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FRONTIERS ARTICLE

Ultrafast optical encoding of magnetic resonance

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ABSTRACT

Temporal resolution in magnetic resonance imaging (MRI) is limited by the time required to encode the position of spins using time-varying (10–100 ms) magnetic field gradients. Here, we demonstrate spatial encoding of MRI images in a time that is three orders of magnitude shorter than what is possible by conventional gradient encoding techniques. Our method exploits the chemically induced dynamic nuclear polarization (CIDNP) effect and is an initial example of a set of approaches that seek to combine the favorable properties of optical spectroscopy with those of NMR for polarization, encoding, and detection.

1. Introduction

Magnetic resonance imaging is an uniquely non-invasive probe of structure and chemical dynamics with numerous applications in fields including structural biology, medicine, rheology [1], and fluid dynamics [2]. MRI differs from optical microscopy in that it is capable of peering deep within unmodified and unlabeled materials, elucidating their structure on length scales from nanometers to meters and their dynamics on time scales from microseconds to seconds. In comparison with optically-detected spectroscopic techniques, however, MRI has much lower sensitivity and temporal resolution, complicating its application in studies of dynamical processes that occur in less than 100 μs. These limitations motivate the development of hybrid optically-MRI techniques that combine the properties of optical detection with those of NMR for polarization [3], detection [4], and now encoding.

In a conventional MRI experiment [5], spatial encoding is achieved through the application of a magnetic field gradient for a duration sufficient to impart a detectable phase or frequency at the resolution of interest. Because of limitations in the construction of gradient circuits, the gradient is almost always applied for several milliseconds, limiting the time resolution of the experiment. While recent experiments employing remote detection of flowing fluids have achieved time resolution in the few microsecond range [6], they do so at the expense of an additional spatial dimension in which the temporal information is encoded and are thus ultimately limited by magnetic field gradients and flow dynamics.

In this Letter, we instead exploit the phenomenon of photo-CIDNP [7–9] to spatially encode nuclear spins on a microsecond timescale. In PhotoCIDNP, hyperpolarization of the nuclear spins occurs because of a photochemical reaction that proceeds through spin-correlated radical pair intermediate, as outlined below. The pattern of spin polarization reflects the pattern of initiating optical radiation, and hence a relevant medium solid or liquid can be encoded at a resolution limited by optical diffraction by shaping the light irradiated on the sample.

Specifically, a suitable chromophore, P, is optically excited from electronic singlet to triplet.

$$^1P \rightarrow {}^3P. \tag{1}$$

This highly reactive radical species reacts with a substrate molecule, Q, through proton or electron transfer, with retention of electron spin symmetry, to form a geminate pair.

$$^3P + Q \rightarrow {}^3[P + Q]. \tag{2}$$

The spin-correlated pair can then either diffuse apart and react with other molecules, X and Y (Eq. (3)), or the geminate pair can undergo triplet–singlet conversion (Eq. (4)) followed by recombination (Eq. (5)).

$$^3[P + Q] \rightarrow PX + QY, \tag{3}$$

$$^3[P + Q] \rightarrow {}^1[P + Q], \tag{4}$$

$$^1[P + Q] \rightarrow P + Q. \tag{5}$$

The rate of triplet to singlet conversion in Eq. (4) is a function of the electron-nuclear hyperfine coupling. As a consequence, the reaction outcome and reaction rate depends on the nuclear spin orientation, terminating either in the generation of PX and PY or the regeneration of P and Q. These products will be respectively enriched in either nuclear spin up or nuclear spin down states.

In the system used in these experiments, where P represents 2′2′ dipyridyl and Q represents n-acetyl tryptophan, the products

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of Eqs. (3) and (5) are the same. This would appear to lead to zero net nuclear polarization. However, the nuclear spin relaxation rate is fast in the radical species, leading to imperfect cancellation of the nuclear polarization [10] and hence non-equilibrium polarization of the nuclei.

Because the polarization evolves on a very fast timescale, PhotoCIDNP has been exploited in the study of fast protein folding dynamics [7,11] and as a method of hyperpolarization for reducing acquisition time in multidimensional protein NMR studies [12]. Here, we apply it to spatial encoding in magnetic resonance imaging experiments. Using a collimated light source, such as a laser beam, one can illuminate a specific region of a sample, enhancing nuclear polarization only in the illuminated volume. By applying an optically dense mask to the output of the light source it is possible to "imprint" a two dimensional image onto nuclear spins in the sample. In this way it is possible to spatially encode or 'tag' a particular volume using a short pulse of light, rather than a magnetic field gradient, significantly reducing the encoding time.

