Progress in Nuclear Magnetic Resonance Spectroscopy 60 (2012) 52–70

Contents lists available at SciVerse ScienceDirect

Progress in Nuclear Magnetic Resonance Spectroscopy

journal homepage: www.elsevier.com/locate/pnmrs

Process and reaction monitoring by low-field NMR spectroscopy

Franz Dalitz [a], Markus Cudaj [b,c], Michael Maiwald [d], Gisela Guthausen [a,*]

[a] *Institute of Mechanical Process Engineering and Mechanics, SRG10-2, KIT, Adenauerring 20 b, 76131 Karlsruhe, Germany*
[b] *Institute for Chemical Technology and Polymer Chemistry, KIT, 76128 Karlsruhe, Germany*
[c] *PSS Polymer Standards Service GmbH, 55120 Mainz, Germany*
[d] *BAM Federal Institute for Materials Research and Testing, 12489 Berlin, Germany*

ARTICLE INFO

Article history:
Received 26 September 2011
Accepted 29 November 2011
Available online 6 December 2011

Keywords:
Process analysis
Low-field NMR spectroscopy
Flow-NMR
Data analysis

Contents

Abbreviations: ALTADENA, adiabatic longitudinal transport after dissociation engenders nuclear alignment; ATR, attenuated total reflection; CFD, computational fluid dynamics; CPACT, center of process analysis an control technology; CPMG, Multi-echo sequence according to Carr, Purcell, Meiboom, Gill; DECRA, direct exponential curve resolution algorithm; DNP, dynamic nuclear polarization; e.g., Lat: exempli gratia, for example; etc., Lat: et cetera, and so forth; ERETIC, electronic reference to access in vivo concentrations; FID, free induction decay; FID-GRAM, free induction decay generalized rank annihilation method; FID-DECRA, free induction decay direct exponential curve resolution; FT, Fourier transformation; FWHM, full width at half maximum; GRAM, generalized rank annihilation method; GC, gas chromatography; HCA, hierarchical cluster analysis; IHM, indirect hard modeling; IPC, in-process control; IR, infra red (spectroscopy); LC, liquid chromatography; LDA, linear discriminate analysis; MAS, magic angle spinning; MSME, multi-slice multi-echo sequence (MRI); MCR, multivariate curve resolution; MRI, magnetic resonance imaging; MR-NMR, medium resolution NMR; MTBE, methyl-tert-butylether; NCCW, non-contact check weigher; NIR, near infrared (spectroscopy); NMR, nuclear magnetic resonance; OPU, oil pick up; PASADENA, para-hydrogen and synthesis allow dramatically enhanced nuclear alignment; PCA, principal component analysis; PCR, principal component regression; PEEK, polyether ether ketone; PHIP, para-hydrogen induced polarization; PLS-R, partial least squares regression; PRESS, predictive residual error sum of squares; QC, quality control; RTD, residence time distribution; SFC, solid fat content; SEVI, spin-echo-velocity imaging; SNR, signal to noise ratio; TD-NMR, time-domain NMR; UV–Vis, ultra-violet–visible (spectroscopy); WATERGATE, water suppression by gradient tailored excitation; WET, water suppression by T_1 effects.

* Corresponding author. Tel.: +49 721 6084 8058; fax: +49 721 6084 4953.
E-mail address: gisela.guthausen@kit.edu (G. Guthausen).

doi:10.1016/j.pnmrs.2011.11.003

Nomenclature

α	conversion	T_1	longitudinal relaxation time
a	parameter of Lorentzian line shape	$T_{1,eff}$	effective T_1-relaxation time
b	parameter of Gaussian line shape	T_2	transverse relaxation time
$\boldsymbol{B}_0$	static magnetic field	$T_{2,eff}$	effective T_2-relaxation time
$\boldsymbol{B}_1$	radio frequency field	t	time
c	concentration	t_{res}	median of the RTD
δ_{max}	(maximum) Chemical shift	t_p	repetition time
γ	gyromagnetic ratio	t_{acq}	acquisition time
Γ	relaxation matrix	t_d	relaxation delay
I_{max}	(maximum) Intensity	$\boldsymbol{v}$	velocity
μ_0	magnetic permeability	$\dot{V}_{max}$	(maximum) volume flow rate
$\mathbf{M}$	magnetization	V	volume
Q	quality factor	ω_0	Larmor frequency
r	distance	$\Delta\omega$	line width
$\boldsymbol{r}$	position vector	x,y,z	Cartesian coordinates
τ_c	correlation time	x	molar fraction
τ	residence time		

1. Introduction

New developments in spectroscopic techniques for process control are in general driven by the shortcomings of existing technology, e.g., when sensitivity, selectivity, robustness, etc. do not meet the demands. The perfect process analytical method would be based on a robust, non-invasive and easy to handle customized technique operating in real-time. The ideal instrumentation comes without any need for calibration, is an absolute method, has a professional support, and is compliant to increasing regulatory requirements. At least for NMR a trend can be observed towards such an all-in-one device suitable for every purpose, also in NMR.

In process control, the usually measured parameters are temperature, pressure, flow rate, feedstock and product composition, most often as a function of time. One major issue is the time-relevant feedback, which cannot be provided by most of the standard off-line techniques. Sometimes density and viscosity (torquemeter) are also monitored. The aim of reaction monitoring is commonly to follow material properties time-resolved for the purpose of guidance and optimization of a given process. This is driven by the need to save human and natural resources by an optimized process (Section 2.1).

Alternative techniques used in process control are optical spectroscopy (UV–VIS, IR and especially NIR), ultrasonic velocity and attenuation measurements. Most of these methods are nowadays widely used as on-line instrumentation. In the case of commonly applied optical methods, reliability is not guaranteed in case of heterogeneous materials, and they usually require a considerable calibration effort. Gas chromatography requires extensive sampling and is time-consuming. Above all it is not completely non-invasive. For heterogeneous materials the question about the representative sample volume has to be addressed. NMR has the potential to reflect both structural and conformational changes according to spectral, diffusional and relaxation parameters. NMR may be a valuable alternative to commonly used methods despite the higher technical efforts required because it is unique with respect to chemical selectivity.

Quantitative high-resolution on-line NMR spectroscopy can be applied to the investigation of complex fluid mixtures containing analytically similar compounds. The development of on-line (flow) techniques has tremendously increased the value of NMR spectroscopy as a non-invasive method for process development applications. Small low-field NMR systems equipped with permanent magnets are available for quantitative analysis in quality control, also as on-line instruments in production environments. These devices typically work at magnetic field strengths up to about 2 T, corresponding to 85 MHz ^{1}H-frequency. In classic low-field NMR, relaxation times and relaxation weighted signals represent product, educt or process relevant variables. It should be mentioned that ultra low-field NMR with ^{1}H-Larmor frequencies in the kHz range is not considered in this review. The interpretation of ultra low-field NMR spectra is complicated because of small chemical shift differences and is difficult to use for multi-component samples. The selective enhancement by hyper-polarization effects is impressive but it probably cannot be generalized for each and every process apart from the requirement of additional instrumentation. Different spectrometer hardware is required for this type of NMR, too, and even small time dependent magnetic fields in the surrounding have to be avoided.

The focus in this review is on a robust low-field spectroscopic technique which has the potential to be widely applicable in an industrial or technical environment. The development is related