Weekend course, WE-06, Saturday 8 am, ICC Capital Hall 1

Encoding Diffusion:
Advanced gradient design and relaxation-weighting

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LUND UNIVERSITY

Declaration of Financial Interests or Relationships

Speaker Name: Filip Szczepankiewicz

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

Company Name: Random Walk Imaging AB, Sweden
Type of Relationship: Inventor on patents and shareholder

Overview

- Motivation for ‘advanced’ diffusion-relaxation MRI
- Advanced sequence & gradient waveform designs
  - Beyond the regular spin-echo with EPI
  - Tensor-valued diffusion encoding
  - Restriction and exchange weighting
- Diffusion-relaxation MRI
  - Sequence design for T2-weighting
  - Sequence design for T1-weighting
- The uninvited “cousins of diffusion MRI”
  - Scary stories and potential remedies

The motivation for ‘advanced’ MRI

Why we bother to go beyond the standard experiment and the power of a multidimensional approach

Advanced methods facilitate more information

Diffusivity & direction

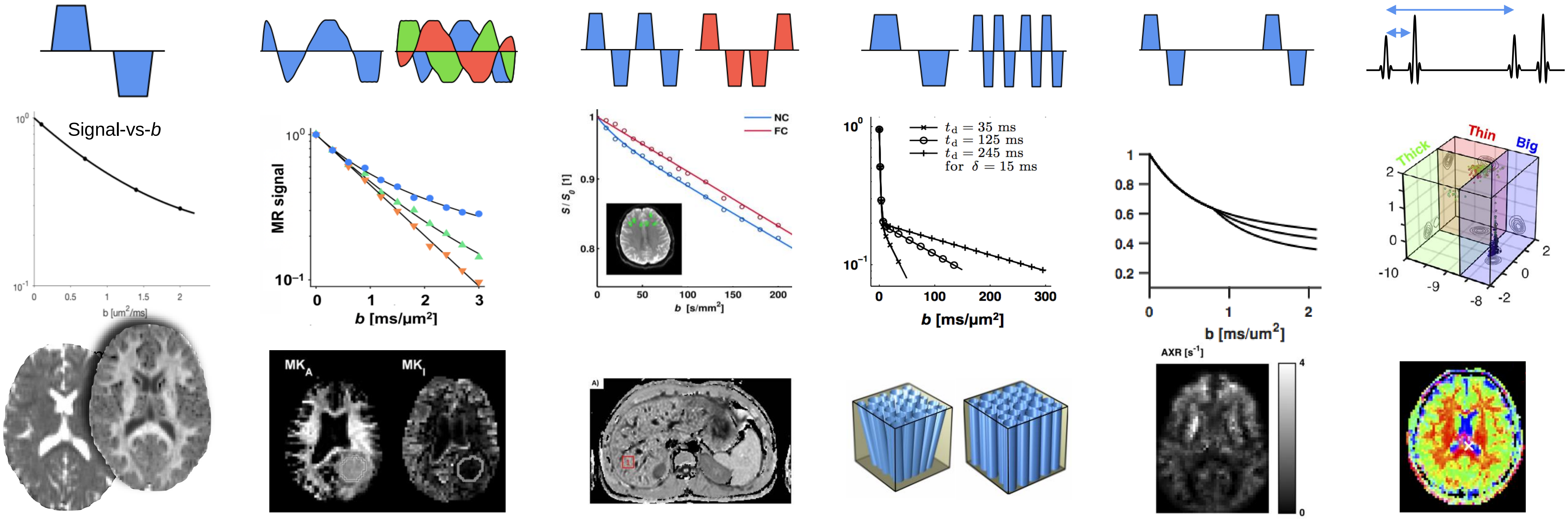
Micro-anisotropy & heterogeneity

Perfusion fraction

Compartment Sizes

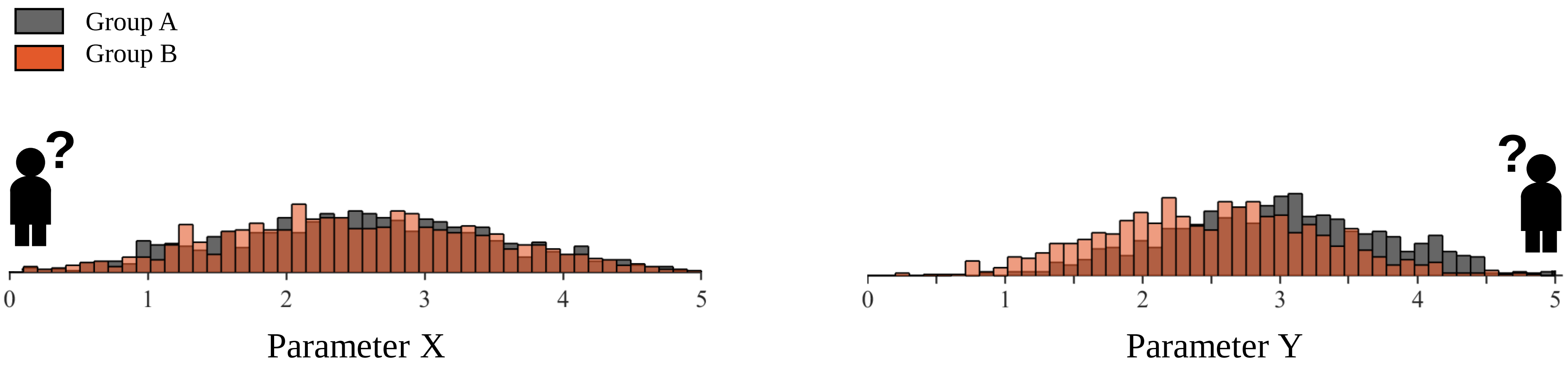
Water exchange

Volume fractions



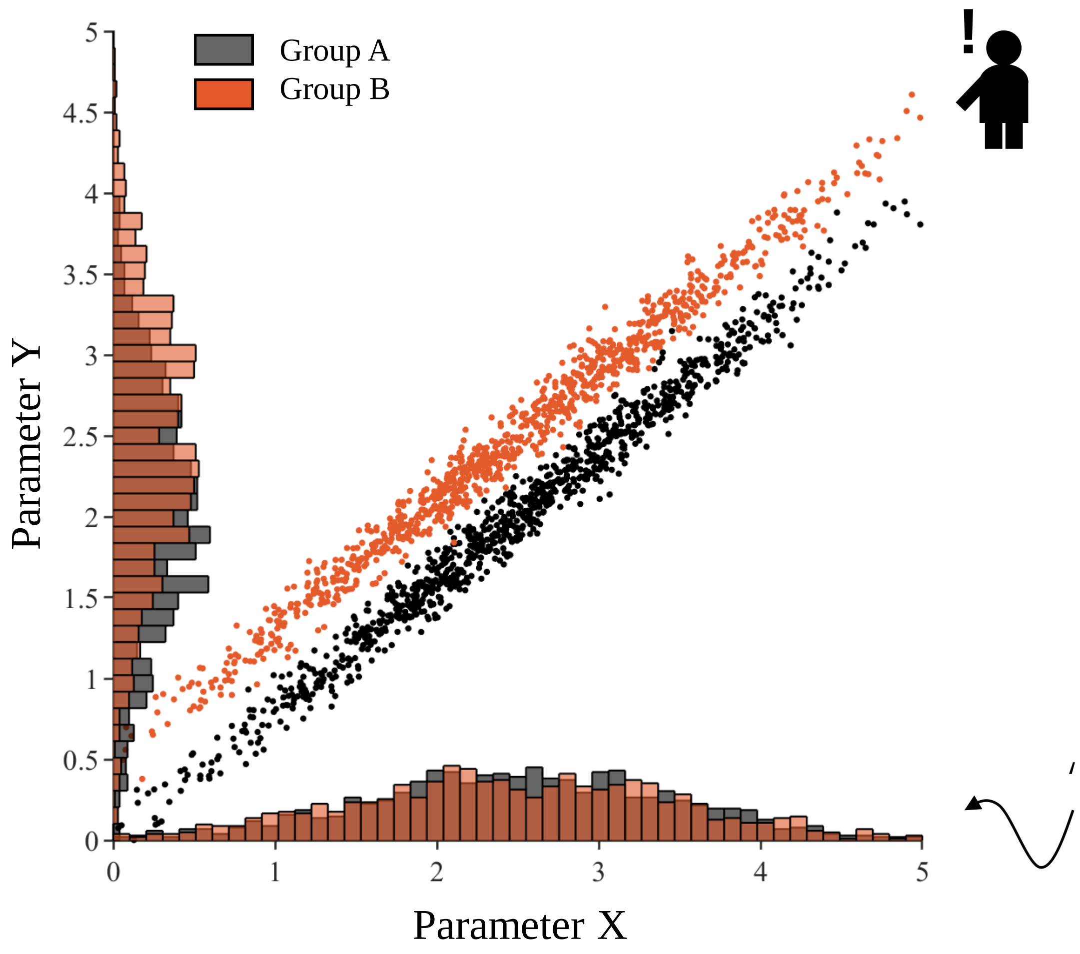
Slide borrowed from Markus Nilsson

Multiparametric imaging



Effect size is too small to be interesting

Multidimensional imaging



By jointly probing X and Y, the correlation between parameters is seen…

… and data can be viewed from a vantage point with a large effect size!