2. Experimental

2,2-Dipyridyl (DP) (shown in Figure 2a) and *n*-acetyltryptophan (TrpH) were obtained in the highest available purity from Sigma Aldrich and used without further purification. 99.99% D_2O was purchased from Cambridge Isotope Laboratory (CIL). Experiments were conducted on solutions of around 0.5 mmol of DP and 3 mmol of TrpH. The solutions were purged of O_2 by bubbling with N_2 for 30 min before each experiment. This process increased the photoCIDNP signal by a factor of two.

The method of coupling the laser light to the solution is shown in Figure 1, in a similar manner to that shown previously by Pienta and Smith [13].

The photoCIDNP imaging experiments were carried out on a 300 MHz (7.04*T*) Bruker Avance 300 spectrometer with a 10 mm Bruker microimaging probe and gradient stack. Images were obtained using a Bruker CSI imaging sequence, using water suppression and presaturation to remove any residual thermal signal before photo-excitation.

3. Results and discussion

Before recording an image, spectra were taken in order to directly observe the photoCIDNP polarization. The polarization enhancement shown in Figure 2b was obtained following a pulse train of 50 laser pulses over a period of 500 ms. The polarization generated following a single pulse was about equal to the thermal polarization and thus necessitated broadband presaturation in order to observe the CIDNP signal.

The imaging experiment consisted of a single 5 ns laser pulse followed by a CSI (chemical shift imaging) pulse sequence. As can be seen from the spectrum of the bulk sample in Figure 2b the photoCIDNP enhancement was greatest for the 3, 4 and 5 positions of DP. Thus the region between 7.5 and 9.0 ppm was selected for the CSI images in order to minimize the effect of any residual thermal polarization of the unenhanced protons.

The UV laser light penetrated about 1 mm into the bulk sample before significant attenuation, so a 1 mm thin slice immediately below the light guide was selected for imaging. The low concentration of DP required the collection of 200 transients per voxel even with significant photoCIDNP signal enhancement. The signal to noise ratio and image resolution was limited by linebroadening caused by the large susceptibility gradient in the area being imaged, in this case directly on the interface between the quartz glass and the aqueous solution.

An example image is given in Figure 3. The spatial encoding time in this experiment is given by the time taken for CIDNP polarization to develop following laser excitation of the photosensitizing agent. Previous time-resolved CIDNP experiments [14,10] have shown this to be in the sub-microsecond timescale.

Our experiments demonstrate that the duration of the encoding step of an MRI experiment can be significantly reduced by manipulating optical transitions that are coupled to spin degrees of freedom, in this case through the photoCIDNP effect. Ultra-fast spatially selective spin labeling could be productively applied to the study of fast protein folding in combination with remotely detected NMR in microfluidic devices [6] or for studying turbulent and dispersive flow at time scales currently inaccessible to MRI.

While we have acquired a conventional image to demonstrate the successful spatial encoding of spins, our method in principle can be extended to obviate the need for gradients all together. In this case, the image can be reconstructed by a point-by-point acquisition, either directly or using chemical exchange or diffusion to yield a large signal enhancement [15]; the sensitivity of the approach will improve dramatically as the voxel dimensions are reduced. Further, because there are numerous technologies to generate a desired spatial pattern of optical irradiation, either by scanning or masking, our method can also be used in a Fourier mode to generate an image of spins in the sample without magnetic field gradients, an example of single pixel imaging [16]. In this case, the resolution might be improved by a two-photon excitation scheme, yielding photoCIDNP excitation only in the region of interaction between multiple laser pulses. More speculatively, approaches based on optical excitation in triplet-forming solutes or in solids [17] may join recently

