

# Accelerated reconstruction of dictionary-based $T_2$ relaxation maps based on dictionary compression and gradient descent search algorithms

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## ABSTRACT

### Background

Quantitative  $T_2$ -relaxation-based contrast maps have shown to be highly beneficial for clinical diagnosis and follow-up. The generation of quantitative maps, however, is impaired by long acquisition times, and time-consuming post-processing schemes. The EMC platform is a dictionary-based technique, which involves simulating theoretical signal curves for different physical and experimental values, followed by matching the experimentally acquired signals to the set simulated ones.

### Purpose

Although the EMC technique has shown to produce accurate  $T_2$  maps, it involves computationally intensive post-processing procedures. In this work we present an approach for accelerating the reconstruction of  $T_2$  relaxation maps.

### Methods

This work presents two alternative post-processing approaches for accelerating the reconstruction of EMC-based  $T_2$  relaxation maps. These are (a) Dictionary compression using principal component analysis (PCA) and (b) gradient-descent search algorithm. Additional acceleration was achieved by finding the optimal MATLAB C++ compiler. The utility of the two suggested approaches was examined by calculating the relative error, produced by each technique.

### Results

Gradient descent method was in perfect agreement with the ground truth exhaustive search matching process. PCA based acceleration produced root mean square error (RMSE) of up to 4% compared to exhaustive matching process. Overall acceleration of  $\times 16$  was achieved using gradient descent in addition to  $\times 7$  acceleration by choosing the optimal MATLAB C++ compiler.

### Conclusions

Postprocessing of EMC-based  $T_2$  relaxation maps can be accelerated without impairing the accuracy of the ensuing  $T_2$  values.

## 1. Introduction

MRI's transverse ( $T_2$ ) relaxation time is one of the most commonly used contrast mechanisms for diagnosis and prognosis of pathologies. This relaxation mechanism is most-commonly utilized in a qualitative manner, involving visual assessment of contrast-weighted images. Quantitative mapping of  $T_2$  relaxation times has also shown to be useful for the diagnosis of pathologies including neurodegenerative diseases

[1–3] cancer [4–6], impaired hip and knee cartilage [7–12], imaging of stroke [13], assessment of diseased and post-transplant myocardial edema [14,15], and investigation of muscle physiology [16]. Quantitative  $T_2$  mapping ( $qT_2$ ) offers several advantages. First, it provides the flexibility to generate any level of  $T_2$  contrast offline [17,18]. Second,  $qT_2$  offer higher sensitivity to subtle tissue changes, allowing to detect pathology in an otherwise normal-appearing tissues [3,19,20]. Third, and no less important, is the scalability of the measured values, which are stable across scanners and scan settings, and thus allow easier

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### Nomenclature

MESE	multi-echo-spin-echo
SE	spin-echo
EMC	echo-modulation-curve
$qT_2$	quantitative $T_2$
ETL	echo train length
ROI	region of interest
PD	proton density

longitudinal and multi-center studies [21].

Notwithstanding the proven utility of  $qT_2$ , this technique is still underutilized due to the difficulties of reliably quantifying this relaxation time. These include the extensive scan times associated with single spin-echo (SSE) acquisitions [20–24] (ca. 1-h scan for clinically relevant spatial-resolutions), and the contamination of rapid multi-echo spin-echo (MESE) protocols by stimulated echoes (STEs) [21,25–27]. These lead to significant overestimation of  $T_2$  values when using a theoretical exponential fitting [25,28], a bias which is moreover not constant as it depends on the scanner and scan parameters being used [20,21,25,28].

Several approaches have been developed for accurate mapping of  $T_2$  values at clinically-relevant scan times. One class of techniques relies on steady state free precession protocols such as inversion recovery TrueFISP [29] and DESPOT2 [30], to avoid contamination of MESE signals by STEs. These protocols are characterized by relatively short scan times on expense of higher sensitivity to main field ( $B_0$ ) inhomogeneities and reduced  $T_2$  encoding quality vs. spin-echo based protocols [25,29,31–33]. The Extended Phase Graph (EPG) algorithm is another useful technique, developed specifically for modeling MESE STEs by tracking all the coherence pathways along the MESE echo train, while also accounting for imperfect slice profiles [22,30,34–36]. Recently, extensive research has been done regarding the use of dictionary-based signal processing techniques such as magnetic resonance fingerprinting (MRF) [37], and the echo modulation curve (EMC) algorithm [25]. Previous reports have shown the superiority of Bloch-equation based fitting for mapping  $T_2$  values [22], as well as the accuracy and reproducibility of the EMC technique across different scan settings [19,32–34,38]. This advantage can be attributed to the fact that methods like the EMC algorithm incorporate the specific protocol implementation and experimental parameter values into its reconstruction process [3]. Notwithstanding their short scan times, these dictionary-based techniques involve intensive data post-processing procedures, as they require matching the experimental signal from each voxel to each dictionary element, in order to find the best fit between theoretical and experimental data. These exhaustive search procedures are often too time-consuming for realtime processing, thereby hindering the integration of such techniques in clinical settings.

Several techniques have been proposed for accelerating the reconstruction of MRF-based parameter mapping. These may be divided to two classes. The first altogether avoids the use dictionaries by relying on iterative data-driven parameter estimation (Kalman's filter [39]), on nonlinear regression models [40], or based on machine/deep-learning approaches [41–45]. These offer a twofold advantage of skipping the dictionary creation and fitting process – both of which involve computationally intensive procedures. The second class is based on accelerating the dictionary matching process, either through dimensionality reduction of MRF data using singular value decomposition (SVD) [46], low-rank approximation [47], and compressed sensing [48,49]; using fast group matching procedures [50]; or using strong GPU-based computational power [51].

In this work we investigate two approaches for accelerating dictionary-based reconstruction of MESE data. The first approach is to reduce the dimensionality of the search space using dictionary

compression based on principal component analysis (PCA) [52,53]; and the second approach improves the efficiency of the dictionary-matching procedure using a gradient descent (GD) search scheme. Improvement in reconstruction times are presented for each approach, demonstrated on in vivo brain and calf data.

## 2. Material and methods

### 2.1. MRI scans

MRI scans were performed on a whole-body 3 Tesla MRI scanner (Prisma, Siemens Healthineers). Brain and calf scans of two healthy volunteers were performed under the approval of the ethics committee at Sheba Medical Center, Ramat Gan, Israel. Calf muscles of a genetically-confirmed dysferlinopathy patient were scanned at the Center for Magnetic Resonance in Biology and Medicine, Marseille, France. The patients' protocol was approved by the local ethics committee (Comité de Protection des Personnes Sud Méditerranée I).

