Restore high-resolution NMR spectra from inhomogeneous magnetic fields using neural network

Xiongjie Xiao[1], Qianqian Wang[1], Xu Zhang[1,2,3], Bin Jiang[1,2,3*], Maili Liu[1,2,3*]

[1]State Key Laboratory of Magnetic Resonance and Atomic and Molecular Physics, National Center for Magnetic Resonance in Wuhan, Wuhan National Laboratory for Optoelectronics, Wuhan Institute of Physics and Mathematics, Innovation Academy for Precision Measurement of Science and Technology, Chinese Academy of Sciences, Wuhan, 430071, China.
[2]University of Chinese Academy of Sciences, Beijing, 100049, China.
[3]Optics Valley Laboratory, Wuhan 430074, China

To whom correspondence should be addressed. E-mail:jbin@apm.ac.cn (Bin Jiang), ml.liu@apm.ac.cn (Maili Liu)

ABSTRACT

High-resolution nuclear magnetic resonance (NMR) spectroscopy is a powerful analytical tool with wide application. However, the conventional shim technique may not guarantee the homogeneity of the magnetic field when the experimental conditions are unfavorable. In this study, we proposed a data post-processing method called Restore High-resolution Unet (RH-Unet), which uses a convolutional neural network to restore distorted NMR spectra that have been acquired in inhomogeneous magnetic fields. The method generates feature-label pairs from singlet peak regions and ideal Lorentzian line shape and trains a RH-Unet model to map low resolution spectra to high resolution spectra. The method was applied to different samples, and showed superior performance than the REFDCON method incorporated in Bruker Topspin software. The proposed method provides a simple and fast way to obtain high resolution NMR spectra in inhomogeneous fields, which can facilitate the application of NMR spectroscopy in various fields.

Keywords: NMR processing, High-resolution NMR, Inhomogeneous magnetic fields, Deep learning

INTRODUCTION

High-resolution nuclear magnetic resonance (NMR) spectroscopy is a powerful analytical tool for studying molecular structure, conformation, composition and dynamics at the level of atoms. It provides detailed information about chemical shifts, J-coupling and relaxation rate, and has been widely used in chemical analysis, structural biology and life sciences [1-3]. The spectral resolution and signal-to-noise ratio are crucial criteria for the quality of NMR spectra. With the continuous development of NMR equipment hardware (e.g., stronger superconducting magnet [4], cryogenic probe [5]) and experimental techniques (e.g., cross polarization [6], hyperpolarization [7]), sensitivity has been greatly improved in modern NMR spectroscopy. On the other hand, the resolution of NMR spectra is also highly valued. Various techniques have been developed to improve the resolution of spectra, such as various decoupling techniques [8] and TROSY [9]. However, ultimately, the resolution of NMR spectra is determined by the uniformity of the magnetic field. The more uniform the magnetic field, the higher the NMR resolution. The resolution of modern NMR spectrometers is usually up to 0.1 Hz, which requires that the magnetic field uniformity must reach 1 part in 10^9. Therefore, before performing NMR experiments, operators should carefully optimize the magnetic field by adjusting the current of shim circuits.

The development of advanced magnets and the implementation of advanced magnetic shimming and deuterium locking techniques have greatly improved the homogeneity of the magnetic field in NMR experiments. However, in some experimental conditions, the magnetic field may still suffer from spatial inhomogeneity or temporal instability, such as measurements on biological tissues with intrinsic magnetic susceptibility variations. Shimming is sometimes difficult to avoid these magnetic field inhomogeneities in some NMR equipment, even for homogeneous samples [10]. In addition, slight disturbance or unsatisfactory shimming can also reduce the homogeneity of the magnetic field. Magnetic field inhomogeneity is a common issue in NMR experiment. If the magnetic field cannot meet the requirements after automatic shimming before sampling, it must take a lot of time to shimming manually, or accept poor spectral quality, which results in missing information about J-coupling and overlapped peak, and makes it challenging to extract useful information from spectra. Therefore, it is necessary to develop corresponding methods to obtain higher resolution NMR spectra under inhomogeneous magnetic field conditions.