'Marginal distribution'

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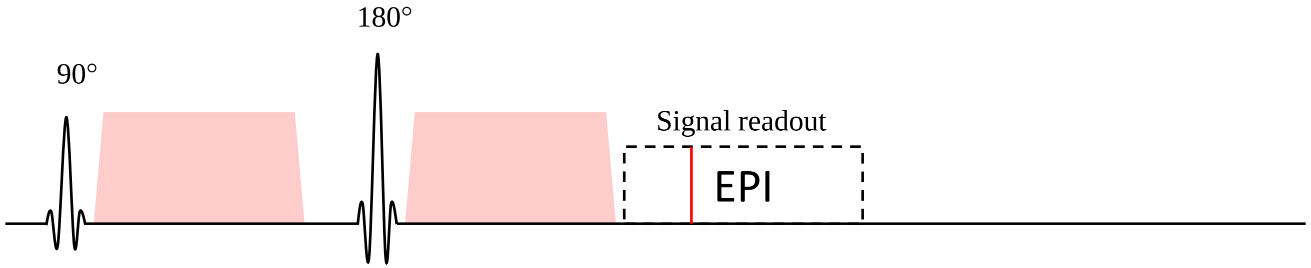
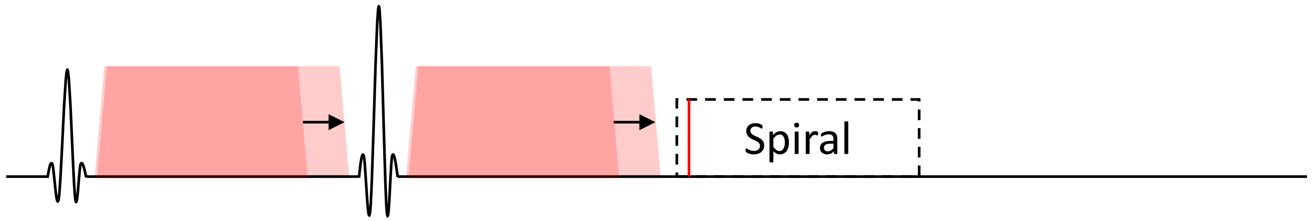
Advanced sequence & gradient waveform designs

Alternatives to the regular spin-echo, tensor-valued encoding and more…

The ‘regular’ spin-echo pulse sequence

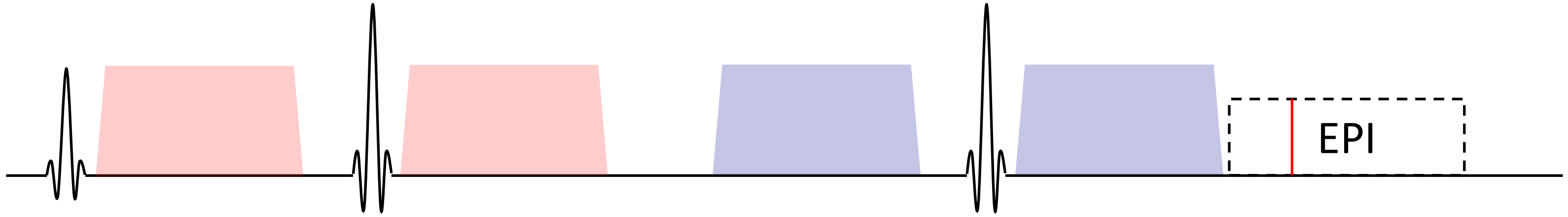


Recomended reading: Translational Dynamics and Magnetic Resonance, Callaghan 2011



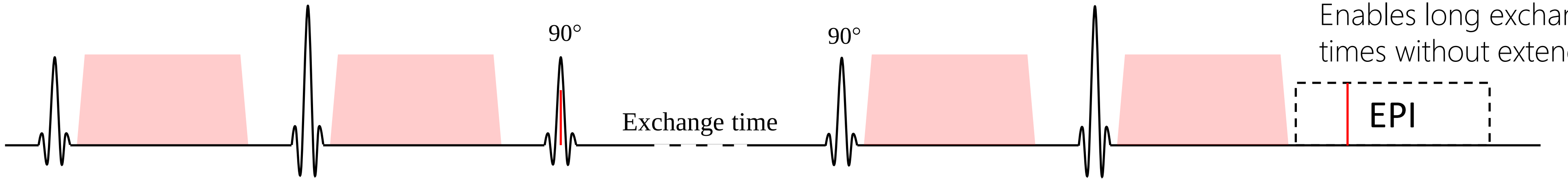
Spiral readout can increase time available for diffusion encoding

Increases diffusion time without extending TE



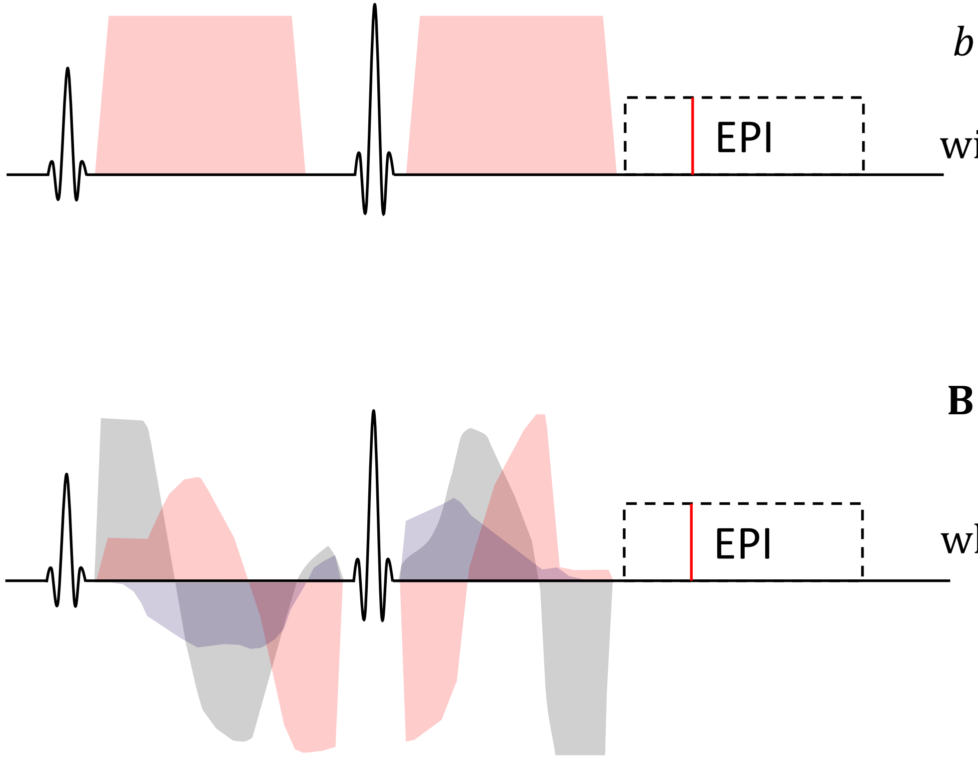
Enables DDE with independent gradient configurations

Enables long exchange/mixing times without extending TE



Recomended reading: Lee et al. MRM 2020; Burstein Conc Magn Reson 1996; Lasič et al. MRM 2011

'Free waveforms' instead of trapezoids

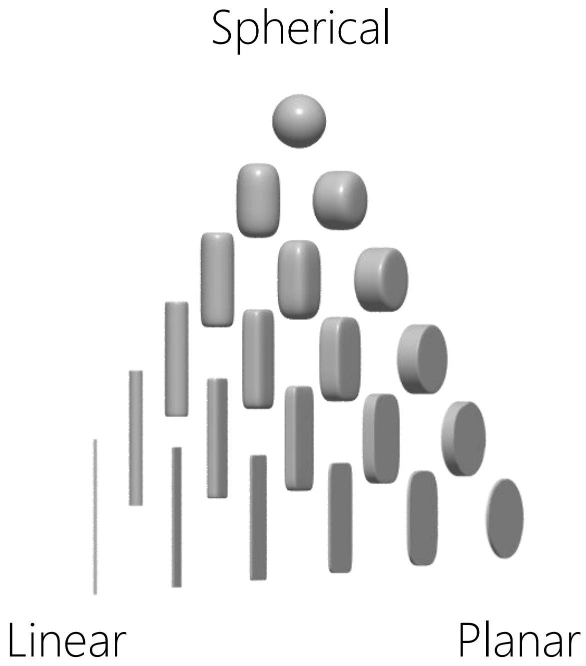


$$b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

with direction $\mathbf{u}$

$$\mathbf{B} = \int_0^{\mathrm{TE}} \mathbf{q}(t)\mathbf{q}^{\mathrm{T}}(t)\mathrm{d}t$$

where $\mathbf{q}(t) = \gamma \int_0^t \mathbf{G}(t')\mathrm{d}t'$



Westin et al. NeuroImage 2014 and 2016; Sjölund et al. JMR 2015; Topgaard JMR 2017

The origin of non-linear encoding…

Linear b-tensors
sPFG, SDE
Stejskal & Tanner. *J. Chem. Phys. 42* (1965)

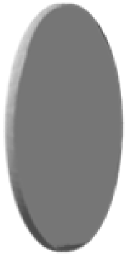
$$\mathbf{B} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Rank ≤ 1

Planar b-tensors
dPFG, DDE
Cory et al., *Polymer Prepr. 31* (1990)

$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

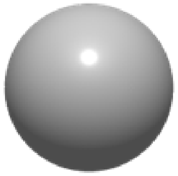
Rank ≤ 2



Spherical b-tensors
TDE, MDE, Trace, Iso
Mori & van Zijl. *Magn. Reson. Med. 33* (1995)
Wong et al. *Magn. Reson. Med. 34* (1995)