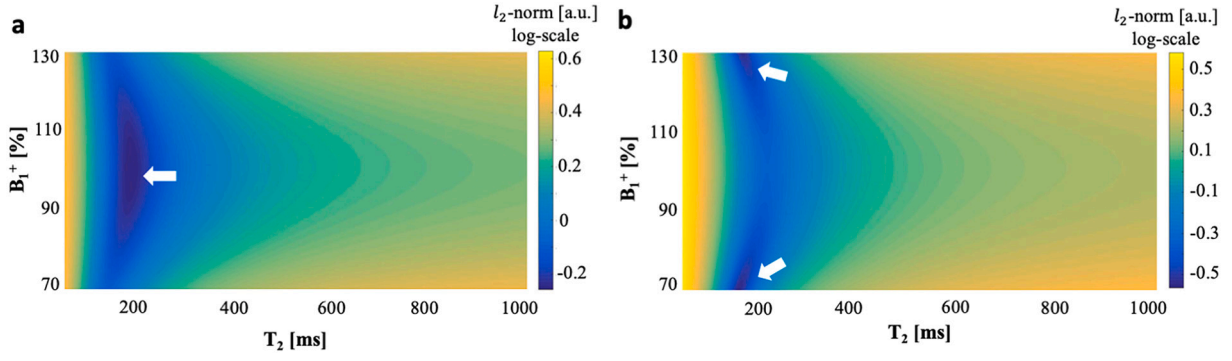
Experimental quantitative  $T_2$  data were acquired using a multi-echo spin-echo (MESE) protocol. Brain scans used a 24-channel receiver coil, and the following experimental parameters: TR/TE = 4072/15 ms, slice thickness = 3 mm, number of slices = 26, acquisition bandwidth = 200 Hz/Px,  $N_{\text{Echoes}} = 10$ , field-of-view =  $220 \times 206 \text{ mm}^2$ , matrix size =  $128 \times 120$ . Healthy subjects' calf scans used a flexible 4-channel receive coil and 4 additional coils embedded in the scanner bed, with the following experimental parameters: TR/TE = 3000/10 ms, slice thickness = 4 mm, number of slices = 5, acquisition bandwidth = 200 Hz/Px,  $N_{\text{Echoes}} = 25$ , field-of-view =  $120 \times 180 \text{ mm}^2$ , matrix size =  $106 \times 160$ . Patients' calf scan was performed on a 1.5 Tesla whole-body MR scanner (Siemens Healthineers), using the following experimental parameters: TR/TE = 2500/8.7 ms, slice thickness = 10 mm, number of slices = 5, acquisition bandwidth = 434 Hz/Px,  $N_{\text{Echoes}} = 17$ , field-of-view =  $192 \times 192 \text{ mm}^2$ , matrix size =  $128 \times 128$ .

### 2.2. Data pre-processing: generation of the EMC dictionary

Quantitative  $T_2$  maps were generated using the EMC algorithm described in [25] and summarized in Appendix A. All procedures were programmed in-house using MATLAB (The MathWorks Inc., Natick, MA), and C++ code compiled to a MATLAB MEX file using the MinGW64 compiler. The EMC algorithm consists of an initial pre-processing stage, in which Bloch simulations of the prospective MESE protocol are performed using the exact RF pulse shapes and other experimental parameter-values used on the MRI scanner. This allows to simulate the actual MESE  $T_2$  decay curve and produce  $T_2$  values that are invariant to the particular choice of scanner and scan settings. Simulations are repeated for a range of  $T_2$  relaxation values and transmit-field ( $B_1^+$ ) inhomogeneity levels ( $T_2 = 1 \dots 1000 \text{ ms}$ ,  $B_1^+ = 70 \dots 130\%$ ), producing dictionary of echo modulation curves (i.e., EMC's), each associated with a unique  $[T_2, B_1^+]$  pair.

### 2.3. Data post-processing: generation of quantitative $T_2$ relaxation maps

Once experimental data is acquired, the signal time-series at each voxel is matched to the dictionary of simulated EMCs, by minimizing the  $l_2$ -norm of the difference between experimental and simulated curves  $\|EMC_{\text{exp}} - EMC_{\text{sim}}\|_2$ . Once a match is found, a unique  $T_2$  value associated with the matched EMC is assigned to the corresponding voxel. Repeating this process for all voxels, yields the desired parametric map. Next, proton density (PD) maps are calculated by extrapolating the image from the first echo time to time  $t = 0$ , based on the calculated  $T_2$  map, under the assumption that purely exponential decay takes place between excitation and the first TE. This assumption is based on the fact that stimulated echoes affect MESE signals only from the second echo and on, while the first echo includes only spins that underwent perfect refocusing.



**Fig. 1.** Graphical representation of the  $l_2$ -norm space of a single voxel with respect to the EMC fitting dictionary. Two-dimensional surf plots show the  $l_2$ -norm values over the dictionary of EMCs for two representative voxels. (a)  $l_2$ -norm space for a voxel where  $B_1^+$  is homogenous resulting in a single minimum point. (b)  $l_2$ -norm space for a voxel where  $B_1^+$  is inhomogeneous (e.g.  $B_1^+ \pm \Delta B_1^+$ ), leading to two local minima, and only one global minimum point.

The above fitting process can be implemented using an exhaustive search over the set of  $N_{T_2} \times N_{B_1^+}$  dictionary entries ( $\sim 10,000 \dots 20,000$  elements). Calculation of the  $l_2$ -norm of each element also depends on the MESE echo train length (ETL), which eventually leads to extensive reconstruction times. To overcome this limitation, we investigated two different acceleration approaches: PCA compression of the EMC dictionary and experimental data, and optimized traversal of the dictionary search space using a GD search scheme.

#### 2.4. Accelerated reconstruction using PCA compression

SVD is a mathematical factorization method for real or complex matrices. Every matrix  $A \in \mathbb{C}^{n \times m}$  can be written using the SVD as:

$$A = U \Sigma V^* \quad (1)$$

where  $U \in \mathbb{C}^{n \times n}$  and  $V \in \mathbb{C}^{m \times m}$  are real or complex unitary matrices, and  $\Sigma \in \mathbb{R}^{n \times m}$  is a diagonal matrix with nonincreasing and nonnegative real numbers, which are the singular values  $\sigma_1, \dots, \sigma_{\min(n,m)}$  of the matrix  $A$ . The columns of  $U$  are denoted as  $u_1, \dots, u_n$  and the columns of  $V$  are denoted by  $v_1, \dots, v_m$ .

One of the common applications of SVD, is to approximate  $A$  using a matrix  $A^{(r)}$  with lower dimensions. An  $r$ -rank approximation of  $A$ , where  $r \leq \min(n, m)$ , is produced by truncating  $U$  and  $V$ , and using only the first  $r$  columns of  $U$  and  $r$  rows of  $V^*$ , corresponding to the  $r$  largest singular values. This can be written as

$$A^{(r)} = \sum_{i=1}^r \sigma_i u_i v_i^* \quad (2)$$

The energy of a matrix  $A$  is then defined by

$$E = \sum_{i=1}^{\min(m,n)} \sigma_i^2 \quad (3)$$

and the *energy ratio* represents the energy conserved in the  $r$ -truncation of the matrix, defined by

$$E(r) = \frac{1}{E} \sum_{i=1}^r \sigma_i^2 \quad (4)$$

The energy ratio is an important criterion for choosing the truncation rank  $r$ , so as to retain most of the energy from the original matrix  $A$ . The implementation of PCA as part of a reconstruction procedure is similar to the pattern recognition problem of facial recognition using SVD [54]. In the context of this work, we apply SVD to the dictionary  $D$  of simulated EMCs

$$D = U \Sigma V^* \quad (5)$$

where  $U \in \mathbb{R}^{(N_{T_2} \times N_{B_1^+}) \times (N_{T_2} \times N_{B_1^+})}$ ,  $V \in \mathbb{R}^{N_{ETL} \times N_{ETL}}$ ,  $\Sigma$  is as described before, and  $D \in \mathbb{R}^{(N_{T_2} \times N_{B_1^+}) \times N_{ETL}}$  is a dictionary with rank  $d$ . The truncated dictionary can then be written as

