MISST

MICROSTRUCTURE IMAGING SEQUENCE SIMULATION TOOLBOX

DOCUMENTATION

Contents

1 Introduction

Microstructure Imaging Sequence Simulation Toolbox (MISST) is a practical diffusion MRI simulator for development, testing, and optimisation of novel MR pulse sequences for microstructure imaging. MISST is based on a matrix method approach and simulates the signal for a large variety of pulse sequences and tissue models. Its key purpose is to provide a deep understanding of the restricted diffusion MRI signal for a wide range of realistic, fully flexible scanner acquisition protocols, in practical computational time.

MISST uses the 3D extension of the Matrix Method (Callaghan [1997]) presented in Drobnjak et al. [2011].

To put our method in perspective, the following table summarizes different computational methods used to compute the diffusion signal:

Computational method	Pulse sequence	Restricted diffusion substrate	Performance
Gaussian Phase Distribution (GPD) approximation	PGSE, OGSE, SWOGSE	Parallel planes, Cylinder, Sphere, Triangles (eigenvectors of the diffusion propagator are needed)	Very fast to compute; Accurate within limits
Matrix Method (MM), Multiple Correlation Function (MCF)	Any	Parallel planes, Cylinder, Sphere, Triangles (eigenvectors of the diffusion propagator are needed)	Medium fast to compute; Accurate
Monte Carlo (MC)	Any	Any	Slow to compute, especially for more complex substrates; Accurate

2 Detailed explanation

In order to generate the diffusion signal, we need to specify the diffusion pulse sequence and the tissue model.

2.1 Diffusion pulse sequence

The information about the pulse sequence is stored in a structure, commonly denoted as protocol. There are three mandatory fields needed to generate the diffusion signal:

protocol.pulseseq	**='GEN' the name of the sequence required to generate diffusion signal from discrete generalised gradients**
protocol.G	**- discrete gradient waveforms which contain the gradient components (G_x, G_y and G_z) at each point in time from the beginning of the measurement until the readout**
protocol.tau	**- time interval between two consecutive points of the gradient waveform (sampling interval)**

Optional fields:

protocol.smalldel	**- gradient duration**
protocol.delta	**- time interval between the onset of the first and second gradients**
protocol.mirror	**=0 - the 2nd gradient is the same as the 1st gradient; =1 - the 2nd gradient is the mirror of the 1st gradient**

Specifying the fields 'smalldel' and 'delta' if the diffusion sequence has two gradient intervals reduces computation time.

The gradient waveform (protocol.G) is a M x 3K matrix, where M is the number of diffusion measurements and K is the number of gradient points in one measurement.

The gradient waveform has the following structure:

meas 1:	$G_x(1)$	$G_y(1)$	$G_z(1)$	$G_x(2)$	$G_y(2)$	$G_z(2)$	...	$G_x(K)$	$G_y(K)$	$G_z(K)$
meas 2:	$G_x(1)$	$G_y(1)$	$G_z(1)$	$G_x(2)$	$G_y(2)$	$G_z(2)$	...	$G_x(K)$	$G_y(K)$	$G_z(K)$
...	...	...	...	...	...	...	...	...	...	...
meas M:	$G_x(1)$	$G_y(1)$	$G_z(1)$	$G_x(2)$	$G_y(2)$	$G_z(2)$	...	$G_x(K)$	$G_y(K)$	$G_z(K)$

For a diffusion MRI experiment the integral of the gradient at the echo time must be 0.

Note: The gradient waveform (protocol.G) should contain the effective gradient, i.e. for a PGSE sequence the second gradient is the negative of the first one. Where necessary, imaging gradients should be included for more accuracy.