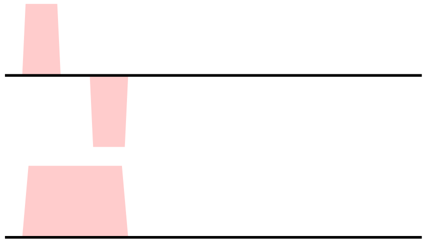
$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

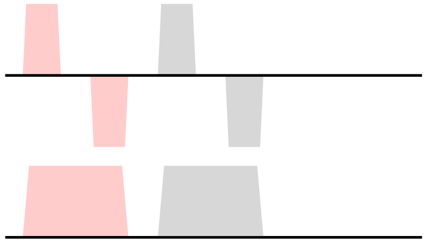
Rank ≤ 3

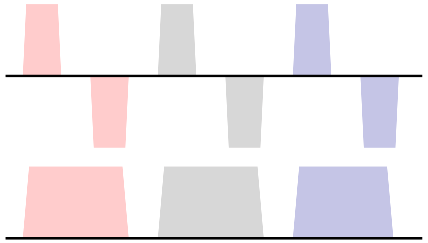


$\mathbf{g}(t) =$

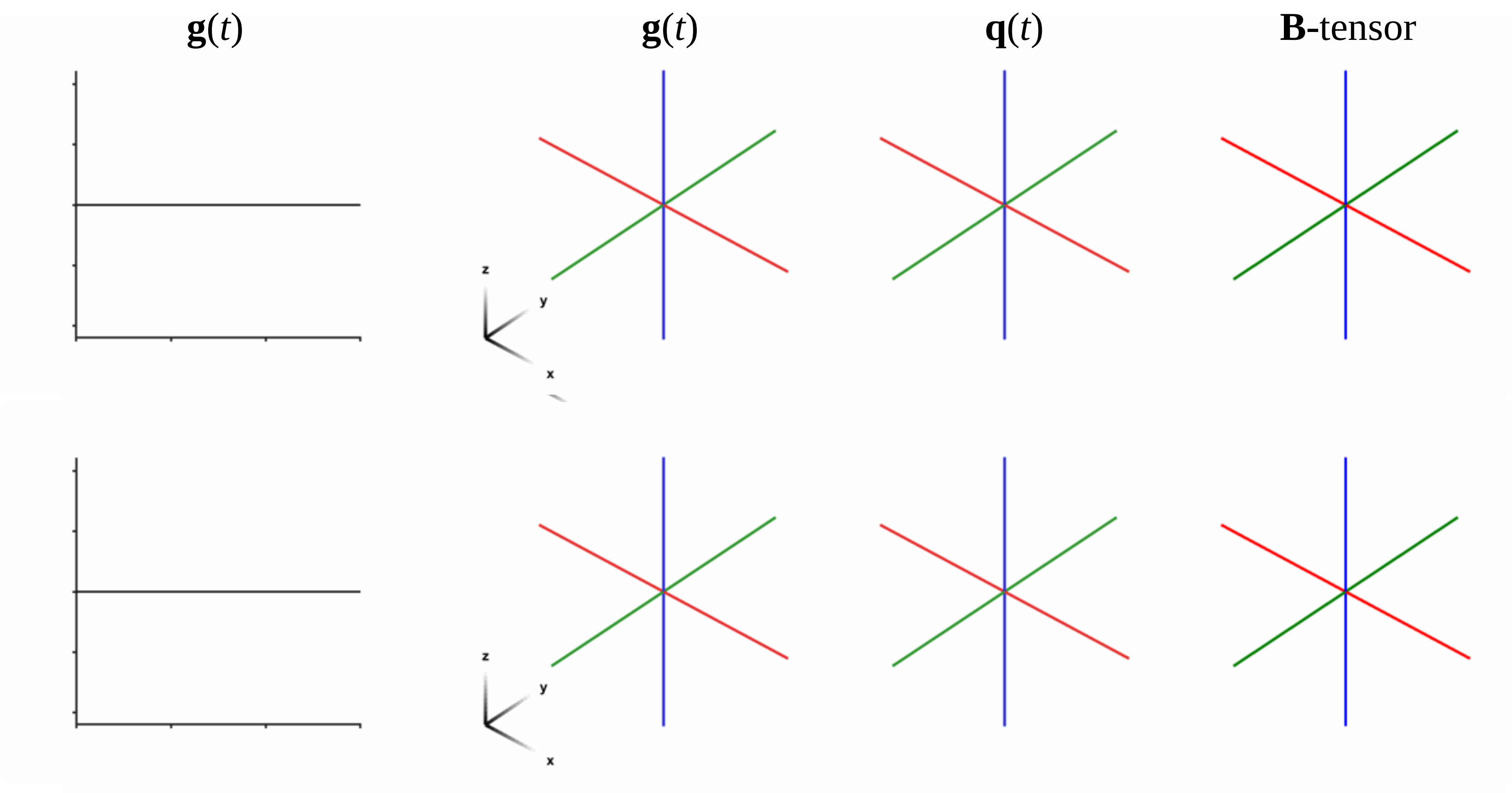
$\mathbf{q}(t) =$







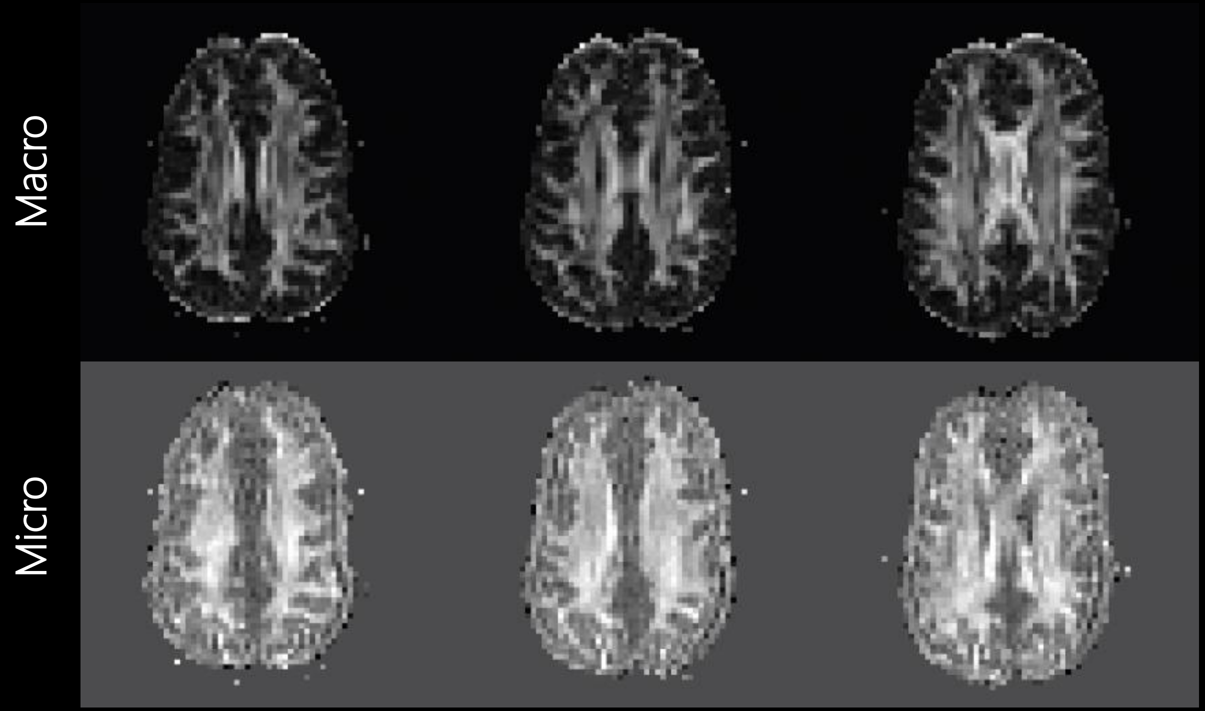
Numerically optimized waveforms

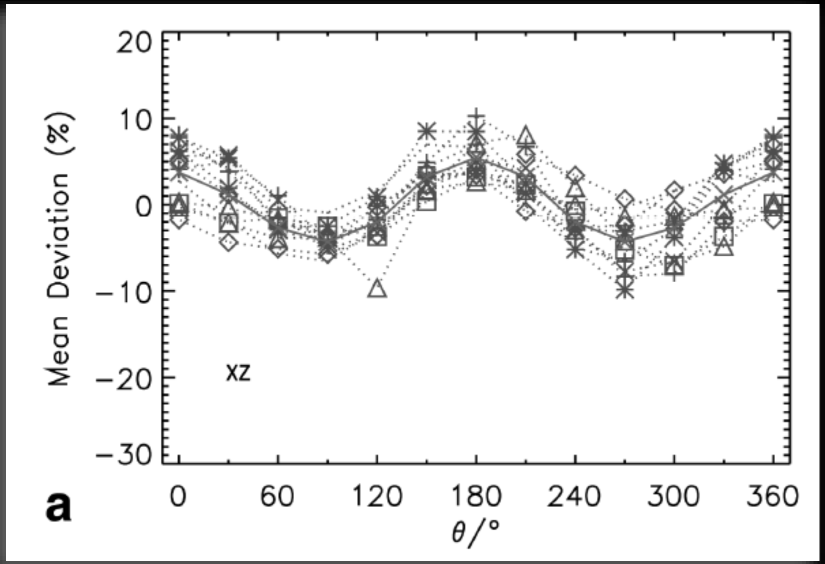


https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/gwf_lte_stejskaltanner.gif
https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/gwf_ste.gif

Sjölund et al. JMR 2015; Szczepankiewicz et al. MRM 2019; open-source optimizer at https://github.com/jsjol/NOW