There are several techniques that have been proposed to achieve this goal [11]. Chen et al reviewed three types of experimental techniques that can measure high-resolution NMR spectra free from the influence of inhomogeneous magnetic fields [11]. These are the techniques based on intermolecular multiple-quantum coherences (iMQCs) that originate from long-range dipolar interactions among spins in different molecules [12], the techniques based on nutation echo and/or z-rotation pulse [13], and the techniques based on spatial encoding and phase correction that make direct phase compensation for the dephasing caused by field inhomogeneities [14]. In addition to

the experimental techniques mentioned above, high-resolution spectra can also be obtained from inhomogeneous magnetic fields using data post-processing methods [15, 16]. Compared with experimental techniques, data post-processing methods have better compatibility and can be used in conjunction with various pulse sequences [17]. The representative of this type of method is the reference deconvolution method, which can correct the effects of instrumental distortion including field inhomogeneity [11].

In recent years, deep learning has made significant progress and has been successfully applied in many disciplines such as image processing [18], natural language processing [19], etc. Deep learning has also been successfully applied in the NMR for spectrum denoising [20], spectral reconstruction of undersampled data [21, 22], fast shimming [23], etc. In this work, we proposed a data post-processing method that uses Restore High-resolution Unet (RH-Unet) to correct and restore low-resolution ^{1}H NMR spectra collected in inhomogeneous magnetic fields, which will help expand the application range of NMR spectroscopy.

METHODS

In NMR experiment, the acquired signal comes from the sum of all nuclear spins across the whole sample. In inhomogeneous field, nuclear spins at different position may experience different field strength, and have different resonance frequencies, therefore, inhomogeneous magnetic field will cause peak broadening and distortion in NMR spectra. For the same reason, each spectral peak in the spectrum should share the same peak broadening and shape distortion. Therefore, for a NMR spectrum collected from an inhomogeneous magnetic field, if the ideal line shape of a distorted singlet peak is known in prior, then a certain image transformation which can correct the distorted singlet peak to the ideal line shape, could correct the line shapes of other peaks in the spectrum too. Based on the above principle, a singlet peak with known correct chemical shift and line shape is chosen as the reference peak from a spectrum distorted by inhomogeneous field, and a neural network is designed and trained to correct the reference peak into an ideal peak, then other resonance peaks should also be corrected simultaneously, which is just the idea of the proposed method in this research. The neural network is derived from Unet [24] to restore high resolution spectrum from NMR spectra acquired in inhomogeneous fields, so this method is called Restore High-resolution Unet (RH-Unet).

In machine learning, it is common to split the input data into three datasets: training dataset, validation dataset, and test dataset, where training dataset is used to fit the model parameters, validation dataset is used to evaluate the model performance and tune the model hyperparameters, and test dataset is used to estimate the final performance of the model [25]. However, every NMR spectrum is unique, which means that we can only use this one NMR spectrum for model training, and the trained model can only handle this one spectrum too. For other spectra that need to be corrected, each

spectrum needs to train a separate neural network. In fact, this method can be classified as one-shot learning [26]. Fortunately, we found later that the model training time is very short and within a tolerable range.

The first step of this method is to construct a dataset for model training. A singlet signal in the original spectrum is chosen as the reference peak, whose chemical shift should be known in prior. It is recommended to choose NMR internal standard as the reference peak. Since the reference peak is singlet, its ideal shape should be Lorentzian line shape, and could be simulated. The dataset consists of two NMR spectra, which are the input spectrum and the reference spectrum. The input spectrum is just the preprocessed original spectrum with distorted peaks due to magnetic field inhomogeneity. Preprocessing mainly involves rescaling the amplitudes of datapoints in the spectrum. The reference spectrum is actually a copy of the input spectrum, but all the peaks in the reference spectrum are replaced with ideal Lorentzian line shapes. These peaks are detected by a peak picking program [27, 28], regardless of whether there are false peaks caused by magnetic field inhomogeneity. The most important step in the RH-Unet method is to generate the feature-label pair, which is based on the peak pick conducted by the find_peaks function from the scipy.signal package [27]. After these peaks are detected, Lorentzian line shapes are simulated based on their chemical shifts and intensities, and these simulated peaks replace the original ones. A special case is the reference peak, which is replaced by a Lorentzian line shape regardless of how many local peaks it is split into by the magnetic field inhomogeneity. The role of the reference spectrum is to calculate the loss function for model training together with the output spectrum obtained by the neural network model from the input spectrum. The replacing of peak shape in reference spectrum is to impose necessary constraints on the model training.