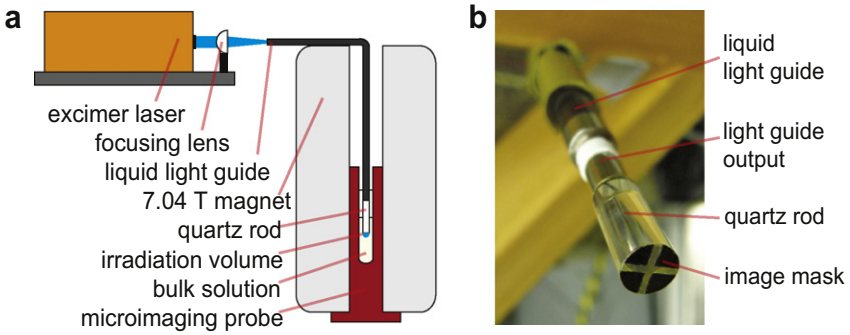

Figure 1. (a) A XeCl (308 nm) MPB Communications excimer laser was used for sample illumination, triggered by transistor–transistor logic (TTL) pulses. Its peak pulse energy was approximately 100 mJ, with a pulse duration of 5 ns. Coupling to the NMR probe was achieved by focusing the output UV light onto the end of a 7 mm diameter liquid light guide. The magnetic susceptibility mismatch between the metallic sheath of the light guide and the solution necessitated the addition of a 1 inch length of quartz rod butted up against the output of the light guide. The mask was applied to the end of the quartz rod using a UV-absorbing ink. Losses of around 95% of light over the path from laser output to sample were recorded. (b) Detail showing output of light guide apparatus.

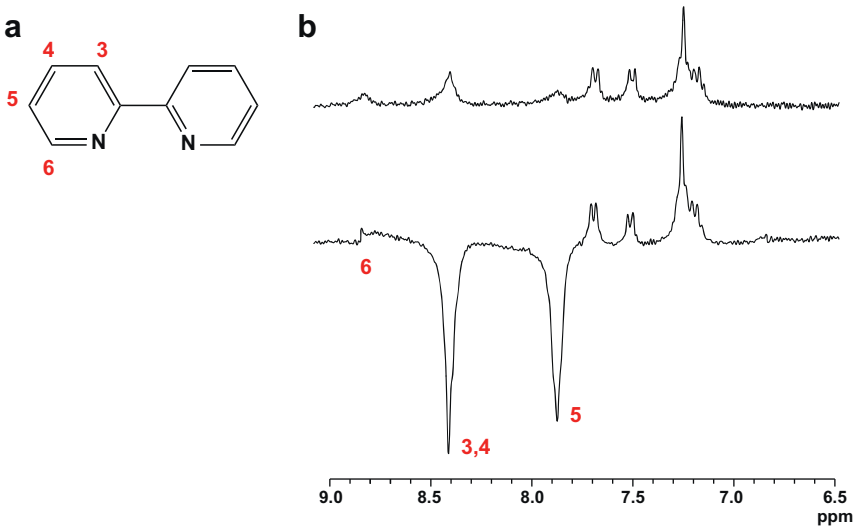

Figure 2. (a) 2′2′-dipyridyl. (b) The solution spectrum before irradiation (top) and immediately after irradiation (bottom). The labelled peaks correspond to the numbered positions of DP in part (a). Significant photoCIDNP enhancement was observed for the 3, 4 and 5 positions of DP. The unlabelled peaks between 7.0 and 7.7 ppm correspond to aromatic protons on TrpH. A small photoCIDNP enhancement is visible for the resonances at 7.2 and 7.7 ppm. Shimming of the magnetic field was complicated by the susceptibility mismatch between the quartz rod and the solution, leading to the broad lines in these spectra.

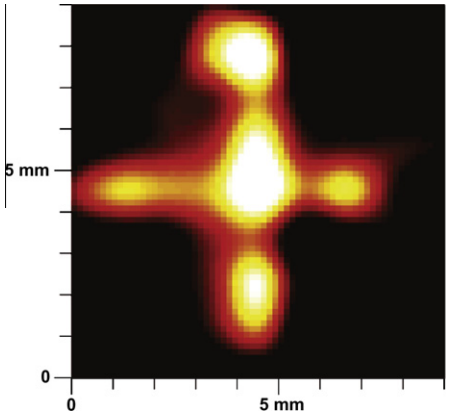

Figure 3. 9 × 9 Pixel image of the applied mask, with a resolution of about 900 microns.

proposed schemes for nanoscale optical detection of MRI [18,19], in which case the optical excitation of the sample or an optically active substrate on which the sample has been deposited may be used for spatial encoding of all-optical MRI experiments.

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