Macro & micro-anisotropy in brain using DDE





Lawrenz and Finsterbusch MRM 2013

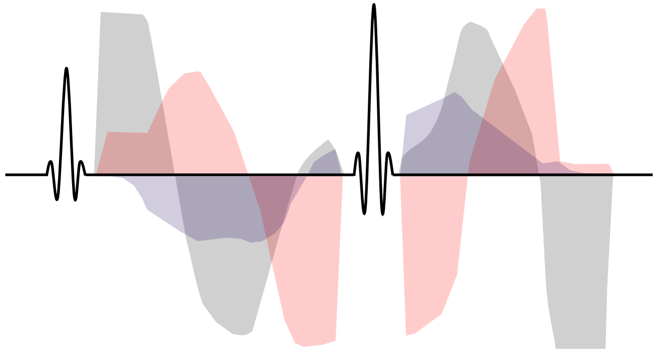
Healthy brain in vivo using linear and spherical b-tensors

Macro-anisotropy | Micro-anisotropy | Orientation order

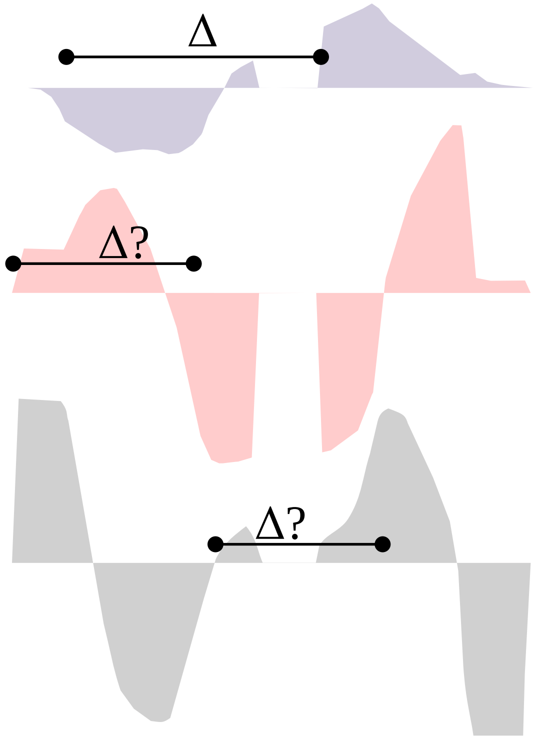
Szczepankiewicz et al. NeuroImage 2015

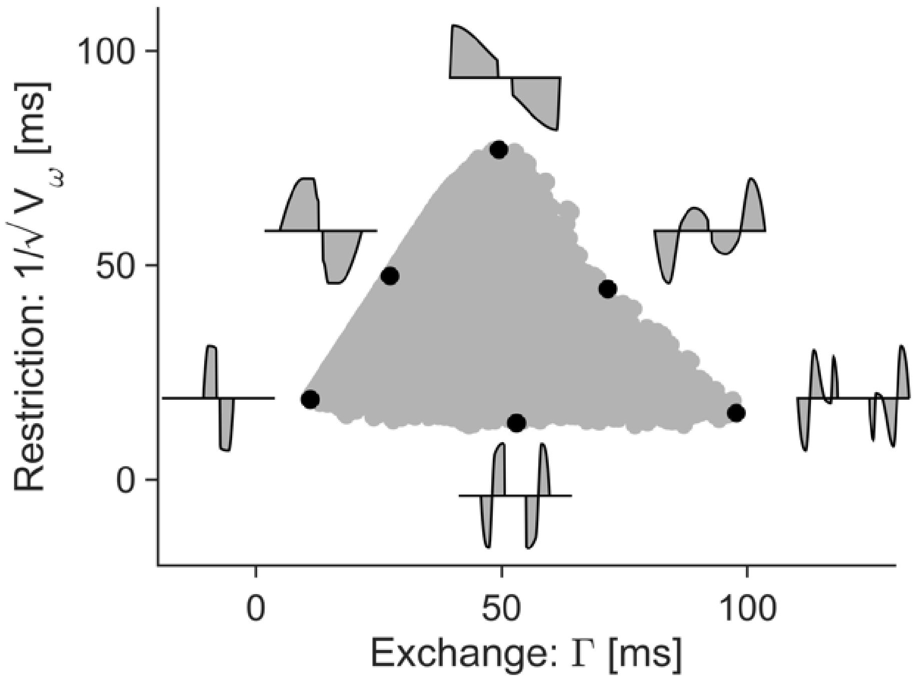
Restriction and exchange weighting

What is the diffusion time?
Is it the same in all directions?
How about exchange weighting?