$$D \approx D^{(r)} = U_r \Sigma_r V_r^* \quad (6)$$

with  $r \leq d$ . An important property of the SVD is that the right singular vectors form an orthonormal basis for the rows of  $D$ . Thus, each entry from the original dictionary can be written as linear superposition of these orthonormal vectors, allowing to express the dictionary in a lower-dimensional space  $C^r$  according to

$$D^{(r)} = D V_r \quad (7)$$

The same compression can be applied to the experimental signals using the truncated  $V_r$  matrix,

$$EMC_{exp}^{(r)} = EMC_{exp} V_r \quad (8)$$

This being done, the exhaustive procedure of matching experimental and theoretical curves can be done using the compressed dictionary and data. Total computation time includes, in this case, the time required for data compression and for the matching process. The PCA process itself requires  $r \times ETL \times N_{voxels}$  operations, while number of computations required for  $T_2$  matching process is  $N_{T_2} \times N_{B_1^+} \times r \times N_{voxels}$  vis-à-vis the original matching process which costs  $N_{T_2} \times N_{B_1^+} \times N_{ETL} \times N_{voxels}$ . The number of computations is thus reduced by a factor of  $\sim \frac{ETL}{r}$ .

#### 2.5. Accelerated reconstruction using gradient descent (GD) search scheme

GD is a first-order optimization algorithm for finding local minimum of a differentiable function. This technique minimizes an objective function  $F(x)$ , parameterized using  $x \in \mathbb{R}^d$ , by updating the parameters in the negative gradient direction of  $F$  using  $\nabla_x F(x)$ . Optimization then follows

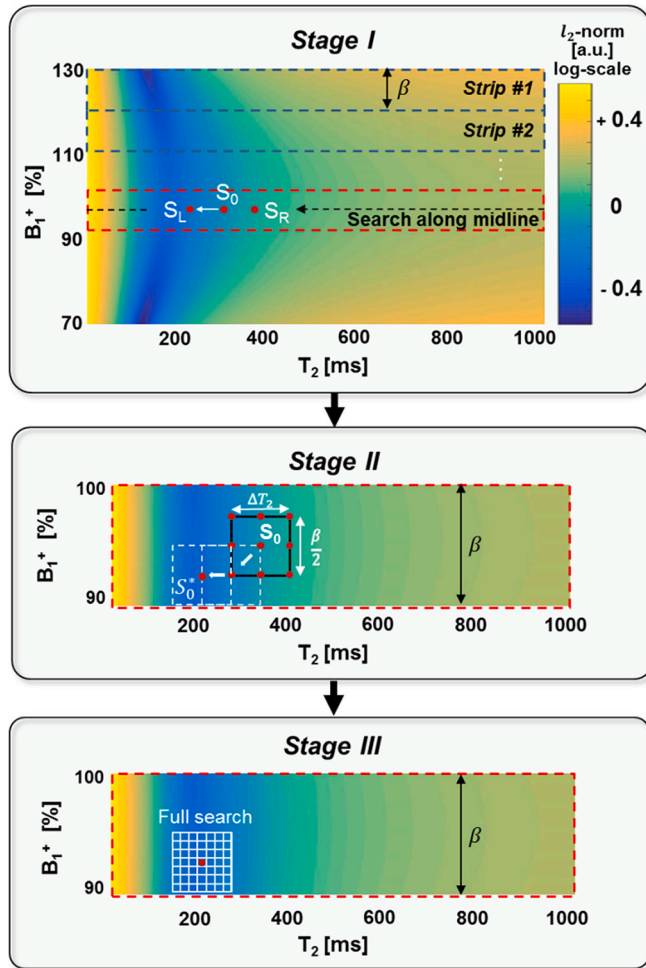
$$x_{n+1} = x_n - \eta \nabla_x F(x) \quad (9)$$

where  $\eta \in \mathbb{R}^+$  is the step size, and for  $\eta$  small enough we have a decreasing monotonic set  $F(x_0) \geq F(x_1) \geq F(x_2) \geq \dots$ . Unlike the continuous case described above, the EMC dictionary involves discrete  $T_2$  and  $B_1^+$  values. A discrete search problem can be formulated, in this case, using graph theory where the set of vertices  $S$  denote locations in dictionary space:

$$S = \left\{ (T_2, B_1^+) \mid T_2 \in [T_{2min}, T_{2max}] \text{ and } B_1^+ \in [B_{1min}^+, B_{1max}^+] \right\} \quad (10)$$

and the set of edges  $E \subseteq S \times S$  denote the connection between each pair of vertices. The problem of finding a unique pair  $[T_2, B_1^+]$  with the minimal  $l_2$ -norm  $\|EMC_{exp} - EMC_{sim}\|_2$ , now translates to searching through a *weighted* graph, where the weight between edges is defined as:

$$w(S_1, S_2) = \|EMC_{exp} - EMC_{sim,S_1}\|_2 - \|EMC_{exp} - EMC_{sim,S_2}\|_2 \quad (11)$$



**Fig. 2.** Gradient-descent search algorithm. The algorithm implements fast traversal over the  $l_2$ -norm space of every voxel in order to find the minimal  $[T_2, B_1^+]$  value pair. *Stage I:* the  $l_2$ -norm space is divided into strips, where  $\beta$  represent number of  $B_1^+$  values in each strip. A three-vertices search scheme ( $S_L, S_0, S_R$ ) is performed, until the mid-point  $S_0$  assumes the minimal value. *Stage II:* A nine-vertices search scheme is performed (nine red dots in the Figure). In each iteration the center vertex of the search window (solid black rectangle) is shifted to the minimum valued vertex ( $S_0^*$ ) until the center vertex assumes the minimal value out of the nine vertices. *Stage III:* A full exhaustive search is performed across all vertices in the search window, centered around  $S_0^*$ . (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

where  $EMC_{exp}$  is the experimental EMC being analyzed, and  $EMC_{sim, s_1}$  and  $EMC_{sim, s_2}$  denote the simulated EMCs for values of  $[T_2, B_1^+]$  assigned to vertex  $S_1$  and  $S_2$ , respectively. Using these definitions, it is possible to implement a discrete GD procedure, with the gradient between two vertices defined as the weight of the edge connecting them.

The  $l_2$ -norm difference between the experimental EMC of an arbitrary voxel and the dictionary of simulated EMCs can be graphically represented as a function of  $T_2$  and  $B_1^+$  as shown in Fig. 1. This graphical representation highlights two important properties of the  $l_2$ -norm search space: first, it is monotonic in the neighborhood of each local minima, and second, it can have either one or two minima. A voxel residing in a region where  $B_1^+$  is homogeneous would have a single minimum point, while regions of inhomogeneous  $B_1^+$  fields will result in two minima due to the symmetry of  $B_1^+$  around its undistorted value (see supplementary Fig. S.1). GD search through this space is done in three stages. *Stage I:* the  $l_2$ -norm space is divided into horizontal strips along the  $B_1^+$  dimension, i.e. each strip consists all the simulated  $T_2$  values and a limited range of

$\beta = 10 B_1^+$  values, resulting in  $N_{B_1^+}/\beta$  strips (see Fig. 2 Stage I). The local minimum within each strip is found by sampling the  $T_2$  dimension using a three-vertices search scheme. These are defined as:

$$\begin{aligned} S_0 &= [T_2^0, B_1^{+0}] \\ S_L &= \left[ T_2^0 - \frac{\Delta T_2}{2}, B_1^{+0} \right] \\ S_R &= \left[ T_2^0 + \frac{\Delta T_2}{2}, B_1^{+0} \right] \end{aligned} \quad (12)$$

Here  $\Delta T_2 = 20$  ms is the configurable width of the search window, the initial  $B_1^{+0}$  is set to be the middle of the strip, the initial  $T_2^0$  is set to 100 ms, and  $S_{L/R}$  are the left/right edges of the search window. The use of  $\Delta T_2 \gg 1$  allows fast traversal through the strip, thereby accelerating the search procedure. As long  $w(S_0, S_L) \leq 0$  or  $w(S_0, S_R) \leq 0$ , another iteration is done and the center vertex  $S_0$  is updated to be  $S_L$  or  $S_R$ , respectively. The stopping criterion is when both weights of the edges are positive.

