Available online at www.sciencedirect.com
ScienceDirect
Journal of Magnetic Resonance 189 (2007) 286–292
JMR Journal of Magnetic Resonance
www.elsevier.com/locate/jmr

DOUBLESLICING: A non-iterative single profile multi-exponential curve resolution procedure Application to time-domain NMR transverse relaxation data

Letícia Andrade [a,b,*], Elisabeth Micklander [b], Imad Farhat [c], Rasmus Bro [b], Søren Balling Engelsen [b]

[a] University of Nottingham, Division of Food Sciences, Sutton Bonington Campus, Loughborough LE12 5RD, UK
[b] University of Copenhagen, Faculty of Life Sciences, Department of Food Science, Quality & Technology, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark
[c] Firmenich SA, Route de la Bergère 7, 1217 Meyrin, Switzerland

Received 26 June 2007; revised 6 September 2007
Available online 29 September 2007

Abstract

A new non-iterative curve resolution technique for resolving single decay profiles is proposed. The new technique, called DOUBLESLICING, is based on the DECRA (Direct Exponential Curve Resolution Algorithm) principle. While the original DECRA was designed to resolve several decay curves simultaneously and thus fitting *common* pure exponentials, DOUBLESLICING can resolve single decay profiles by a simple double data transformation followed by an analytical and unique three-way decomposition. The new approach is successfully demonstrated on experimental NMR CPMG relaxation data, measured on combinations of unmixed paramagnetic $CuSO_4$ solutions. Decay signals of the water component were acquired following an innovative experimental design that ensured no interaction between the components present in each sample under observation. DOUBLESLICING proved to be accurate in estimating relaxation times differing in one order of magnitude (range: 19.6–159.4 ms). Its performance was comparable to discrete exponential fitting with the advantage of being much faster – in terms of computation time, DOUBLESLICING outperformed exponential fitting by a factor of four.

Keywords: Low field time domain NMR; Multi-exponential curve resolution; DECRA; DOUBLESLICING; Discrete exponential fitting

1. Introduction

Low Field Nuclear Magnetic Resonance (LF NMR) is an established method in many food and material science applications as a technique that combines useful complex information about species with mobile protons, with speed of analysis and minimal perturbation to the sample. In the time domain, transverse LF NMR relaxation data are a sum of exponentials [1]. The ability to resolve such data and extract the underlying characteristic relaxation times (associated to the different components of the sample under observation) is very valuable and is becoming more and more popular as it is the reference method in analysis of time domain NMR data. The time constants and amplitudes associated are usually calculated by multi-exponential fitting, but often algorithmic and mathematical problems such as ill-conditioning and local minima make the solutions difficult to interpret and validate. Provencher has presented methods to overcome and deal with data limitations related to random noise, baseline and number of exponentials that can be extracted from a decay data signal [2,3]. Istratov and Vyvenko have discussed general limitations of exponential analysis and summarized the algorithms applied to resolve exponential

* Corresponding author. Address: University of Copenhagen, Faculty of Life Sciences, Department of Food Science, Quality & Technology, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark. Fax: +45 35 33 32 45.
E-mail address: lman@life.ku.dk (L. Andrade).

1090-7807/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmr.2007.09.018

decays [4]. In recent years, many algorithms have been developed to overcome some of these limitations. NMR relaxometry, when combined with methods such as DECRA, represents a unique approach for studying, for example, water compartmentalization in gels, meat, dough, bread and dairy products, and for the determination of solid/fat content in edible oils [5–9].

This work presents DOUBLESLICING as an alternative method to resolve LF NMR relaxation curves, emphasizing its relation to and advantages over alternative procedures.

DOUBLESLICING is based on the DECRA (Direct Exponential Curve Resolution Algorithm) principle [10]. DECRA has attracted much attention due to its capability to uniquely and non-iteratively resolve sets of multi-exponential decay functions into common underlying pure exponentials. DECRA has been used in several industrial applications ranging from food monitoring to chemical production [10,11]. This approach is appealing, because the algorithm, although utilizing highly redundant information, requires no initial value guesses and provides non-iterative and unique mono-exponential solutions. When compared to standard numerical curve-fitting algorithms, the main advantages of DECRA are its dramatically improved speed (independent of number of components extracted) and somewhat improved diagnostics [6]. DECRA, and consequently DOUBLESLICING, is based on the application of generic approaches to determine the right number of components, identify outlying samples, etc., giving rise to robust solutions [12].

