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Recent MRI Studies on Heterogeneous Catalysis

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**Abstract**

Applications of magnetic resonance imaging to the studies of heterogeneous catalytic processes are relatively rare. At the same time, magnetic resonance toolkit is able to provide valuable insight into the key dynamic processes in an operating reactor which govern its efficiency and safety, such as heat and mass transfer, phase transitions and chemical transformations. Thanks to the versatile nature of image contrast in MRI, it can provide valuable parameter maps with a rich and diverse information content. Achieving a reasonably high spatial and temporal resolution requires high NMR detection sensitivity, and is thus particularly challenging in MR studies of gases because their spin density and relaxation times are considerably smaller than those of liquids. Remarkably, the reaction that so far was addressed with MRI most, the heterogeneous hydrogenation of unsaturated compounds such as liquid and gaseous olefins and alkynes, provides a useful solution to the sensitivity problem. By simply utilizing parahydrogen instead of normal hydrogen in the reaction, one can hyperpolarise nuclear spins of reaction products and intermediates, thereby achieving a several orders of magnitude enhancement of their NMR signals. Another interesting yet challenging development is the MRI/MRS of operating microreactors where conventional NMR/MRI instruments and techniques fail to provide adequate sensitivity. An elegant solution to boost the sensitivity in such studies is the use of the remote detection NMR approach, either alone or in combination with hyperpolarisation techniques. The examples we discuss are intended to demonstrate the current achievements of this research area and the challenges that need to be addressed before such applications can become routine and widespread.

**Keywords:** magnetic resonance imaging, operando spectroscopy, MRI of gases, operating catalytic reactor, microreactors, heterogeneous hydrogenation, reaction conversion map, spatially resolved thermometry, remote detection NMR, parahydrogen-based hyperpolarization

**1. Introduction and general information**

Magnetic resonance imaging (MRI) is a versatile technique broadly used in modern medical diagnostics. Its capabilities and applications extend well beyond the simple morphological imaging and today cover such areas as functioning of a human body as well, ranging from angiographic studies of blood flow [1,2] and perfusion [3,4], uptake of exogenous and endogenous substances by tissues and organs, in vivo MRI thermometry to monitor local tissue temperature in hypo- [5,6] and hyperthermia [7,8] treatments, to functional MRI of normal and pathological human brain [9,10] and in vivo studies of metabolism in molecular and cellular MRI [11-14]. In addition to advanced methods of medical care, achieving higher standards of human life and well-being also requires further progress in modern industrial processes, including chemical industry that provides fuels, pharmaceuticals, detergents, personal care and health products, textiles, foods, fertilizers, polymers, plastics and coatings, and a lot more. Most of the industrial chemical processes rely heavily on catalysis, and the majority of them are based on heterogeneous catalysis [15-17]. Heterogeneous catalytic process is a complex combination of numerous individual processes such as mass and heat transport at various length and timescales in addition to the chemical transformation of reactants into various reaction intermediates and final products and byproducts. It is desirable to make industrial scale catalytic processes better, i.e., cheaper, safer, greener, etc. To achieve this, it is imperative to have access to spatially and temporally resolved information on the processes taking place inside a catalytic reactor. A much better understanding of reaction conversion and selectivity, mass transport (flow and diffusion) of reactants and products, adsorption processes, heat transport (local temperatures and their gradients, formation of hot spots), etc., are essential to improve overall reactor performance. At the same time, there aren’t many instrumental techniques that could provide such information, especially in a non-invasive manner.

MRI is quite unique in this respect, as it has certainly proven its power to visualize non-invasively the morphology and function of a human body. In a sense, a living organism (e.g., a human body) can be viewed as a very sophisticated bioreactor, while MRI is a versatile advanced toolkit for an efficient non-invasive visualization of its morphology and function. Thus, given that the most sophisticated catalytic reactor is not nearly a match in its complexity to a mammal, it may appear that applying MRI to study the inner structure and function of a man-made reactor [18-27] would be a piece of cake. However, when trying to extend the application of MRI to heterogeneous catalysts and catalytic reactions, one inevitably arrives at the following revelation: the NMR properties of a human or an animal body are almost ideal for an MRI study. In fact, it would be quite hard to come up with a better fit even if one had an opportunity to redesign a human being from a scratch. In contrast, most of the materials and non-living objects are difficult and sometimes impossible to explore with the MRI technique. The primary reason for this difference is that human body is mostly water (ca. 55-75% depending on age and gender), providing the high sensitivity of 1H NMR detection. The only nucleus that could have provided a higher sensitivity is tritium (3H), for which the resonance frequency is ca. 6.6% higher compared to that of 1H at a given magnetic field, but apparently we were not intended to glow in the dark. In addition, the nuclear spin relaxation time of mobile water molecules is in the very comfortable range (seconds); much longer relaxation times could significantly increase image acquisition times, while much shorter relaxation times would lead to significant signal loss and thus to degraded sensitivity and image quality as well as spatial resolution. In addition, a body is composed of materials that are compatible with an NMR experiment in a broader sense. In contrast, the presence of foreign objects and materials in a body often leads to major complications with application of MRI including severe image distortions, or even completely precludes an MRI examination if patients have magnetic implants, pacemakers, etc.

Therefore, to successfully apply MRI to study catalytic processes, one needs to design and build a reactor which is compatible with NMR/MRI experiments, keeping in mind several key and sometimes interrelated issues and goals: (i) to ensure personnel safety and prevent damage to expensive NMR/MRI equipment, as flammable gases and liquids, explosive gas mixtures and high temperatures and pressures may be involved; (ii) to ensure the reactor design is compatible with MRI experiments; in particular, one needs to avoid magnetic materials and electrically conducting parts to avoid undesirable interaction with high magnetic fields, eddy currents induced by pulsed magnetic field gradients, to ensure thermal insulation of the reactor to avoid overheating of the hardware, in particular the gradient coils; (iii) to ensure realistic and meaningful reaction conditions such as pressure, temperature, reactor size, shape and orientation. In addition, it is always useful and desirable to supplement spatially resolved information on the reaction progress with other useful measurements such as temperature, reaction conversion and selectivity, etc.

In the design and implementation of such experiments, a lot will depend on the particular type of imaging system to be used, which can be a vertical bore system, such as an NMR spectrometer equipped with (micro)imaging accessories (a microimaging instrument), or a horizontal bore system such as preclinical or clinical MRI scanner. Alternatively, a bench-top or a mobile NMR/MRI system can be utilized, but such systems are usually characterized by lower magnetic fields and thus reduced signal-to-noise ratio (SNR) compared to high-field systems equipped with superconducting magnets, unless spin hyperpolarisation is employed as discussed in section 3 below.

The type of the imaging pulse sequence to be used in the experiments and its optimization are highly important. As SNR is a universal limitation in such studies, signal losses need to be minimized. In particular, it is essential to minimize the delay between the excitation radiofrequency (RF) pulse and signal detection (nominally, the echo time TE, even if the pulse sequence used does not formally produce an echo-type signal). Detecting gases is even more difficult compared to liquids, first of all because of the much lower NMR signal intensity due to low spin density in gases even if elevated pressures are used. Adsorption of gases on porous materials such as catalysts can increase the SNR but may also complicate the picture, In addition, gases diffuse much faster than liquids, and rapid diffusion in the presence of a magnetic field gradient leads to further signal losses. Therefore, the gradient amplitudes, their durations and placement in the pulse sequence should be chosen wisely, particularly with regard to the slice selection gradient which is on for all data points in k-space including k=0. As acquisition of spectral data is often desired, frequency encoding of one of the spatial coordinates is normally not applicable, and pure phase encoding is used, which increases imaging time and further reduces attainable spatial resolution.

**2. Conventional MRI studies of catalytic processes**

**2.1. Mapping of the liquid phase distribution and dynamics**

While a lot of useful information can be obtained when studying model “reactors” without an actual reaction taking place in them, the ultimate goal of such studies is to better understand processes taking place in a reactor under realistic operating conditions. Therefore, relevant information can be obtained only by means of the in situ and operando studies performed on an operating reactor. The interest to such studies based on the development and use of various spectroscopic and imaging techniques is growing steadily in the recent years [18,28-35]. Depending on the capabilities of a particular technique employed and the information desired, the operating reactors can range from a single catalyst pellet studied under reaction conditions to packed catalyst beds, structured catalysts (monoliths, honeycombs), etc.

To address the processes taking place on the length scale of a single catalyst pellet or bead, a single-catalyst-pellet reactor can be quite useful. Its relatively small size in comparison to, e.g., a packed catalyst bed makes it easier to safely conjugate it with an MRI instrument. The first reported studies of gas-liquid-solid catalytic processes by MRI addressed heterogeneous catalytic hydrogenation of α-methylstyrene (AMS) over a single cylindrical Pt/γ-Al2O3 pellet [18-20,36-42]. AMS was supplied to the catalyst as liquid or vapour or their combination, leading to very different spatial distributions of the liquid phase within the catalyst pellet. Notably, AMS was observed as a liquid within the pellet even when only its vapour was supplied to the reactor, which is reasonable because the temperature of the gaseous feed (ca 70 °C) was lower than the AMS boiling point (ca. 167 °C). Different steady states and hysteresis phenomena were observed by visualizing the liquid phase distribution in the pellet with MRI. As the MRI experiment was performed in such a way that no spectroscopic information was available, the efficiency of catalytic conversion of AMS to cumene was monitored indirectly by recording the pellet temperature with an implanted thermocouple. It was established that the highest reactor productivity was achieved when the upper part of the pellet to which liquid AMS was supplied remained filled with the liquid phase while the lower pellet part was essentially dry. In such a regime, the liquid-filled upper portion of a pellet served as a pool of reactant which can be readily evaporated and rapidly delivered to the dry lower portion of the catalyst pellet where a very efficient AMS to cumene conversion could take place in the vapour phase over the vast exposed catalyst surface available for the reaction.

Access to dynamic processes was facilitated by impregnating the catalyst pellets (1 wt% Pd/γ-Al2O3) with paramagnetic Mn ions (0.1 mass%), which made it possible to reduce the 2D image acquisition from ca. 4 min to ca. 0.5 min [19,41,43,43-46]. As a result, a number of fascinating dynamic processes were visualized in the operating single-pellet reactor, such as liquid phase redistribution during catalyst ignition events (Figure 1), liquid content oscillations and a reciprocating motion of the liquid front in the catalyst pellet [19,43,46]. Mathematical modelling of the experimental results [47] showed that the experimentally observed complex dynamic behaviour involving temperature and liquid distribution oscillations was the result of the coupling of heat and mass transfer and phase transitions with the chemical conversion within the operating reactor.

[Insert Figure 1 here]

Figure 1. The dynamics of liquid phase redistribution in a single catalyst pellet (Pd/γ-Al2O3, diameter 4.5 mm, length 12 mm) during an ignition event in the AMS hydrogenation process. The 2D images of an axial (a) or transverse (b) slice 2 mm thick were detected sequentially every 34 s, with image number in the sequence indicated above each image. Temperatures measured with a thermocouple implanted in the lower part of the pellet are indicated below each image. The location of the thermocouple in the pellet is indicated with white arrow (a, image 1). Note that the subsets of images shown in (a) and (b) are from different experimental runs. Lighter shades of grey correspond to higher liquid contents; in white areas the signal intensity is below the noise level. H2 flow rate was 10.9 cm3/s, its temperature was 77-78 0C, the AMS flow rate was 8.7×10-4 g/s. Transverse slice shown in (b) is located about 2.5 mm below the pellet centre. (Ref. [19]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

While the studies of single-pellet reactors are useful, they are certainly unable to capture the behavioural complexity of more realistic reactors such as packed beds and structured reactors. Indeed, the behaviour of an ensemble of pellets can be drastically different from that of a single pellet, for instance because of a different length scale and the presence of cooperative phenomena in the ensemble of pellets which would be impossible for a single pellet. In addition, studies of catalyst beds can demonstrate unambiguously the drastic differences in the processes that take place under reactive and model non-reactive conditions. This was convincingly demonstrated, for instance, by applying MRI to study heterogeneous catalytic hydrogenation of 1-octene [48]. In the experiments, liquid 1-octene feed was kept constant, while the reaction was switched on or off by supplying either H2 or N2 in the gas feed, respectively. The spatial maps of external and internal liquid holdup extracted from the 2D images revealed major qualitative differences in the liquid phase distribution within the catalyst bed which tended to be much less uniform when the hydrogenation reaction was taking place.