*Stage II:* once the region of the minimal value is found, a 9-vertices search scheme is applied on a rectangular window centered at the output vertex of previous scheme. The window has a width  $\Delta T_2$  along the  $T_2$  dimension and height  $\beta/2$  along the  $B_1^+$  dimension. The 8 other vertices are the corners of the search window mid-points at each side (see Fig. 2 Stage II). Same GD scheme is then applied to shift the window center to the vertex with the largest gradient from the center vertex. This continues until all the edges (the gradients) have positive values, i.e. the center vertex has the minimal value amongst all the 9 vertices. At *Stage III*, an

exhaustive search is performed within the  $\Delta T_2 \times (\beta/2)$  rectangular search window, i.e. iterating across all dictionary entries within this window and calculating their  $l_2$ -norm value to find the minimal one. Once a minimal value is found for each strip, the global  $l_2$ -norm minimum value is obtained as the minimal value across all strips, producing the voxels  $[T_2, B_1^+]$  value pair. Repeating this process for each voxel produces full  $T_2$  and  $B_1^+$  maps.

Once these three stages are performed, the calculated  $B_1^+$  map is re-processed to remove outliers and perform spatial smoothing in order to reflect a realistic continuous transmit profile (see Appendix A). The resulting map  $B_1^+$  is inputted into a second matching process, which is similar to the first one, albeit having only a limited range of  $B_1^+$  values per voxel, equal to the input values  $\pm 3\%$ . The second iteration is thus done on only one strip, around the inputted  $B_1^+$  from the first iteration.

## 2.6. Estimation of relative error when using accelerated reconstruction

The accuracy of each accelerated reconstruction technique was estimated vis-à-vis full exhaustive search of the entire dictionary space. The relative percent error was then estimated at each voxel and for each reconstruction technique. Mean and standard deviation were then calculated across all voxels in the slice. To focus the error estimation on the physiologically relevant  $T_2$  range we excluded  $T_2$  values larger than 200 ms and smaller than one TE (typically 10 ms). The two assayed anatomies were reconstructed using dictionaries having the same number of entries. This was done in order to factor out the effect of the number of entries on the reconstruction time, and the resulting acceleration factors.

## 2.7. C/C++ MATLAB compiler considerations

All computations were performed using MATLAB on a standard desktop computer. Part of the reconstruction is implemented in C++ function, which is compiled using one of MATLAB's recommended compilers, and invoked using MATLAB's MEX interface. In this work the performances of two compilers, the default Microsoft Visual Studio Compiler (MSVC) and minGW-64, were tested for variation in



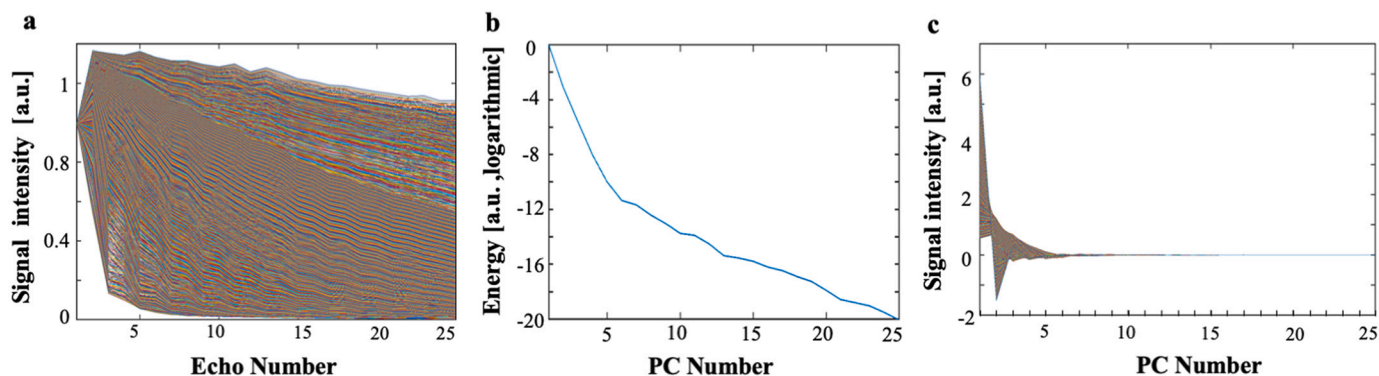


Fig. 3. PCA based compression of an EMC dictionary. Dictionary compression was done by calculating the energy of each principal component in the SVD, in order to evaluate the number of principal components that contain meaningful information and are needed for image reconstruction. (a) Original EMC dictionary. (b) Relative energy of each principal component [logarithmic scale]. (c) EMC dictionary, spanned in PCA space, attesting to the low rankness of the dictionary matrix and its compressibility.