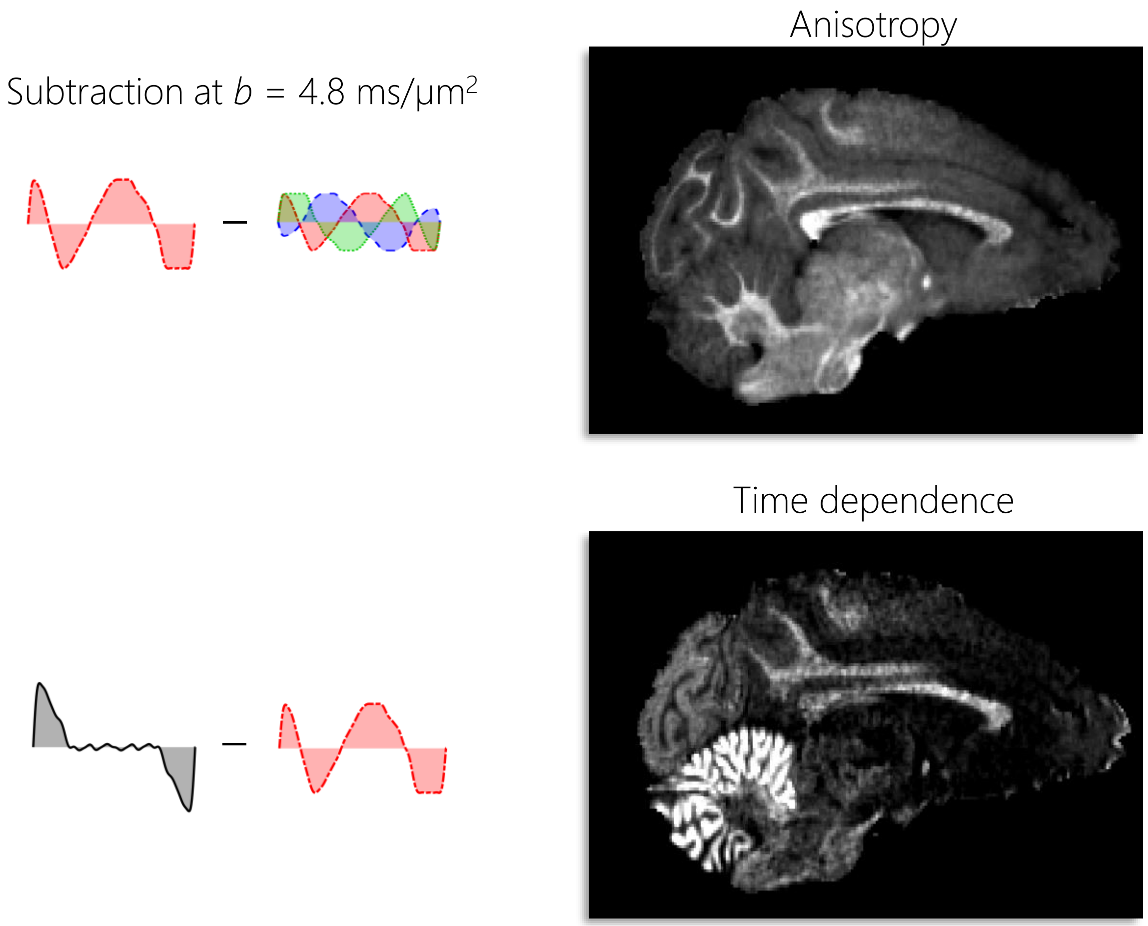
Restriction and exchange weighting





Chakwizira et al. arXiv 2021; Stepišnik PhysB 1993

Time dependent diffusion in ex vivo brain

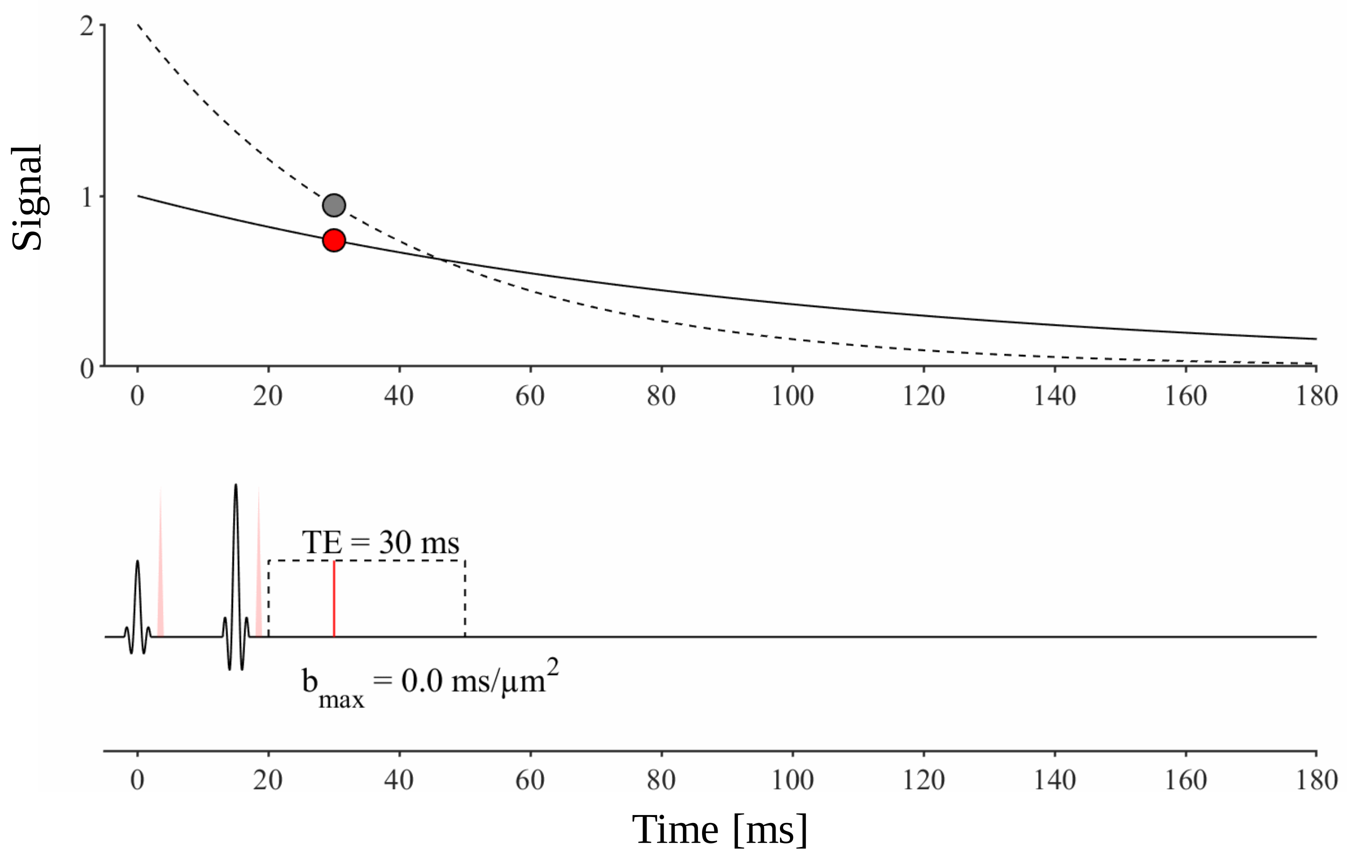


Lundell et al. Sientific Reports 2019

Diffusion-relaxation MRI

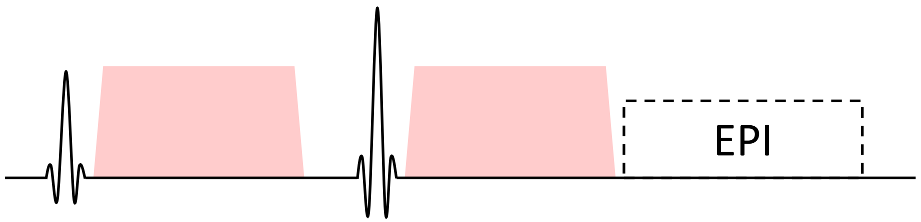
Multidimensional measurements of diffusion and relaxation

T2-weighting by changing the echo time (TE)

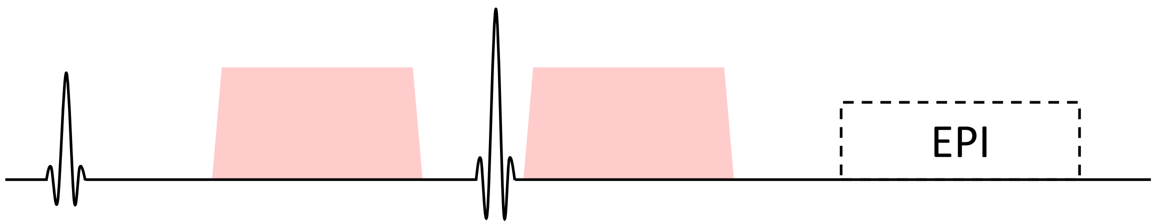


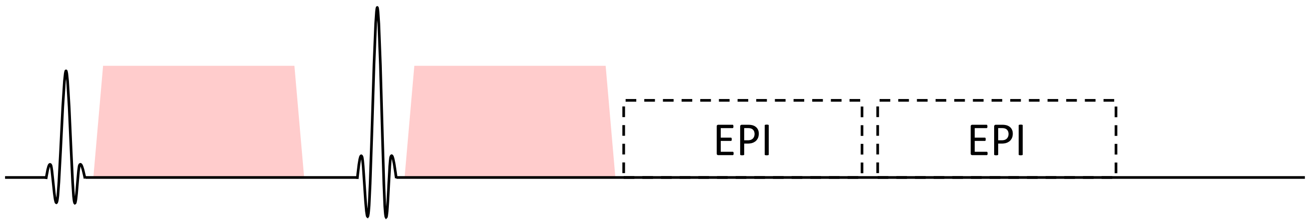
https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/T2-weighting%20by%20TE.gif

Regular with 'short' TE

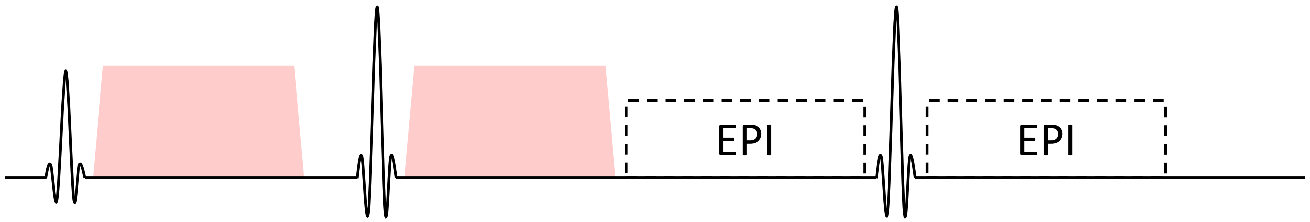


Regular with 'long' TE. Same timing as 'short' variant.

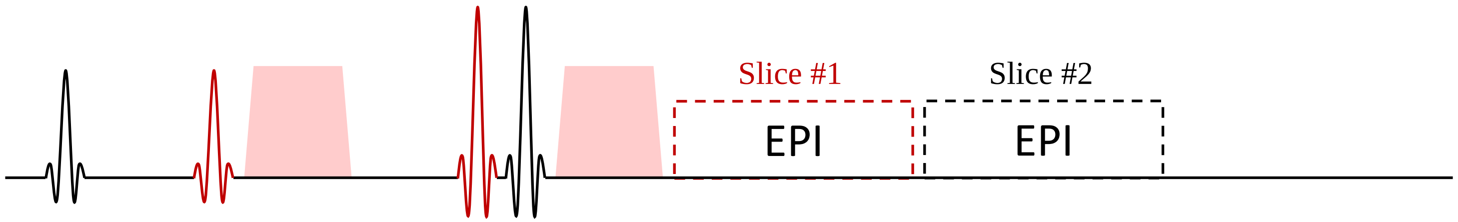




Addition of T2*-weighted image



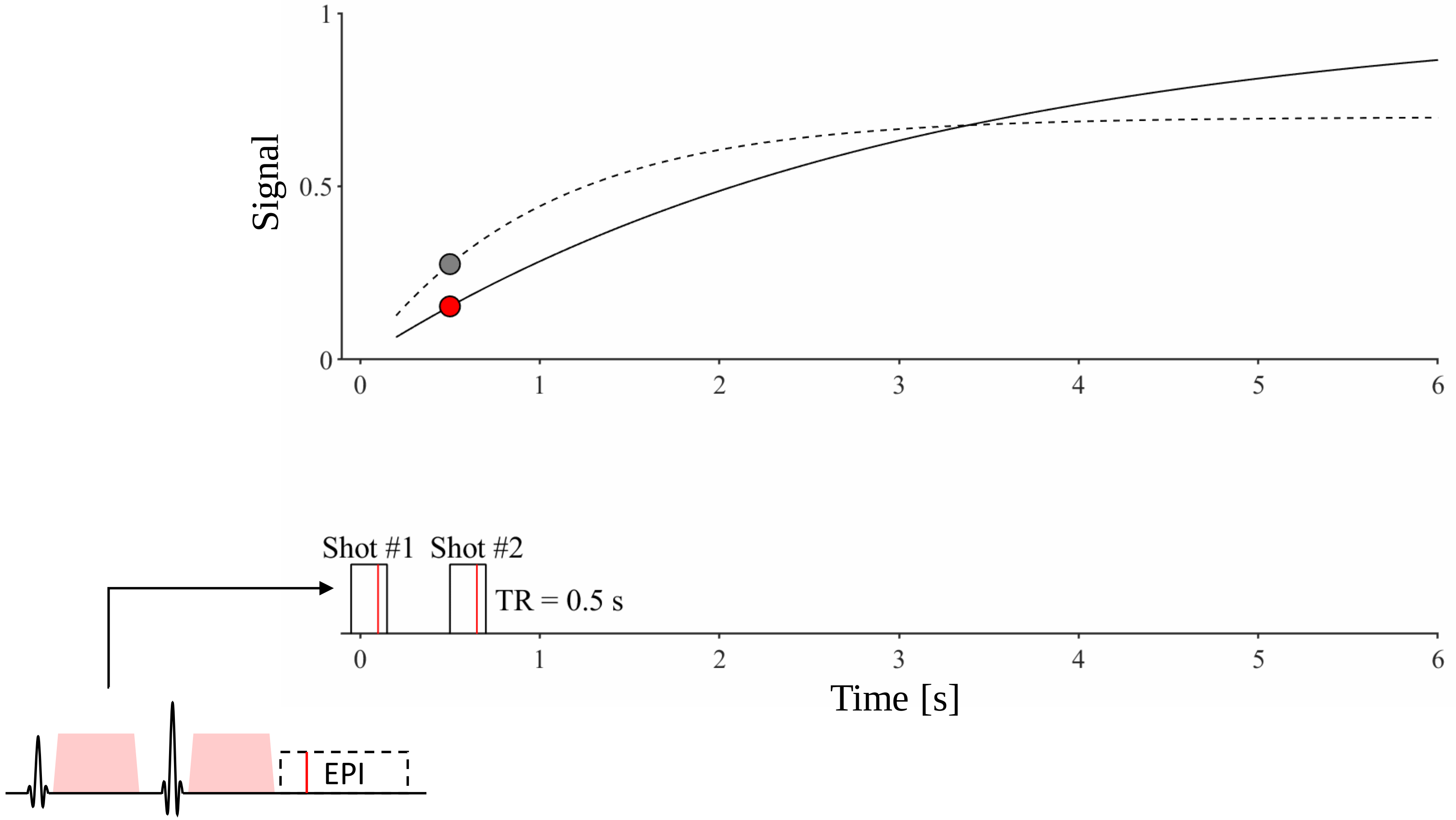
Addition of another T2-weighted image with longer TE.