For relatively small catalyst pellets and beads (below ca. 1-2 mm) it is usually not possible to map liquid distribution within individual catalyst particles in the bed with sufficient spatial resolution [19,41,45,46]. At the same time, with larger catalyst pellets (e.g., 3-4 mm) an MRI experiment can provide spatial information on the length scale of both the bed and the individual catalyst pellets. This can provide access to some interesting and important dynamic phenomena. For instance, in the hydrogenation of olefins in the catalyst bed comprised of 4 mm beads of 1% Pd/γ-Al2O3 catalyst [19,41,45,46], ignition of individual catalyst pellets was revealed, leading to a prolonged existence of such pellets in a liquid-free state while their immediate neighbours remain filled with the liquid phase, providing very efficient conditions for the hydrogenation reaction similar to those described above for partially filed catalyst pellets in a single-pellet reactor (Figure 2). Redistribution between the dry and wetted neighbour pellets was also visualized in some of the experiments. It was also demonstrated that catalyst pellets in the bed could be partially filed with the liquid phase, with a sharp front of liquid exhibiting back-and-forth motion within the pellet. Rapid imaging pulse sequences implemented in later studies made it possible to reduce imaging time of (a set of) 2D slices to 2-3 s and of the entire 3D image to 20-30 s [18,20,49-52], thus providing access to faster dynamic processes in the operating model packed bed reactors. Another study addressed the peculiarities of reactor behaviour upon periodic modulation of the liquid reactant supply upon 1-octene hydrogenation [51], an approach which is known to be able to increase reactor productivity. A significant influence of reactant feed modulation on the liquid holdup and catalyst wetting efficiency was revealed.

[Insert Figure 2 here]

Figure 2. 2D 1H images of the liquid phase distribution in a regularly packed bed of spherical catalyst beads (Pd/Al2O3, 4.2 mm in diameter) detected in the course of 1-octene hydrogenation. Rows 1–5 correspond to the respective layers of the catalyst beads shown schematically in (b). Each column of the images represents a subset of the entire set of images detected for an extended period of time for visualizing dynamic processes in the reactor. The time elapsed from the reactor startup is indicated above the columns of images. Lighter shades correspond to higher signal intensity (more liquid). (Reprinted from ref. [49], Copyright (2007), with permission from Elsevier.)

Another catalytic reaction which was addressed by MRI in several studies is the decomposition of hydrogen peroxide (H2O2) over heterogeneous catalysts. Decomposition of H2O2 over a single pellet of Fe/Al2O3 catalyst revealed slow (4 min image acquisition time) chaotic motion of the liquid phase within the pellet, presumably caused by gas bubbles formation and growth as well as heat evolution in this exothermic reaction [53]. Another study [38,42] used Ag/γ-Al2O3 catalyst pellet and showed that H2O2 was decomposing rapidly in a thin surface layer of the catalyst pellet, thus preventing H2O2 from diffusing deeper into the catalyst. Velocities of convective transport of the liquid phase around the catalyst pellet induced by gas evolution during the reaction were mapped as well [38]. A later study addressed reaction-induced transport of the liquid phase around the catalyst pellet during decomposition of H2O2 over a Cu- or Pt-doped Al2O3 pellet [54].

**2.2. Mapping reactants and products with spectroscopic resolution**

An early example of the application of MRI/MRS to study heterogeneous catalytic reactions is the room-temperature liquid-phase esterification reaction which converted methanol and acetic acid into methyl acetate and water in a packed bed of small beads of acidic ion exchange resin [55,56]. In the 1H NMR spectra, the signals of the OH groups of water, acetic acid and methanol gave a single NMR line due to the fast proton exchange. The chemical shift of this broadened combined signal was shown to depend on the relative concentrations of all three components, and this was used to extract spatially resolved information on reaction conversion. Changes in conversion along the bed and its variations in the transverse direction could be deduced by extracting conversion data either along the bed axis (chemical shift imaging, CSI) or in a number of selected volume elements within the reactor (volume-selective spectroscopy, VOSY). In these experiments, only the interparticle liquid contributed to the observed NMR signal while the intraparicle fraction was not detected. In the later studies, both measured and numerically calculated velocities of liquid flow in the catalyst bed were correlated with the experimentally evaluated data on conversion [57].

Clearly, the approach to concentration data evaluation based on the chemical shift of a single spectral line characterizing several reactants and products at once [55-57] is not fully quantitative, and has limited applicability in terms of the scope of chemical reactions that can be addressed this way. A more general approach would be based on the detection of partial or complete NMR spectra in which the lines belonging to different molecules (reactants and products) are clearly separated. This approach is exemplified, for instance, by the study of an enzymatically catalyzed esterification of propionic acid with 1-butanol into butyl propionate and water. In the experiment, a single calcium alginate bead containing an immobilized enzyme was used as the catalyst [58]. The reaction within the bead was monitored by detecting 1H NMR spectra with 1D spatial resolution. The gradual conversion with time of reactants into products was evident from the experimental data.

Given the major broadening and distortion of NMR signals often encountered for fluids confined in porous materials and a limited range of chemical shifts generally provided by 1H NMR spectra, it may be advantageous in certain cases to employ heteronuclear MRI/MRS instead. In particular, 13C NMR spectra of organic compounds are usually characterized by an order of magnitude broader range of observed chemical shifts, leading in many cases to much less overlap between the broadened signals of various reactants and reaction products. However, this advantage is not easy to use in practice because it can be outbalanced by several disadvantages that the detection of 13C (and other heteronuclei) can entail. The major drawback in switching from 1H to heteronuclear NMR detection is associated with a significant loss in sensitivity. Several reasons for this include lower gyromagnetic ratio (i.e., a lower nuclear spin magnetization combined with a lower detection frequency) and often lower concentrations of nuclear spins (for instance, 13C natural abundance is only 1.1%, while the abundant 12C isotope is NMR-silent). In addition, spin-lattice relaxation times of heteronuclei tend to be longer compared to the T1 times of 1H nuclei (e.g., tens of seconds for 13C vs. seconds for 1H), making acquisition of the same number of scans substantially more time-consuming for the former. For nuclei such as 19F, the sensitivity can be relatively high, but the utilization of fluorinated compounds in MRI of heterogeneous reactions may be rather limited. Therefore, detection of heteronuclei in the MRI/MRS experiments on catalytic reactions and reactors usually requires some means of signal enhancement. For heteronuclei characterized by a low natural abundance, this could be achieved by using isotope-enriched samples, but this approach is not practical because of the involved costs. Another possibility to improve sensitivity when detecting heteronuclei is to apply existing pulse sequences (e.g., INEPT, DEPT) which transfer thermal equilibrium polarization of 1H nuclei to their counterparts with a lower γ value (X), leading to signal enhancements of the order of the ratio of the gyromagnetic ratios of the two nuclei (γ(1H)/γ(X)) or even slightly larger.

The latter approach was demonstrated in the study of the competitive etherification of 2-methyl-2-butene (MB) into tert-amyl methyl ether (TAME) and its hydration to tert-amyl alcohol (TAOH) in liquid phase in a fixed bed of H+ ion-exchange resin beads [56]. In the experiments, the 13C NMR spectra were spatially resolved in two spatial dimensions (a 3D experiment) with 2.5 mm × 3.75 mm spatial resolution using DEPT (distortionless enhancement by polarization transfer) 13C NMR signal enhancement pulse sequence. The entire data set took 16 hours to acquire on an operating reactor. The spectroscopic information obtained in this experiment was used to evaluate both conversion of MB and reaction selectivity to TAME, and to map their variations in the two spatial dimensions (axial and transverse).

The same approach based on the spatially resolved 13C DEPT spectroscopic experiment was used to study esterification of acetic acid with ethanol to produce ethyl acetate in a bed of an ion-exchange resin at ambient temperature and pressure [59]. The composition of the interparticle liquid phase was quantified along the reactor. Anoter experiment in the same study addressed the intra- and interparticle diffusivities of the reacting mixture components which were evaluated with a 6 mm spatial resolution along the catalyst bed. Ethyl acetate concentration was observed to be higher in the intraparticle liquid than in the liquid phase between the particles, evidencing the presence of mass transfer limitations on the reaction progress. The entire diffusion experiment performed with spatial and spectral resolution took ca. 55 hours.

Several studies report the use of MRI/MRS to address heterogeneous catalytic hydrogenation of unsaturated compounds with H2. The early example in this field is the gas-liquid-solid hydrogenation of α-methylstyrene (AMS) to cumene in an operating trickle bed reactor over a bed of 1% Pd/γ-Al2O3 catalyst beads 1 mm in diameter using the CSI approach [18-20,43,46]. As already mentioned, under these conditions the signals in NMR spectra are significantly broadened due to large inhomogeneities of the local magnetic fields caused by the magnetic susceptibility differences between different phases (solid, liquid, and gas), as well as by the significantly faster nuclear spin relaxation for liquids confined in the catalyst pores. In particular, the linewidths in the 1H NMR spectra of AMS in the packed bed reactor were about 300 Hz at 130 °C (7 T field, 300 MHz 1H NMR frequency). However, the chemical shifts of AMS and cumene are sufficiently different, making it possible to distinguish the two compounds in the spectra despite such significant line broadening. The CSI experiment performed on the operating hydrogenation reactor yielded a 2D spatial image of a 2 mm thick axial slice within the catalyst bed with the spatial resolution of 170 μm × 330 μm within the axial imaging plane, with a 1H NMR spectrum available for each image voxel (Figure 3). The AMS to cumene conversion was observed to increase along the reactor, as expected, with some pronounced variations of conversion observed in the transverse direction.

[Insert Figure 3 here]

Figure 3. 1H NMR spectra detected with spatial resolution during AMS hydrogenation in a bed of 1 mm Pt/γ-Al2O3 catalyst beads. Each spectrum corresponds to a 170 × 330 × 2000 μm3 voxel. Spectra 1,3,5 correspond to the same radial position within the operating reactor and are detected in its top, middle and bottom parts, respectively, while spectra 2-4 correspond to voxels at the same vertical position in the operating reactor but shifted horizontally by 1.3 mm relative to each other. In the spectra 6 and 7, the traces with narrow lines were detected for liquid AMS (6) and cumene (7), while the traces with broad lines were obtained by mathematically broadening the experimentally observed lines to 300 Hz. Reproduced from Ref. [21] with permission from the Royal Society of Chemistry.

The reaction of 1-octene with H2 in a gas-liquid-solid model reactor with a fixed bed of 1 wt% Pd/Al2O3 catalyst trilobes operating under co-current gas-liquid downflow was addressed using 13C MRI to overcome line broadening complications [25,56,60]. The MRI experiment with one spatial (axial) and one spectral dimensions was implemented using 13C distortionless enhancement by polarization transfer (DEPT) spectroscopy pulse sequence for signal enhancement (Figure 4). The 13C NMR spectra obtained at each axial position along the reactor with a spatial resolution of 3 mm revealed a facile isomerisation of 1-octene into 2-octene and formation of n-octane upon their hydrogenation, with significant amounts of 3- and 4-octenes observed at higher flow rates of H2. The concentrations of 1-octene, 2-octene and octane were observed to reach their steady-state values at different axial positions. It took the authors ca. 17 min to acquire the data.

