Two-dimensional nanoscale nuclear magnetic resonance spectroscopy enhanced by artificial intelligence

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Two-dimensional Nuclear Magnetic Resonance (NMR) is essential to molecule structure determination [1]. Nitrogen vacancy (NV) center in diamond has been proposed and developed as an outstanding quantum sensor to realize NMR in nanoscale [2, 3]. However, it is still lack of two-dimensional nanoscale NMR spectroscopy which is crucial in structure analysis. In our work, combined two-dimensional quantum controls with an artificial intelligence algorithm [4], the two-dimensional nanoscale NMR spectroscopy is realized on a pair of coupled 13C nuclear spins by NV sensor. Meanwhile, the data consuming time is speeded up by one order with artificial intelligence and compressed sensing protocol, which make the nanoscale NMR more practical. The two-dimensional nanoscale NMR will be the cornerstone to realize nanoscale or even single molecule structure analysis.

Molecular structure analysis is the cornerstone of biology, chemistry and medicine. Among three vastly used techniques for structure analysis, X-ray [5], electron microscopy [6], and nuclear magnetic resonance (NMR) [7, 8], NMR is the most promising technique to reveal the structure of a single molecule in ambient environments. Towards this goal, nanoscale two-dimensional NMR spectroscopy (2D NMR) is a crucial step. With the virtue of high sensitivity and atomic scale of NV centers [9, 10], nanoscale magnetic resonance spectroscopy has been developed rapidly over the past decades. One-dimensional nanoscale NMR [11–13], single spin sensitivity NMR [14], single molecule magnetic resonance [2, 3], and the detection of macroscopic-scale chemical shift and J-coupling [15, 16] has been realized step by step with NV centers. Although these works on nanoscale NMR make it possible to provide an unprecedented insight into molecule structure formation, nanoscale 2D NMR is highly required to reveal the structure of molecule (Fig. 1(a)). However, there are two challenges for realization of 2D NMR. One is the control techniques on nuclear spins combined with the NV sensor. The other is the large consuming time for statistics especially compared to one dimensional NMR.

To overcome those two challenges, new two-dimensional quantum control pulses and artificial intelligence enhanced compressing sensing have been employed in our experiments. With these two achievements, we demonstrate a 2D NMR spectroscopy technique on a system which consists of two coupled 13C nuclear spins.

A two-dimensional protocol, in analog to COSY in conventional NMR, has been developed to investigate such correlation map of target nuclear spins, as shown in Fig. 1(b). For the NV sensor and nuclear spins system, the Hamiltonian is $H = \omega_L (I_{1z} + I_{2z}) + S \cdot (A_1 \cdot I_1 + A_2 \cdot I_2) + I_1 \cdot J \cdot I_2$. A nuclear spin $I_1$ is initialized by a resonant dynamical decoupling sequence on the coupled NV quantum sensor. During a free evolution time $t_1$, the two nuclear spins $I_1$ and $I_2$ interact and phase $\phi_1 = (\omega_L + A_{1z} S_z + J m_{1z} m_{2z}) t_1$ accumulates in the first nuclear spin, where $A_{1z}$ is the parallel component of the hyperfine interaction of the NV sensor with $I_1$, $J$ is the coupling between nuclear spin $I_1$ and $I_2$. Then a half $\pi$ pulse is applied to $I_2$ to mix the coherence. The first phase is recorded in the altitude angle of the Bloch vector, as illustrated in Fig. 1(b). During the second time interval $t_2$, another phase $\phi_2 = (\omega_L + A_{1z} S_z + J m_{1z} m_{2z}) t_2$ accumulates. In the end, the last dynamical decoupling protocol reads the transverse component of the nuclear spin, which corresponds to the correlation of $\phi_1$ and $\phi_2$. Note that, this sequence on nuclear spin $I_1$ is realized by quantum controls on NV sensor via the hyperfine coupling.

