Grant agreement no. 667510

GLINT

Research and Innovation Action
H2020-PHC-2015-two-stage

D2.1 N-pool Bloch-McConnell simulation software

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Reviewers:	

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PU	Public	YES
CO	Confidential, only for members of the consortium (including the Commission Services)	
CI	Classified, as referred to in Commission Decision 2001/844/EC	

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Contents

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Version log

Version	Date	Released by	Nature of Change
V1	29/06/2016	M. Zaiss	First version

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Definition and acronyms

Acronyms	Definitions
BM	Bloch-McConnell
CEST	Chemical exchange saturation transfer
MT	Magnetization transfer

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Introduction

1.1 Background and the need

To make the best choice for both pre-saturation and MR readout of a glucoCEST MR sequence, a simulation is needed that allows for predicting CEST signal intensities for different setups. At the same time here glucose –OH exchange rates and system parameters flow in that can also be fitted using this simulation and experimental in vitro data.

1.2 Objectives

To simulate the glucoCEST signal 4 problems have to be solved:

1. The signal recovery during a delay time must be simulated
2. The signal behavior of exchanging pools upon pulsed RF irradiation must be simulated
3. The signal behavior during an MR readout must be simulated
4. The actual relaxation and exchange properties of the pool system must be estimated

Steps 1-3 are displayed in figure 1 and can be realized using the N-pool Bloch-McConnell equations with and without RF irradiation.

Step 4 is actually a goal of the whole GLINT project and an initial as well as an improved estimation of glucose CEST pool parameters must be fed back from experiments. Using the given simulation in here, these glucose CEST pool parameters can also be determined from experimental data.

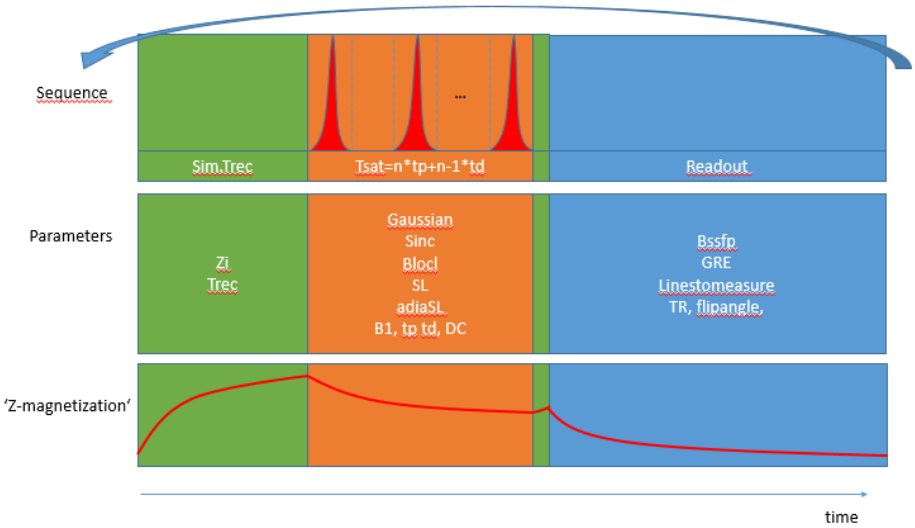

Figure 1: *Visualization of the sequence scheme, possible Parameters and dynamic of Z-magnetization during relaxation delay, pulsed RF saturation and MR readout phase in a typical (Gluco-) CEST experiment.*

1.3 Position of D2.1 in the project

The Bloch-McConnell simulation allows for quantitative characterization of glucose exchange processes. Using these outcomes different saturation scheme can then be simulated for optimizing the effect and use this a s a first step for a real MR sequence. In the end, in vivo measurements have to tell what's the best protocol.

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Methodology and Approach

1. Free and driven magnetization dynamics

The generated Bloch-McConnell simulation is based on the code provided by Shanrong Zhang published in **Woessner, D. E., Zhang, S., Merritt, M. E. and Sherry, A. D. (2005), Numerical solution of the Bloch equations provides insights into the optimum design of PARACEST agents for MRI. Magn Reson Med, 53: 790–799. doi: 10.1002/mrm.20408**. It was extended for multiple pools, including semi-solid MT, and pulsed RF saturation.
Find more in the attached document: **BM_Documentation.docx.**
This allows to generate the principal signal behavior upon RF saturation, MR readout and relaxation delay as shown in figure 1.

2. Pool parameters

Grey and white matter MT and water pool relaxation parameters were taken from **Stanisz, G. J., Odrobina, E. E., Pun, J., Escaravage, M., Graham, S. J., Bronskill, M. J. and Henkelman, R. M. (2005), T_1, T_2 relaxation and magnetization transfer in tissue at 3T. Magn Reson Med, 54: 507–512. doi: 10.1002/mrm.20605**
The pool parameters estimated from a first cw glucoCEST experiment (100mM glucose in PBS => f=0.1/111=0.0009 per –OH) were for each of the 5 hydroxyls (pools B, D, E, F, G).

```
case 'glucose'
        % Pool B
        Sim.dwB=2;
        Sim.R2B=66.66;
        Sim.fB=0.0045;
        Sim.kBA=5000;
        % Pool D
        Sim.dwD=2.2;
        Sim.R2D=66.66;
        Sim.fD=0.0009;
        Sim.kDA=500;
        % Pool E
        Sim.dwE=2.8;
        Sim.R2E=66.66;
        Sim.fE=0.0009;
        Sim.kEA=1000;
        % Pool F
        Sim.dwF=0.6;
        Sim.R2F=66.66;
        Sim.fF=0.0009;
        Sim.kFA=5000;
        % Pool G
        Sim.dwG=1.2;
        Sim.R2G=66.66;
        Sim.fG=0.0009;
        Sim.kGA=5000;
```

These are not yet the final in vivo parameters and this must be adjusted during the whole GLINT project.