[Insert Figure 4 here]

Figure 4. Spatially resolved 13C DEPT NMR spectroscopy of 1-octene conversion in the model reactor loaded with 1 wt% Pd/Al2O3 catalyst in the shape of trilobes. The gaseous and liquid reactants were supplied with the rate of 32 and 1.0 mL/min, respectively, (a) 2D 1H MR image of the spatial distribution of liquid within the bed. The white horizontal lines indicate the boundaries between the catalyst bed and pure Al2O3 pellets packed above and below it. (b,c) 2D spatial-spectral datasets with one spectral (horizontal) and one spatial (vertical, along the length of the catalyst bed) coordinate acquired separately for the olefinic (b) and the aliphatic (c) regions of the 13C NMR spectrum during the steady-state reactor operation. (d,e) Transformation of the 1D 1H NMR spectrum of the liquid phase along the catalyst bed. (a-c) Adapted from Ref. [22], Copyright (2007), with permission from Elsevier. (d,e) Adapted from Ref. [25], Copyright (2010), with permission from Elsevier.

An NMR-compatible reactor [61] made of silicon nitride and capable of withstanding high temperatures and pressures (up to 350 °C and 30 barg) was used to monitor conversion and selectivity during the multi-phase ethylene oligomersation reaction occurring at 110 or 200 °C and 28 barg over a 1 wt% Ni/SiO2-Al2O3 catalyst. The 1H NMR spectra were detected as a function of time-on-stream without spatial resolution. While ethylene (most likely – adsorbed) contributes to the olefinic peak at ca. 5 ppm only, the reaction products contribute to both the olefinic resonance and the “aliphatic resonance” at ca. 1 ppm. The line broadening effects make it impossible to identify the product distribution directly from the 1H NMR spectra. However, the ratio of aliphatic-to-olefinic peak intensities was observed to change with time-on-stream, showing that higher molecular weight species are produced during the first 10-20 min of reactor operation compared to longer times-on-stream. Furthermore, the 1H MR images were acquired during the steady-state operation of the reactor. The signal in those images originates almost entirely from the liquid phase species, making it possible to map the distribution of reaction products in the reactor.

As mentioned earlier, imaging of gases is even more challenging than liquids. To address heterogeneous catalytic hydrogenation of ethylene by MRI, the Bremen group have constructed an NMR-compatible glass tube reactor with an inner diameter of 30 mm placed inside a 72 mm i.d. volume RF coil of a horizontal bore Bruker Biospec system (300 MHz) [62]. The space between the reactor and the RF coil was used for thermal insulation. The reaction of choice was hydrogenation of ethylene with H2 in the packed bed of a Pt/Al2O3 catalyst. The total length of the packed bed was 80 mm. The Pt/Al2O3 catalyst was mixed with the inert Al2O3 pellets in such a way that the amount of catalyst increased from individual Pt/Al2O3 pellets embedded in the Al2O3 packing to ca 50% over the bed length of 40 mm. This mixed Al2O3-Pt/Al2O3 bed was sandwiched on both sides by 20 mm thick layers of Al2O3. The mixture of gases (ethylene, H2, and an inert balance gas) was flown through the reactor. Imaging was performed with a use of a MRSI pulse sequence with the delay between the slice-selective excitation RF pulse and the start of data acquisition reduced to 350 ms. It is based on the pure phase encoding of the spatial information and the acquisition of the FID in the absence of an applied gradient to preserve spectroscopic information. Spatial mapping of the chemical composition was demonstrated within five slices each 3 mm thick, with an in-plane resolution of about 1.5 mm, and a time resolution of about 3.5 minutes was achieved. The spectrum of the reacting gas mixture is rather simple and exhibits two single lines only, one for ethylene and one for ethane; H2 does not contribute because of its very short T2 time and fast diffusion. The chemical shift difference between ethylene and ethane is rather large (exceeds 4 ppm). Despite all that, the reliable separation of the signals of ethylene and ethane for the quantification of their amounts in each pixel required data fitting rather than a simple signal integration (Figure 5). This demonstrates nicely the difficulties one encounters in MRI studies of highly spatially heterogeneous systems such as gas- or liquid-filled packed bed reactors. The spatially resolved studies of reactants/products mixture composition were complemented with the temperature evaluation in the two inert alumina layers located on both sides of the catalyst bed. This was achieved by detecting the 1H NMR spectrum of ethylene glycol enclosed in several glass capsules positioned in the alumina layers.

[Insert Figure 5 here]

Figure 5. (a) A typical magnitude NMR spectrum of a mixture of ethylene and ethane with a superimposed fitted magnitude spectrum. (b-e) Volumetric concentration maps of ethane (vol.%) extracted from the data of a typical spatially resolved experiment, with the data for five out of the seven detected slices shown in the figure. The measurements were performed at (b) t =−5 min, (c) t = 2 :30 min, (d) t = 1 :31 : 52 h, and (e) t = 1 :43 : 15 h; all time information corresponds to the middle of the measurement duration. (Reprinted from ref. [62], Copyright (2015), with permission from Elsevier.)

In the later work [63], the authors extended their experiments to the study of ethylene hydrogenation with the use of a coated sponge packing or a honeycomb monolith catalysts. Specifically, a γ-Al2O3 sponge (10 picks per inch, PPI) packing or a cordierite honeycomb monolith (600 cells per square inch, cpsi) 50 mm long were used (Figure 6). Both were coated with 1 wt.% Pt/Al2O3. The outlet pressure of the reacting mixture of gases was kept at 1.3 bar. During the operation, the reactor was cooled with pressurized air. A magnetic resonance spectroscopic imaging (MRSI) experiment was performed with 3 spatial coordinates and one spectral coordinate, with ca. 20 min measurement time per dataset, providing 22 slices along the 50 mm long catalyst bed. While the images of the gas in the sponge packing reflect its morphology, the spatial resolution in the imaged slices (ca. 1×1 mm2) was insufficient to see the structure of the honeycomb monolith. Steady-state distributions of ethylene and ethane concentrations were visualized at various reaction conditions, once again using the numerical fitting of the time domain data in each voxel. Nevertheless, the limited SNR and spectra distortions prevented the authors from quantifying the ethane/ethylene ratio in some of the voxels of the detected image. The experimental findings were compared to a one-dimensional mathematical model of the process.

[Insert Figure 6 here]

Figure 6. (a) A photograph of the monolithic sponge packing consisting of three stacked 10 PPI sponge segments with 25 mm diameter and 20 mm (front and back segment) resp. 10 mm (central segment) length; the green dotted lines indicate the positions of the segments. (b) A photograph of the coated cordierite honeycomb monolith (600 cpsi). (c) 1H MR inverted greyscale image of ethylene for the cross-section of the catalytic sponge packing at z = 32 mm (arrow in (a)) acquired in a 3D MRSI experiment during a constant flow of a non-reacting mixture of ethylene and argon. (d,e) Volumetric ethane concentration maps of the same slice of the monolithic sponge packing reconstructed for low (d) and high gas flow rate (e) experiments. (f) H MR image of ethylene for the cross-section of the honeycomb catalyst at z = 32 mm acquired in a 3D MRSI experiment during a constant flow of a non-reacting mixture of ethylene and argon. (g,h) Volumetric ethane concentration maps of the same slice of the honeycomb catalyst reconstructed for low (g) and high gas flow rate (h) experiments. All concentrations are given in vol%. (Reprinted from ref. [63], Copyright (2016), with permission from Elsevier.)

A more detailed comparison of the experimental findings with modelling results was attempted in a later study [64]. In order to take proper account of heat transport processes for the exothermic reaction of ethylene hydrogenation, long but thin (0.68 mm in diameter) glass capillaries were filled with ethylene glycol and placed in the cylindrical monolithic catalyst bed, one along the axis and another near the reactor wall. This enabled the authors to perform spatially resolved temperature measurements in the centre and at the wall of the catalyst bed, thus providing the temperature boundary conditions necessary for modelling. Temperature profiles and conversions were compared for the honeycomb and foam packing catalyst beds, revealing differences associated with the different radial heat conduction properties of the two catalyst types. The experimental temperature and concentration fields were compared with the results of model calculations based on the numerical solution of the set of coupled equations describing heat and mass transfer and the reaction kinetics. It was not possible to perform a quantitative comparison of the experimental and simulated concentration profiles in each voxel because of the insufficient SNR of the individual spectra. Therefore, the averaged longitudinal concentration profiles in the axial direction were used. The authors note that the heterogeneous structure of the foam packing leads to distortions and SNR loss in the individual spectra, which precludes any spectral analysis in some of the voxels.

When gases are involved, an accurate quantification and modelling of concentration fields and reaction conversion requires the due account of gas adsorption processes. Indeed, the local amount of a hydrocarbon gas (reactant or product) adsorbed on a porous catalyst support can often significantly exceed the amount of the same hydrocarbon in the gas phase. These effects were unambiguously observed in various studies [65-67]. The supplementary experiments in the studies described above [62-64] also confirm that local concentration of the gas can increase measurably owing to the presence of the porous solid. However, these effects still need to be studied and analyzed in detail. This is not easy to accomplish as gas adsorption will depend on many parameters including the nature of the adsorbent and the adsorbing gas, local temperature and gas mixture composition, etc. These effects and the adsorption-desorption processes need to be accounted for in the future efforts on quantitative modelling of an operating catalytic reactor.

**2.3. Spatially resolved thermometry**

The importance of heat transport during catalytic reactor operation makes it desirable to map temperature distributions to better understand the reactor behaviour. While NMR/MRI cannot measure temperature of a sample directly, there is still a possibility to use NMR signal sensitivity to temperature to perform such a measurement indirectly. NMR “thermometers” are used routinely in NMR, they usually represent a chemical which demonstrates a pronounced and well-characterized chemical shift dependence on temperature. Some examples are ethylene glycol for which the separation of its two 1H NMR signals provides a reliable measure of its temperature, and water for which chemical shift changes by 0.01 ppm/degree. There are other possibilities to implement an NMR-based temperature measurement, based on the temperature dependence of other properties of an NMR signal, e.g., signal intensity, relaxation times, molecular diffusivity, etc. However, such an indirect temperature measurement is complicated by the fact that all these parameters are sensitive not only to temperature but to other experimental conditions as well. For instance, all these characteristics of an NMR signal of a liquid confined in catalyst pores will change with changes in the amount of the liquid in the pores, making it essentially impossible to single out the contributions from temperature variations. For measuring temperatures in a catalyst bed, one potential solution is to make sure that the amount of liquid in an NMR “thermometer” is not changing.

In the study of 1-octene hydrogenation in a bed comprised of Pd/Al2O3 trilobes, four glass bulbs 4 mm in diameter were filled with ethylene glycol and placed in various parts of the catalyst bed. Their volume-selective 1H NMR spectra were used to evaluate temperatures of these bulbs during reactor operation quite accurately (ca. ±2 °C). Long thin capillaries filled with ethylene glycol were also used to measure temperature distributions in the catalyst bed along its axis and near the reactor wall during ethylene hydrogenation, as mentioned in the previous section [64].