Although 2D NMR reveals much more information of spectrum, the two-dimensional protocols are quite time consuming. Fortunately, artificial intelligence can learn superhuman proficiency to recognize special patterns in the two-dimensional spectrum. Deep learning (DL), using multi-layered artificial neural networks which mimic the network of neurons of human brain, has been demon-
FIG. 1. Schematics of the experimental protocol. (a) The schematic of nanoscale 2D NMR enhanced by artificial intelligence. NV center is a state-of-art quantum NMR spectrometer. A single NV center (red) is fabricated underneath several nanometers from diamond surface while a target molecule is placed on the surface. 2D NMR method can help to reveal the molecule structure in nanoscale. Artificial intelligence is able to recover full spectrum from sparse sampled experiment data. (b) Analog to the conventional COSY sequence, the nuclear spin is firstly initiated in the x-y plane and evolves for $t_1$ time. Then the mixing time follows. In the end, the nuclear spin is detected after $t_2$ time. The evolution trajectory of the nuclear spins in Bloch sphere is shown downside. (c) Deep learning convolutional neural networks. The experiment is performed on the time domain. The results are converted to the missing on the frequency domain. One encoder-decoder convolutional neural network (CNN) is chosen here. In the encoder (left half) part, a sequence of hierarchical filters is utilized to recognize the image features, enabling to encode the global structure of the correlation maps in the neural network. In the decoder (right half) part, contrary operations are performed. The network is trained by simulated data to get optimal performance.

We use a single NV center in a CVD-grown diamond with a natural 1.1% abundance of $^{13}$C nuclear spins (Fig. 2(a)). The NV electron spin is used as a quantum sensor to probe $^{13}$C nuclear spins cluster (Fig. 2(b)) through dynamical decoupling spectroscopy [23, 24]. The electron spin is prepared in a superposition state $|\psi\rangle = (|0\rangle + |\bar{1}\rangle)/\sqrt{2}$ as a magnetic sensitive state. During the controlled evolution (Fig. 2(b)), the coherence of NV electron spin decreases, which causes a dip on resonance by $\tau = 1/2(\omega_L - A_\parallel / 2)$. The dips of the spectrum in Fig. 2(c) reveal nuclear spins with different hyperfine interactions.

The high resolution correlation spectroscopy [25, 26] is applied to the NV and nuclear spins system to resolve the fine structure of spectrum, the red region in Fig. 2(c) with center frequency $\omega_L = 1.71$MHz is mainly investigated here. We apply dynamical decoupling protocol with time interval resonant with $\omega_L$. And the correlation between the first and the second dynamical decoupling protocols is recorded. During the free evolution in between, the nuclear spin evolves under different electron spin states $m_s = 0, -1$. Thus, the spectrum shows different peaks centered at $\omega_0 = \omega_L$ and $\omega_{-1} = \omega_L - A_\parallel$. However, the spectrum in Fig. 2(c) shows 4 peaks. Clearly, this spectrum has a number of different interpretations. The spectrum may correspond to a two coupling nuclear spin cluster or three isolated nuclear spins (see [27] section IIA). The one-dimensional NMR spectrum provides no indication as to which NMR peaks are generated from the same spin system, and which are generated from the different spin systems. It is not possible to attribute the peaks to corresponding spin systems by examining the one-dimensional NMR spectrum alone. A two-dimensional correlation map is then necessary to provide those important information.

Two-dimensional NMR protocol is shown in Fig. 3(a).
focus on a monodim nuclear spin dimer. (a) An [111]-orientated CVD-grown diamond is used in the experiment. The $^{13}$C concentration is natural 1.1%. We study a NV-nuclear spins system while focus on a $^{13}$C nuclear spin dimer. (b) The pulse sequence for dynamical decoupling spectroscopy. (c) Dynamical decoupling spectroscopy show the resonant frequency of the nuclear spins with $\omega_L + A_1/2$. Different peaks will correspond to one or several nuclear spins. The fine spectrum is necessary to be investigated by high resolution correlation spectroscopy. We focus on the region labeled with red. (d) The pulse sequence for correlation spectroscopy. (e) The high resolution correlation spectroscopy show the fine structure of the spectrum. Four peaks are found but hard to directly attribute to nuclear spin system.

t_1 and t_2 in sequence are swept from 4 $\mu$s to 0.9 ms and the correlation map is shown in Fig. 3(b). The 2D fast Fourier transformation (FFT) spectrum shown in Fig. 3(c) finds correlations of peaks of the one-dimensional spectrum, clearly showing which peaks belong to the same spin system. The cross peaks (Fig. 3(c)) between $3^{rd}$ and $4^{th}$ peaks indicate they belong to a coupled spin system. From the spectrum, we obtain the bond length of off-axis $^{13}$C dimer nuclear spins to be 1.52±0.02 Å [27] (section II D). The spectra shown in Fig. 3(b) and (c) are extracted from almost full (80%) data. The two-dimensional experiment was carried out for about a week, which is an obstacle for real-world applications.

