Null-Biased Fast-FieldCycling NMR Sequences

Stanislav Sýkora - Gianni Ferrante

Stelar Srl, Via E.Fermi 4, Mede (Pv), Italy I-27035

Introduction

The standard pre-polarized and non-polarized measurement sequencies used in fast-field-cycling (FFC) NMR relaxometry [1] suffer from two major drawbacks:

(a) The longitudinal nuclear magnetization of the sample evolves with $\tau \to \infty$ towards non-zero values which, moreover, are difficult to predict due to the fact that the magnetization evolves even *during the field-switching intervals*. Consequently, FFC-NMR magnetization evolution curves *must* be fitted with an adjustable 'offset' parameter, in addition to the decay rates and weights of individual sample components (for example, three parameters are needed in the case of a mono-exponential fit).

(b) Measurements are carried out combining two different sequences, a non-polarized one at high relaxation fields and a pre-polarized one at low relaxation fields (the crossover field being approximately half of the polarization field). Occasionally, this leads to statistically significant discrepancies between the two sections of the resulting NMRD profile.

We propose a family of novel measurement sequences consisting in a combination of RF phase cycling, receiver cycling *and* magnetic-field cycling, such that all the offset effects get cancelled, while the components of the decays due to sample polarization get enhanced. In such sequences, the acquired signal S(τ) decays to exact zero for $\tau \to \infty$ (which is the reason why we call them **null-biased**).

Basic traditional FFC-NMR sequences

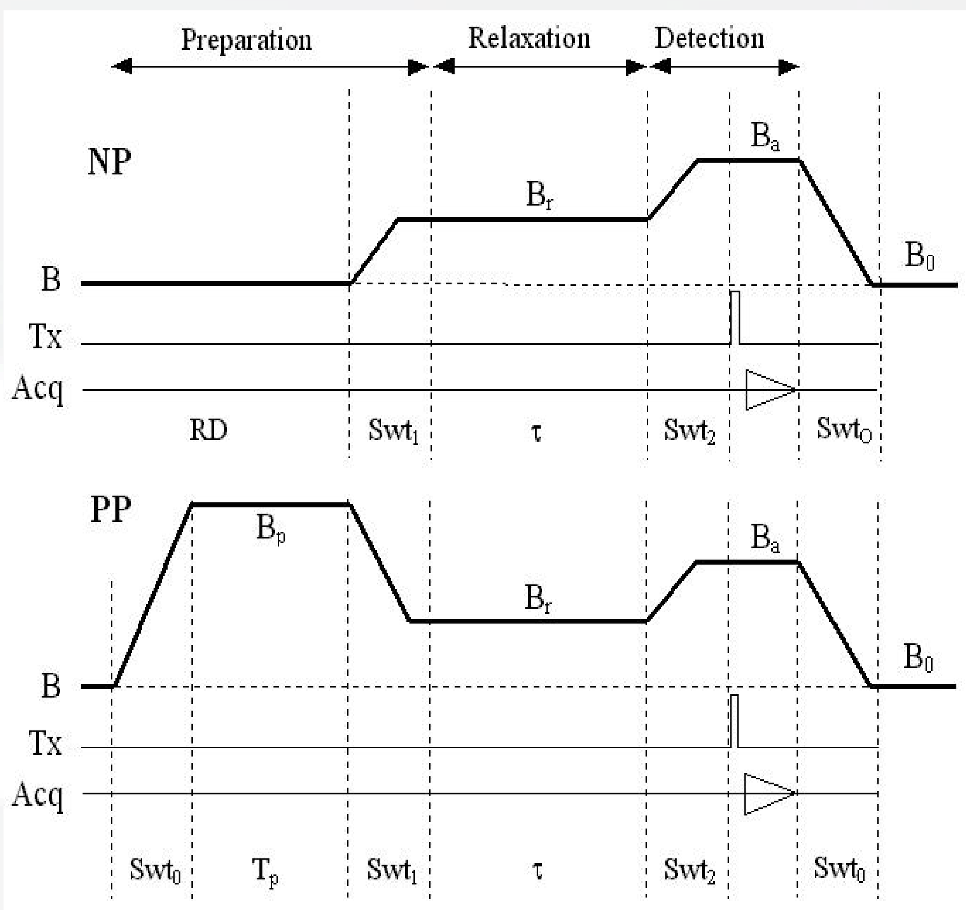


Fig.1. Non-polarized (NP) and pre-polarized (PP) sequences

The thick line shows the switching of the main magnetic field B between four pre-programmed values (off B_o, polarization B_P, relaxation B_r and acquisition B_a). The pulser control lines for the RF transmitter (T_x) and data-acquisition trigger (Acq) are also shown. Normally, the switching periods Swt_0 are omitted since they do not affect the acquired data, while the switching periods Swt_1, Swt_2 are set to a common value Swt. The pre-programmed slewing rates of all the linear switching ramps are all identical.

