Quantum control for magnetic resonance spectroscopy

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Aim

In-vivo identification of biomarkers and metabolites with MRI/S is an extremely challenging task:

- Spectral peaks frequently overlap making it difficult to differentiate certain metabolites in the spectrum.
- Various sources of noise in MRI add unclarity to the spectrum, leading to broadening and shifting of peaks, and low signal levels being lost to background noise.

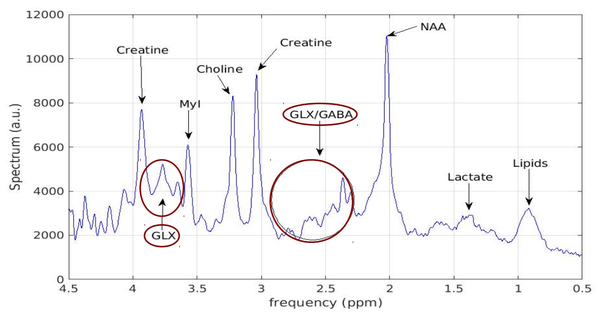


Figure 1 : Example MRS spectrum, displaying the difficulty of individual identification, Glutamine – Glutamate are commonly grouped together as 'Glx' as they are not individually resolvable in many cases. .

Quantum control provides methods to selective excite specific proton groups in molecules. This can be exploited to avoid overlap of peaks in the spectra and clearly assign individual peaks to molecules. Moreover, pulses can be found that are robust to a range of noise sources.

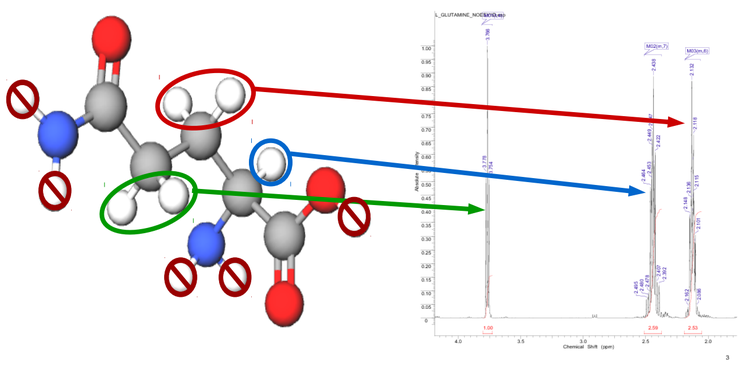


Figure 2: structure of Glutamine and the contributions of protons to resulting FID spectrum [1]. Some have been ignored here, as their resonances are much higher than the usual spectroscopy range

Conventional MRS

Magnetic resonance spectroscopy (MRS), is an analytical technique for analysing the composition of tissue. Spectra are created by exciting all protons with a 90 RF pulse, recording the returning RF signal, and performing a Fourier transform on it. The frequency components of the returning signal can be roughly decomposed into individual contributions from a wide range of molecules. However, due to numerous noise sources, scanner uncertainties, relaxation and overlap between molecule spectrum, this poses an additional challenge to combat.

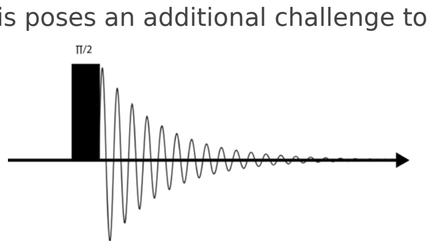


Figure 3 : A basic free induction decay (FID) pulse sequence, a 90° excitation pulse followed by a readout [2].

We aim to excite selected protons of interest per metabolite, leaving those which produce undesirable spectroscopy characteristics, producing no signal. This is achieved by computing a new excitation pulse using optimal control techniques. This exploits the quantum nature of the molecules, driving more complex dynamics that excite only the desired proton groups.

Method

Metabolite sets are manually chosen, we are initially using Glutamine, Glutamate and GABA,Creatine as these propose difficult and medically relevant targets. Target states are also manually selected, attempting to achieve peaks which are maximally apart for a set of metabolites.