To obtain the image transformation that corrects the distorted spectral peaks into ideal spectral peaks, a neural network model called Restore High-resolution Unet (RH-Unet) was designed based on U-Net [24]. U-Net is a popular neural network and has wide application in image segmentation, and image noise suppression [20]. As shown in Figure 1, the architecture of RH-Unet consists of a down-sampling path and an up-sampling path. The down-sampling path mainly consists of convolutional layers and pooling layers, which are used to extract features of NMR spectrum, and the up-sampling path consists of deconvolutional layers and skip connections, which are used to restore the high-resolution NMR spectrum. The architecture is actually an encode-decoder network [29]. The down-sampling path is the encoder, and the up-sampling path is the decoder. The details of the RH-Unet are shown in the SI.

A loss function is a mathematical function that measures how well a model performs on a given dataset. Model training is to adjust model's parameters to minimize the value of loss function. The loss function of model training is the mean square error (MSE) of each data point of output spectrum and reference spectrum. There is a special feature in this method, which is using the normalized MSE of the reference peak in the output and reference spectra as the criterion for stopping model training. The reason for using the normalized MSE is that there may be a large fluctuation in the absolute value

of MSE in the training of different spectra. After the model training stops, the corrected spectrum is obtained by the inverse operation of preprocessing on the output spectrum.

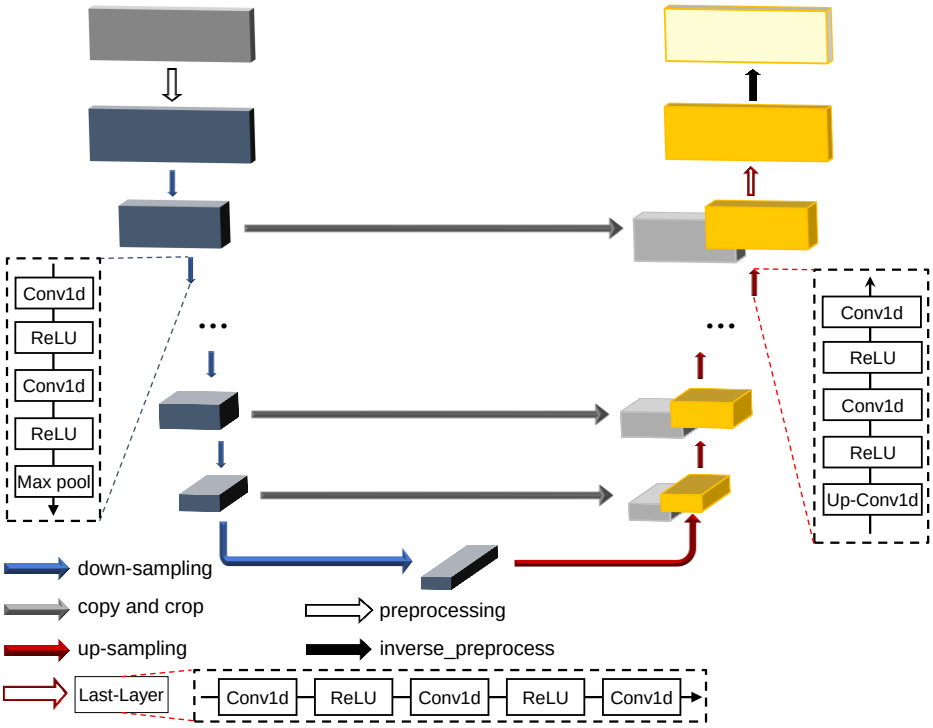

Figure1. The overall architecture of the RH-Unet includes down-sampling, up-sampling and skip connections. The network consists of convolutional neural network (CNN) layer and encoder-decoder (ED) structure. It adopts the splicing method of skip connection to realize feature fusion, and its structure is simple and stable. The model consists of a contraction path that captures context and a symmetric expansion path that contains location information. The encoder and decoder structures of the network consist of a convolutional layer and a deconvolution layer, respectively. The convolutional layer is directly connected to the corresponding deconvolution layer to preserve the spectral details of the output of the deconvolution layer. In the encoder module, the maximum pooling layer operation realizes the down-sampling, while in the decoder module, the deconvolution layer realizes the up-sampling.