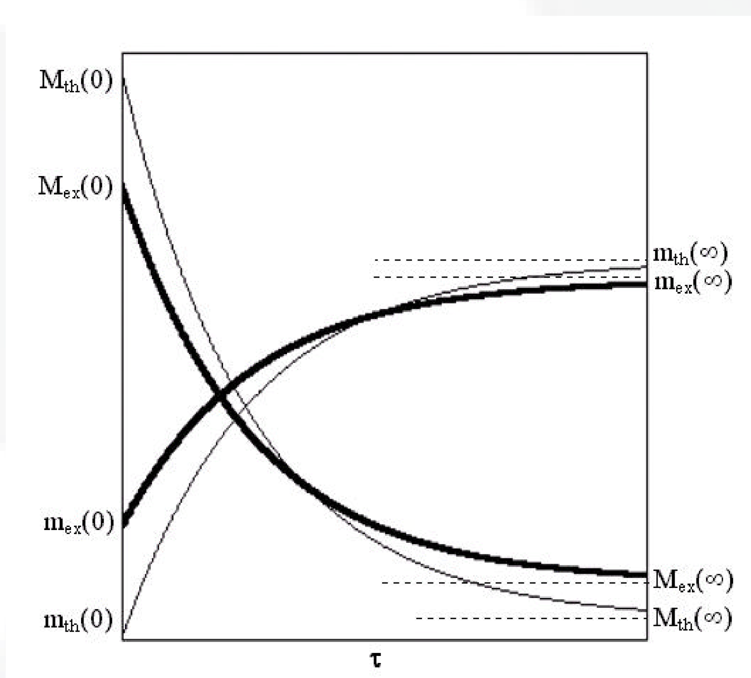


Fig.2. Effects of field-switching intervals on the magnetization evolution curves M(τ)

The differences between the theoretical (thin) and experimental (thick) lines represent the effects of switching intervals on the magnetization evolution curves.

In the NP experiment (increasing curves), the theoretical $m_{th}(\tau)$ function starts at 0 and increases toward the value $m_{th}(\infty) \equiv m_r$, corresponding to the relaxation field b_r. The experimental curve $m_{ex}(\tau)$ starts at $m_{ex}(0)>0$ because of the switching interval from zero field to B_r. It then grows toward $m_{ex}(\infty) \neq m_r$ because of the switching interval from B_r to B_a (we assume $B_a<B_r$ so that the discrepancy has a negative sign).

In the PP experiment (decreasing curves), the theoretical $M_{th}(\tau)$ function starts at $M_{th}(0) \equiv M_p$ and decreases toward the value of $M_{th}(\infty) = M_r$, corresponding to the relaxation field B_r (assumed to be quite small). The experimental curve $M_{ex}(\tau)$ starts at $M_{ex}(0)<M_p$ because of the switching interval from B_p to B_r. It then falls toward $M_{ex}(\infty)>M_r$ because of the switching interval from B_r to the (higher) acquisition field B_a.

Despite the apparent discrepancies between the theoretical and experimental curves, their relaxation rate constants the same (all curves plotted in this Figure have the same relaxation rate R).

The principle of Null-Biased sequences

With reference to Fig.1, notice that the relaxation and detection periods of the classical sequences NP and PP are completely identical. What differs is the sample magnetization at the beginning of the relaxation period. We can therefore arrange an experiment which (i) cycles alternatively through two distinct sequences with different preparation periods but identical relaxation and detection periods and identical relaxation fields and (ii) accumulates the data by adding the signals associated with the first sequence and subtracting those arising from the second one.

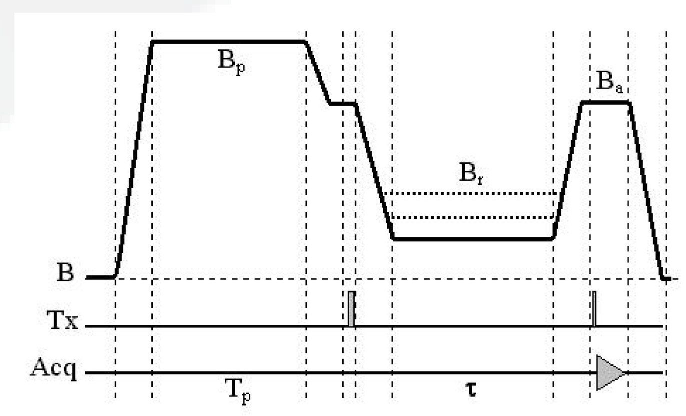
The accumulated data then reflect the difference in the preparation periods but contain no switching artifacts due to the switching interval Swt_2. Since the relaxation field is the same in both sequences, the accumulated signal difference necessarily decays to zero with increasing τ value. For reasons listed below, this is an extremely desirable result.