The DECRA approach utilizes the linear relationship between exponentials to upgrade a set of one-dimensional relaxation curves to a pseudo two-dimensional structure and thus facilitate the unique advantages offered by trilinear mathematical models. The method is based on the fact that two different time "slices" of a given multi-exponential decay curve consist of the same underlying features (*quality*: characteristic decay times), but in a new linearly related combination of amounts (*quantity*: concentrations or magnitudes) [6]. In the simplest case, chosen in the original DECRA [10], one relaxation curve can be translated one data point, called *lag* 1, and added to the data matrix in a new direction called *slab* (*slab* 2). The relaxation data is now transformed into a $2 \times J - 1$ array, in which J represents time. If several relaxation decay curves, M, are to be evaluated, a $M \times 2 \times J - 1$ data cube is obtained, which can be analyzed by trilinear methods. It is possible to perform such pre-transformation, i.e. translate a relaxation curve one data point, twice or more and thus, from a single relaxation curve, generate a trilinear data cube.

In this work DOUBLESLICING is presented as an extension to DECRA in which the translation pre-transformation is performed twice. The idea of "cutting" data into a number of overlapping slices, repeated twice, has given rise to the name selected for this approach: DOUBLESLICING. It is shown that the application of DOUBLESLICING enables the generation of a trilinear data cube from a single relaxation curve, which can then be resolved by trilinear models into pure mono-exponentials. First, the principle behind DOUBLESLICING is outlined and the reasons why DECRA slicing is not adequate for resolving singe relaxation curves are presented and explained. Finally, DOUBLESLICING is applied to a real data set which consists of low field time domain NMR transverse relaxation data of 30 samples of distinct paramagnetic copper sulphate ($CuSO_4$) concentrations. The new method is then tested against standard numerical methods for exponential curve fitting.

2. Theory and methods

In this section the DOUBLESLICING algorithm is developed and explained in relation to relevant alternative methods.

DECRA can be classified as a multi-curve multi-exponential fitting algorithm. As outlined in the Introduction section, in order to determine the time constants inherent to the exponential decays (T_2 values), a set of NMR transverse relaxation curves has to be analyzed. DECRA does not allow the determination of T_2 values from a single exponential decay, which can be very useful and advantageous when the set of relaxation curves under study cannot be described by one set of *common* profiles. For this purpose, single-curve multi-exponential fitting algorithms, such as discrete exponential fitting and DOUBLESLICING, have to be applied.

The T_2 of a single physico-chemical component is dependent on several factors such as the temperature at which the relaxation decays are acquired. Moreover, it also depends on local magnetic fields arising from intramolecular and intermolecular interactions in the sample, which depend on the concentration. The development of a method enabling the determination of the different T_2 values (each one corresponding to the behavior of one component within the same sample) from a single relaxation curve is, therefore, crucial. In this way, it is possible to analyze, for example, the gradual changes induced by the effect of temperature or concentration on T_2, from a set of relaxation curves acquired for a single sample. In this work, however, and in order to test and compare the performance of the single exponential fitting algorithms, temperature was kept constant during all measurements and it was ensured (by the experimental design) that there were no interactions between the components in the samples – T_2 values (of the four mother solutions that will be described later) were similar in all samples (even though their concentrations were different). The application of single-curve multi-exponential fitting algorithms to this particular data set (30 relaxation curves of samples with different concentrations of the same components) enabled the determination of the T_2 values of each component and the concentration of each sample. In this way, DOUBLESLICING could be tested in 30 independent relaxation decays. In order to assess and compare the performance of DOUBLESLICING, the T_2 values of the 30 samples were also determined by discrete multi-exponential curve fitting,

which has been the classical numerical approach to extract T_2 values from NMR relaxation decays.

2.1. DOUBLESLICING

The rationale behind DOUBLESLICING is to *slice* the data twice and thus from a single relaxation profile generate a three-dimensional data array that can be resolved by trilinear mathematical models [9]. Fig. 1 shows in schematic form the principle behind DOUBLESLICING. In the first operation, a number of *pseudo*-samples are created which all have the same underlying relaxation components, but in different relative amounts. The number of *slabs* (*pseudo*-samples) is usually equal to, or larger than, the number of components one wishes to extract. DOUBLESLICING involves a second data pre-processing step in which the previous slicing procedure is repeated along the columns, resulting in a three-way data matrix containing low-rank trilinear variation that can then be analyzed using multiway techniques [9].