Target states represent which protons are selected for excitation. Simulation is done using a Hamiltonian model, in the Lindblad equation to enable a fully dissipative simulation, models are based upon well known J-Coupling and Chemical Shift data [3]. Simulation of the full spin ensemble is computationally expensive but necessary, as the hyper-fine structure of the molecules can be utilised by the optimisation when producing complex pulse sequences. Control update during optimisation is performed concurrently, using a gradient based algorithm to modify the excitation pulse[4]. Pulse shape and duration is initially randomly generated before optimisation. Scanner uncertainties and noise sources are integrated into the target function, to allow for a range of B0 and B1 instabilities. Performance in the presence of relaxation is assessed post-optimisation.

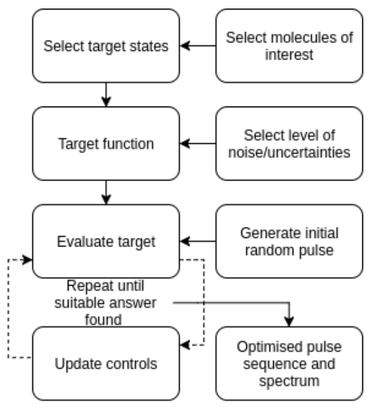


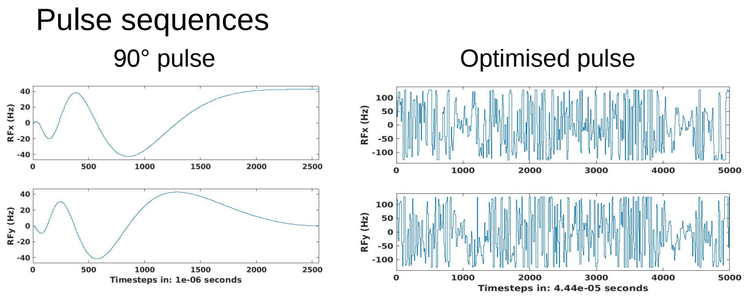
Figure ? : Program flow, optimisation loop terminates when convergence falls below a tolerance level.

Glutamine-Glutamate Results

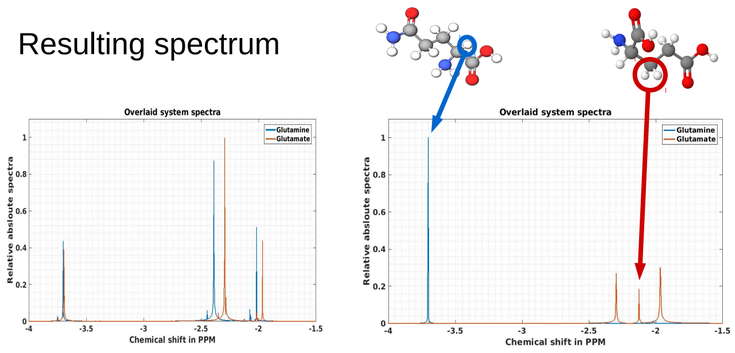
Pulse sequences

90° pulse

Optimised pulse

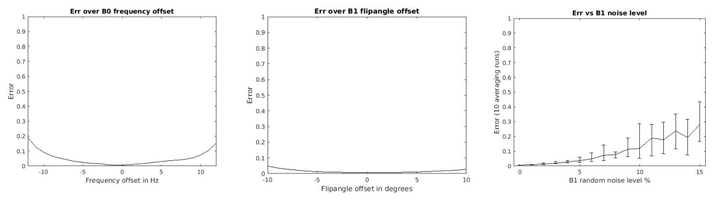


Resulting spectrum



Above: Comparison of a 90° excitation pulse (left) and an optimised pulse(right). Optimised pulse is stable to 10Hz B0, 10° flip angle T=222ms.