In practice, the principle can be implemented in a large number of ways. In what follows we discuss the NBIR sequence which is one of the most important of such implementations.

NBIR: the Null-Balanced Inversion-Recovery sequence

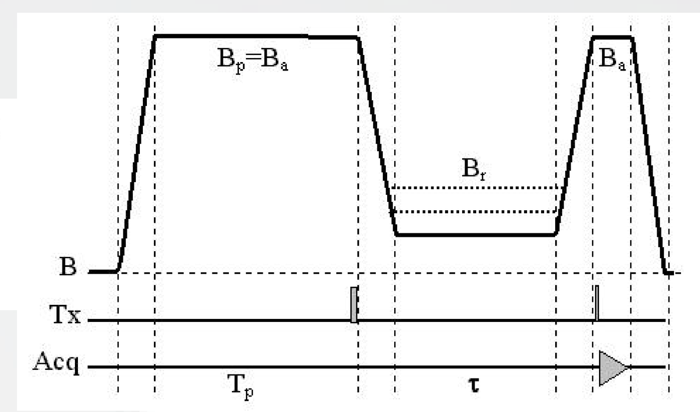
A neat way of achieving the goal is by using exactly the same field cycle in both sequences and causing the difference in polarization by alternatively gating ON and OFF a 180° RF pulse positioned at the very end of the polarization interval. This has the advantage of being easily implementable by means of the standard phase-cycling mechanism. The diagram of the complete sequence is shown below, at left. It can be further simplified (below right) when one uses the same field value both for acquisition and for polarization (this has an additional merit of freeing one of the field settings for other uses).

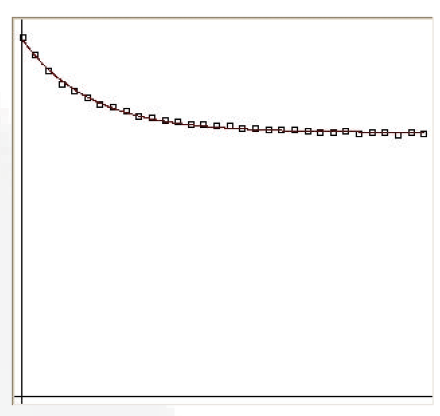
The two diagrams are actually identical to those of the plain FFC IR sequences [1]. What differs is the 'phase' cycle which, reduced to its minimum length of 2, is as shown below (center).



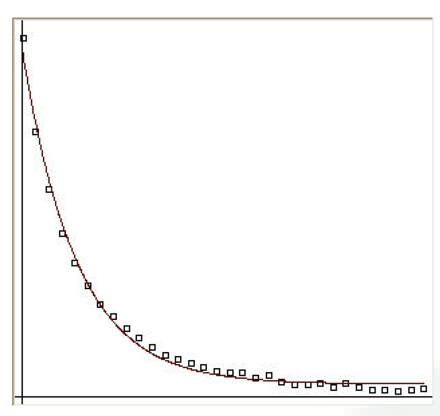
⇐ **NBIR, NBIR/S** **NBIR0, NBIR0/S** ⇒

Cycle #	Pulse 1	Pulse 2	Receiver
1	none	90°x	Add
2	180°x	90°x	Subtract

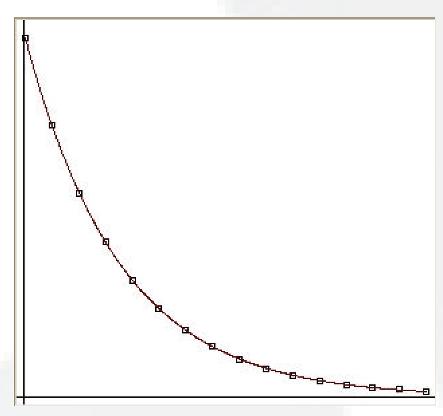




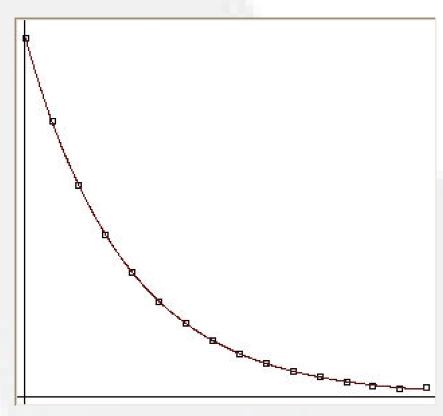
#1) Paraffin
Sequence: **PP/S**
B_P = 12 MHz, B_r = 8 MHz.
NP sequence would be better here, but PP illustrates nicely the large signal S(∞) value and the small signal variation.