Example waveforms

We provide a set of examples how to generate the discrete gradient waveforms for several diffusion sequences. The examples we offer include:

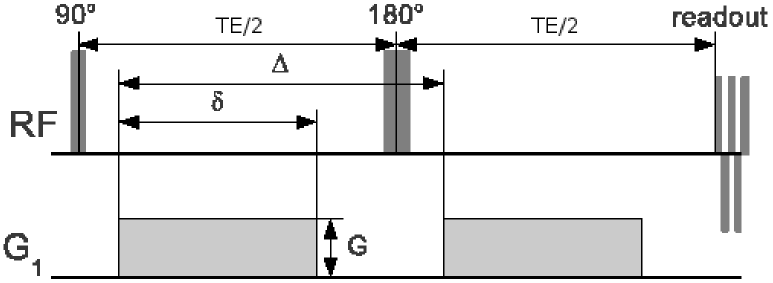
- pulsed gradient spin echo sequences (PGSE)
- sinusoidal oscillating gradients (OGSE)
- square oscillating gradients (SWOGSE)
- trapezoidal oscillating gradients (TWOGSE)
- square oscillating gradients with multiple orientations (SWOGSE_3D)
- double pulsed field gradients (dPFG)
- stimulated echo sequences (STEAM)
- helical gradients (Helical)

Note: If the sequence you are interested in is not listed here, you have to create it yourself. We show how to do this in example 2 on our web page our web page: `http://cmic.cs.ucl.ac.uk/mig//index.php?n=Tutorial.MISST`.

For these examples, the discrete gradients required to generate the diffusion signal are created as follows: `G = wave_form(protocol)`. In this case the protocol structure contains information about the sequence which is being discretised and has the following fields:

PGSE

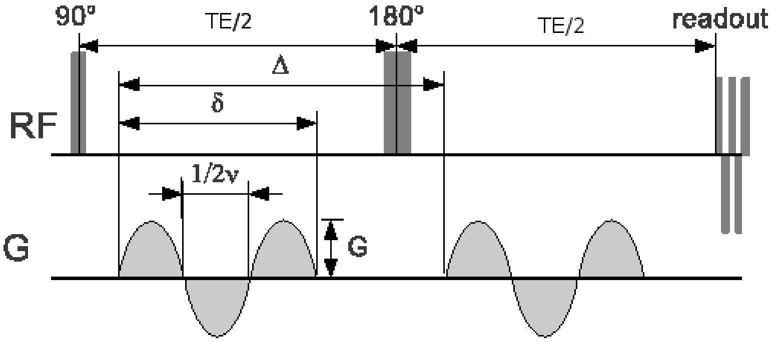
standard pulsed gradient spin echo sequence



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude	T/m
protocol.grad_dirs	direction of each gradient	unit vector
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s

OGSE

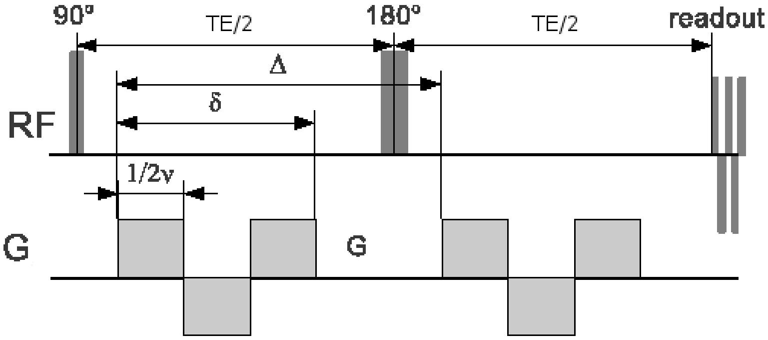
sinusoidal oscillating gradients



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude	T/m
protocol.grad_dirs	direction of each gradient	unit vector
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.omega	$= 2\pi\nu$ - gradient angular frequency	1/s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s
Optional		
protocol.phase	phase of the gradient waveform; default value 0	-
protocol.mirror	=0 - the 2nd gradient is the same as the 1st gradient; =1 - the 2nd gradient is the mirror of the 1st gradient; default value 0	-
protocol.apodisedcos	=1 - returns an apodised cosine waveform, in which the first quarter of a period is replaced by a sine wave with double frequency. This is needed for practical implementations of OGSE sequences. A detailed explanation can be found in Does et al. [2003]; This option works only if the angular frequency of the waveform corresponds to a integer number of lobes. If the phase is specified, it must be $\pi/2$ or $-\pi/2$	-