It may appear an unnecessary complication to create a three-way data array with highly redundant information from a single relaxation curve to solve the simple discrete multi-exponential fitting problem. However, with suitable resampling, DOUBLESLICING produces practically the same results as traditional exponential fitting, but with significantly shorter computation times, especially when more than two components are extracted [9] (as will be demonstrated in Section 3 of this paper).

2.2. Discrete multi-exponential curve fitting

In this classical approach, the relaxation profiles are individually decomposed into a limited number of pure exponential curves (typically less than 5) [2–4]. Despite the ill-conditioning property of the exponential-sum fitting and the initial value problem, in practice, numerical methods have become fairly robust, but unfortunately the iterative methods are rather time consuming. In this work we use an algorithm which is based on Nelder–Mead simplex minimization [13] for estimation of the non-linear parameters with a least squares fit of the linear parameters inside the function evaluation call. This algorithm has proved to be robust and reliable in the analysis of time domain NMR data, but similarly to all other multi-exponential curve fitting techniques, the results remain dependent on the number of exponential components extracted [4,6].

2.3. Experimental design

In order to test the different algorithms evaluated in this paper, an experimental design was carried out which resulted in a set of 30 samples consisting of combinations of paramagnetic $CuSO_4$ solutions with known concentrations (three of the samples in duplicate). For each sample, the transverse relaxation signal of the water component was collected by the acquisition of CPMG (*Carr–Purcell–Meiboom–Gill*) [14,15] NMR signals as a function of time.

Samples were prepared using four mother solutions of different $CuSO_4$ concentrations, 55, 26, 13, and 6.5 mM, which correspond approximately to T_2 relaxation constants of 20, 40, 80, and 160 ms, respectively. Later, from the mono-exponential fitting of the experimental relaxation curves of the mother solutions to exponential decays, T_2 values of 19.6, 40.6, 81.4, and 159.4 ms were calculated and were henceforth considered the reference values. The mono-exponential fitting was very successful, since no systematic patterns were observed in the residuals plots (difference between data acquired and data calculated using the fitting parameters). To emphasize the quality of the fitting, it was decided to report the root mean square errors of the residuals – 954, 915, 852, and 875, respectively, corresponding to approximately 1.5% of the total signal of each mother solution.

A four-component (D-optimal) design with seven levels (representing concentrations) was used to ensure no interaction between the components present in each one of

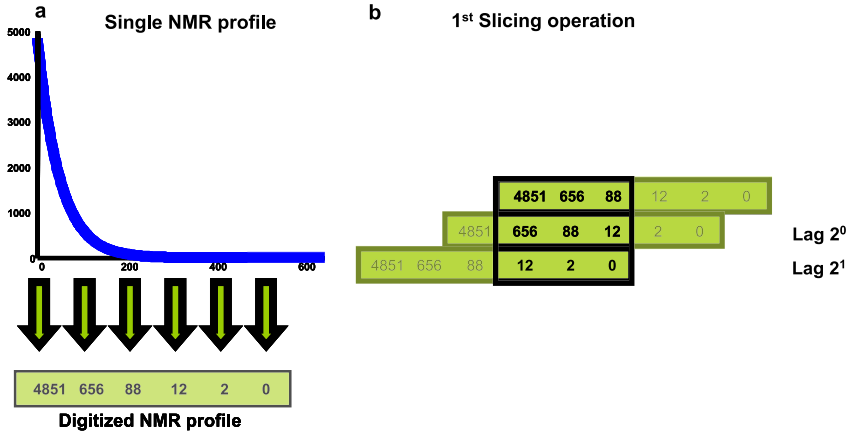

Fig. 1. Illustration of the principle behind DOUBLESLICING. (a) Digitizing the relaxation profile; (b) Lagging scheme of the first three slices in the time direction.

the 30 samples prepared. This design was achieved placing seven small tubes, filled with pure mother solutions, in the 18 mm NMR tube. Concentration values (reflecting the filling of the small tubes) are presented in units from 1 to 7 (Table 1), each unit representing one seventh of the tube sampling volume. Each of the four mother solutions was present in as many tubes as designated by the design (for example, for sample 1 all the small tubes were filled with mother solution number 4).