However, it would be desirable to perform such temperature measurements without the need to perturb the structure of the reactor and the catalyst bed. One possibility to achieve this would be to address the NMR signal of either the reactants/products or the catalyst itself. As mentioned above, in gas-liquid-solid reactors the local liquid content in the catalyst pores and packed bed voids may vary significantly during reactor operation, thus masking any NMR signal changes associated with temperature, while spin density of gases is too low to provide a reliable mapping of their NMR signals for a spatially resolved evaluation of their temperature. At the same time, the solid phase (the catalyst bed) remains rather unchanged during reactor operation, and thus its NMR signals could be suitable for temperature evaluation. This requires the detection of the NMR signal of the nuclei of a solid material (catalyst, support). NMR/MRI of solid materials is often performed using specialized solid-state techniques, which could be an obstacle for such measurements. For instance, magic angle sample spinning often used in solid-state NMR spectroscopy is normally not feasible when the sample is an operating model reactor with its supply and exhaust lines, etc. However, clever approaches are feasible that may allow one to find ways of doing such experiments. One possibility is to redesign a MAS NMR probe into a flow-MAS probe [68,69] which allows one to run a catalytic reaction continuously while a packed catalyst bed is spinning at a high rate in a MAS rotor. Another interesting solution explores a different strategy which is based on the idea that, in terms of NMR spectroscopy, a rotating sample in a static magnetic field may be similar to a static sample in a rotating field [70]. However, these clever approaches are yet to be developed to the level when their routine application becomes feasible. Fortunately, in certain cases nuclei of solid materials can be used for imaging with conventional MRI hardware and techniques [19,45,49,52,71-76]. In particular, the 27Al nucleus of Al2O3 catalyst support possesses acceptable relaxation times, and the temperature dependence of its signal is suitable for temperature evaluation [18,20,44,72]. Based on these facts, temperature distribution along the bed of Pd/γ-Al2O3 catalyst was monitored qualitatively during propylene hydrogenation reaction at various propylene supply rates [18,77]. The 1D 27Al MR images were acquired in ca. 3 min with the spatial resolution better than 1 mm along the reactor axis. As expected, the 27Al NMR signal intensity decreased with the increase of the catalyst temperature which was monitored with a thermocouple, but remained unchanged with the variation of gas feed composition at a constant temperature, validating the assumption that signal intensity can be used for the evaluation of catalyst temperature. In the later studies, the experiment was extended from a qualitative 1D temperature visualization to a semi-quantitative 2D temperature mapping [78]. The experiments were performed using catalytic oxidation of H2 with molecular oxygen over a single cylindrical pellet of Pt/γ-Al2O3 catalyst 4.2 mm in diameter and ca. 10 mm long. The pellet was placed eccentrically in a 10 mm o.d. glass tube reactor (Figure 7). As the flow rate of H2 increased, the signal intensity in the transverse 2D 27Al MR images of the pellet (image acquisition time 21 min, spatial resolution 0.4 mm × 0.4 mm, no slice selection) decreased and developed a more pronounced intensity gradient in the image plane, with stronger signals near the contact of the pellet with the glass reactor wall and weaker ones in the pellet parts that were further away from the glass. This was expected, as the eccentric pellet placement geometry was intended to provide a non-uniform flow of reactants around the pellet. To convert 2D MR images to 2D pellet temperature maps, the results of an independent calibration experiment were used which related quantitatively the 27Al NMR signal intensity with alumina temperature measured with a thermocouple. At the highest H2 flow rates used in the experiments, temperatures up to 700 K were observed in the reconstructed temperature maps. As the NMR signal intensity decreases with increasing temperature, this leads to the decrease in SNR, and thus to the decrease of temperature evaluation accuracy (ca. 10–12 K at 400 K, ca. 30 K at 500 K). It is essential that, despite a number of problems and complications, this approach allows one to evaluate the actual and relevant temperature of the catalyst with spatial resolution in a non-invasive manner.

[Insert Figure 7 here]

Figure 7. (a) Geometry of Pt/Al2O3 pellet positioning for the MRI thermometry experiment during catalytic gas phase oxidation of H2. (b) 2D 27Al MR image of the catalyst pellet and the reactor glass tube. (c) 2D temperature maps of the catalyst pellet derived from the images of the catalyst pellet detected at different H2 flow rates using the calibration curve that relates the 27Al NMR signal intensity to the actual temperature of alumina. Reproduced from Ref. [21] with permission from the Royal Society of Chemistry.

A different approach to the thermometry of gases in a model catalytic reactor was suggested and tested in Ref. [79]. It is based on the inverse relationship between an NMR linewidth and temperature when the NMR spectra are detected in the presence of a weak magnetic field gradient, as proposed by the authors. The gradient (0.05 – 0.1 G/cm) needs to be weak enough as not to convert an NMR spectrum into a MR image, but strong enough to provide measurable signal broadening. This approach was tested by the experiments aimed at non-invasive mapping of gas temperatures during the hydrogenation of propylene in reactors packed with metal nanoparticles and metal–organic framework catalysts. Given the rather counter-intuitive interrelation between the spectral linewidth and gas temperature (diffusivity), an independent verification of the general validity of these findings would be desirable.

**3. MRI/MRS studies with hyperpolarisation-based signal enhancement**

As mentioned earlier, many applications of the MRI and MRS techniques are limited by the SNR available in an experiment. A relatively low sensitivity is indeed the main disadvantage of NMR-based techniques [80]. It is caused by the fact that the difference between the spin levels populations at thermal equilibrium is rather small. A method to increase this difference significantly and, as a result, to largely increase the signal intensity, is the hyperpolarisation of nuclear spins [81-84]. The principle of the hyperpolarisation techniques is based on the feasibility to overpopulate some of the spin levels with respect to their thermal equilibrium populations. Nowadays the most utilized hyperpolarisation techniques for liquid and gaseous samples are dynamic nuclear polarization (DNP) [85-90], spin-exchange optical pumping (SEOP) [91-95], and parahydrogen-induced polarization (PHIP) [96-99].

In the DNP approach [100], polarization of the spins of unpaired electrons in paramagnetic compounds is transferred to various types of magnetic nuclei. Polarization of spins at thermal equilibrium is proportional to γB0/T, i.e., it depends on gyromagnetic ratio, magnetic field strength and temperature. To maximize the equilibrium polarization of electron spins which is then transferred to nuclei, the setup for a DNP experiment needs a strong superconducting magnet, a helium cryostat to cool down the sample, free radicals or paramagnetic metal ions, and a microwave source for polarization transfer.

The SEOP method generates nuclear spin polarization of noble gases (3He [101,102], 129Xe [93,103], 83Kr [104,105]). To achieve this, a circularly polarized laser beam with an appropriate wavelength is used to selectively depopulate one of the electronic ground levels of an alkali metal [103], thereby producing electron spin polarization in the alkali metal atoms. Gas-phase collisions then lead to the transfer of polarization from the alkali metal electrons to the nuclei of the noble gas which is mediated by the Fermi-contact interaction. An optical pumping cell containing a noble gas and alkali metal, a laser, a magnetic field of tens of Gauss and an oven for alkali metal evaporation and temperature control are needed for SEOP experiments [106].

Both DNP and SEOP require rather complex and thus expensive hardware. In contrast, the PHIP approach is simple and does not utilize sophisticated or expensive hardware [107]. Parahydrogen is one of the two modifications (nuclear spin isomers) of H2 molecule; the latter can exist in two different modifications, namely orthohydrogen and parahydrogen. Parahydrogen is the spin isomer of hydrogen molecule which has zero total nuclear spin (singlet spin state) [97]. A direct detection of this species by NMR is impossible because it has no spin. However, if both H atoms of parahydrogen are added to an unsaturated substrate in such a way that they end up in chemically or magnetically non-equivalent positions, this often leads to a substantial NMR signal enhancement. During this hydrogenation reaction the H atoms which formed an A2 spin system in H2, are converted to, e.g., an AX spin system after the pairwise hydrogen addition. The spins of the hydrogen atoms may remain correlated. In such case, while the symmetry of the singlet state of parahydrogen molecule gets broken, the spin state is preserved but is no longer an eigenstate of the formed AX spin system. As a result, only some of the spin states of the products and intermediates become highly overpopulated compared to thermal equilibrium [108].

The shape of the enhanced NMR signals observed in such studies depends on the type of the PHIP experiment. Usually, two basic types are distinguished, namely Adiabatic Longitudinal Transport After Dissociation Engenders Nuclear Alignment (ALTADENA) [109] and Parahydrogen And Synthesis Allow Dramatically Enhanced Nuclear Alignment (PASADENA) [99]. In a PASADENA experiment, the hydrogenation reaction is conducted at a high magnetic field, often directly within the probe of an NMR instrument. If upon the reaction the two hydrogen atoms form an AX spin system in the reaction product or intermediate, the |αβ> and |βα> spin states get overpopulated because the initial singlet spin state (|αβ> - |βα>)/√2 of these two hydrogens that they inherit from parahydrogen is composed of these two states. Of the four signals observed in the NMR spectrum of such AX spin system, two signals appear in emission (that is, exhibit a negative intensity) and the other two in absorption (Figure 8a) [99,110]. In an ALTADENA experiment, hydrogenation reaction is conducted in a low (e.g., Earth’s) magnetic field followed by an adiabatic product transfer to the high magnetic field of a spectrometer. As a result, one energy level is overpopulated, and two peaks are observed in the corresponding NMR spectrum, with one of them in emission and another in absorption (Figure 8b) [97]. As a result of PASADENA or ALTADENA experiments, the NMR signals with enhancement factors of up to 104-105 can be observed [111].

[Insert Figure 8 here]

Figure 8. (a) PASADENA and (b) ALTADENA experiments. Spin energy levels and the resulting NMR spectra. The NMR signal patterns shown in the figure are observed when the excitation pulse flip angle is smaller than 900; in particular, the antiphase PASADENA pattern shown in (b) is maximized with a 450-pulse.

The very first and many subsequent observations of PHIP effects were demonstrated using homogeneous catalytic hydrogenation reactions performed with the use of a transition metal catalyst and a suitable unsaturated substrate with a multiple chemical bond in solution [112]. At the same time, one of the major driving forces for the entire hyperpolarisation research field is the potential possibility to combine signal enhancements with biomedical MRI and MRS studies. This necessarily requires the ability to overcome the main disadvantage of homogeneous catalysis, that is, the problem of catalyst separation/removal. The toxicity of metal complexes makes it undesirable or even not permissible to use solutions of hyperpolarised substances in the in vivo studies if they also contain a metal complex catalyst [113]. One potential solution of this problem is the use of heterogeneous hydrogenation instead of the homogeneous one, which can be preferable for such studies [114-117]. There is no necessity to additionally purify a hyperpolarised fluid after a heterogeneous catalytic reaction, because the solid catalyst can be removed by a simple filtration procedure, or alternatively a hyperpolarised reaction product which is free from the catalyst can be collected directly if the reaction is performed using a flow reactor [118]. Also, solid catalyst is recyclable and can be reused several times, which is desirable for a further reduction of the cost of the production of hyperpolarised fluids [119].