SWOGSE

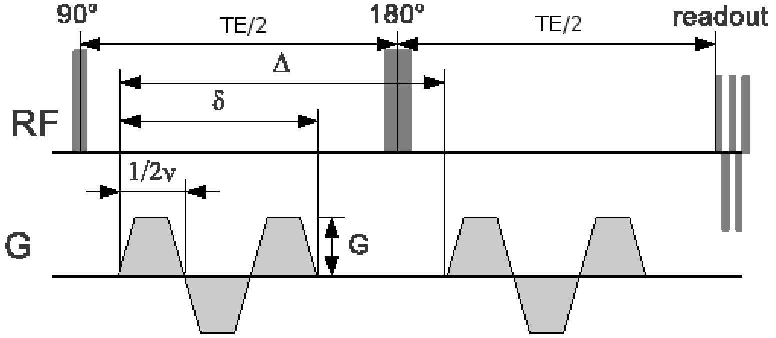
square wave oscillating gradients



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude	T/m
protocol.grad_dirs	direction of each gradient	unit vector
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.omega	$= 2\pi\nu$ - gradient angular frequency	1/s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s
Optional		
protocol.phase	phase of the gradient waveform; default value 0	-
protocol.mirror	=0 - the 2nd gradient is the same as the 1st gradient; =1 - the 2nd gradient is the mirror of the 1st gradient; default value 0	-

TWOGSE

trapezoidal wave oscillating gradients



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude	T/m
protocol.grad_dirs	direction of each gradient	unit vector
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.omega	$= 2\pi\nu$ - gradient angular frequency	1/s
protocol.slew_rate	the slew rate of the gradient	T/m/s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s
Optional		
protocol.phase	phase of the gradient waveform; default value 0	-
protocol.mirror	=0 - the 2nd gradient is the same as the 1st gradient; =1 - the 2nd gradient is the mirror of the 1st gradient; default value 0	-
protocol.apodisedcos	=1 - returns an apodised trapezoidal waveform with a slightly increased duration $\delta + rt$ and $\Delta + rt$ ($rt = G/slew\_rate$ is the rise time of the gradient). This ensures that the area of the first lobe is half the area of a full lobe in order to have a similar diffusion spectrum to a cosine waveform. A detailed explanation can be found in Ianus et al. [2012]. This option works only if the angular frequency of the waveform corresponds to a integer number of lobes. If the phase is specified, it must be $\pi/2$ or $-\pi/2$	-

SWOGSE_3D

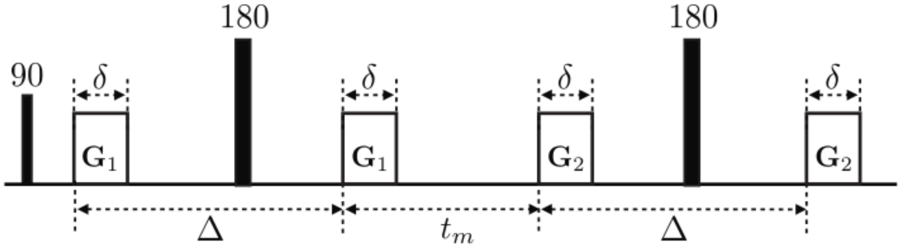
square wave oscillating gradients with different components in different directions

Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.Gx	gradient amplitude in x direction	T/m
protocol.Gy	gradient amplitude in y direction	T/m
protocol.Gz	gradient amplitude in z direction	T/m
protocol.omegax	angular frequency of the gradient in x direction	1/s
protocol.omegay	angular frequency of the gradient in y direction	1/s
protocol.omegaz	angular frequency of the gradient in z direction	1/s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s
Optional		
protocol.phix	phase of the gradient waveform in x direction	-
protocol.phiy	phase of the gradient waveform in y direction	-
protocol.phiz	phase of the gradient waveform in z direction	-