By setting up the experiments in this particular way, it was possible to control the exact contribution of each of the components to the overall NMR signal, while avoiding cross-interactions which typically arise when concentrations are varied; however, the division of the NMR tube into compartments can lead to artefacts arising from the void spaces between the small tubes (susceptibility issue). In this work, this problem was circumvented by the randomization of the position of the small tubes in the 18 mm tube. A second artefact that can arise from the division of the NMR tube into compartments is related to the fact that different amounts of the same sample (placed in different compartments) may be experiencing slightly different magnetic fields (B_0, magnetic induction field, and potentially, B_1, excitation field). This, however, should be a minor issue, especially the impact of B_0 on the acquired CPMG NMR signals – CPMG pulse sequence was developed to minimize the impact of field inhomogeneities on the NMR signal acquired [14,15]; moreover, measurements were performed in a low-field NMR machine.

Table 1
The experimental design: concentration of the 30 samples in units of 1–7, each unit representing one seventh of the NMR tube sampling volume; samples labeled according to concentration

Sample no.	Sample concentration on mother solution number				Sample label
	1 ($T_2 = 19.6$ ms)	2 ($T_2 = 40.6$ ms)	3 ($T_2 = 81.4$ ms)	4 ($T_2 = 159.4$ ms)	
1	0	0	0	7	0007
2	1	0	1	5	1015
3	0	6	0	1	0601
4	1	0	6	0	1060
5	1	6	0	0	1600
6	0	0	6	1	0061
7	0	2	0	5	0205
8	2	5	0	0	2500
9	0	5	2	0	0520
10	0	0	7	0	0070
11	0	6	1	0	0610
12	0	5	0	2	0502
13	0	0	2	5	0025
14	6	0	1	0	6010
15	0	0	5	2	0052
16	0	1	0	6	0106
17	0	2	5	0	0250
18	1	5	1	0	1510
19	1	0	0	6	1006
20	2	0	5	0	2050
21	6	1	0	0	6100
22	0	0	1	6	0016
23	5	2	0	0	5200
24	7	0	0	0	7000
25	6	0	0	1	6001
26	0	7	0	0	0700
27	5	0	2	0	5020
28	0	2	0	5	0205
29	0	1	6	0	0160
30	5	0	0	2	5002
31 (16)	0	1	0	6	0106
32 (8)	2	5	0	0	2500
33 (9)	0	5	2	0	0520

Samples 31, 32, and 33 are duplicates of samples 16, 8, and 9, respectively.

Fig. 2 illustrates the CPMG NMR signals acquired on four representative samples – a mother solution (one-component solution), sample 2 (three-component solution) and samples 20 and 30 (two-component solutions). In order to highlight the differences between the relaxation decays of the samples, the time axis is presented in log scale.

The signal-to-noise ratio is an important parameter, as it can significantly influence the performance of the algorithms [2–4,7]. The signal-to-noise ratio (S/N) of each sample (individual CPMG curves) was determined using Eq. (1)

$$S/N = \frac{B}{\mathrm{STDEV(noise)}} \tag{1}$$

where B is the first point of the CPMG signal and STDEV(noise) is the standard deviation of the noise, which was calculated as the standard deviation of the last 1500 points acquired (1.0–1.6 s). From a careful inspection of the CPMG signals of the 30 samples under study, it was clear that after 1.0 s acquired data corresponded only to noise (sample had already decayed). Data S/N varied between 2105 (Sample 22) and 7279 (Sample 9), with a mean value of 5444, which perfectly fulfills the requirements of the algorithms under study concerning the S/N of the computed data. Istratov and Vyvenko [4] have reported that the maximum resolution limit that can be reached in experimental setups, $(T_2)_{i+1}/(T_2)_i$, is approximately 2 for data