Furthermore, in contrast to homogeneous catalytic reactions, heterogeneous hydrogenations can be performed not only in the liquid phase but also in the gas phase. Therefore, demonstration of PHIP effects in heterogeneous hydrogenation reactions paved the way to the studies involving hyperpolarised hydrocarbon gases that were not possible before. The relative simplicity of the PHIP technique and the high NMR signal enhancement it provides allow one to apply MRI to visualize gaseous products of heterogeneous catalytic hydrogenations despite their low spin density in comparison to liquids. Indeed, hyperpolarised propane gas produced using the heterogeneous version of the PHIP experiment (HET-PHIP) was successfully imaged inside various phantoms [114]. Nowadays, the most popular gases in the case of hyperpolarisation are helium-3 (3He) and xenon-129 (129Xe) mentioned earlier, and propane [81]. Compared to the noble gases, propane gas has some benefits. In propane, hydrogen atoms are hyperpolarised, and the gyromagnetic ratio of hydrogen γ(1H) is larger than γ(3He) and especially γ(129Xe); the natural abundance of the magnetic isotope of 1H is 99.985%, which is more than 3-fold larger than that of 129Xe (26.44%), and 7×105-fold larger than for 3He (0.00014%) [120]. Importantly, the standard NMR/MRI instruments are equipped with 1H detection coils, while detection of other nuclei requires specialized heteronuclear radiofrequency channels and probes. Propane is a non-toxic asphyxiant and therefore can be potentially administered to humans for lung imaging at gas concentrations significantly exceeding its upper explosive limit (UEL) > 9.5% (20,000 ppm). Moreover, brief inhalation exposures to 10,000 ppm propane cause no symptoms in humans [121]. These properties show that propane is a promising gas for a potential use in medical MRI. The main limitation of the hydrocarbon gas use can be its fast relaxation time T1, which for propane gas at high magnetic fields and ambient pressure is approximately 1 s because of the high efficiency of the spin-rotation relaxation mechanism in the gas phase [122]. However, there are ways to overcome this disadvantage and to prolong the relaxation time of hyperpolarised propane by up to 10- to 50-fold, for instance using low magnetic fields, high pressures, increasing propane percentage in the reacting mixture and by dissolving propane in an appropriate solvent [122-124]. Therefore, MRI of chemical reactors, lungs and other materials becomes feasible with the use of propane hyperpolarised via PHIP.

The first demonstration of the possibility to use hyperpolarised propane for MRI experiments in heterogeneous catalysis was reported in 2007 [114]. The gas-phase reaction of propylene hydrogenation to propane with parahydrogen over solid catalyst was implemented. In an ALTADENA experiment, a mixture of propylene and parahydrogen-enriched hydrogen (50% parahydrogen content) in a ratio 1:4 flowed through the reactor packed with immobilized Wilkinson's catalyst supported on phosphine-modified silica gel ([RhCl-(PPh3)2PPh2(CH2)2]–SiO2). Later, other similar immobilized catalytic systems were shown to be active in the pairwise hydrogen addition to unsaturated substrates [125,126]. Heterogeneous hydrogenation of propylene to propane with parahydrogen was carried out at 150 ⁰C. Despite the high temperature within the reactor, the flowing gaseous reaction product propane cooled down significantly by the time the hyperpolarised propane was delivered to the bottom of a 10 mm NMR tube which was placed inside the probe of a 300 MHz NMR magnet. The gas was transferred from the reactor to the NMR tube through a 1/8 inch polytetrafluoroethylene (PTFE) tube which ended with a 1/16 inch PTFE capillary. The resulting 1H NMR spectrum showed an enhancement of NMR signals of propane by about 300-fold compared with the NMR signals of propane at thermal equilibrium. Importantly, this fairly large signal enhancement factor was actually observed in the experiments, i.e., it was obtained directly, without any extrapolation or correction based on a consideration of the relaxation effects [127].

For the MRI experiments, two handmade PTFE phantoms were used. The first one had a shape of a cross. The gas flowed from the capillary into the empty spaces around the cross (Figure 9c). The second phantom consisted of a large number of PTFE capillaries and imitated a porous medium. The phantoms were placed near the bottom of a 10 mm NMR tube and were positioned in the sensitive area of the RF probe. Utilizing the pure phase-encoding protocol [127], the high resolution images of these model objects were obtained. The estimated SNR in the experiments with the cross-shaped phantom was about 150 in the channels where the signal had the minimum intensity and about 200 where the signal had the maximum intensity. For the comparison of the quality of MR images, the cross-shaped phantom was then filled with water and an MR image was acquired (Figure 9a). It was shown that the quality of the image of the water-filled phantom was only slightly better than for the one containing hyperpolarised gas despite the dramatic difference in the proton spin density of the water and gas samples. The yield of propane in the reaction of heterogeneous propylene hydrogenation was estimated as ca. 5%, that is, well below 100%. In addition, the signal enhancement was significantly reduced in these ALTADENA experiments because of the relatively short relaxation time T1 of propane and the resulting relaxation losses of propane hyperpolarisation during the time it took for the gas to flow from the reactor to the detection zone. Additionally, the interaction of hyperpolarised product with the porous catalyst support can cause extra losses of hyperpolarisation. Despite that, these experiments demonstrated the feasibility of such studies, and they can be further improved by, e.g., utilizing more efficient pulse sequences with shorter recycle delay.

[Insert Figure 9 here]

Figure 9. (a) 1H MRI of water flowing through the phantom with the cross shape. A small circle is the Teflon capillary; (b) 1H MRI of thermally polarized propylene gas (CH2 peak). The image contains zero-frequency artefacts; (c) 1H MRI of hyperpolarised propane in ALTADENA experiments (CH3 peak); (d) 1H MRI of thermally polarized propylene gas flowing through the phantom that imitated porous medium; (e) 1H MRI of hyperpolarised propane in ALTADENA experiments with the second phantom. (Ref. [114]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

Therefore, this MRI observation promotes future applications of hyperpolarised hydrocarbon gas produced via PHIP such as absorption studies and gas-phase kinetics studies. Moreover, the above-mentioned results initiated many subsequent investigations and applications of MRI approach in heterogeneous hydrogenation processes with parahydrogen [81].

In a recent study [128], the ultrashort echo time (UTE) pulse sequence [129,130] was successfully exploited to image both thermally polarized and hyperpolarised propane with 1H MRI. It was shown that even thermally polarized propane can be efficiently imaged using this pulse sequence. Other pulse sequences intended for rapid imaging, such as rapid acquisition with relaxation enhancement (RARE) [127] or echo-planar imaging (EPI) [131] may not be suitable for MRI of every object. In particular, these sequences are inefficient in the experiments with propane gas which has a relatively short T2 time. In the case of fast spin-echo (SE) methods [132], application of a 180⁰ pulse is required, which may be difficult to achieve for samples with for short T2 times. The UTE pulse sequence performs much better in the experiments with short T2 samples. In addition, using radial sampling of k-space one can achieve shorter effective echo times [133] and gain in sensitivity. Heterogeneous hydrogenation of propylene was carried out in a reactor containing Rh/TiO2 catalyst and maintained at 250 ⁰C. The experiments performed with the use of parahydrogen were done in the ALTADENA mode. A mixture of propylene and parahydrogen (1:4) flowed at the rate of 20 mL/s through the reactor, producing hyperpolarised propane. After exiting the reactor, hyperpolarised propane flowed through a PTFE capillary to the bottom of a 10 mm NMR tube placed in the probe of a wide bore microimaging instrument. The resulting images were obtained for both non-flowing thermally polarized propane and flowing hyperpolarised propane (Figure 10). Even for the thermally polarized gas, the images had good quality and spatial resolution. A comparison of the images of hyperpolarised propane and thermally polarized propane showed that the image with hyperpolarised propane was enhanced only by two-fold, while the corresponding 1H NMR spectra showed an enhancement factor of about 10.

[Insert Figure 10 here]

Figure 10. (a) 1H MR image of 10 mm NMR tube with non-flowing thermally polarized propane; (b) 1H MR image of 10 mm NMR tube with hyperpolarised propane acquired during gas flow. The experiments were performed on an Avance III 400 MHz NMR spectrometer (Bruker) equipped with microimaging accessories using the commercial 15 mm i.d. RF coil. The UTE (Bruker ParaVision) pulse sequence was used with 15⁰ flip angle pulses, radial trajectories in k-space were filled starting from the centre using 100 different projections. Field of view FOV = 3 cm × 3 cm, matrix size 32 × 32, spatial resolution 0.94 mm × 0.94 mm, slice thickness 10 mm, TR/TE= 20 ms / 0.226 ms. The total scan time was 2 s. Reproduced from Ref. [128].

For certain MRI studies, chemically selective imaging (chemical shift selective imaging, CSSI) by selectively exciting or suppressing the signals of the molecules of interest may be beneficial [134]. To achieve this, experiments performed with a suppression of the signals of one of the gases in a binary mixture were implemented [128]. For these experiments, a 10 mm NMR tube with propylene was coaxially inserted in a 15 mm NMR tube with propane. First, the unmodified UTE pulse sequence was used, with the number of different projections increased to 400, which increased the spatial resolution in the images. It is important to note that the images acquired (Figure 11a) did not have any significant artefacts. Both gases (propylene and propane) could be seen in the MR images, with the signal intensity of propylene gas being somewhat lower than that of the propane gas This difference is associated with the choice of the pulse sequence parameters. The latter were optimized for propane imaging (Figure 10). This choice can be suboptimal for propylene as propane and propylene have different relaxation times.

[Insert Figure 11 here]

Figure 11. 1H MR image (a) and 1H NMR spectrum of a 10 mm NMR tube with propylene placed in a 15 mm NMR tube containing propane. 1H MR image (c) and 1H NMR spectrum acquired with selective suppression of the propane signals. The images were acquired using 400 projections, 100 kHz spectral width, FOV = 5 cm × 5 cm, matrix size 128 × 128, spatial resolution 0.39 mm × 0.39 mm. The total scan time was 8 s. The spectra were acquired by turning off the gradients and reducing the spectral width appropriately. Reproduced from Ref. [128].

For the next set of experiments, the ultrashort TE (UTE) pulse sequence was modified by adding a selective excitation pulse before the imaging module to suppress the signals of the methylene (CH2) and methyl (CH3) groups of propane. This also led to the suppression of the signal from the CH3 group of propylene (Figure 11d) as these signals are close to each other in resonance frequencies. As a result, the dominating signals in the NMR spectrum were those from the CH and CH2 groups of propylene. The intensity of those signals was appropriate for imaging, and MRI experiments showed that propane gas was suppressed in the resulting image (Figure 11c), while the propylene gas had almost the same intensity as before saturation (cf. Figure 11a and Figure 11c). Therefore, the developed approach can provide the opportunity to perform imaging selectively with respect to different molecules in the gas phase.

Later, the above-mentioned approach with the acquisition of MR images from the selectively exited signals was used for dissolved hyperpolarised propane [124], and for hyperpolarised propylene gas formed during heterogeneous hydrogenation of propyne with parahydrogen over the single-site Pd-In catalyst [135]. It was mentioned above that gases including propane have short relaxation times which significantly limits the flexibility in hyperpolarised propane gas visualization. However, it was shown that this problem can be easily overcome by dissolution of propane in appropriate organic solvents [124]. A mixture of propylene and parahydrogen in the ratio 1:4 passed through a reactor containing Rh/TiO2 catalyst maintained at 200 ⁰C placed in the Earth’s magnetic field (ALTADENA experiment), then the hyperpolarised propane flowed through a 1/16-inch o.d. PTFE capillary to the bottom of a 10 mm NMR tube containing 2 mL of a solvent (acetone-d6 or methanol-d4), which was placed inside a microimaging instrument. The concentration of dissolved propane was approximately 50 mM. NMR spectra were recorded with a 10⁰ excitation pulse. The results of NMR experiments showed that T1 of hyperpolarised propane dissolved in the solvent is approximately 50 times longer than the T1 of gaseous propane (35 s vs. 0.6 s, respectively). The change of the main relaxation mechanism that takes place upon dissolution of hyperpolarised propane is the main reason of T1 prolongation, because the spin-rotation mechanism which dominates in the gas phase becomes significantly less efficient once a molecule finds itself in the liquid phase. It is essential for such experiments that hyperpolarised gas can preserve polarization upon dissolution [136]. The signal enhancement in the experiments with acetone-d6 was approximately 17-fold, which was quite useful for performing imaging studies.