Note: If the gradient is not desired in a certain direction, then the respective gradient strength, frequency and phase should be set to 0;

dPFG

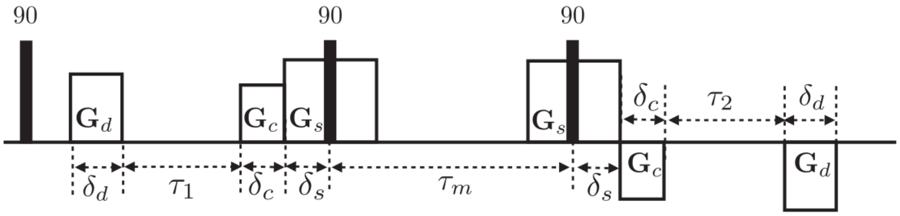
double pulsed field gradient



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude (same for both gradient pairs)	T/m
protocol.smalldel	gradient duration (same for both gradient pairs)	s
protocol.delta	duration between the onset of the first and second pulses (same for both gradient pairs)	s
protocol.tm	mixing time	s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s
protocol.theta	Angle between the first gradient direction and z axis.	-
protocol.phi	Azimuthal angle of the first gradient direction; $G_z = G \times \cos(theta); G_x = G \times \sin(theta) \times cos(phi); G_y = G \times \sin(theta) \times \sin(phi);$	-
protocol.theta1	Angle between the second gradient direction and z axis.	-
protocol.phi1	Azimuthal angle of the second gradient direction; $G_z = G \times \cos(theta1); G_x = G \times \sin(theta1) \times cos(phi1); G_y = G \times \sin(theta1) \times \sin(phi1);$	-

STEAM

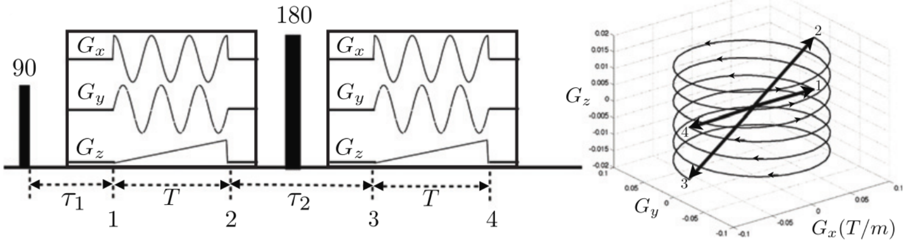
pulsed gradient with stimulated echo sequence



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	diffusion gradient amplitude	T/m
protocol.grad_dirs	direction of diffusion gradients	unit vector
protocol.Gc	crusher gradient amplitude - fixed direction along z	T/m
protocol.Gs	slice select gradient amplitude - fixed direction along z	T/m
protocol.smalldel	diffusion gradient duration	s
protocol.sdelc	crusher gradient duration	s
protocol.sdels	slice select gradient duration	s
protocol.tau1	time interval between the first diffusion gradient and crusher gradient	s
protocol.tau2	time interval between the second crusher gradient and the second diffusion gradient	s
protocol.tm	mixing time	s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s

Helical

helical gradient waveforms



Field name	Description	Units
protocol.pulseseq	the name of the sequence	-
protocol.G	gradient amplitude	T/m
protocol.smalldel	gradient duration	s
protocol.delta	duration between the onset of the first and second pulses	s
protocol.omega	gradient angular frequency: $G_x = G \times \cos(omega \times t), G_y = G \times \sin(omega \times t)$	1/s
protocol.slopez	slope of Gz: $G_z = G \times slopez \times t$	1/s
protocol.tau	sampling interval of the gradient; recommended value 1E-4 s	s

Limitations

The signal is accurate up to the level of discretization. If the imaging parameters are on the order of ms, then a sampling interval tau = 0.1 ms should be enough. However if you want to see the effect on a sorter time scale, then tau should be decreased.