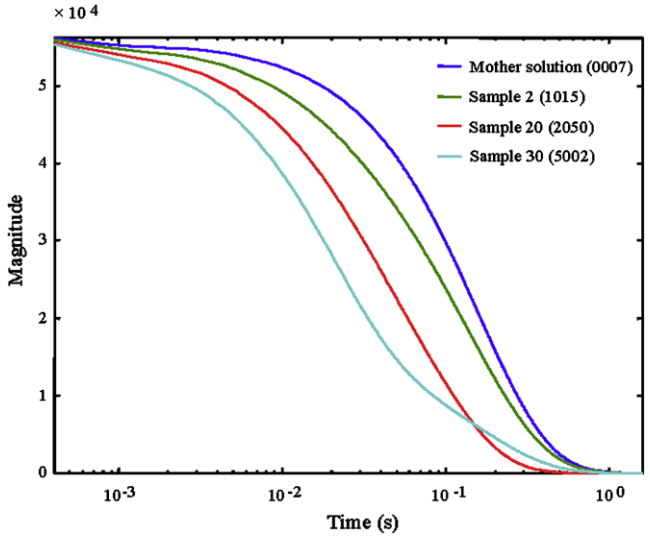

Fig. 2. CPMG relaxation profiles of four $CuSO_4$ representative solutions (known concentrations) – a mother solution (one-component solution), sample 2 (three-component solution) and samples 20 and 30 (two-component solutions); time axis in log scale.

with a S/N value of 10^3. In the present study, the minimum T_2 value ratio is indeed 2 and the S/N values of the relaxation decays are in the order of 10^3.

3. Results and discussion

The main advantage of the DOUBLESLICING algorithm is its capability to resolve single exponential profiles within very short computation times. For example, when applied to a single CPMG NMR data curve, characterized by being a sum of exponentials, the ability of DOUBLESLICING to yield mono-exponential loadings enables the determination of the number of compounds in the sample as well as the estimation of the respective concentrations and decay times (T_2 values). This feature can be very valuable in the analysis and understanding of variations of the T_2 values of the different components within a sample.

However, before accepting and promoting a new algorithm, its performance must be evaluated and compared with existing related algorithms. As mentioned before, the experimental design, which resulted in a set of 30 samples with known concentrations and T_2 values, allowed for 30 independent tests of the DOUBLESLICING algorithm and the comparison of its performance to the performance of the classical approach, the so-called discrete multi-exponential curve fitting.

As a first step, the relaxation time values (T_2 values) of the four components present in the 30 samples were obtained from DECRA. DECRA was run using four factors, equal to the maximum number of different components (each one corresponding to a single T_2 value) that could be present in the 30 samples under study. In Table 2, DECRA T_2 results (obtained by the analysis of the entire data set) are reported.

From Table 2 it is clear that DECRA does not provide accurate T_2 results, failing in the determination of the highest T_2 values. It is worth mentioning that the T_2 estimates obtained by DECRA improved significantly when the initial data points, which deviated from an exponential behavior, were excluded from the computations. However, DECRA was identified as a non-robust method, since its results were strongly dependent on the number and selection of the removed data points.

The second step was to test and compare DOUBLESLICING to discrete exponential fitting. Both algorithms were independently applied to each one of the 30 CPMG signals in order to estimate the relaxation decay times of the underlying exponential components. For each sample, the algorithms were run using a number of factors equal to the number of different components present in the sample (for example, one factor was computed for sample 1, while three factors were computed for sample 2). Fig. 3 compares the resulting performance of the two numerical approaches.

The plot indicates that DOUBLESLICING and exponential fitting were similarly accurate and precise in the determination of T_2 values. Moreover, by statistical analysis (not shown), DOUBLESLICING proved to give slightly better results – it follows that the dispersion of each one of the calculated T_2 estimates by DOUBLESLICING was narrower than the results obtained by exponential fitting (DOUBLESLICING more precise), centered at a value closer to the reference T_2 (DOUBLESLICING more accurate).

When examining the average algorithm speed, DOUBLESLICING outperformed exponential fitting by a factor of approximately four (on average). The speed advantage also allows for more elaborate validation of the number of components and quality of the fit by, for example, jack-knifing [8].

In addition, the computation time for DOUBLESLICING increased slightly with the number of components, which was in stark contrast to exponential fitting, for which the computation time increased dramatically with the number of components.