MRI experiments were performed on a Bruker Avance III 400 MHz NMR spectrometer with imaging accessories. The conventional two-dimensional fast low-angle shot (FLASH) [137] pulse sequence was used. Utilizing small flip angles, this pulse sequence decreases the delays between measurements which decreases the total scan time. To perform the imaging of a liquid solution, the gas flow was interrupted during acquisition to prevent perturbations of the magnetic field homogeneity in the sensitive area of the probe. The excitation pulse in the FLASH sequence was equal to 5⁰, with the selective RF pulse applied at the resonance frequency of the CH3 group of hyperpolarised propane produced in ALTADENA type experiments. Enhancement of the NMR signals provided by the ALTADENA experiments gave an opportunity to visualize hyperpolarised propane and even to resolve a 1/16“ capillary despite the short duration of image acquisition, which was complete in about 1.7 s (Figure 12a). Such good spatial resolution could not be achieved in the case of thermally polarized propane (Figure 12b).

[Insert Figure 12 here]

Figure 12. (a) 1H MR image of a 10 mm tube containing hyperpolarised propane dissolved in acetone-d6. The imaging experiment was performed right after the gas flow was stopped. SNR = 17.2. (b) 1H MR image of thermally polarized dissolved propane. The standard ParaVision 5.1 software (Bruker TopSpin 3.0) was used to control the experiments. The gas flow rate was adjusted by Aalborg rotameter and varied from 1.89 to 3.313 mL/s. FLASH pulse sequence was used with 50 kHz spectral width, FOV = 5 cm × 5 cm, matrix size 64 × 64, spatial resolution ca. 0.8 mm × 0.8 mm, slice thickness 50 mm, TR/TE = 26.8 ms / 14.8 ms. The total scan time was ca. 1.7 s. Reprinted from Ref. [124]. Copyright (2017) American Chemical Society.

Selective hydrogenation of a triple carbon-carbon bond to a double bond is a major challenge in modern chemical industry [138]. Therefore, development and utilization of new catalytic systems for this semihydrogenation reaction and of new analytical tools for the detection of reaction intermediates and products is of high priority. PHIP can play a role of a very sensitive approach for intermediate/product detection [139,140]. In the context of the development and application of novel catalytic systems for producing PHIP-based hyperpolarisation, the utilization of catalysts with a single atom distribution of an active metal is a new and promising concept for semihydrogenation of a triple bond [135,141]. To this end, the reaction of selective semihydrogenation of propyne with parahydrogen over the single-site Pd-In catalyst was investigated [135]. It was established that high levels of enhancements of the NMR signals can be achieved via pairwise hydrogen addition to an unsaturated substrate. The behaviour of single-site active centres can be analogous to that of the metal centres of homogeneous catalysts [142]. Therefore, catalysts with a well-defined single-site structure of an active centre could be promising for achieving high levels of pairwise hydrogen addition in experiments with parahydrogen [108].

The Pd-In/Al2O3 [143] catalyst was usedin semihydrogenation of propyne with parahydrogen in an ALTADENA experiment. 1H NMR experiments were done on a 300 MHz Bruker AV 300 NMR spectrometer with the use of a 90**°** excitation pulse. In the NMR experiments, the mixture of propyne with parahydrogen (1:4) flowed through the reactor with Pd-In/Al2O3 (30 mg)single-site catalyst at 400°C. This catalyst provided high levels of hyperpolarisation (9.3%), conversion (20%) and selectivity to propylene (up to 98%). The NMR signal of the reaction product, hyperpolarised propylene, demonstrated high signal enhancement (about 3400-fold) and high conversion that was sufficient for the selective imaging experiments. The enhancement factor was high because of the high degree of pairwise addition of parahydrogen (9.3%) to propyne provided by the single-site Pd-In/Al2O3 catalyst. It was the highest enhancement reported for heterogeneous PHIP experiments presented to that date [135,144]. The MRI experiments were done on a 400 MHz microimaging instrument (Bruker). Compared to the spectroscopic experiments, the amount of the catalyst was increased to 100 mg to provide higher reaction conversions. 1H MR images of continuously flowing hyperpolarised propylene in a 10 mm NMR tube were acquired using the fast low-angle shot (FLASH) pulse sequence, which was modified for frequency-selective excitation. The modification consisted in the replacement of the hard RF pulse with a soft selective pulse. The shape of the pulse was Hermitian for the CH3 group of propylene and Gaussian for CH and CH2 groups of propylene. To achieve the maximum signal intensity for the gradient echo pulse sequence used in the experiments, the flip angle was set to the Ernst angle value (arccos(exp(-TR/T1)), which for the experiments with propylene was equal to 12.6° for the CH3 group and 14.3**°** for the CH and CH2 groups (Figure 13).

The results of MRI experiments showed that in the case of thermally polarized propylene the NMR signal intensity is insufficient to acquire good quality images (Figure 13, bottom row), whereas in the case of hyperpolarised propylene good quality images with high SNR were obtained. Such demonstration is unique and allows one to use the approach based on the combination of MRI and PHIP with selective hydrogenation and selective detection for medical or industrial applications.

[Insert Figure 13 here]

Figure 13. Selective 1H MRI of hyperpolarised (top row) and thermally polarized propylene (bottom row) in a 10 mm NMR tube. The reaction was performed at 400 °C. Each column corresponds to a certain group of hydrogen atoms propylene (labels above the top row of images). The images of thermally polarized propylene show almost no signal. The images were acquired while the gas was flowing. Gradient echo pulse sequence, matrix size 64 × 64, spatial resolution 0.8 mm × 0.8 mm, TE was equal to 4.9 ms for the selective excitation of CH3 group and 6.9 ms for CH and CH2 groups. The total acquisition time was 700 ms for CH3 group and 956 ms for CH and CH2 groups. (Ref. [135]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

In all the PHIP-MRI experiments discussed so far, 2D images of hyperpolarised substances were acquired, but the developed approaches can be further extended to imaging in the three-dimensional (3D) space. The first experiments related to the 3D visualization of hyperpolarised gas (propane) were reported in 2014 [119]. To achieve that, propylene was hydrogenated to propane with parahydrogen over a supported metal catalyst, whereby the mixture of propylene and parahydrogen in a ratio of 1:2 flowed through a reactor with the catalyst under conditions of an ALTADENA experiment. The temperature of the reactor was maintained at 100 °C. Three different catalysts, Pd/TiO2, Pt/TiO2 and Rh/TiO2, were used for propylene hydrogenation in these experiments. The best results were obtained with the Rh/TiO2 catalyst, which demonstrated the highest catalytic activity for the pairwise addition of hydrogen to propylene molecules, i.e., the largest NMR signal enhancements. In the high-resolution 1H NMR experiments, the hyperpolarised propane flowed to the probe of a Bruker 400 MHz NMR spectrometer with the flow rate of 15 mL/s through the system of capillaries. The achieved NMR signal enhancement was about 70-fold (Figure 14).

[Insert Figure 14 here]

Figure 14. (a) Reaction scheme of propylene hydrogenation with parahydrogen. (b) 1H NMR spectra acquired in an ALTADENA experiment for hyperpolarised propane produced over Pd/TiO2, Pt/TiO2 and Rh/TiO2 supported catalysts. (c) Comparison of the 1H NMR spectra of thermally polarized and hyperpolarised propane for Rh/TiO2 catalyst.

MRI experiments were done on a Varian 4.7 T (200 MHz) animal imaging instrument. For the phantoms for acquiring MR images, TygonTM tubes (3/32 in. i.d., 3/16 in. o.d.) were bent to form the letters "NSU" (Novosibirsk State University) and "VU" (Vanderbilt University) and wrapped around a piece of cardboard to preserve the shape (Figure 15). During the acquisition, the hyperpolarised propane was flowing through the letters. For imaging, 3D gradient echo (GRE) pulse sequence was used. In comparison with the conventional spin echo (SE) pulse sequence, the gradient echo sequence utilizes flip angles that are less than 90° and requires less time to acquire an image.

[Insert Figure 15 here]

Figure 15. 3D GRE 1H MRI of (a) "NSU" and (c) "VU" phantoms, and (b) the photo of the former. The image of water in the "VU" phantom (d) is provided for comparison of the SNR. 3D gradient echo (GRE) pulse sequence (ge3d, Varian version; VNMRJ version 3.3 software suite) was used for 1H MRI experiments, RF pulses had Gaussian shape and 15° flip angle and were 500 μs long. Spectral width 40 kHz, FOV = 80 mm × 80 mm × 20 mm, matrix size 128 × 128 × 32, spatial resolution 0.625 mm × 0.625 mm × 0.625 mm. TR / TE = 4.2 ms / 2.1 ms. The total scan time was 17.4 s. (Ref. [119]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

The results showed that 3D images of hyperpolarised propane were of reasonably high quality, but there were some imaging artefacts. The intensity of the signal decreased at the locations where the gas had higher velocity, which is likely associated with the gas leaving the imaged area during the application of the pulse sequence (on the order of 1 ms). The SNR of the image of the same phantom filled with water was a factor of 3 higher than the SNR of the phantom with hyperpolarised propane. However, it is important to note that with the catalyst used, the contribution of the pairwise addition of parahydrogen to propylene was only about 1.3%, and yet the quality of the image was comparable to that of the water image. The results thus demonstrate the feasibility of performing 3D MRI of hyperpolarised propane for imaging of porous media or in medical applications, where it can overshadow the background signal of water [119].

While gas imaging is useful in studies of catalysis [46], porous media [18] and lungs [103], it is challenging due to low density of gases. In this respect, gases polarized via PHIP provide a unique opportunity for significantly advancing such studies. Most PHIP hyperpolarised agents significantly benefit from the further increase in signal enhancement and lifetime upon deuteration of their molecular precursors [18]. Therefore, investigation of the deuterated propylene precursor for the production of hyperpolarised propane-d6 and its use in NMR at high and low magnetic fields are useful. The results reported in [145] demonstrate for the first time the 2D low-field MRI and 3D high-field MRI of propane-d6. To this end, the mixture of propylene-d6 and parahydrogen (1:2) was passed through the reactor containing Rh/TiO2 catalyst and equipped with an oven, which was held at the temperature of 100 °C.

In high-field 1H NMR experiments, hyperpolarised propane-d6 (ALTADENA conditions) flowed through a 1/16 inch PTFE tube to a 5 mm NMR tube positioned in the probe of a 400 MHz Bruker Avance NMR spectrometer. The signal enhancement measured by comparing the NMR spectrum of flowing hyperpolarised gas and the NMR spectrum of thermally polarized non-flowing gas was about 100-fold.

For 3D MRI, a 200 MHz Varian MRI scanner (Varian, Palo Alto, California) and a custom-built dual-channel MRI coil (38 mm i.d.) were used. A special phantom for imaging with a spiral shape was made of the TygonTM tube (3/32 in. i.d., 3/16 in. o.d.), which was wrapped around a plastic syringe for dimensional representation. The gas was continuously flowing through the phantom during an MRI experiment. The pulse sequence was the 3D gradient echo (ge3d). The resulting images were not interpolated or smoothed (Figure 16). For comparison of the quality of the images, the phantom filled with water (55 M concentration) containing 5 mM CuSO4 was used. The images of hyperpolarised propane-d6 (Figure 16) had a factor of two better spatial resolution (comparing voxel size) than the images of hyperpolarised non-deuterated propane (Figure 15). In addition, the quality of images of hyperpolarised propane-d6 and water was similar and SNR values were comparable (15 and 24, respectively).

