

[0015] FIGS. 4A and 4B provide graphs of J-coupling data for methanol.

[0016] FIGS. 5A and 5B provide graphs of experimental and simulated zero-field NMR spectra for ethanol 2 ($^{13}\text{CH}_3\text{-}^{12}\text{CH}_2\text{-OH}$) and ethanol 1 ($^{12}\text{CH}_3\text{-}^{13}\text{CH}_2\text{-OH}$), respectively.

[0017] FIG. 6 is a plot of noise as a function of frequency, the smaller plot insert in the main panel shows the optical response vs. frequency for an alternative arrangement where a second, pump laser has been employed along with a first, probe laser.

[0018] FIG. 7 shows a scheme for detecting parahydrogen induced polarization at zero magnetic-field in accordance with an exemplary embodiment of the present invention.

[0019] FIG. 8 shows a single-shot zero-field PHIP J-spectra (imaginary component) of ethylbenzene- $\beta^{13}\text{C}$ (a) and ethylbenzene- $\alpha^{13}\text{C}$ (b), polarized via addition of parahydrogen to labelled styrene, as obtained via the present invention.

[0020] FIG. 9 shows a zero-field J-spectrum (imaginary component) of ethylbenzene, produced via parahydrogenation of styrene with ^{13}C in natural abundance, as obtained via the present invention.

[0021] FIG. 10 shows a zero-field PHIP spectra for several compounds in accordance with an exemplary embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0022] Scalar couplings of the form $J_{I_1 I_2}$ between nuclei impart valuable information about molecular structure to nuclear magnetic-resonance spectra. Examples of the present invention demonstrate direct detection of J-spectra due to both heteronuclear and homonuclear J-coupling in a zero field environment, where the Zeeman interaction is completely absent. It is shown here that characteristic functional groups exhibit distinct spectra with straightforward interpretation for chemical identification. Detection is performed with a microfabricated optical atomic magnetometer, providing high sensitivity to samples of microliter volumes. In examples of the present invention, linewidths of 0.1 Hz were obtained and scalar-coupling parameters with 4-mHz statistical uncertainty were measured. It is anticipated that the technique described here may provide a new modality for high-precision “J spectroscopy” using small samples on microchip devices for multiplexed screening, assaying, and sample identification in chemistry and biomedicine.

[0023] The present invention provides for the direct detection of hetero- and homonuclear scalar coupling in a zero field environment or a low field environment using an optical atomic magnetometer. Examples of the present invention show that characteristic functional groups have distinct spectra, with straightforward interpretation for molecular structure identification, allowing extension to larger molecules and to higher dimensional Fourier NMR spectroscopy. A magnetically shielded, zero field environment provides high absolute field homogeneity and temporal stability, which provides a capability to obtain 0.1-Hz linewidths without using spin echoes, and to determine scalar coupling parameters with a statistical uncertainty of 4 mHz. Such linewidths and measurement uncertainties are far better than were previously available for J-coupling measurements, providing a super-sensitive means for detection of subtle differences in chemical structure.

[0024] As used herein, the term “zero field” refers to a static magnetic field having a zero or near-zero magnitude in which

the magnetic field is small enough that the Larmor precession frequency is small. For a sample with protons, a smallest competing timescale is the relaxation rate, so that the precession frequency should be less than $1/(2\pi T_2)$ or ~ 100 mHz, corresponding to about 2.5 nT. Thus, a zero field includes a static magnetic field of 0.1 nT or an oscillating magnetic field with a near zero average magnitude. As used herein, the term “low field” refers to a static magnetic field having a magnitude less than about 1 mT and more typically less than about 100 μT . Zero field and low field are in contrast to high field (i.e. a static magnetic field having a high magnitude), where a typical high field in the context of NMR has a magnitude on the order of 3 to 10 T.

[0025] An embodiment of a system for detecting J-coupling in accordance with an embodiment of the present invention is illustrated in FIG. 1. The system 100 includes an optical atomic magnetometer, a fluid handling system 101, magnetic shields 114, coils 120, and an oven 122. According to an embodiment, the atomic magnetometer includes a laser 116 (e.g., an external-cavity diode laser that produce light at the D1 resonance), an alkali vapor cell 112 (e.g., an ^{87}Rb alkali-vapor cell), a photo-diode 118, a lock-in amplifier 132, polarizers 128, and a quarter wave plate 130. According to an embodiment, the fluid handling system 101 includes a syringe pump 102, a reservoir 104, a polarization volume 106, a Halbach array 108 (e.g., 1.8-T Halbach array), a solenoid 124, a detection volume 110 (e.g., an 80- μL detection volume), and a pressurized reservoir 126.

[0026] In operation, the syringe pump 102 pushes fluid from the reservoir 104 into the polarization volume 106, which is within the Halbach array 106, and then into the detection volume 110, which is adjacent to the alkali-vapor cell 112. The vapor cell 112 and the detection volume 110 are housed within the oven 122, which is inside the set of magnetic shields 114. Circularly polarized light from the external-cavity diode laser 116 at the D1 resonance is used to optically pump and probe the alkali spin polarization within the vapor cell 112. The circularly polarized light that passes through the vapor cell 112 is detected by the photodiode 118. The set of coils 120 inside the magnetic shields 114 is used to zero the residual magnetic field, apply pulses to the sample in the y-direction, and to oscillate a small magnetic field in the z-direction. The oven 122 heats the vapor cell 112 to $\sim 170^\circ\text{C}$. to maintain sufficient alkali vapor density. The detection volume 110 may be separated from the vapor cell 112 by a gap so that it operates at a lower temperature than the vapor cell 112. Also, the detection volume 110 may be cooled, for example, by attaching it to a heat sink that is outside of the oven 122. In an alternative embodiment, the oven 122 is replaced by a heat source that is attached to the vapor cell 112. The solenoid 124 provides a quantizing magnetic field (about 50 μT) to help maintain the orientation of the polarization of the analyte as it is transferred from the polarization volume 106 to the detection volume 110. The pressurized reservoir 126 receives the analyte after it has been analyzed in the detection volume 110. Linear polarizers 128 are used to polarize light from the laser 116. A quarter wave plate 130 circularly polarizes the laser light. A lock-in amplifier 132 detects the signal from the photodiode 118. A data acquisition system 134 may record the signal from the photodiode 118. A spectrum analyzer 136 may be used to view the data acquired in experiments.

[0027] An embodiment of a method of detecting a J-coupling of the present invention includes providing a polarized analyte adjacent to the vapor cell 112 of the atomic magne-