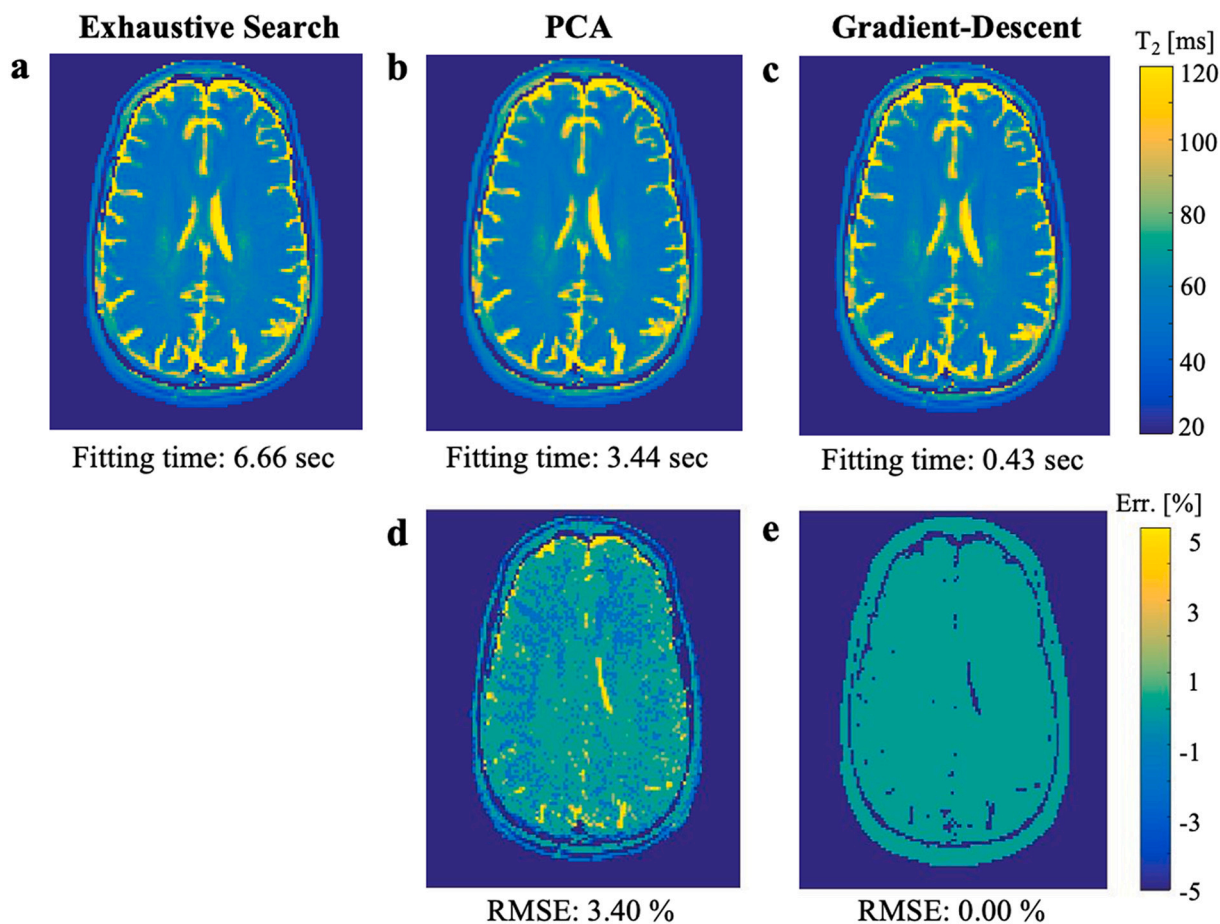


Fig. 4. Accelerated reconstruction of  $T_2$  maps of the brain. Quantitative  $T_2$  maps and relative-error maps, using PCA and GD accelerated reconstruction schemes. (a)  $T_2$  map reconstructed using exhaustive search method, with fitting time of 6.66 s per slice [matrix size =  $120 \times 128$ ]. (b-c)  $T_2$  maps that were fitted using the PCA and GD techniques, with fitting times of 3.44 and 0.43 s per slice respectively. (d-e) Relative-error of the PCA and GD accelerated reconstruction schemes produced RMSE of 3.40% and 0.00% respectively.

computation speed.

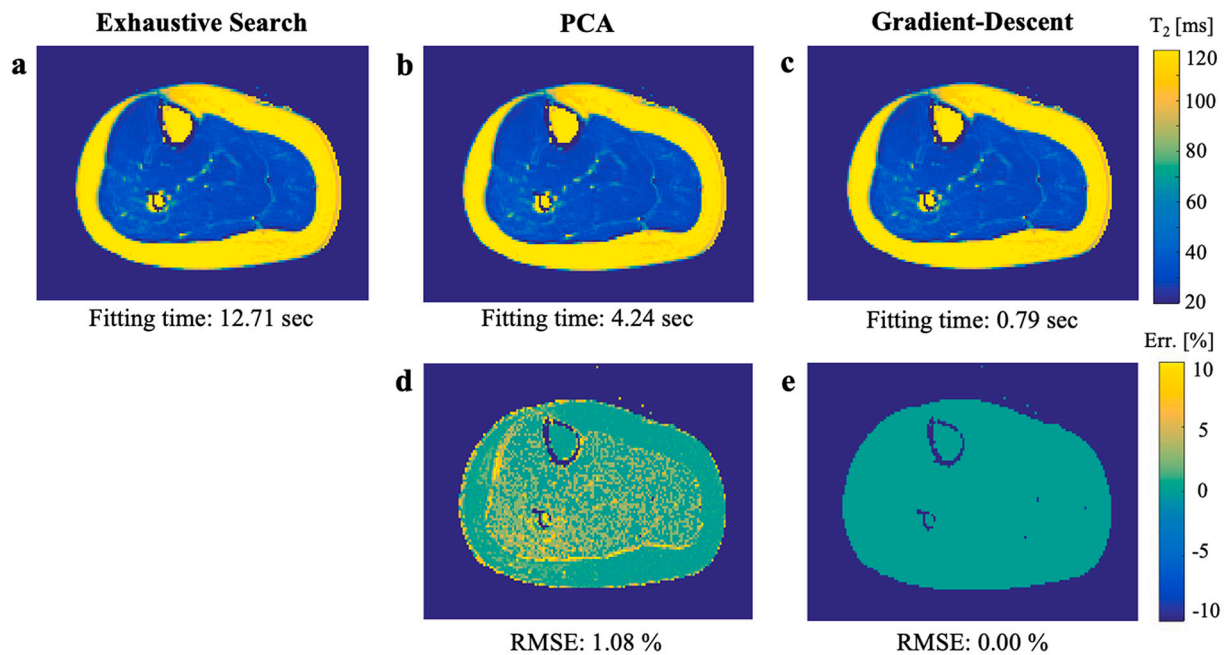
### 3. Results

Comparing the postprocessing times of several datasets we found that the minGW-64 compiler provided superior performance, leading to a significant x7 decrease in reconstruction times compared to the MSVC

compiler. The results presented hereon are thus shown for the minGW-64 compiled MEX libraries.

#### 3.1. Accelerated reconstruction of $T_2$ maps using SVD dictionary compression

Fig. 3 shows the feasibility of compressing an EMC dictionary using



**Fig. 5.** Accelerated reconstruction of  $T_2$  maps of the calf. Quantitative  $T_2$  maps and relative-error maps, using PCA and GD accelerated reconstruction schemes. (a)  $T_2$  map reconstructed using exhaustive search method, with fitting time of 12.71 s per slice [matrix size =  $106 \times 160$ ]. (b-c)  $T_2$  maps that were fitted using the PCA and GD techniques, with fitting times of 4.24 and 0.79 s per slice respectively. (d-e) Relative-error of the PCA and GD accelerated reconstruction schemes produced RMSE of 1.08% and 0.00% respectively.

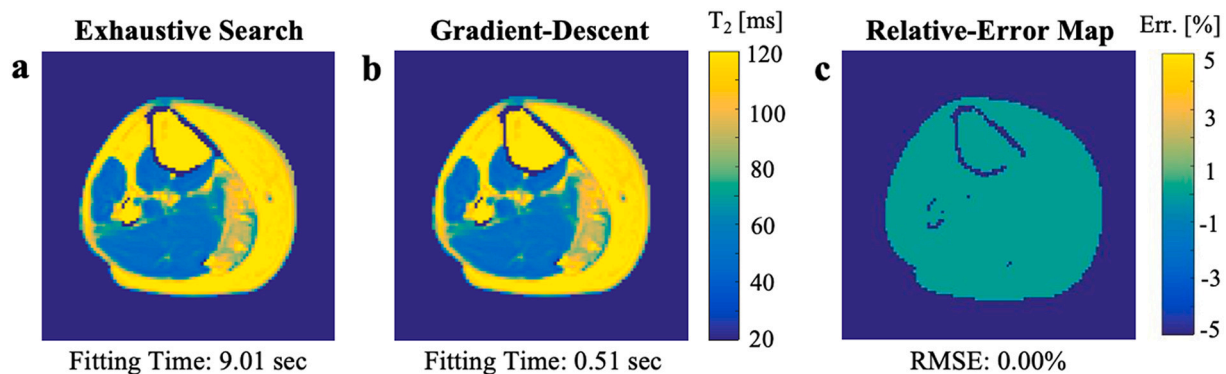
PCA. A graph of the relative energy of each PC is shown in Fig. 3b for a representative dictionary. The PC values are sorted in logarithmic nonincreasing order, exhibiting a fast drop in each PC's energy and a change in slope of the graph beginning at approximately the 5th PC. Fig. 3a and c show the original and compressed dictionaries after the PCA projection. Consistent with the slope in Fig. 3b, most of the signal in the PCA projected dictionary is concentrated in the first 5–6 PCs, suggesting that it is possible to project the dictionary (and the experimental EMC data) onto the first five eigenvectors in order to accelerate the dictionary search process.