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Report Activities carried-out and results

Optimization of glucoCEST

Using the parameters given in the previous section sequence parameters can be varied. For this system we simulated the glucoCEST in white matter upon saturation using a train of n conventional off-resonant spinlock pulses for the field streghts 9.4T (dots in Fig. 2) and 3T (crosses in Fig. 2).
A first estimation of the optimal saturation parameters is given by (Figure 2):
At 9.4 T: B1 =3.2 µT, Trec=2.5 s, n=5, DC=70%
At 3 T: B1 =1.5 µT, Trec=2.5 s, n=7, DC=70%
Thus, due to spillover effects the optimal power at 3T is much lower than at 9.4T. Thus, due to lower labeling, also the maximum effect strength is approximately 2.5 times smaller for 3T than for 9.4T. This does not yet include the SNR gain for the readout at 9.4T.

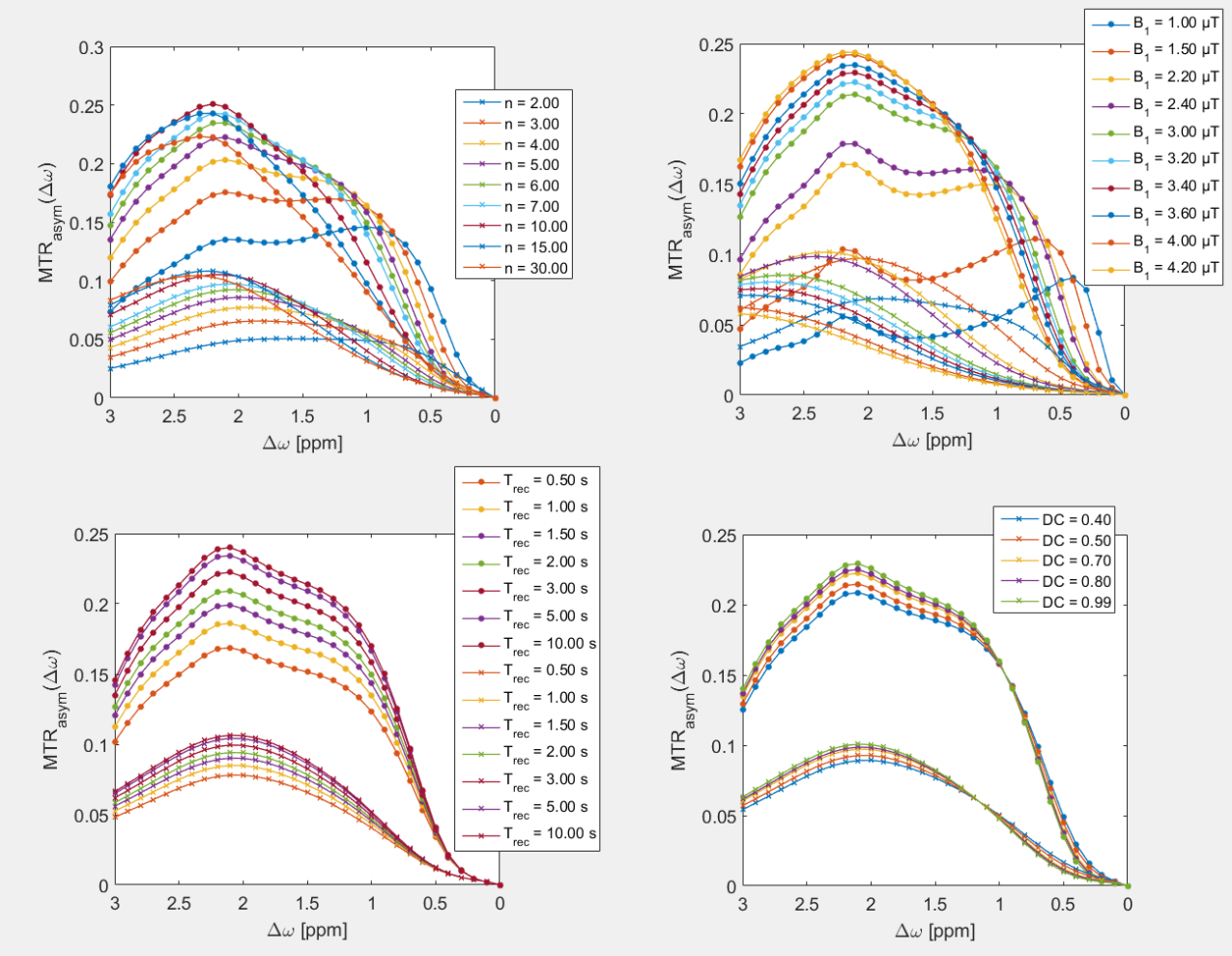

Figure 2: GlucoCEST RF and relaxation parameter optimization at field strengths 9.4T (dots) and 3T (crosses).

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Conclusions

With this code a framework is established to optimize the glucoCEST signal. CEST pool parameters have to be determined more accurately especially in the in vivo condition of injected glucose. Then simulation and experiments can be run iteratively to finally globally optimize the glucoCEST sequence. The whole simulation with documentation is published under GPL online on the website www.cest-sources.org as well as on github: https://github.com/cest-sources/BM_sim_fit.

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