Simultaneous acquisition of multiple slices with different TE.

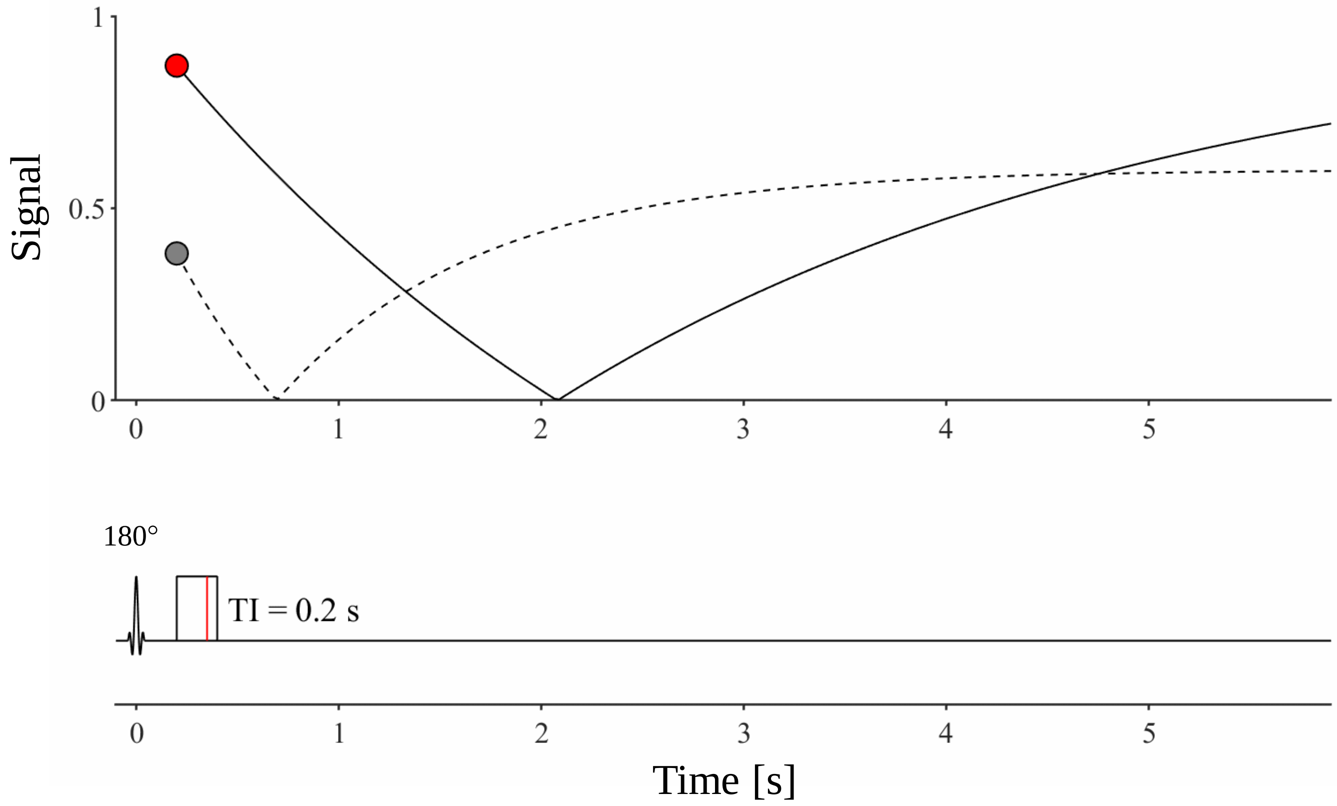
Recomended reading: Slator et al. MRM 2019; Ji et al. MRM 2021

T1-weighting by changing the repetition time (TR)



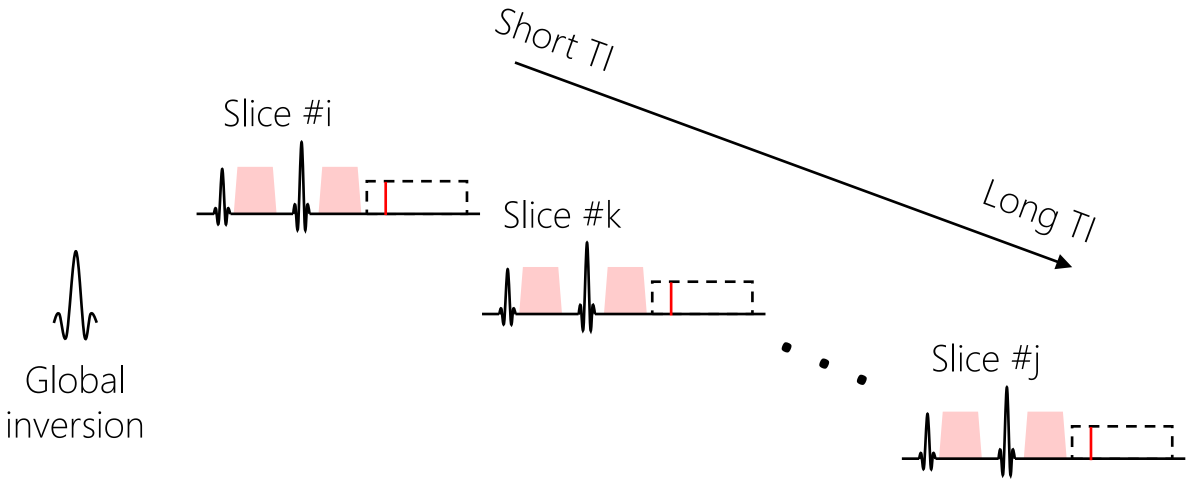
https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/T1-weighting%20by%20TR.gif

T1-weighting by changing the inversion time (TI)

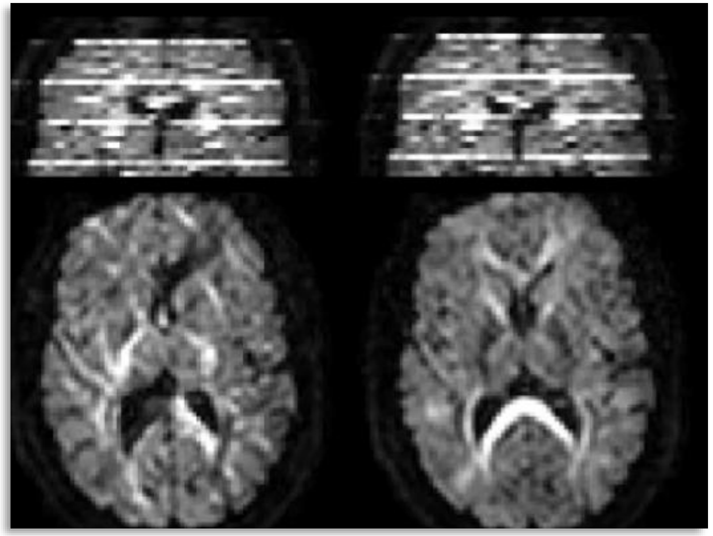


https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/T1-weighting%20by%20TI.gif

Diffusion-T1-correlation by 'ZEBRA'