Additionally, quantitative information from the application of discrete multi-exponential fitting and DOUBLESLICING was evaluated using the estimates of the concentration of each of the 30 samples (Fig. 4). To assess Fig. 4, it is worth recalling that samples were prepared by transferring different amounts of four mother solutions into an 18 mm NMR tube, which sampling volume was previously divided into

Table 2
Summary table: T_2 estimates using DECRA, discrete exponential fitting and DOUBLESLICING; for the single-curve multi-exponential fitting algorithms (discrete exponential fitting and DOUBLESLICING), mean T_2 values are presented; reference T_2 values in the first row

T_2(ms)	19.6	40.6	81.4	159.4
DECRA	17.5	56.9	179.2	347.2
Single-curve multi-exponential fitting algorithms				
Discrete exponential fitting	19.2	40.7	81.6	160.7
DOUBLESLICING	19.5	40.7	81.7	159.9

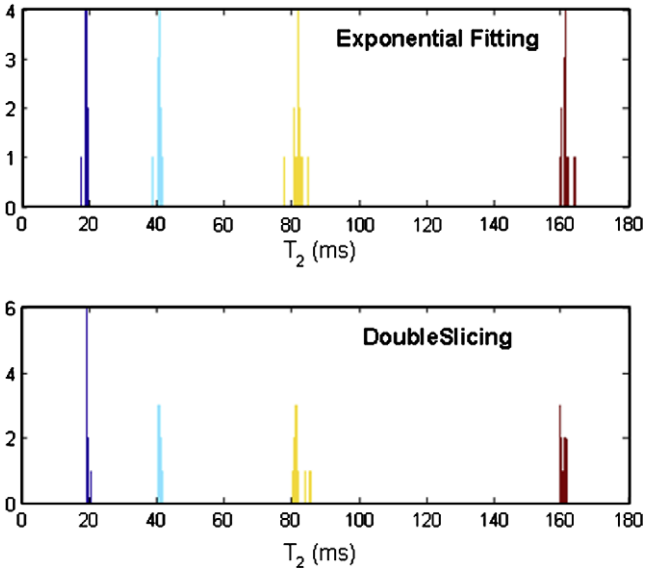

Fig. 3. Dispersion of T_2 values found by discrete exponential fitting and DOUBLESLICING.

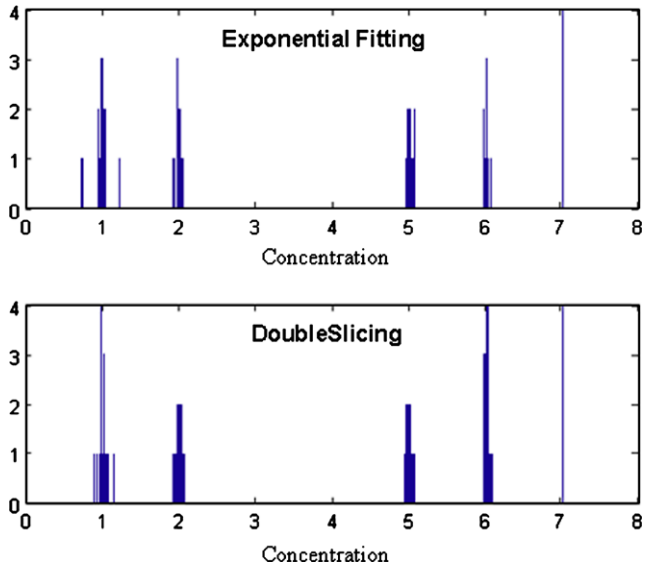

Fig. 4. Bar graph displaying the distribution of concentration values (each unit corresponding to one compartment, i.e. one small tube placed in the 18 mm NMR tube) for the 30 samples under study, as a function of the curve fitting algorithm used: discrete multi-exponential fitting and DOUBLESLICING.

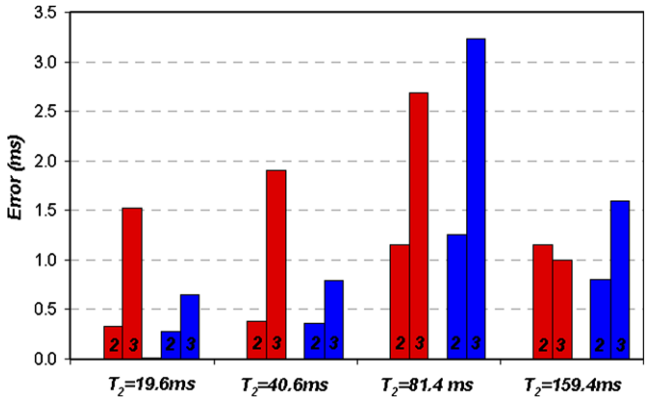

Fig. 5. Bar graph presenting the errors associated with T_2 calculations by discrete multi-exponential fitting (red) and DOUBLESLICING (blue), fitting two and three components to the CPMG relaxation data (numbers in the bars). The errors that resulted from fitting a single component were insignificant when compared to the ones presented.

seven identical compartments – concentration values in units from 1 to 7 (refer to Experimental Design, Section 2, Table 1).