Figs. 4b and 5b show quantitative  $T_2$  maps produced using PCA-based accelerated reconstruction of brain and calf anatomies of healthy subjects. A full exhaustive search produces the ground truth maps are shown in Figs. 4a and 5a, with the voxel-wise error maps shown in Figs. 4d and 5d respectively. Error values represent absolute relative error with respect to the full exhaustive search, producing mean RMSE of 3.4% for the brain anatomy, and mean RMSE of 1.1% for the calf anatomy, using the PCA acceleration. Total fitting time for the brain anatomy using the PCA scheme is 89.44 s (for 26 slices), reflecting a

reduction of 48.3% with respect to the fitting time using exhaustive search. For the calf anatomy the total fitting time is 21.2 s (for 5 slices), reflecting a 66.6% decrease with respect to the exhaustive search scheme.

### 3.2. Accelerated reconstruction of $T_2$ maps using gradient descent method

The second approach for accelerating the EMC fitting process was based on an efficient search pattern in the dictionary search-space. Fig. 1 shows two typical  $l_2$ -norm spaces for two representative voxels. Figs. 4c, e and 5c,e show quantitative  $T_2$  maps reconstructed using GD search pattern along with the corresponding fitting errors for healthy brain and calf anatomies scans. The GD scheme produced 100% accuracy in the  $T_2$  calculated values. Total fitting time for the brain anatomy (26 slices) using the GD scheme is 11.18 s, reflecting a reduction of 93.5% in the overall fitting time compared to the exhaustive search scheme. For the calf anatomy (5 slices), the total fitting time is 3.95 s, reflecting a reduction of 93.8% in the overall fitting time compared to the exhaustive search scheme. Fig. 6 shows a quantitative  $T_2$  map for a patient with



**Fig. 6.** Accelerated reconstruction of  $T_2$  maps of a dysferlinopathy patient's calf anatomy. (a)  $T_2$  map reconstructed using exhaustive search, with fitting time of 9.0 s per slice [matrix size =  $128 \times 128$ ]. (b-c) Gradient descent fitting of the same anatomy took 0.5 s per slice, with zero RMSE.

**Table 1**

Performance and accuracy of the accelerated PCA and gradient descent (GD) fitting techniques for brain and calf anatomies.

Fitting method↓	Anatomy [# slices]→	Brain [26]	Calf #1 [5]	Calf #2 [5]
	No. of voxels →	366,782	78,758	67,939
	Matrix size →	120 × 128	106 × 160	128 × 128
Exhaustive search [ground truth]	Total duration [sec]	173.2	63.6	45.3
	Duration per slice [sec]	6.66	12.71	9.01
	Duration per voxel [ms]	0.47	0.81	0.67
PCA	Total duration [sec]	89.4	21.2	20.9
	Duration per slice [sec]	3.44	4.24	4.19
	Duration per voxel [ms]	0.24	0.27	0.30
Gradient descent	Acceleration Factor	1.9	3.0	2.2
	Relative error [%]	3.4 ± 1.6	3.0 ± 5.4	4.5 ± 6.0
	Total duration [sec]	11.1	3.9	2.6
	Duration per slice [sec]	0.43	0.79	0.51
	Duration per voxel [ms]	0.03	0.05	0.04
Gradient descent	Acceleration Factor	15.5	16.1	17.5
	Relative error [%]	0.0 ± 0.0	0.0 ± 0.04	0.0 ± 0.0

The exhaustive search approach produced ground truth maps which were compared against the two accelerated techniques. Measured parameters include the mean and standard deviation of the relative error across all voxels within the examined anatomy. Voxels with  $T_2$  values larger than 200 ms, and shorter than 10 ms were excluded as they correspond to tissues with lower clinical relevance (excluding CSF, which requires an entirely different range of experimental TEs in order to be estimated). As can be seen, the GD technique achieved perfect reconstruction, with acceleration factors of 15–18 for a dictionary comprised of  $203 T_2 \times 41 B_1^+$  entries.

dysferlinopathy. Fig. 6a shows the original  $T_2$  map reconstructed using the exhaustive search process, while Fig. 6b shows the  $T_2$  map reconstructed using the accelerated GD scheme. Similar to the healthy subjects' results, no error was produced when employing the GD reconstruction scheme, which offered 94.3% reduction in the map's fitting time.

### 3.3. Evaluating reconstruction properties

Table 1 summarizes the acceleration factors and corresponding relative errors achieved for each anatomy. GD-based method produced almost perfect reconstruction, with improved acceleration factors compared to the PCA dictionary compression approach. Reconstruction times were calculated for both multi-slice scans and also per single/voxel. These acceleration factors depended mainly on the dictionary size, namely, the number of simulated  $T_2$  and  $B_1^+$  values, as well as on the number of acquired echoes (experimental ETL). The ETL defines, in this case, the number of core operations involved in matching the experimental signal in a single voxel to a single dictionary element. Thus, shorter ETLs resulted in higher relative acceleration factors, although the absolute change in processing time remained the same. The performance of the GD acceleration technique depended on the  $l_2$ -norm space of the fitted voxel (which depends mainly on  $B_1^+$  uniformity), and on the different range of  $T_2$  values in each anatomy, affecting the number of echoes used in the calculation of the  $l_2$ -norm between experimental and simulated EMCs.

## 4. Discussion

In this study we investigated two approaches for accelerated fitting of dictionary-based  $T_2$  mapping from MESE data. The original and straightforward fitting procedure involved an exhaustive search over an entire dictionary space, which is time consuming and limits the clinical applicability of EMC-based  $T_2$  mapping. Our results show that the GD search pattern affords significant reduction in the processing time and that choosing the right C++ compiler also has a dramatic effect, which can reduce the overall reconstruction times by an additional  $\times 7$  factor.

The PCA-based dictionary compression approach resulted in non-negligible inaccuracies in the fitted  $T_2$  values. These inaccuracies may be a result of two inherent issues of the PCA algorithm. First, the compression process involves reducing the dimensionality of the dictionary using an SVD approximation process and removing PCs below a certain threshold. This involves an unavoidable loss of information, creating a trade-off between the accuracy of the reconstruction process and the number of principal components retained in the compressed dictionary. Secondly, the  $l_2$ -norm search spaces are different for different  $T_2$  baselines, leading to  $T_2$  dependent errors in the PCA fitting process.

A few important insights can be drawn regarding the search process by examining the  $l_2$ -norm space of fitted voxels. First observation is that an ambiguity arises in this search space at areas of inhomogeneous  $B_1^+$ , resulting from symmetry of the Bloch equations around the central  $B_1^+ = 100\%$  value. This ambiguity leads to the emergence of two local minima, which requires to separate the graph to two sub-graphs, and perform a separate search in each one. The final (absolute) minimum [ $T_2, B_1^+$ ] value pair is then found by comparing the two local minima. The ambiguity of the  $l_2$ -norm search-space also highlights the importance of the  $B_1^+$  map smoothing process during the second-stage of the matching process. As the  $B_1^+$  map is expected to be smooth, this constraint helps to overcome cases where one of the two local minima is wrongly identified as the global minimum due to noise. This is particularly important at low SNR settings or when fitting short  $T_2$  components, which are inherently noisy due to their fast signal decay.