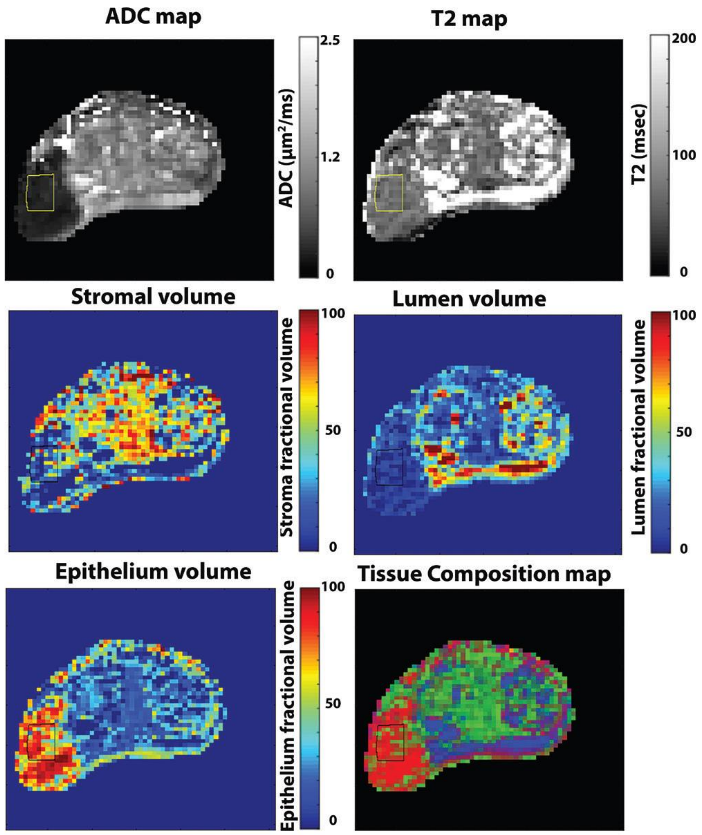


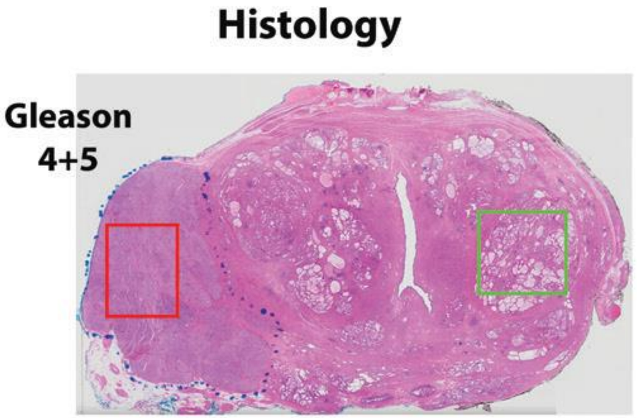
Data from ZEBRA



Hutter et al. Scientific Reports 2018

Diffusion-T2-relaxation for volume fraction estimation in prostate





Chatterjee et al. Radiology 2021

The “uninvited cousins” of diffusion MRI

Scary stories and potential remedies

There is a lot to look out for

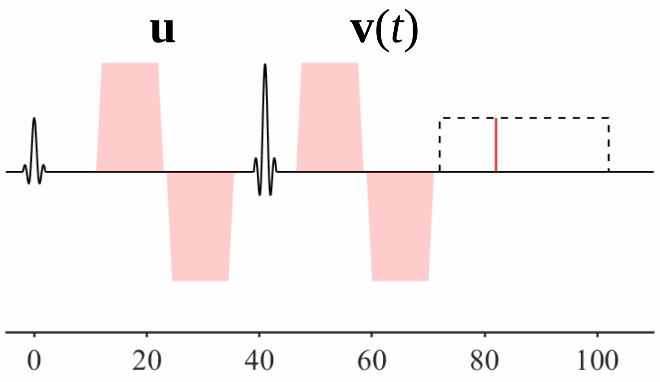
- Motion encoding
- Concomitant gradients
- Cross-terms
- Gradient balance
- Gradient non-linearity
- Eddy-currents
- Energy consumption / heating
- Vibration and acoustic noise
- Nerve stimulation

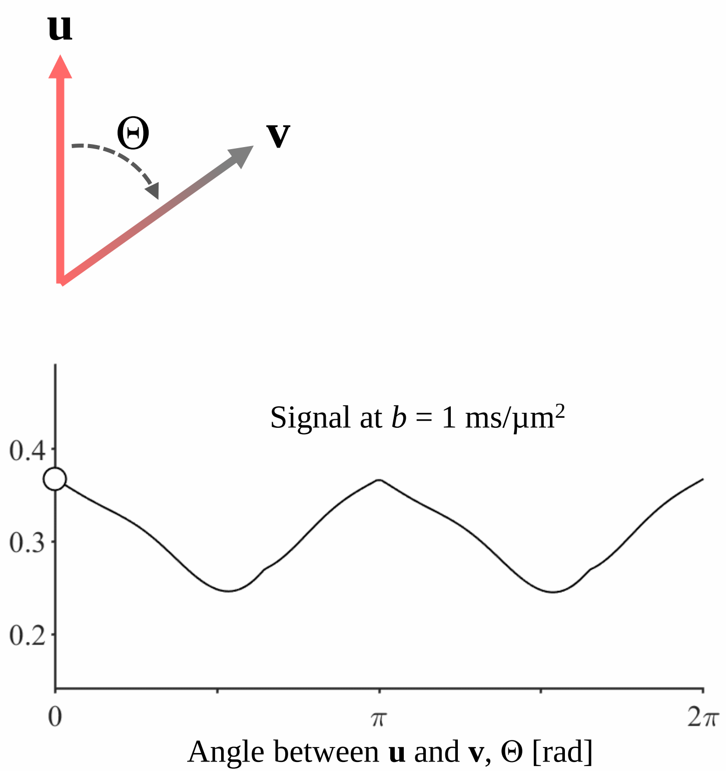
…

Filip Szczepankiewicz

Concomitant gradients that do not balance!

Double diffusion encoding in single spin-echo.

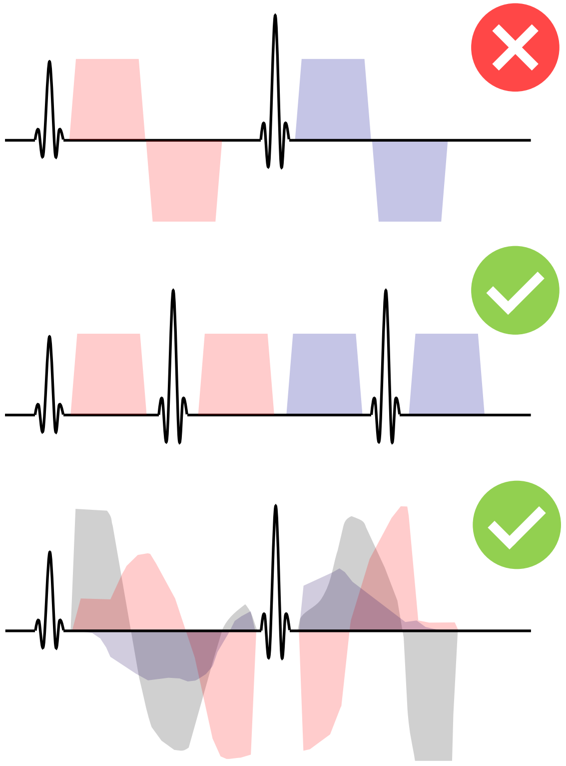




https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/Concomitant%20gradient%20example.gif

Concomitant gradients

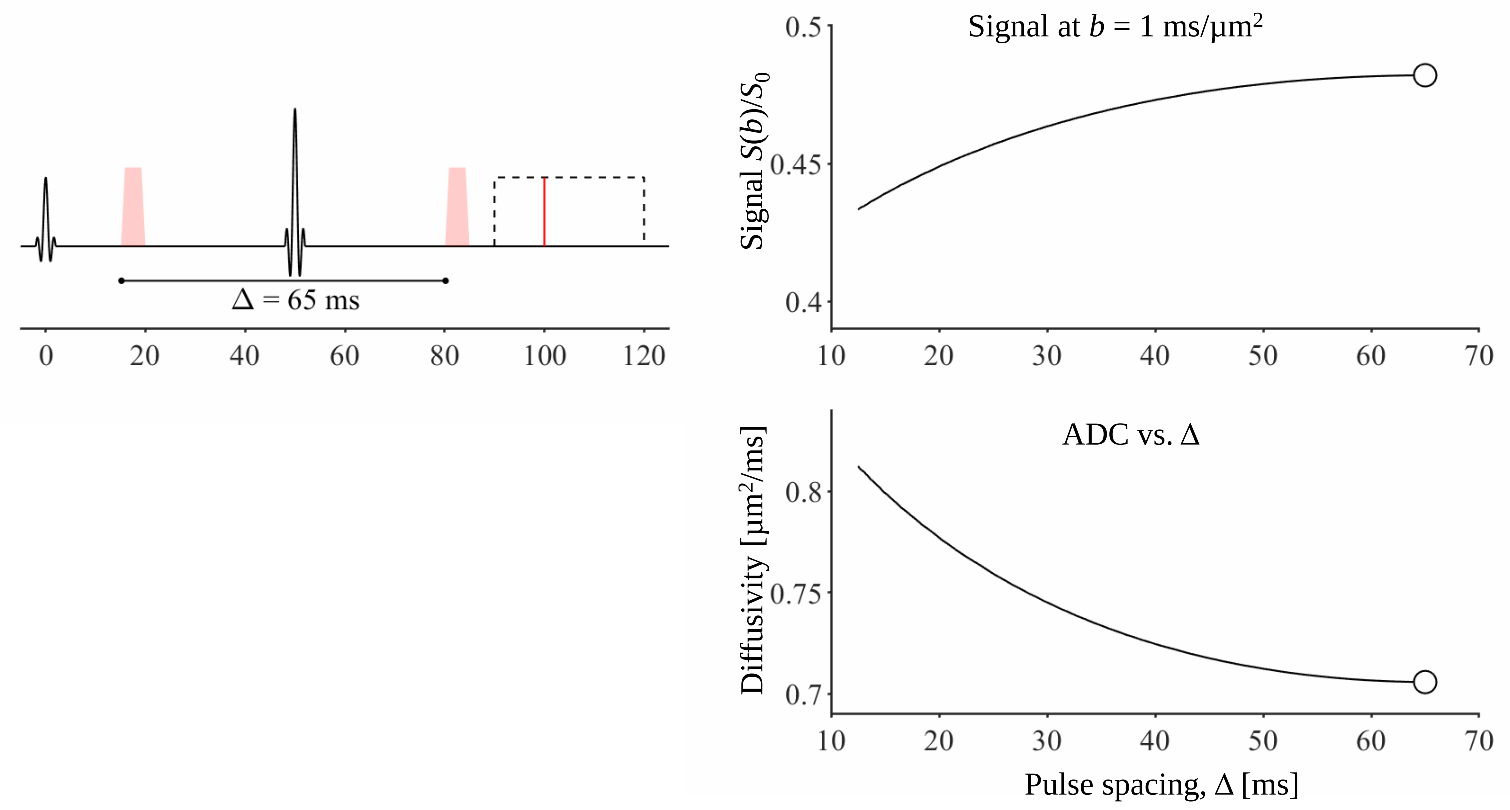
- Main issue is residual dephasing, *not* an error in b-value
  - Easy to predict for any given setup/waveform [1,2]
  - Gets worse for increasing slice thickness and distance to isocenter
- 'Symmetric' waveforms have balanced concomitants!
  - Stejskal-Tanner is symmetric
  - DDE in *double* spin-echo
- Design your waveforms with concomitants in mind!
  - "Waveform reshaping" for linear encoding [3]
  - "Maxwell-compensation" for tensor-valued encoding [2]



