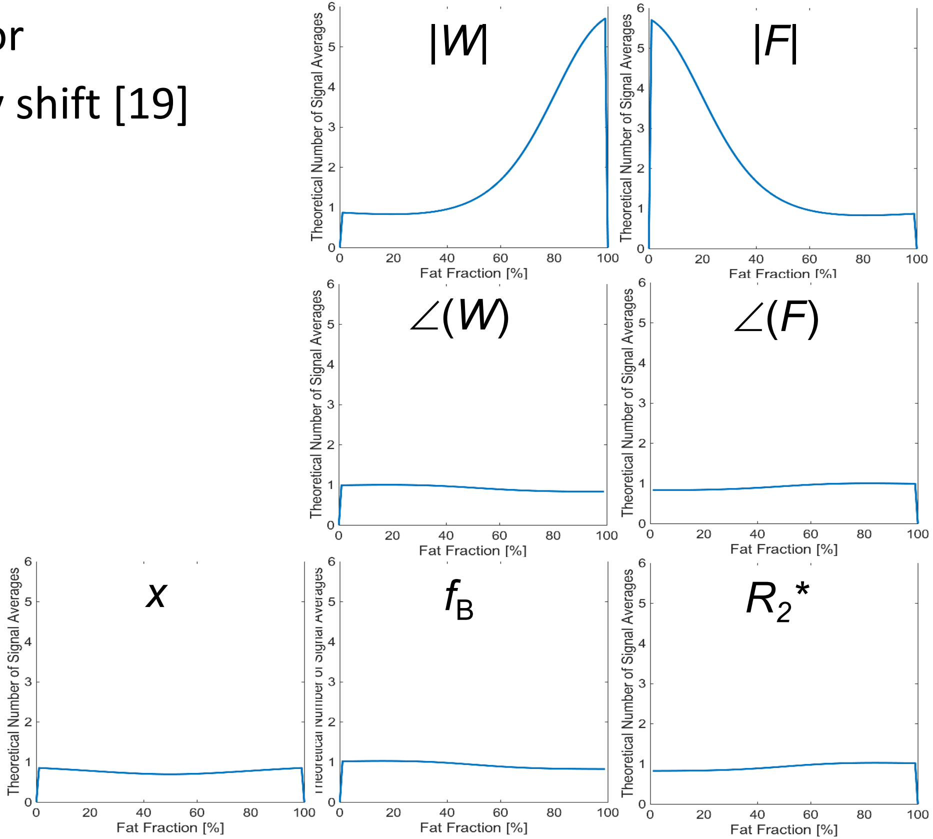


[12] Pineda, MRM 2005, 10.1002/mrm.20623;

Application

Parameter maps & Cramér–Rao analysis for single-R_2^* water–fat model with frequency shift [19]





[19] Karampinos, MRM 2012, 10.1002/mrm.24157;

Summary

General *M*-species model,
observation to matrix formulation

$$S(t) = \sum_{m=1}^{M} \varrho_m e^{i\phi_m} e^{i(\omega_m + i r_m)t}$$

$$\vec{S} = A(\vec{\omega}, \vec{r}) P(\vec{\phi}) \vec{\varrho}$$

$$J = \left[\frac{\partial \vec{S}}{\partial \vec{\rho}}, \frac{\partial \vec{S}}{\partial \vec{\phi}}, \frac{\partial \vec{S}}{\partial \vec{\omega}}, \frac{\partial \vec{S}}{\partial \vec{r}} \right]$$

$$= [APC_\varrho, iAP\,\mathrm{diag}(\vec{\varrho})C_\phi, iTAP\,\mathrm{diag}(\vec{\varrho})C_\omega, -TAP\,\mathrm{diag}(\vec{\varrho})C_r]$$

Model specification in the Jacobian via **constraints matrices**

parameter mapping

$$\Delta\beta_{\mathrm{nonlin}} = J^+(\vec{S} - A\beta_{\mathrm{lin}})$$

noise & bias analysis

$$F = \frac{1}{\sigma^2} J^\dagger J$$

Acknowledgements

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