Notwithstanding the fitting accuracy, the acceleration factor was very similar across data sets when using dictionaries with similar number of entries. The acceleration factor of the PCA method is a result of using truncated dictionaries. The search process itself is, in this case, the same as in the exhaustive search scheme and therefore depends only on the number of simulated [ $T_2, B_1^+$ ] pairs and the ratio between ETL and the number of principal components used. The common factors, affecting both acceleration schemes are the matrix-size and number of slices in the scanned dataset – both of which have a linear effect on the acceleration factor as the algorithm iterates over all the pixels in the reconstructed  $T_2$  map and over all slices.

The reconstruction time of the GD search scheme is mainly affected by the number of entries in the simulated dictionary, which can increase the steps that are needed to convergence. Although it is very important property which can be controlled by the resolution of the simulated dictionary, the gradients across the  $l_2$ -norm of the map are the most significant property, affecting the reconstruction time. These gradients depend on strength, or level of the  $T_2$  encoding, e.g., using refocusing flip angles smaller than  $180^\circ$  would lead to weaker  $T_2$  weighting, thereby influencing the ability to discern between neighboring  $T_2$  values by decreasing the convexity of the  $l_2$ -norm search space, hence the optimal GD step size. The use of  $l_2$ -norm is also an important factor as it determines the computational complexity of each step during the matching process (either PCA or GD based). Other criteria for comparing the similarity between experimental and simulated curves can be implemented, e.g., simple correlation, or dot product. These, however, are more suitable for dictionaries in which the entries are orthogonal to one another, in contrast to the low-rank EMC dictionary used here. A small improvement in processing time can be achieved by switching to a simpler similarity criterion, yet, this will not significantly change the



overall runtime process, as each of these criteria involve an  $O(n)$  number of operations (where  $n$  is the vectors' length).

## 5. Conclusions

In this paper, we present two approaches for accelerating the reconstruction of quantitative  $T_2$  maps from MESE data using the EMC algorithm. The PCA based compression method is used to reduce the dimensions for both the simulated dictionary and acquired data so as to perform the search over shorter vectors. This approach, however, results in inaccuracies in the calculated  $T_2$  maps, while providing only moderate acceleration factors. The GD-based approach, on the other hand, yielded significant acceleration factors and close to perfect fitting

accuracy in comparison to a full exhaustive search. In addition to accelerating the reconstruction process, we have also accelerated the dictionary generation process as can be seen in Appendix B. We believe that these advances will facilitate integration of realtime quantitative  $T_2$  mapping in clinical settings. Future work may be focused on further acceleration using advanced hardware solutions, e.g. using GPUs or artificial intelligence tools.

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## Appendix A. The EMC Algorithm

This appendix contains a concise description of the steps for generating  $T_2$  maps using the EMC algorithm, covering the data acquisition, pre-processing, and post-processing procedures.

### Step 1 – MRI data acquisition

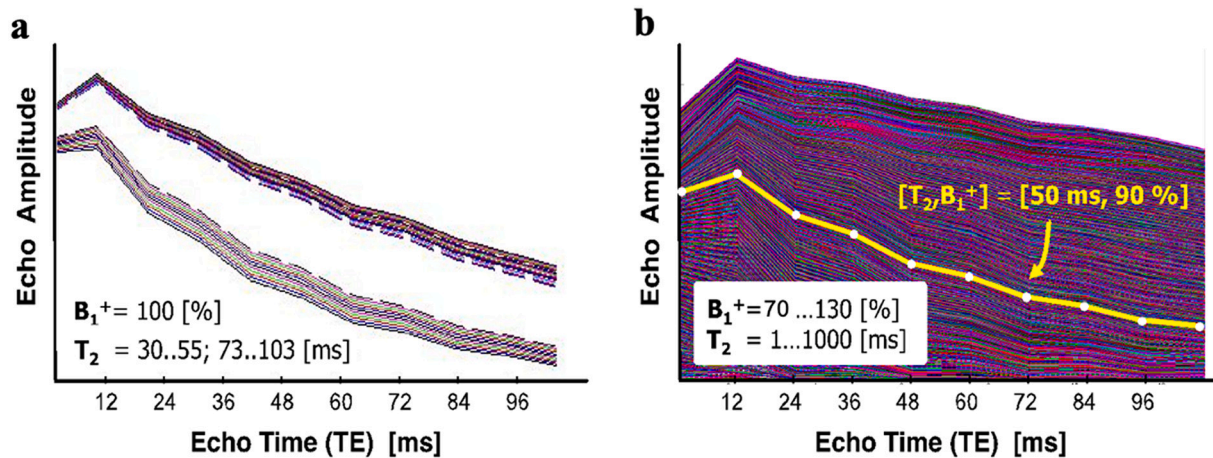
Experimental data is acquired using a multi-echo spin-echo (MESE) protocol, producing a time-series of  $T_2$  weighted DICOM images, corresponding to increasing echo-times (TEs).

### Step 2 – Pre-processing: Generation of a simulated EMC dictionary

Tracking the precise magnetization evolution during a MESE scan is done using simulations of the prospective pulse sequence, programmed in-house in C++ and MATLAB (The MathWorks Inc., Natick, MA) and based on time and space propagation of Bloch equations. The exact pulse sequence scheme and the corresponding parameter values are obtained through offline simulation of the pulse sequence diagram extracted using Siemens's POET sequence testing tool. This provides information regarding the amplitudes and timing of each RF and gradient pulse. The actual RF pulse shapes were read from the pulse sequence source code and imported into MATLAB.

Although full volumetric simulations would have been ideal for EMC modeling, such simulations are not feasible due to their extreme computational intensity, and the extended runtimes that are needed in order to track a pool of  $10^3 \dots 10^4$  spins in a high resolution four-dimensional space ( $x, y, z, t$ ). To facilitate this process, reduced one-dimensional imaging simulations are carried out solely along the slice dimension (see ref. [6] for justification of this procedure). The internal spatial resolution of these simulations is set high enough to accurately account for intra-voxel dephasing (10–100  $\mu\text{m}$  for data acquired on standard clinical scanners), while the temporal resolution is matched to the one used in the actual MESE experiment.

Each run of the simulation generates a single echo-modulation-curve, designating the intensity of a MESE echo train for a given parameter set. A dictionary of simulated EMCs is thus constructed by repeating the simulations for a range of  $T_2 = 1 \dots 1000$  ms, and transmit field ( $B_1^+$ ) inhomogeneity scales of 70% and 130%, where a value of 100% corresponds to a purely homogeneous  $B_1^+$  field (see Fig. A.1). The total simulation time depends on the echo train length and number of  $T_2$  and  $B_1^+$  values simulated, with typical times ranging between 1 and 4 h on a multi core desktop PC.



**Fig. A.1.** Two examples of simulated echo-modulation-curve (EMC) dictionaries for a multi-echo spin-echo (MESE) protocol. (a) A simplified dictionary containing two limited ranges of consecutive  $T_2$  values. (b) Full dictionary, spanning  $T_2$  range of 1...1000 ms and  $B_1^+$  inhomogeneity scales of 70%...130%. The yellow line illustrates an experimentally acquired EMC for a single pixel, which was matched to the dictionary of simulated EMCs producing a specific pair of  $[T_2, B_1^+]$  values.