RESULTS AND DISCUSSION

The proposed method utilizes a specially designed method to generate feature-label pair for model training, and then employs the RH-Unet model to correct realistic low-resolution ^{1}H NMR spectra that have been acquired in inhomogeneous magnetic fields. To verify the performance of RH-Unet, the method was applied to several samples with different magnetic field homogeneities and the results were compared with the reference deconvolution method. The first sample was a D_2O solution of L-glutathione (GSH) with DSS as an internal standard, and it was a representative of the sample with complex J-coupling peaks. The second sample was a chloroform solution of cholesterol with TMS as an internal standard, and it was a representative of the sample with overlapping peaks. The third sample was a chloroform solution of

azithromycin with TMS as an internal standard, and it was a representative of the sample with two reference peaks. The NMR spectra of these three samples were collected on Bruker 850MHz and 700MHz spectrometers respectively, and each sample not only collected a spectrum in a homogeneous magnetic field, but also collected spectra under slight and moderate magnetic field inhomogeneity conditions respectively. Here, slight field inhomogeneity means that the field inhomogeneity causes some broadening of resonance peaks, but does not cause obvious distortion of peak shape. And moderate field inhomogeneity means that the field inhomogeneity not only causes peak broadening, but also causes obvious distortion of peak shape, such as the DSS peak that should be a single peak splitting into two peaks. The processing of the reference deconvolution method was implemented through the macro called REFDCON provided in Bruker TopSpin3.6.5 software. The processing of RH-Unet was performed using a homemade Python program. See SI for the detailed parameters of acquisition and processing.

The spectra of GSH acquired in homogeneous and slight inhomogeneous fields were shown in Figure 2a and 2b. Most of the peaks in the NMR spectra of GSH shown complex J-coupling. Compared with the spectrum shown in Figure 2a, the peaks shown in Figure 2b were significantly broadened and the resolution was poor. The spectrum shown in Figure 2b was processed using the reference deconvolution method and RH-Unet respectively, and the results were shown in Figure 2c and 2d respectively. The results showed that both methods can correct the influence of field inhomogeneity on NMR spectrum and improve spectral resolution, when field inhomogeneity is slight.

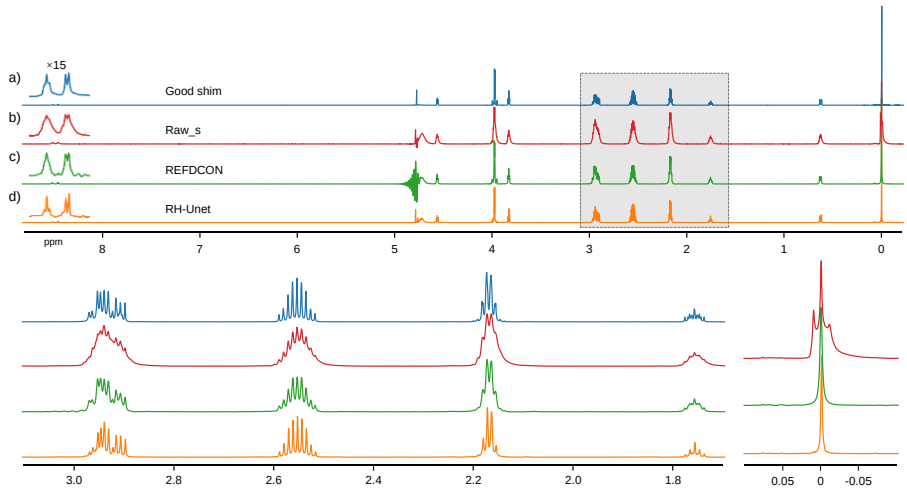

Figure 2. 1D ^{1}H NMR spectrum of 65mM GSH in deuterium oxide (D_2O) with DSS as the internal standard. The spectrum was acquired on a Bruker 850 MHz AVANCE III spectrometer equipped with a cryoprobe. (a) Spectrum collected with 8 scans in the homogeneous magnetic field. (b) Spectrum collected with 8 scans in a slightly inhomogeneous magnetic field. Spectrum obtained after correcting the spectrum in panel b by using the reference deconvolution method (c) and RH-Unet method (d).