[Insert Figure 16 here]

Figure 16. High-resolution 3D GRE MRI of the phantom filled with (a) hyperpolarised propane and (b) water. Excitation RF pulses were Gaussian in shape, 500 μs long, and the flip angle was 15° for gas and 2° for water. Spectral width 20 kHz, FOV = 32 mm × 32 mm × 32 mm, matrix size 64 × 64 × 64, spatial resolution 0.5 mm × 0.5 mm × 0.5 mm (125 nL voxel). TR/Te = 4.3 ms / 2.2 ms. The total scan time was 17.7 s. Reprinted from Ref. [145]. Copyright (2014) American Chemical Society.

In addition, low-field NMR and MRI experiments were performed with a Kea2 0.0475 T NMR spectrometer (Magritek, Wellington, New Zealand) with a custom-built frequency optimized dual-channel RF 1H-X probe. In the low field NMR experiments, hyperpolarised propane-d6 was transferred into a phantom with the volume of approximately 2 mL which was placed inside the spectrometer. The gas transfer time did not exceed 0.3 s in these experiments. The phantom was filled for about 1 s with the inflowing hyperpolarised propane-d6 produced at 100 °C with subsequent gas flow termination (Figure 17). The RF pulses had a rectangular shape and a flip angle of 45°. The signal enhancement achieved in these low-field experiments was estimated as 6000.

[Insert Figure 17 here]

Figure 17. Experimental setup for the low-field MR experiments. A mixture of propylene-d6 and parahydrogen flowed from the mixing chamber to the reactor. The reactor contained Rh/TiO2 catalyst and was heated to 100 °C. The resulting hyperpolarised propane-d6 gas flowed out of the reactor to the phantom (2 mL volume) which was placed inside a 0.0475 T NMR spectrometer. Transfer time from the reactor to the phantom was ca. 0.3 s.

The effective T1 value for propane-d6 measured at low magnetic field was equal to 6 s, which is a factor of 10 longer than the high magnetic field value of ~0.6 s. This effect was named Nuclear Alignment of Spin Hyperpolarisation via Interactions in Long-lived Low-field Ensembles (NASHVILLE) [145]. The main feature of this effect is the creation of population differences between the spin states of nascent parahydrogen protons with extended lifetimes. Such increase in hyperpolarisation lifetime is sufficient in principle to perform MRI of the lungs of a patient during one breath-hold.

2D low-field MRI experiments were conducted utilizing a conventional 2D gradient echo pulse sequence without slice selection (Figure 18). After transferring the hyperpolarised gas to the phantom, the MR images were acquired every 3 s. The centre of the image has a higher intensity compared to the rest of the image because of the phantom shape. These results are the first demonstration of low field MRI of hyperpolarised hydrocarbon gas. Low-field MRI approach has several advantages. Low-field MRI spectrometers have lower cost in comparison with high-field MRI instruments which require superconducting magnets. In addition, for the same level of nuclear spin polarization the SNR in low-field MRI can be even higher than in high-field MRI [146]. The image of 55 M water was acquired using eight signal accumulations and is presented for comparison in Figure 18.

[Insert Figure 18 here]

Figure 18. 1H MR imaging of hyperpolarised propane-d6 at the low magnetic field. The images correspond to the sequence of experiments with one scan acquired every 3 s. The rightmost image is that of thermally polarized water detected using 8 scans. Conventional gradient echo sequence was used, with a rectangular excitation RF pulse, 7° flip angle and 6 μs long. Spectral width 5 kHz, FOV = 28 mm × 28 mm, matrix size 32 × 32, spatial resolution 0.88 mm × 0.88 mm, TR/Te = 20 ms / 7 ms. The total scan time was ca. 0.7 s with one acquisition. All images were interpolated to 1024 × 1024 matrix using zero-filling prior to Fourier transformation. Reprinted from Ref. [145]. Copyright (2014) American Chemical Society.

The hyperpolarisation stored in the long-lived spin states can be transformed into observable magnetization more efficiently using specialized pulse sequences [147]. The lifetime of hyperpolarised propane can be extended by populating its long-lived spin states using PHIP, which can significantly increase the hyperpolarisation decay times. Long-lived spin states of propane were created by the use of the low magnetic field of 0.0475 T in the experiments [148]. The direct detection of the resulting NMR spectrum was shown to be possible, but the signal intensity was approximately 2-3 orders of magnitude lower than the expected value. Moreover, a detailed analysis of the spectrum shows that the peaks are in fact the 13C satellites arising due to the one-bond 1J(1H-13C) couplings in those propane molecules that contain 13C nuclei. The experiments were performed at the natural abundance of the 13C isotope in propane molecules. Therefore, isotopic enrichment of the reactant (propylene) with 13C could potentially lead to much larger signal intensities in such experiments. Moreover, observation of enhanced 13C satellites shows that larger signal enhancements can be potentially achieved for the main propane NMR signal corresponding to propane molecules that do not contain the 13C label.

To check this possibility, the hyperpolarised propane produced in the reaction of heterogeneous hydrogenation of propylene with the use of Rh/TiO2 ascatalyst at the Earth’s magnetic field was detected using the 0.0475 T NMR spectrometer (Magritek, Wellington, New Zealand). To convert the long-lived spin state of propane prepared in the Earth’s magnetic field, which is not immediately observable in the NMR experiments, into the significantly enhanced magnetization observable at 47.5 mT, the Spin-Lock Induced Crossing (SLIC) pulse sequence [146] was employed. The use of the SLIC pulse sequence provided the signal enhancement of about 5100, which is two orders of magnitude higher than the enhancement factor obtained for hyperpolarised propane detected without SLIC.

In the MRI experiments, the same phantom, reaction conditions, magnetic field and pulse sequence as reported in [145] were used. The resulting image (Figure 19) showed a good spatial resolution (0.88 mm × 0.88 mm) for a gas mixture with non-deuterated propane. The scan time of the propane imaging experiment was 0.7 s. A further decrease in scan time is limited by an electronic response of the receiver. The corresponding image of thermally polarized water is also presented in Figure 19 for comparison.

[Insert Figure 19 here]

Figure 19. MRI of hyperpolarised propane and water. The images were interpolated to 1024 × 1024 matrix using zero-filling prior to Fourier transformation. The dashed circle shows the location and shape of the phantom. (Ref. [148]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

**4. MRI studies of operating microreactors**

Microfluidic devices have attracted significant attention due to several advantages provided by small length scales [149-152]. The progress in this area was advanced greatly by the success of microengineering technologies providing unprecedented control and reproducibility for the manufacturing process. The idea of miniaturization of reaction processes has attracted enthusiastic researchers who have created microfluidic devices for various chemical engineering processes like mixing and separation and for performing a chemical reaction itself. The benefits of small length scales such as high surface-to-volume ratio and mechanical stability, efficient heat exchange and stable laminar flows made microreactors very interesting objects to explore.

As demonstrated with a number of examples discussed above, MRI is one of the rare methods providing versatile means for visualization of reaction processes and mass transport in heterogeneous catalysis. The low sensitivity of the method, however, sets significant obstacles in the studies of microreactors. For this reason, the first attempt to use NMR imaging in microreactor studies [153] was reported only after the demonstration [116] of the possibility to use PHIP to hyperpolarise reaction products produced via heterogeneous hydrogenations. In this study [153], PASADENA experiments were performed to enhance the signals of propane and to visualize and, in a sense, to control the spatial and temporal dynamics of its polarization in two model microreactors made of a 1/8’’ o.d. tubing packed with two different catalysts. The first microreactor contained a tightly packed bed of Wilkinson’s catalyst immobilized on silica gel. The catalyst was packed between two layers of 200 μm glass beads. In the second reactor, the bed of powdered Wilkinson’s catalyst was much less uniform and had voids up to 2 mm in size. In both cases, the mixture of propylene and parahydrogen flowed through the reactor 145 °C, which was placed in the RF probe of a microimaging instrument.

The pulse sequence used in the experiments is shown in Figure 20. The resulting NMR signal enhancement factor was estimated as ca. 300, which is essential in view of the low filling factor of the RF probe (the sample to RF coil volume ratio was less than 0.01). The pure phase encoding protocol was used for imaging with chemical-shift selection and good spatial resolution.

[Insert Figure 20 here]

Figure 20. The spin echo pulse sequence which was used in the MRI experiments. Isotropic mixing was achieved using the DIPSI-3 module prior to imaging. Tm is mixing time, Td is time delay. From [153] Adapted with permission from AAAS.

The antiphase 1H NMR signal of hyperpolarised propane, typically observed in PASADENA experiments, can result in signal reduction or even complete cancellation. Therefore, the spin echo pulse sequence π/4-TE/2-π-TE/2-echo was used, so that evolution under J-coupling would produce an in-phase signal and avoid the signal cancellation problem. The signal was detected from the gas phase in the void space of the catalyst bed. As a result, it was possible to map the distribution of the hyperpolarised propane gas inside the model reactors (Figure 21a). In addition, the quantification of the mass transport was attempted by acquiring flow velocity maps (Figure 21b).

[Insert Figure 21 here]

Figure 21. (a) 1H NMR image acquired from a 5 mm thick Rh catalyst bed, and (b) corresponding flow map of the reaction gas mixture from propylene hydrogenation with parahydrogen in a 1/8’’ tube model microreactor. FOV= 2.3 mm (x) × 7.0 mm (z), spatial resolution 20 µm × 60 µm. The orientation and length of the arrows in the map indicate the direction and the magnitude of the local flow velocity, respectively. From [153]. Adapted with permission from AAAS.

The results showed that images of thermally polarized propylene gas could not be acquired because of the insufficient SNR, while the image of hyperpolarised propane showed a good quality and sufficiently high spatial resolution. In addition, hyperpolarisation was crucial to mapping gas flow. These maps revealed that the flow was not uniform, which can be explained by the manner of the catalyst packing.

In addition, decoupling in the presence of scalar interactions (DIPSI-3) module was used for isotropic mixing in order to control the lifetime of the non-equilibrium spin state of propane produced in the reaction of propylene with parahydrogen. The duration of the mixing period Tm was sufficient to lock the non-equilibrium spin state of propane until it flows out of the catalyst bed. The optimal Tm depended on the average velocity of the flow. After the mixing the long-lived spin state transformed into an observable one during the time delay Td. These results were intended to demonstrate the extended control of the distance travelled by the molecules produced in a long-lived non-equilibrium spin state in the model catalytic reactor.

It should be pointed out, however, that the study discussed above [153] the diameter of the reactor channel was on the order of thousands of µm, which is an order of magnitude larger as compared to tens to hundreds of µm commonly used in microfluidics [154]. Nevertheless, this study was the first of its kind, showing the use of parahydrogen to enhance sensitivity for the imaging of relatively small beds of heterogeneous catalysts. The ability to image model packed bed microreactors of smaller sizes (down to 150 µm) was demonstrated in the later studies [66,155-157] by employing methodology of the so-called remote detection (RD) NMR. RD NMR imaging method was established in the group of A. Pines [158]. It allows substantial detection sensitivity boost in the studies when the imaged fluids occupy only a small fraction of the volume of the RF probe [159], i.e. when the filling factor of the probe is small. The detected NMR signal is directly proportional to the filling factor. In the remote detection, the information about spatial distribution of fluids is encoded with a large RF coil accommodating the entire microfluidic device, whereas the detection is performed by a small microcoil of optimized size when the fluid flows outside the device (Figure 22) [160].

[Insert Figure 22 here]

Figure 22. Schematic representation of RD NMR experiment with a model microfluidic reactor. Reagent mixture is supplied to the microreactor positioned inside a large RF coil to encode information about instant spatial distribution of reagents and products of a reaction taking place inside. The directions of the flow streams are indicated with small arrows. When the fluid flows out of the microreactor, the spatial information is detected by using the sensitive microcoil wound around the outlet capillary. The much better detection conditions lead to the significant sensitivity improvement.