Artificial intelligence DLMC algorithm is utilized here to improve the data acquisition efficiency. The intrinsic bias problem of the deep learning algorithm is alleviated while combined with the matrix completion method. As shown in Fig. 3(d), the result obtained by the DLMC algorithm on the 40% sampled data shows less noise and resonant peaks in the upper-right corner compared to the MC method. For the 10% sampled data (Fig. 3(e)), the MC method fails to recover the spectrum while DLMC is still able to recover the spectrum. From the residual analysis in [27], the spectrum processed by DLMC on the 10% sampled data has less residuals compared with the spectrum recoved by the MC method from the 40% sampled data. Thus, the performance of DLMC on the 10% sampled data is better than that of the MC method on the 40% sampled data.

Overall, the first nanoscale 2D NMR spectrum by NV quantum sensor is demonstrated. With deep learning, the full two dimensional spectrum can be recovered from 10% of the data thus, the experimental time is shortened by an order of magnitude, where the compression ratio can be improved with more training. Together with previous work on nanoscale NMR spectroscopy, the speed-up nanoscale 2D NMR can yield valuable structural information as opposed to bulk NMR, where such interactions typically hamper the structure analysis. Such as the sensitivity can be further improved by using weak measurement readout [28, 29], in which weak condition intuitively stands for realistic external molecule detection. In addition, the Qdyne technique [30, 31] largely allows the enhancement of the spectral resolution to approach the chemical-shift resolution (5 p.p.m.) even in a low magnetic field [10]. Equipped with a high sensitive NV sensor, the length of chemical bonds can be resolved under two-dimensional NMR. In the future, it is possible to construct the whole three-dimensional structure of the molecule from enough information of the lengths and angles of chemical bonds obtained by the high-speed 2D NMR.

ACKNOWLEDGMENTS

The authors at University of Science and Technology of China are supported by the National Key R&D Program of China (Grant No. 2018YFA0306600, No. 2016YFA0502400, No. 2018YFF01012501, and No. 2017YFA0305000), the National Natural Science Foundation of China (Grants No. 81788101, No. 91636217, No. 11761131011, No. 31470835, No. 11722544, and No. 11775209), the CAS (Grants No. GJJSTD2017001, No. QYZDY-SSW-SLH004, and No. YIPA2015370), Anhui Initiative in Quantum Information Technologies (Grant No. AHY050000), the CEBioM, the Thousand-Young-Talent Program of China, and the Fundamental Research Funds for the Central Universities, the Innovative Program of Development Foundation of Hefei Center for Physical Science and Technology (Grants No. 2017FXCXY05). Wu’s research work was partially supported by the grant CCF-1733742 from US National Science Foundation.
There are cross peaks between the 3rd spectroscopy then converts to frequency spectroscopy in (c) by two-dimensional FFT transformation. (c) 2D NMR spectrum.

and commented on the manuscript. All authors discussed the results carried out the simulations. X.K., Z.Y., L.Z., X.W. and F.S. implemented the experiments. X.K. and Z.L. carried out the simulations. X.K., Z.Y., L.Z., X.W. and F.S. wrote the manuscript. All authors discussed the results and commented on the manuscript.

We thank Fedor Jelezko and Bensheng Qiu for helpful discussions.

**AUTHOR CONTRIBUTIONS**

J.D. supervised the entire project. J.D., F.S. and X.K. designed the experimental scheme. L.Z. and X.W. programmed and trained the artificial intelligence algorithm. X.K., Z.Y., K.Y., Y.W. and P.W. prepared the setup. X.Q. and X.R. prepared the arbitrary sequence generator. P.Y. prepared the diamond sample. Z.Y., X.K. and F.S. implemented the experiments. X.K. and Z.L. carried out the simulations. X.K., Z.Y., L.Z., X.W. and F.S. wrote the manuscript. All authors discussed the results and commented on the manuscript.

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