When the magnetic field homogeneity further deteriorates, the peak broadening becomes more serious and the peak shape is obviously distorted, such as the spectrum of GSH collected under moderate field inhomogeneity condition shown in Figure 3b.

The results of processing the spectrum using the reference deconvolution method and RH-Unet were shown in Figure 3c and 3d. In Figure 3c, the corrected spectrum from the reference deconvolution method showed a vibrating baseline and lost some peaks nearby. In the spectrum processed by RH-Unet shown in Figure 3d, all the peaks were corrected for peak shape and line width. As shown in the expanded view of the shadowed region (1.7-3.1 ppm), those peaks with fine J coupling splitting, which were broadened and distorted into wide bubbles by the field inhomogeneity, can also be correctly displayed by J coupling splitting after being processed by RH-Unet. In contrast, in the spectrum processed by the reference deconvolution method in Figure 3c, it is difficult to correctly recover these J coupling splitting.

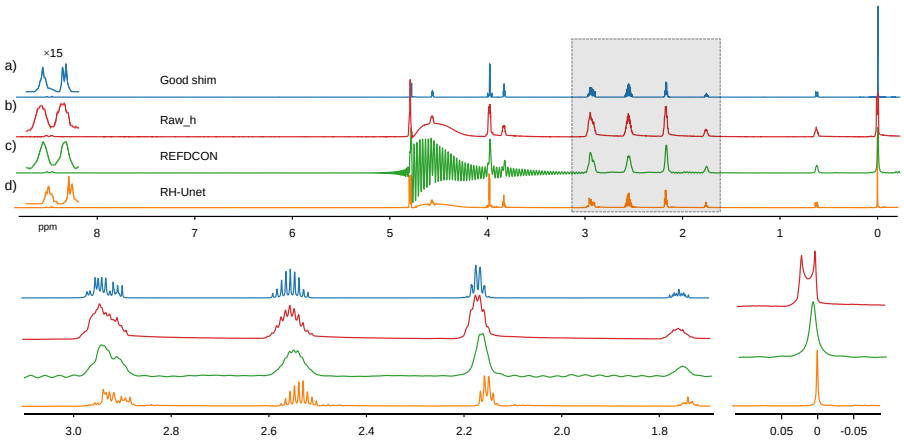

Figure 3. 1D ^{1}H NMR spectrum of 65mM GSH in deuterium oxide (D_2O) with DSS as the internal standard. The spectrum was acquired on a Bruker 850 MHz AVANCE III spectrometer equipped with a cryoprobe. (a) Spectrum collected with 8 scans in the homogeneous magnetic field. (b) Spectrum collected with 8 scans in a severely inhomogeneous magnetic field. Spectrum obtained after correcting the spectrum in panel b by using the reference deconvolution method (c) and RH-Unet method (d).

In Figure 2 and Figure 3, we can observe that the two distorted spectra can be corrected by the RH-Unet model, while the reference deconvolution method limited by the reference peak lineshape, resulting in a corrected spectrum that contains a vibrate baseline.

Peak overlapping usually makes the peaks appear irregular in shape, and look similar to the peak distortion caused by field inhomogeneity from the appearance, so peak overlapping will make it more difficult to obtain high-resolution spectra from inhomogeneous fields through post-processing method. Like the example demonstrated above, the spectra of cholesterol were collected in different fields, and processed using the reference deconvolution method and RH-Unet. The ^{1}H spectra of cholesterol acquired in homogeneous and slight inhomogeneous field were shown in Figure 4a and 4b. The spectrum in Figure 4b was processed by the reference deconvolution method and RH-Unet respectively, and the results were shown in Figure 4c and 4d. As can be seen from Figure 4, both methods had good performance, but in terms of details, RH-Unet has a better recovery effect on the spectral peaks near 1.8 ppm. From the two expanded view of the regions marked in shadow rectangles (0.60-1.05 ppm and 1.02-

2.35 ppm), the complex overlapped regions in the low-resolution spectrum of Figure 4b was restored by RH-Unet method (Figure 4d), which allows for the extraction of useful splitting information and the correction of spectrum keep the prominence peaks.