Similarly to the results obtained for the T_2 estimates, Fig. 4 indicates a comparable (and even narrower) distribution of the concentration values calculated by DOUBLESLICING, when compared to the results obtained by exponential fitting. However, although more precise, DOUBLESLICING was found to be slightly less accurate in the concentration estimates when compared to the exponential fitting approach (results not shown).

When compiling the results obtained, T_2 and concentration estimates, DOUBLESLICING can be thought as a method which has been optimized for the determination of relaxation decay times (T_2 values). The optimization of this particular task is probably responsible for the slight loss of accuracy in the determination of the concentration values (compromising effect).

For exponential fitting as well as DOUBLESLICING it was verified that the error in the estimation of the four T_2 values increased with the number of components fitted during the performance of the algorithm – for example, the determination of the T_2 value associated with mother solution number 1 was more accurate when computing relaxation curves of samples composed of only this solution; the results were gradually poorer when the decays of samples with an increasing number of components (mixture of different amounts of distinct mother solutions) were computed. Fig. 5 illustrates this behavior.

Error values were determined using Eq. (2), which represents the root mean square error of prediction ($T_{2,\text{calculated}}$ are the T_2 estimates obtained by discrete exponential fitting and DOUBLESLICING, and n is the respective number of estimates).

$$\text{Error}(ms) = \sqrt{\frac{\sum_{i=1}^{n}(T_{2,\text{reference}} - T_{2,\text{calculated}})^2}{n}} \quad (2)$$

From the analysis of Fig. 5 it is verified that the error increased when fitting an increased number of components, both for exponential fitting and DOUBLESLICING. This fact is in agreement with the Provencher study [3] in which the results showed that the resolving power of the Fourier method under analysis (for the resolution of decay exponentials) decreased as the number of closely spaced components increased.

Fig. 5 also indicates that small T_2 values are usually estimated more accurately – the error associated with T_2 estimates increased when T_2 increased from 19.6 ms to 81.4 ms (the inverse behavior observed for $T_2 = 159.4$ ms is probably due to statistical uncertainty and numerical problems). This may be associated to the nature of the CPMG NMR data – in a sample, components with small T_2 values relax fast. Information about these components is then captured in the initial time values which correspond to data with higher signal-to-noise ratio (when compared to the data representative of components with high T_2 values; information about these components is mainly obtained in the final time values due to their long relaxation decay times). Additionally, the exponential nature of the signals intrinsically makes the uncertainty of higher T_2 values higher, because the profiles get increasingly more correlated for the same absolute difference in T_2 values at higher levels.

Finally, Fig. 5 shows that discrete multi-exponential fitting and DOUBLESLICING are comparable algorithms in terms of accuracy – neither method could be clearly identified for being more stable in T_2 estimates (when increasing the model complexity, i.e. by fitting a higher number of components). A similar analysis of the calculations performed to determine concentration values, applying

both algorithms, led to identical conclusions. Future studies need to be conducted to properly characterize and compare the algorithms according to their robustness level.

Table 2 presents an overview of the T_2 estimates obtained applying the algorithms tested in this work. It emphasizes the accuracy of DOUBLESLICING as well as its comparable performance with discrete exponential fitting.

4. Conclusions

In this paper the advantages of using DOUBLESLICING in the resolution of single low field time domain relaxation curves are illustrated. This method was found to be accurate in estimating relaxation times (T_2 values) differing in one order of magnitude (range: 19.6–159.4 ms) and their related concentrations. Its performance was comparable to discrete exponential fitting. The main advantage of DOUBLESLICING resides in its much shorter computation times when compared to traditional methods, such as discrete multi-exponential fitting (in this work, DOUBLESLICING outperformed exponential fitting by a factor of four). The faster computation times give DOUBLESLICING great potential for applications where many oligo-exponential equations need to be resolved or in cases where elaborate resampling schemes are required. DOUBLESLICING can also be applied as pre-processing (super-qualified and relatively unbiased initial guesses) to traditional numerical curve resolution algorithms; in the NMR field it can be used, for example, in mathematical contrasting of MRI images [9].