Stability



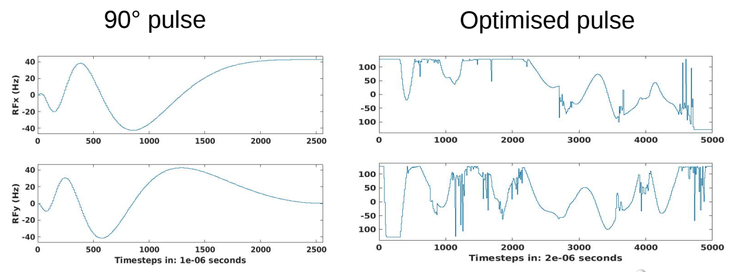
Left: B0 frequency offset versus error. Middle: B1 flip-angle offset versus error. Right: B1 white noise level vs error order 10 averaging runs. Error is (1-fidelity), where an error of 0 would represent a perfect match between target state and actual state produced by the pulse sequence. A flatter landscape represents a more stable pulse.

Glutamine-Glutamate proposes a extremely difficult target, as the structure of the molecules is very similar. However, this technique is able to utilise the structure of the molecules to find an appropriate control, which is relatively stable to B0 and B1 uncertainties

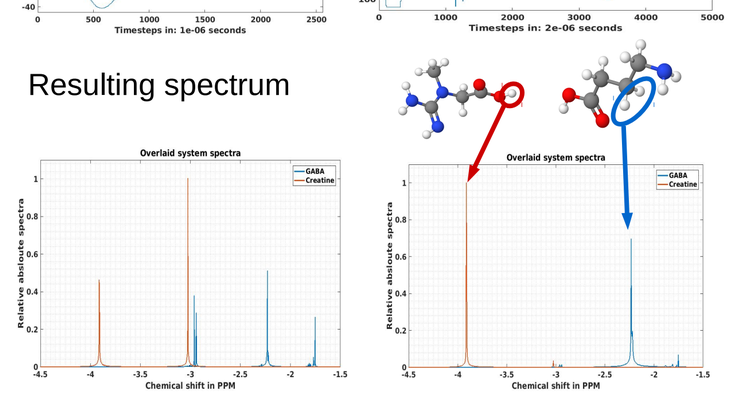
GABA-Creatine Results

90° pulse

Optimised pulse

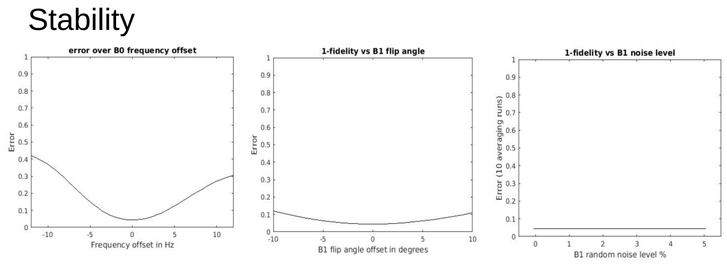


Resulting spectrum



Above: Comparison of a 90° excitation pulse (left) and an optimised pulse (right). Optimised pulse is stable to 10Hz B0, 10° flip angle T=3ms.

Stability



Left: B0 frequency offset versus error. Middle: B1 flip-angle offset versus error. Right: B1 white noise level vs error order 10 averaging runs.

GABA-Creatine proposes a different challenge, with Creatine not fully controllable. The pulse produced here is extremely short at 3ms.

Applications

- Glutamine-Glutamate concentration comparison
- Creatine – GABA – NAA resolve
- Metabolite suppression: e.g. remove the ~2ppm NAA peak
- Shorter, more accurate, robust broadband excitation pulses

Conclusion

Quantum control can be utilised successfully to find pulse sequences to enable molecule differentiation, even if their FID spectrum overlap. Furthermore, pulses can be produced that are robust to a range of B0 and B1 uncertainties and relaxation. This method can be applied to a larger range of metabolites, with available computing power the current limitation.

Advantages of this method:

- Enables molecule concentration comparison
- Robust to scanner uncertainties
- Shorter, lower energy pulses are achievable

Next steps:

- Improving scanner calibration algorithms (shim and flip angle)
- Different / larger range of metabolites (NAA/GABA/Creatine - **tell us what you want to see!**)

References and Acknowledgements

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