1 Bernstein et al. MRM 1998; 2 Szczepankiewicz et al. JMR 2021; 3 Zhou et al. MRM 1998

Cross-terms with background gradients

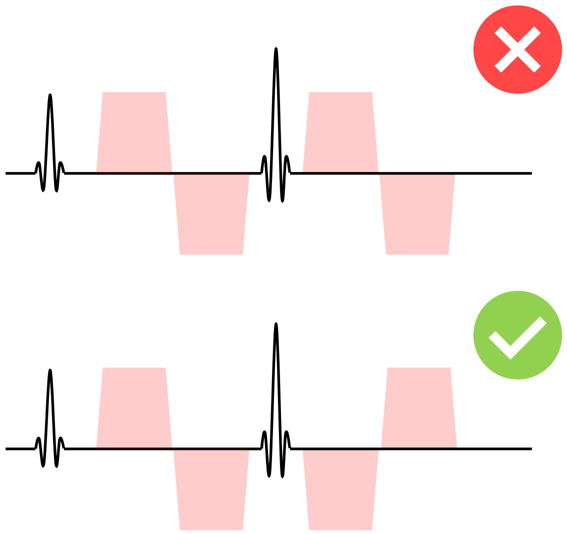
Variable pulse spacing (Δ) at constant b-value.



https://github.com/filip-szczepankiewicz/diff_enc_sim/blob/master/animations/Cross%20term%20example.gif

Cross-terms with background

- Field inhomogeneity due to microscopic and macroscopic heterogeneity in susceptibility
  - Also caused by imaging gradients and poor shimming
- Bias alleviated by antipodal-measurements and geometric averaging [1]
- Sequence/waveform designs exist to alleviate error
  - Explicit measurement + estimation [2]
  - Gradient waveform designs [3-5]



1 Neeman et al. MRM 1991; Jara et al. JMRI 1994; 3 Lawrenz et al. MRM 2019; 4 Hong et al. JMR 1992; Szczepankiewicz et al. JMR 2021

There is a lot to look out for

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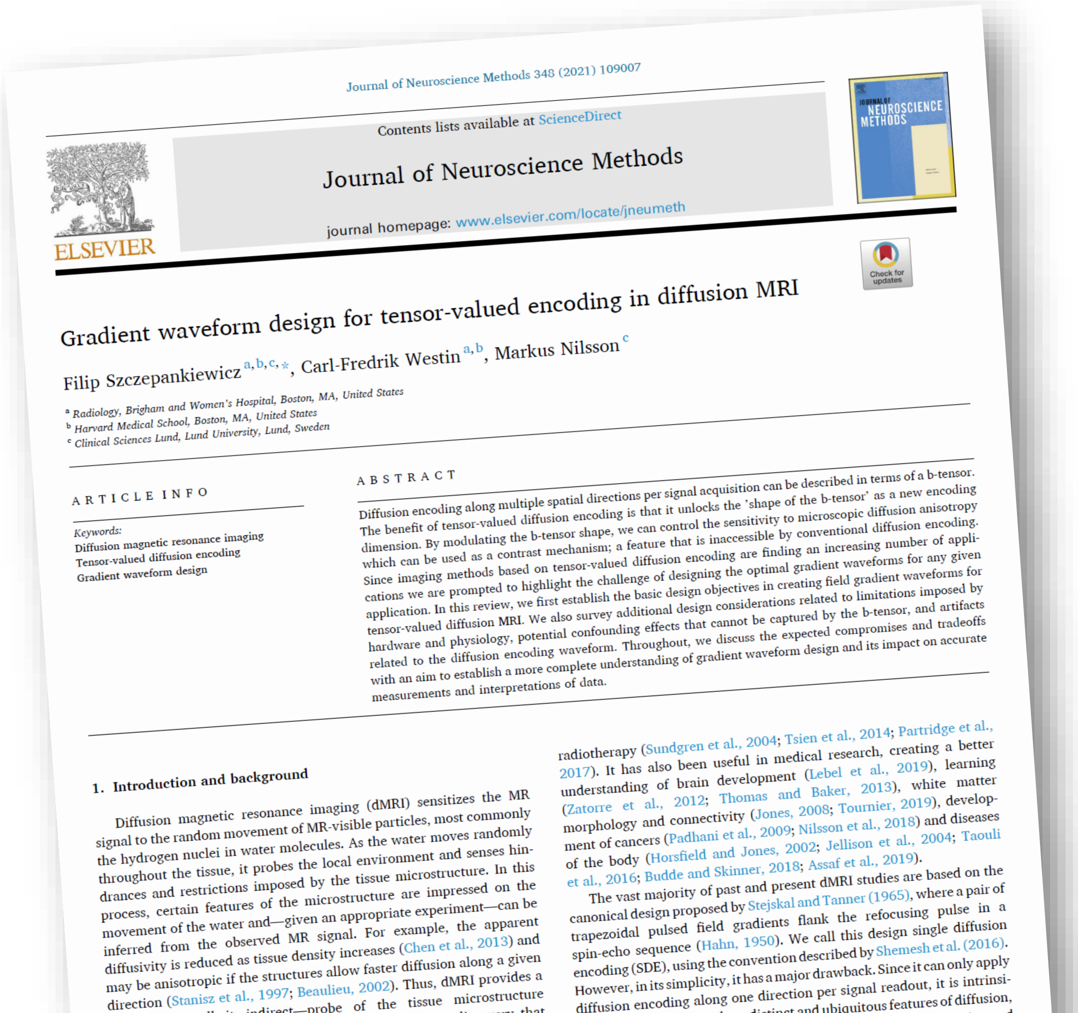

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Gradient waveform design for tensor-valued encoding in diffusion MRI

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Gradient waveform design

ABSTRACT

Diffusion encoding along multiple spatial directions per signal acquisition can be described in terms of a b-tensor. The benefit of tensor-valued diffusion encoding is that it unlocks the 'shape of the b-tensor' as a new encoding dimension. By modulating the b-tensor shape, we can control the sensitivity to microscopic diffusion anisotropy which can be used as a contrast mechanism; a feature that is inaccessible by conventional diffusion encoding. Since imaging methods based on tensor-valued diffusion encoding are finding an increasing number of applications we are prompted to highlight the challenge of designing the optimal gradient waveforms for any given application. In this review, we first establish the basic design objectives in creating field gradient waveforms for tensor-valued diffusion MRI. We also survey additional design considerations related to limitations imposed by hardware and physiology, potential confounding effects that cannot be captured by the b-tensor, and artifacts related to the diffusion encoding waveform. Throughout, we discuss the expected compromises and tradeoffs with an aim to establish a more complete understanding of gradient waveform design and its impact on accurate measurements and interpretations of data.

1. Introduction and background

Diffusion magnetic resonance imaging (dMRI) sensitizes the MR signal to the random movement of MR-visible particles, most commonly the hydrogen nuclei in water molecules. As the water moves randomly throughout the tissue, it probes the local environment and senses hindrances and restrictions imposed by the tissue microstructure. In this process, certain features of the microstructure are impressed on the movement of the water and—given an appropriate experiment—can be inferred from the observed MR signal. For example, the apparent diffusivity is reduced as tissue density increases (Chen et al., 2013) and may be anisotropic if the structures allow faster diffusion along a given direction (Stanisz et al., 1997; Beaulieu, 2002). Thus, dMRI provides a

radiotherapy (Sundgren et al., 2004; Tsien et al., 2014; Partridge et al., 2017). It has also been useful in medical research, creating a better understanding of brain development (Lebel et al., 2019), learning (Zatorre et al., 2012; Thomas and Baker, 2013), white matter morphology and connectivity (Jones, 2008; Tournier, 2019), development of cancers (Padhani et al., 2009; Nilsson et al., 2018) and diseases of the body (Horsfield and Jones, 2002; Jellison et al., 2004; Taouli et al., 2016; Budde and Skinner, 2018; Assaf et al., 2019).

The vast majority of past and present dMRI studies are based on the canonical design proposed by Stejskal and Tanner (1965), where a pair of trapezoidal pulsed field gradients flank the refocusing pulse in a spin-echo sequence (Hahn, 1950). We call this design single diffusion encoding (SDE), using the convention described by Shemesh et al. (2016). However, in its simplicity, it has a major drawback. Since it can only apply diffusion encoding along one direction per signal readout, it is intrinsi-

Thank you for listening!

Pia Sundgren

Markus Nilsson

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Swedish Research Council

Swedish Cancer Society

Royal Physiographic Society of Lund

Animations available at:

github.com/filip-szczepankiewicz/diff_enc_sim