### Step 3 – Postprocessing: Generation of $T_2$ , $B_1^+$ and Proton-Density (PD) maps

Quantitative  $T_2$  values are generated on a pixel-by-pixel basis from the MESE DICOM series by matching the experimental EMC in each pixel to the pre-calculated dictionary of simulated EMCs. Matching is done by calculating the  $l_2$ -norm of the difference between the experimental and simulated EMCs, and choosing the EMC yielding the minimal norm value. Following this procedure, a unique pair of  $[T_2, B_1^+]$  values is assigned to each pixel, yielding the desired  $T_2$  parametric map of the anatomy. Finally, proton density maps are calculated by extrapolating the intensity of each pixel in the image from the first echo-time ( $t = \text{TE}$ ) to the time point  $t = 0$  using the fitted  $T_2$  map according to:



$$PD(x, y) = \frac{S(x, y, t = TE)}{e^{-TE/T_2(x,y)}} \quad (\text{A.1})$$

## Appendix B. Accelerating the generation of EMC dictionaries

Generation of EMC dictionaries requires to simulate the propagation of magnetization in a MESE protocol for a range of  $T_2$  and  $B_1^+$  values. Each run of the simulation generates a single EMC. The time required for simulating an entire dictionary will depend on the range of simulated  $T_2$  and  $B_1^+$  values, and on the echo train length. An effective way to accelerate the generation of EMC dictionaries is to decimate the range of simulated  $T_2$  and  $B_1^+$  values and fill in the missing entries by a much faster interpolation procedure. The type of interpolation may vary from simple linear interpolation to more complex techniques. Here, we employed MATLAB's C2 spline interpolation, which was found to produce the most accurate results [55].

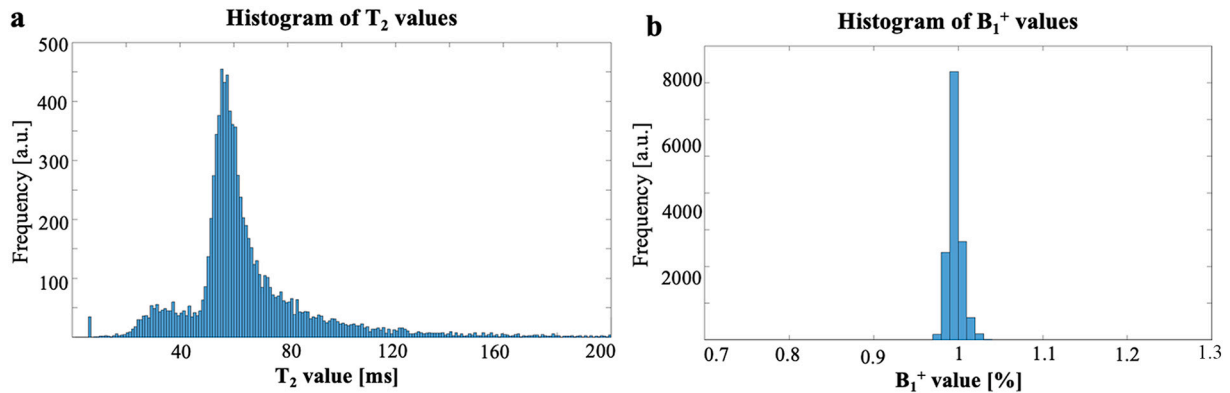


Fig. B.1. Histograms of  $T_2$  and  $B_1^+$  values in a typical brain scan. Values were calculated using the EMC algorithm [56].

To demonstrate the effectiveness of this acceleration technique we consider here a standard dictionary containing 440  $T_2$  values with 1 ms resolution in the range 1...300 ms, and 50 ms resolution in the range 300...1000 ms; and 61  $B_1^+$  values in the range 70...130% and resolution of 1%. Before generating a decimated dictionary, we examined the typical  $T_2$  and  $B_1^+$  content of a brain anatomy (shown in Fig. B.1). As can be seen, this anatomy contains a relatively wide range of  $T_2$  values but only a limited range of  $B_1^+$  values, centered around  $B_1^+ = 100\%$ .

Following this we decimated the original dictionary to contain 21% of the original dictionary's entries, potentially reducing the dictionary generation time by 79%. The ranges of simulated  $T_2$  and  $B_1^+$  values were 1:1:40, 42:2:80, 84:4:160, 200:40:280, 320:80:1000 ms, and 70:2:130% respectively. The mean difference between the interpolated and original dictionaries was  $0.0011\% \pm 0.0033\%$ . This will depend on the level of decimation, which is recommended to follow a logarithmic scale along the  $T_2$  dimension, starting with small spaced sampling at low  $T_2$  values, and gradually increasing towards larger  $T_2$  values. Fig. B.2a–b presents  $T_2$  maps reconstructed using the fully-simulated and decimated dictionaries. A map of the relative-error of  $T_2$  values that were fitted using the two dictionaries is shown in Fig. B.2c. As can be seen, the two fitting procedures produces almost identical maps, except for a few small errors of  $<2\%$ , appearing in the CSF region where  $T_2$  values are well beyond the range of TE's that were sampled during the scan (TE = 10:10:20 ms). These results confirm that the generation of EMC dictionaries can be significantly accelerated without loss of clinical information.

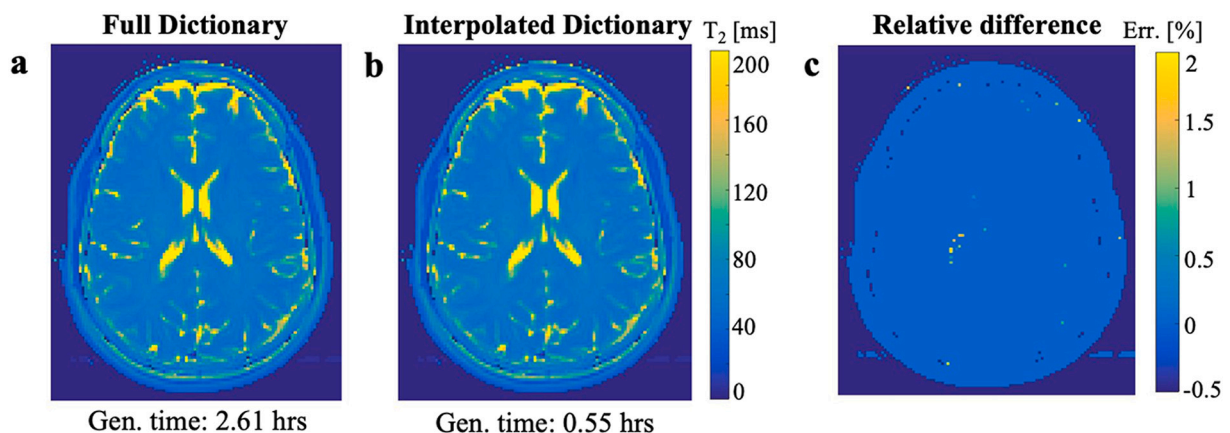


Fig. B.2. Comparison of  $T_2$  maps reconstructed using (a) a fully simulated dictionary vs. (b) a dictionary that was decimated and interpolated. The generation times of the two dictionaries were 2.61 h and 0.55 h respectively. (c) Relative-error between the two maps showing no significant error aside from a few  $<2\%$  errors inside the CSF.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mri.2021.12.006>.

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