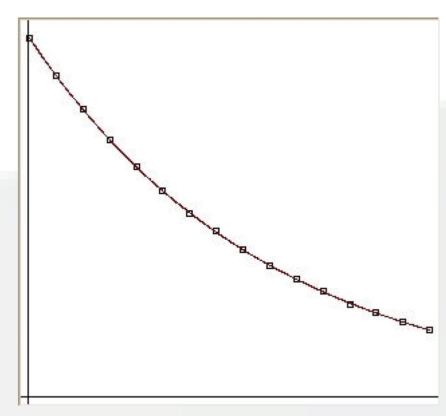
#2) Same sample as #1
Sequence: **NBIR/S**
B_P, B_r are the same as in #1.
The offset has been zeroed. Improved signal variation now permits to assess the non-exponentiality of the decay.



#3) 2 mM $MnCl_2$ in H_2O
Sequence: **NBIR/S**
B_P =8 MHz, B_r = 100 kHz.
Last data point has τ = 48 ms. In this situation, PP/S would have a large S(∞) value due to the last switching interval.



#4) Same sample as #3
Sequence: **NBIR/S**
B_P =8 MHz, B_r = 9 MHz.
Last data point has τ=160 ms. Though B_r is now larger than B_P but we are still using the same sequence.



#5) Same sample as #3
Sequence: **NBIR/S**
B_P =8 MHz, B_r = 4 MHz.
Last data point has τ = 45 ms. The decay is truncated but knowing that it decays to zero permits a good T_1 estimate..

Principle advantages

(1) Since S(∞) is *apriori* known to be exactly null, it does not need to be estimated experimentally. There is therefore no longer the necessity to cover τ-values up to four times T_1. In most cases **one can stop earlier** and save a considerable amount of time (a reasonable default for the maximum τ now becomes 2^*T_1).

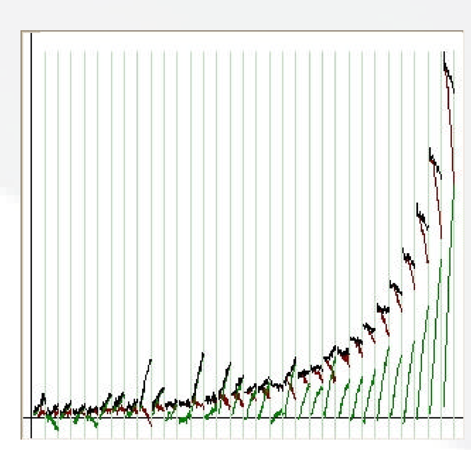
(2) For the same reason, the data can be fitted without the adjustable signal offset parameter (in particular, a two-parameter fit is sufficient in the case of a mono-exponential decay). Considering the strong effect of number of adjustable parameters on their confidance intervals [2], this fact alone **dramatically improves the precision** of the measured T_1's.

(3) As for all the IR-based sequences, **the same sequence** is used to acquire the NMRD profile **over the complete range of field values**. The measured NMRD profiles thus become internally more coherent and no discrepancy between high-field data and low-field data can occur.

(4) Unlike in the plain IR sequence, however, the signal S(τ) in any null-balanced sequence remains always of the same sign (**no zero crossing**). The sequences therefore present no noise-related zero-crossing problem when signal magnitudes are used to evaluate the decay rates.

A minor problem to solve

An *apparent* drawback of the new sequences consists in the fact that they enhance the *visual* impact of random field instabilities between consecutive scans (see the example on the right). Analysis shows, however, that traditional measurements are burdened by exactly the same instabilities, even though they are to a large extent hidden by the large magnetization offsets. Short of redesigning the whole magnet system, there are two viable methods of dealing with such field instability effects:
(a) Using the offset-insensitive CPMG detection technique [1] (sequences **NBIR_CPMG** and **NBIR0_CPMG**),
(b) Applying offset-insensitive data evaluation methods, such as extrapolation to time zero.



References

[1] G.Ferrante, S.Sykora, *Technical Aspects of Fast Field Cycling NMR Relaxometry*, in *Advances in Inorganic Chemistry*, R.van Eldick, Editor, Vol.57 (2005)
[2] C.Radhakrishna Rao, Linear Statistical Inference and its Applications, John Wiley & Sons 1973.