5. Experimental

NMR data acquisition was performed on a 23.2 MHz *Maran* benchtop pulsed ^{1}H NMR spectrometer (*Oxford Instrument*) equipped with an 18 mm diameter variable temperature probe head. The relaxation measurements were performed using CPMG (*Carr Purcell Meiboom Gill*) pulse sequence [14,15]: a total of 4000 data points were acquired, with a 90°–180° pulse spacing (τ) value of 0.2 ms. The relaxation delay between consecutive scans was set to 1 s, and 32 scans were accumulated. The receiver gain (RG) was optimized and kept constant for all measurements (RG = 1.2%). The samples were measured in a random sequence at 25 °C after prior equilibration at the same temperature.

The multi-exponential fitting algorithms applied were from the Low-field NMR toolbox, version 3.0 for MATLAB [6], which can be downloaded from the website www.models.life.ku.dk/source/lfnmr/. Handling of data and all subsequent analyses were performed in MATLAB v. 7.1 (The Math-Works Inc., Natick, USA).

Acknowledgments

The authors gratefully acknowledge The Danish Veterinary and Agricultural Research Council (SJVF) and the Danish Dairy Foundation for financial support. A special thanks to Gilda Kischinovsky for proofreading the manuscript.

References

[1] K. William, NMR in Chemistry – A Multinuclear Introduction, Macmillan, Shepherdstown, WV, USA, 1986.
[2] S.W. Provencher, CONTIN: a general purpose constrained regularization program for inverting noisy linear algebraic and integral equations, Comput. Phys. Commun. 27 (1982) 229–242.
[3] S.W. Provencher, A Fourier method for the analysis of exponential decay curves, Biophys. J. 16 (1976) 27–41.
[4] A.A. Istratov, O.F. Vyvenko, Exponential analysis in physical phenomena, Rev. Sci. Instrum. 70 (1999) 1233–1257.
[5] S.B. Engelsen, H.T. Pedersen, R. Bro, Direct exponential curve resolution by SLICING, in: G.A. Webb (Ed.), Modern Magnetic Resonance – Part III, Applications in Materials Science and Food Science, Springer, Berlin, Heidelberg, New York, ISBN: 978-1-4020-3894-5, 2006, pp. 1823–1830.
[6] H.T. Pedersen, R. Bro, S.B. Engelsen, Towards rapid and unique resolution of low-field NMR relaxation data: trilinear SLICING versus two-dimensional curve fitting, J. Magn. Reson. 157 (2002) 141–155.
[7] S.B. Engelsen, R. Bro, PowerSlicing, J. Magn. Reson. 163 (2003) 192–197.
[8] H.T. Pedersen, L. Munck, S.B. Engelsen, Low-field ^{1}H nuclear magnetic resonance and chemometrics combined for simultaneous determination of water, oil, and protein contents in oilseeds, J. Am. Oil Chem. Soc. 77 (2000) 1069–1076.
[9] E. Micklander, L.G. Thygesen, H.T. Pedersen, F. van den Berg, R. Bro, D.N. Rutledge, S.B. Engelsen, Mutivariate analysis of time domain NMR signals in relation to food quality, in: G.A. Webb, D. Rutledge, (Eds.), Magnetic Resonance in Food Science – Latest Developments, 2003, pp. 239–254.
[10] W. Windig, B. Antalek, Direct exponential curve resolution algorithm (DECRA): a novel application of the generalized rank annihilation method for a single spectral mixture data set with exponentially decaying contribution profiles, Chemom. Intell. Lab. Syst. 37 (1997) 241–254.
[11] B. Antalek, J.M. Hewitt, W. Windig, P.D. Yacobucci, T. Mourey, K. Le, The use of PGSE NMR and DECRA for determining polymer composition, Magn. Reson. Chem. 40 (2002) 60–71.
[12] A. Smilde, R. Bro, P. Geladi, Multi-way Analysis: Applications in the Chemical Sciences, Wiley, SLU Robacksdalen, Sweden, 2004.
[13] D.M. Olsson, L.S. Nelson, The Nelder–Mead simplex procedure for function minimization, Technometrics 17 (1975) 45–51.
[14] S. Meiboom, D. Gill, Modified spin-echo method for measuring nuclear relaxation times, Rev. Sci. Instrum. 29 (1958) 688–691.
[15] H.Y. Carr, E.M. Purcell, Effects of diffusion on free precession in Nuclear Magnetic Resonance experiments, Phys. Rev. 94 (1954) 630–638.