

# Uncertainty Volume Analysis - A Measure for Protocol Performance

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## Motivation:

The amount of information that is extracted by a MRI protocol is usually determined by error analysis based on standard deviations that are very specialized and only applicable to a very limited family of problems. Each parameter that is subject to quantification is commonly acquired using a dedicated protocol with specifically optimized sequence parameters<sup>1</sup>. The model fitting process becomes more complex and intransparent as the model complexity increases, possibly leading to a poor choice of sequence parameters, misinterpretation of error sources, bias, or the need for numerous acquisitions – especially when the parameters cannot be investigated separately. A measure for sequence performance, adjustable to the specific context, is highly desirable for protocol optimization, the optimization of the information extraction process, the investigation of image quality and error source analysis.

The MR Fingerprinting approach<sup>2</sup> aims to optimize the model parameter extraction by simulation-supported optimization of a sequence. Inversely, the approach presented here reveals and quantifies the distinguishability of model parameters in a collection of sequences that is given.

Since model parameters and optimization strategies are plentiful, a measure for sequence performance should be applicable without imposing more restrictions on the sequences and models as urgently needed. This work suggests a workflow to quantify information content and rate sequences by their contribution to the information density of the protocol.

## Method:

For a given model parameter domain (e.g. T1, T2, proton density), the signal response of a collection of sequences was calculated. For images acquired with these sequences, equally weighted squared residuals were used for parameter fitting and following uncertainty analysis. Based on the voxel-specific range of objective function value, an uncertainty threshold was determined and the resulting uncertainty volume is then used as a measure of sequence collection performance for the given model parameter problem and fitting process. The optimization routine is based on the simulated annealing algorithm<sup>3</sup> since it is able to cope with local minima, non-continuous objective functions and is insensitive to initial values. The uncertainty volumes are the results of a 3D region grow starting at seeds acquired by the optimization algorithm with the capped objective function. The decision to use the simulated annealing algorithm in this step allows for a correct volume, even in the presence of disconnected components. Consequently, the algorithm is robust and can be expected to produce correct results even for very ill-behaved objective functions, allowing for careful investigation of future optimization routines that aim to speed up this method.

## Application:

The algorithm was applied to a protocol consisting of 30 TSE sequences with varying TE, TR, refocusing flip angle, turbo factor, the usage of an inversion pulse and TI. The signal responses to the model parameters were generated using a previously described algorithm<sup>4</sup>. Corresponding brain images were acquired on a clinical 3T system (Magnetom Skyra, Siemens Healthcare, Erlangen, Germany). To find the sequences that contribute most to the information content with respect to the optimization at hand, the uncertainty volume measure was calculated while removing the contribution of each one of the images. The image with the worst uncertainty volume performance - the one that leads to the best performance of the remaining sequences - was then eliminated iteratively, yielding a ranking of the sequence performance for the optimization problem.

## Results:

The algorithm was able to identify the sequences with the most diverse signal responses for the measured tissue types; the four most relevant sequences

- TurboFactor=7, TE=25 ms, TR=3000 ms,  $\alpha_{\text{Refoc}}=180^\circ$ , no inversion
- TurboFactor=7, TE=87 ms, TR=3000 ms,  $\alpha_{\text{Refoc}}=180^\circ$ , no inversion
- TurboFactor=34, TE=60 ms, TR=1200 ms,  $\alpha_{\text{Refoc}}=120^\circ$ , TI=900ms
- TurboFactor=7, TE=12 ms, TR=2000 ms,  $\alpha_{\text{Refoc}}=180^\circ$ , no inversion

were sufficient for generating the parameter maps [A-C]. The uncertainty volume map [D] gives hints about the tissue types that might be poorly fitted. Further analysis of the uncertainty volume shape at specific voxels reveals the nature of this uncertainty [E-F]. In these pictures ([E-F]) the volume of the top 1% possible objective function value range is displayed (T1 and T2 range from 0ms to 4000ms, M0 ranges from 0 to the observed maximum). The ranking was robustly reproducible.

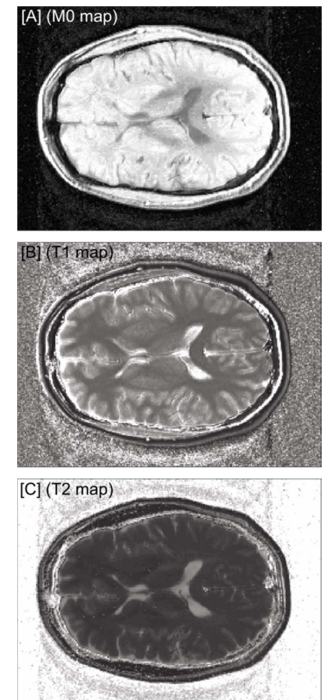
## Discussion:

The presented algorithm is a useful tool for measuring the performance of a combination of sequences for model parameter extraction, ranking the interplay of the combined sequences that are not required to be of the same sequence family. It does so by providing a novel contrast that depends on the optimization routine and can further explain the nature of the uncertainty by revealing the shape of the uncertainty voxel-specifically, unlike standard deviations. It does not depend on simplifications or approximations and can be applied to a large set of optimization problems, it also does not require specific sequence types or model parameter domains, not even the exclusiveness of MRI measurements – given a suitable model.

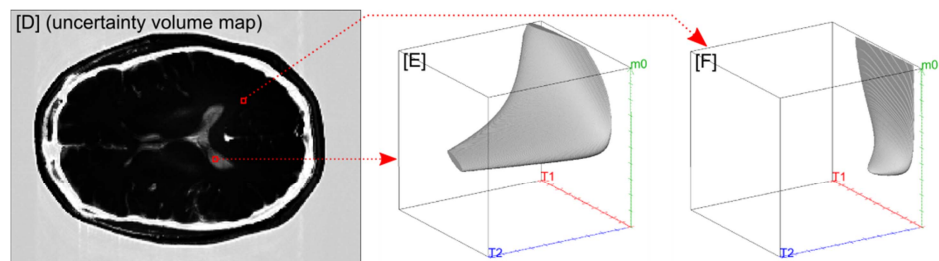
This method can be further improved to develop more meaningful measures for information density. Following this approach, it is possible to judge the absolute information content with respect to a given model and suggest a sequence to reduce the uncertainty efficiently.

## References:

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2. Ma D, et al. Magnetic Resonance Fingerprinting. Nature 2013;495:187-192.
3. Kirkpatrick S, et al. Optimization by Simulated Annealing. Science 1983;220:671-680.
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**Figure [A-C]:** Parameter maps using only the four best-performing sequences.



**Figure [D]:** Uncertainty volume map of the parameter maps [A-C].

**Figure [E]:** The error volume shape reveals a significant T2 influence of the uncertainty at the indicated voxel, suggesting the need for a sequence that increases T2 distinguishability.

**Figure [F]:** The error volume at this voxel is much smaller and suggests the reliability at this specific position.