2.2 Tissue models

For the diffusion substrates, we follow the naming scheme presented in Panagiotaki et al. [2012]. The following substrates are available in MISST:

Basic compartments with Gaussian diffusion:

- Ball (isotropic free diffusion)
- Zeppelin (anisotropic, cylindrically symmetric diffusion tensor)
- Tensor (full diffusion tensor)
- Stick (Unidirectional diffusion)
- AstroSticks (isotropically oriented sticks)

Basic compartments with restricted diffusion:

- Cylinder (diffusion inside a cylinder)
- AstroCylinders (isotropically oriented cylinders)

- Sphere (diffusion inside a sphere)
- Dot (no diffusion at all)

Multi-compartment models:

- ZeppelinCylinder
- TortZeppelinCylinder (same as ZeppelinCylinder, but with tortuosity constraint on volume fraction)
- TortZeppelinCylinderBall

Other substrates can be easily implemented. See Advanced section. All the information related to the diffusion substrate is stored in a structure called model. For the purpose of signal generation, model has only two fields:

model.name - the name of the model

model.params - the values of the model parameters in S.I. (m, s, etc.); the order of the parameters is the same as in the next table (top-bottom)

The next table summarizes the parameters of different models:

Model name	Parameters	Units
Ball	d - free diffusivity	m/s^2
Zeppelin	d$_{\|\|}$ - parallel diffusivity	m/s^2
	d$_h$ - hindered diffusivity	m/s^2
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
Tensor	d$_1$ - diffusivity along main direction	m/s^2
	d$_2$ - diffusivity along second direction	m/s^2
	d$_3$ - diffusivity along third direction	m/s^2
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
	ψ - angle giving the third direction of the tensor	-
Stick	d$_{\|\|}$ - parallel diffusivity	m/s^2
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
AstroSticks	d$_{\|\|}$ - parallel diffusivity along each stick	m/s^2
Cylinder	d$_{\|\|}$ - diffusivity	m/s^2
	R - cylinder radius	m
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
AstroCylinders	d$_{\|\|}$ - diffusivity	m/s^2
	R - cylinder radius	m
Sphere	d$_{\|\|}$ - diffusivity	m/s^2
	R - sphere radius	m
Dot	No parameters	-

ZeppelinCylinder	f - volume fraction of intracellular compartment	-
	$d_{\|\|}$ - parallel diffusivity	m/s^2
	d_h - hindered diffusivity	m/s^2
	R - cylinder radius	m
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
TortZeppelinCylinder	f - volume fraction of intracellular compartment	-
	$d_{\|\|}$ - parallel diffusivity	m/s^2
	R - cylinder radius	m
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-
TortZeppelinCylinderBall	f_i - volume fraction of intracellular compartment from the anisotropic part (1-fiso)	-
	$d_{\|\|}$ - parallel diffusivity	m/s^2
	R - cylinder radius	m
	f_{iso} - volume fraction of isotropic space (eg CSF)	-
	d_{iso} - parallel diffusivity	m/s^2
	θ - angle from z axis	-
	φ - azimuthal angle from x axis	-

3 Running the code

- A step-by-step guide can be found on our web page: `http://cmic.cs.ucl.ac.uk/mig//index.php?n=Tutorial.MISST`
- Run the script files corresponding to the examples shown on our web page. They are located in the folder MISST/example. RunMISST.m includes Example 1 (square waveforms) and Example 2 (random waveforms) and PublishedExamples.m includes the waveforms used in Drobnjak et al. [2011].

References

P. T. Callaghan. A simple matrix formalism for spin echo analysis of restricted diffusion under generalized gradient waveforms. *Journal of Magnetic Resonance*, 129:74–84, 1997.

M. D. Does, E. C. Parsons, and J. C. Gore. Oscillating gradient measurements of water diffusion in normal and globally ischemic rat brain. *Magnetic Resonance in Medicine*, 49: 206–215, 2003.

I. Drobnjak, H. Zhang, M. G. Hall, and D. C. Alexander. The matrix formalism for generalised gradients with time-varying orientation in diffusion NMR. *Journal of Magnetic Resonance*, 210:151–157, 2011.

A. Ianus, B. Siow, I. Drobnjak, H. Zhang, and D. C. Alexander. Gaussian phase distribution approximations for oscillating gradient spin echo diffusion mri. *Journal of Magnetic Resonance*, 227:2534, 2012.

E. Panagiotaki, T. Schneider, B. Siow, M. G. Hall, M. F. Lythgoe, and Alexander D.C. Compartment models of the diffusion mr signal in brain white matter: A taxonomy and comparison. *NeuroImage*, 59:2241–2254, 2012.