The detection sensitivity boost in this case can reach several orders of magnitude, providing novel possibilities for NMR imaging of microfluidic devices. Moreover, as the fluid flows from the encoding RF coil to the detection coil, RD NMR naturally allows one to obtain time-of-flight (TOF) information [161], providing details about mass transport in the microfluidic device.

The first application of RD NMR for imaging of chemical reactions in microreactors was demonstrated by using propylene hydrogenation as a model process over Rh/SiO2 and Rh/TiO2 catalysts [66]. In addition to the sensitivity boost provided by RD NMR, additional NMR sensitivity gain was achieved by utilizing parahydrogen instead of normal hydrogen, which yielded hyperpolarised propane (Figure 23a), the approach considered in detail in section 3. The total sensitivity boost provided by the combined use of RD and PHIP was estimated to be 5×104-fold compared to the normal detection scheme and the normal hydrogen use. Such a significant sensitivity improvement allowed quantifying the distribution of the hyperpolarised propane inside the model packed-bed microreactors with channel diameters from 800 down to 150 µm. For instance, Figure 23b shows TOF RD images with spatial encoding along the axis (z axis) of a 150 µm i.d. cylindrical channel packed with Rh/SiO2 catalyst. The NMR pulse sequence used to acquire this z-encoded TOF RD NMR image is shown in Figure 23c. The vertical coordinate of the image corresponds to the position (z coordinate) at which the product propane was detected, whereas the horizontal coordinate corresponds to the travel time that was required for the gas to travel from the particular position in the catalyst bed to the detection coil. The graph to the right of the image shows the fitting result to the experimentally determined reaction yield inside the catalyst bed as a function of position in the packed-bed channel. These data allowed estimation of the parameters of reaction kinetics. The flow velocity information was determined from the same image by measuring the slope of maximum signal intensity as a function of travel time.

[Insert Figure 23 here]

Figure 23. (a) 1H NMR spectra acquired with a 360 µm detection microcoil from propylene hydrogenation reaction mixture. The spectra correspond to the experiments with parahydrogen and normal hydrogen. A 150 µm inner diameter microfluidic channel packed with Rh/SiO2 catalyst was used as a microreactor. (b) The z-encoded TOF RD NMR image acquired from the 150 µm microreactor and the reaction yield curve as a function of position in the microreactor obtained from the image. (c) The z-encoded and (d) yz-encoded RD NMR imaging pulse sequences, respectively. Enc = encoding coil, Det = detection coil, grad = magnetic field gradient. (e) The yz-encoded TOF RD NMR images obtained in the experiment with the 150 µm microreactor. The first image is the sum of the images for different travel time instances that are presented as well. The travel times are shown in the latter images in ms with the white numbers. (Ref. [66]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Adapted with permission.)

It was also demonstrated that the sensitivity improvement achieved by combining RD and PHIP was sufficient to measure TOF images with the spatial encoding in two dimensions (y and z coordinates) in a reasonable time of about 13 min, Figure 23e. The first image in the figure shows the time projection, i.e. the sum of individual RD NMR images acquired at different travel time instances, which are also shown in the figure. These yz-encoded TOF images were acquired by using the pulse sequence shown in Figure 23d.

The achievements of this study include pushing significantly the limits of channel sizes accessible by NMR, the demonstration of quantitative measurements of the reaction product distribution, kinetic parameters estimation and multidimensional mass transport visualization. Moreover, a manifestation of adsorption phenomenon in the packed catalyst bed was visible in the TOF RD images, which was used to estimate the amount of gas adsorbed in the Rh/SiO2 and Rh/TiO2 catalysts. The observation of absorption in these experiments has presented a foundation for the RD NMR adsorption measurement method discussed briefly later in this section.

In the next demonstrations, RD NMR method was applied to perform studies of lab-on-a-chip type microreactors [155-157]. The chip reactors were made by etching parallel channels in silicon wafers (Figure 24a), and supporting the catalytically active component by using advanced microengineering techniques. Thin films of sputtered Pt [155,156] or Pt nanoparticles [157] were used as the active component in the model reaction of propylene hydrogenation. RD NMR method in these cases was applied without generating hyperpolarisation via PHIP, because the utilized catalysts didn’t produce any nuclear hyperpolarisation when parahydrogen was used as a reagent. Nevertheless, the sensitivity provided by RD NMR allowed the authors to perform NMR imaging of the hydrogenation process in the microreactors, albeit at a price of a longer data acquisition time.

[Insert Figure 24 here]

Figure 24. (a) RD NMR experimental setup for imaging experiments of chip microreactors with sputtered Pt on the channel inner surface. The channel dimensions are shown in the inset. (b) The yz-encoded TOF RD images constructed by using propylene and propane 1H NMR signals from propylene hydrogenation performed in the reactor. Adapted from Ref. [155] with permission from the Royal Society of Chemistry.

In the initial study, it was shown that by using RD NMR principles and the phase encoding of spatial information it is possible to get chemical resolution of the reagent (propylene) and the product (propane) and to construct substance-sensitive TOF RD images. In particular, this advancement allowed the authors to visualize active zones in the microreactors. Figure 24b shows the time projection images corresponding to a 10 mm long chip microreactor. Constructed by using propane and propylene signals, respectively, these images demonstrate localization of propane production in the right part of the microreactor, highlighting the imperfections of chip fabrication. The individual images for different travel times from particular positions in the microreactor to the detection coils were also measured. These data showed that the flow velocity in the propane rich region is lower than in the propylene rich one, implying expectedly that short residence times lead to a less efficient reaction process in the left part of the chip.

It was noticed also that nuclear spin magnetization encoded in propylene molecules has revealed itself in propane molecules. Therefore, this magnetization was inherited by the produced propane after the chemical transformation. Because of this effect, images constructed for propane in some cases revealed NMR signal at the very inlet part of the microreactors, where propane was not expected to be present. This was a clear indication that precise correspondence between the detected signal of propane and its position in the microreactors is not fully straightforward. In the next study, however, this discrepancy was resolved by applying the principles of Hadamard NMR [156]. It was shown that Hadamard NMR spectroscopy principles [162] allow one to gain benefits of multidimensional 2D EXSY techniques to discriminate between the sources (propylene or propane) of magnetization encoding in the imaging experiments, while the data acquisition time does not increase significantly. The developed method was based on the use of selective pulses to excite nuclear spins of propane and propylene, whereas the phases of the signals were selected according to the signs of the 2×2 Hadamard matrix, Figure 25b [163].

[Insert Figure 25 here]

Figure 25. (a) RD-EXSY NMR pulse sequence for exchange spectroscopy experiments in microreactor studies. (b) Hadamard-encoded RD-EXSY pulse sequence for experiments with spatial resolution in the propylene hydrogenation study. (Ref. [156]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Adapted with permission.)

These phases make straightforward the combining of measured NMR signals to obtain the correct contribution that resulted from the signal of interest while the contribution of the other signal vanishes. RD-EXSY and Hadamard-encoded RD-EXSY methods were established in this work, Figure 25 [156], demonstrating the capabilities of spatially resolved RD NMR to study chemical reactions with the tools similar to those widely applied in conventional multidimensional NMR spectroscopy.

The recent study on NMR imaging of microreactors with heterogeneous catalysts concerns characterization of chip-based microreactors with supported Pt nanoparticles on the inner surface of microfluidic channels [157]. It should be noted that this work presented a technologically new design of the microreactors as atomic layer deposition (ALD) was applied to form TiO2 support coating, and the Pt nanoparticles were formed by using ALD as well. In addition to the ALD TiO2 surface, Piranha-treated silicon support was used in the manufacturing process of the microreactors. Hydrogenation of propylene to propane was used as a model reaction process. RD NMR imaging with resolution in two spatial dimensions was used to characterize mass transport inside the microreactors, to measure kinetic parameters and consequently to quantify catalytic activity of different types of Pt surfaces for the microreactors of different particle sizes. Based on the previous developments, this particular study has used RD NMR as a tool for the characterization of promising microreactor design rather than investigating the method itself. Mass fluxes and reaction conversions were determined using RD NMR, highlighting the qualitative transformation of this method to a powerful technique for advanced studies in the field of microreactors.

TOF RD NMR imaging was demonstrated to be useful also for quantification of molecular adsorption by porous materials. The methodology is based on the comparison of mass transport velocities in packed and empty microfluidic channels – the information available from the z-encoded TOF RD NMR images. It was discovered experimentally in the study on microreactor imaging [66], and further developed in the recent work [67]. The ratio of the velocities was shown to be dependent on the number of adsorbed molecules per unit surface area of a porous material, *nua*. The latter quantity can be determined by using the following formula,

, (1)

where *up* and *uo* are the mass transport velocities in the packed and empty channels, respectively. Other parameters are the inner diameters of the packed and empty channels (*dp* and *do*), the gas pressure (*P)*, the temperature (*T*), the universal gas constant (*R*), the specific surface area of the porous material (*s*), the porosity associated with the voids between the particles (*ϕ*), the specific pore volume (*vpore*) and the density of the solid skeleton of the particles (*ρsolid*). Figure 26a shows the experimental setup for the adsorption measurements: the packed-bed capillary with a porous material under investigation is connected to the empty outlet capillary so that they both are visible in the z-encoded TOF RD image, Figure 26c.

[Insert Figure 26 here]

Figure 26. (a) Experimental setup for the RD NMR adsorption measurements. (b) Pulse sequence of the z-encoded TOF RD NMR imaging experiment. (c) The z-encoded TOF RD NMR image of propane flowing through CPG237 mesoporous material at room temperature. The slopes indicated by black dashed lines show the flow velocities in the packed bed and empty outlet capillary regions. Adapted from Ref. [67], Copyright (2017), with permission from Elsevier.

The image is acquired using the pulse sequence shown in Figure 26b to determine flow velocities from the slopes of the maximal signal. The experimental ratio of the two velocities is used in Equation 1 to determine *nua*. It was demonstrated that this technique provides a way to rapidly perform adsorption measurements under continuous flow conditions for a single gas (propylene or propane) as well as for a two-component gas adsorption (propylene/propane mixture) [67]. Since the gases are resolved in the detection coil spectra, RD NMR provides TOF images for the individual components. This advantage made the study of competing adsorption with the use of RD NMR an easy task.

**5. Summary**

MRI of heterogeneous catalytic processes remains a challenging area of scientific research. The studies reported to date in this field demonstrate that, despite this fact, such applications are attractive and potentially useful. The main limitations of such studies are associated with an insufficient sensitivity, which limits both spatial and temporal resolution in the studies of dynamic processes taking place in an operating reactor. This issue is particularly significant if gases are to be addressed with MRI/MRS instead of liquids. A major sensitivity boost is achievable via the combination of MRI/MRS studies with modern nuclear spin hyperpolarisation techniques. Hyperpolarisation is a rapidly growing and advancing area of research, and even if at the moment the number of chemicals that can be hyperpolarised and the number of reactions that can be studied this way may be limited, further rapid progress in this field is a certainty. Thus, novel possibilities for combining hyperpolarisation with MRI/MRS to address catalytic processes will inevitably emerge. Another limitation is associated with the significant line broadening of fluids in porous media which experience both significant acceleration of spin relaxation processes and a major inhomogeneity of the applied magnetic field. All this makes acquisition of useful spectroscopic information difficult at best. Therefore, reliable spatially resolved spectroscopic studies of operating model reactors call for the development of robust and efficient techniques that are able to recover useful spectroscopic information for highly non-uniform samples. Despite all the difficulties, magnetic resonance has a clear potential to be able to characterize a broad range of processes in an operating reactor, including mass and heat transport, phase transitions and the chemical conversion itself, as the examples of the experimental results considered above hopefully demonstrate.

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