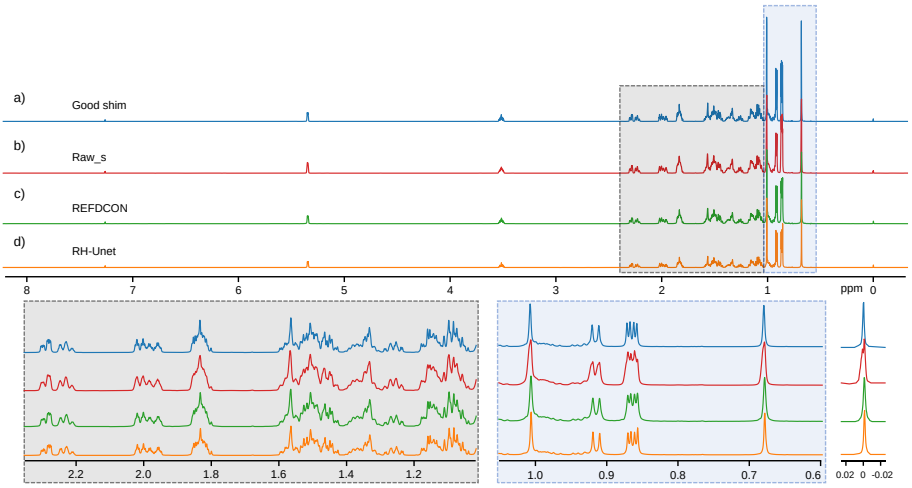

Figure 4. 1D ^{1}H NMR spectrum of 167mM cholesterol in deuterochloroform ($CDCl_3$) with TMS as the internal standard. The spectrum was acquired on a Bruker 700 MHz AVANCE III spectrometer equipped with a cryoprobe. (a) Spectrum collected with 32 scans in the homogeneous magnetic field. (b) Spectrum collected with 32 scans in a slightly inhomogeneous magnetic field. Spectrum obtained after correcting the spectrum in panel b by using the reference deconvolution method (c) and RH-Unet method (d).

After deliberately increasing the inhomogeneity of the magnetic field, the spectrum was sampled again and shown in Figure 5b. Compared with Figure 4b, the resolution of this spectrum was obviously further reduced. The reference deconvolution method and RH-Unet were applied again to process this spectrum, and the results showed the latter has a much better recovery performance than the former, as shown in Figure 5c and 5d.

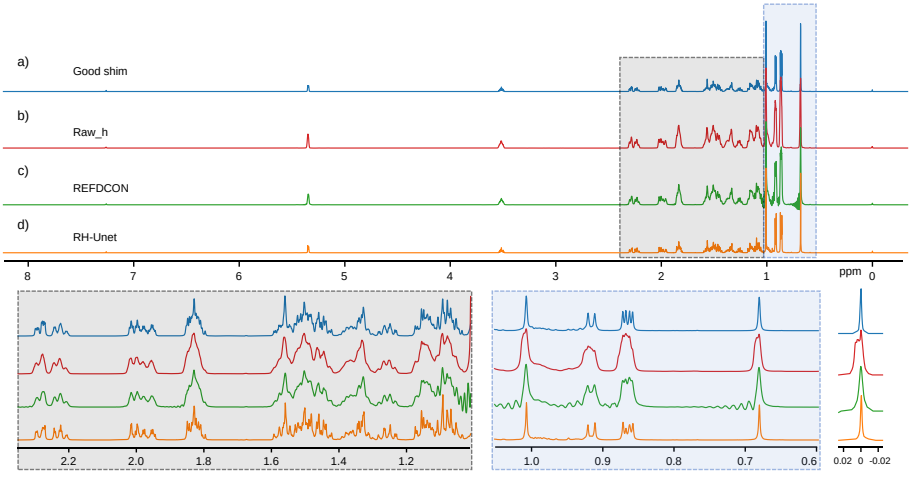

Figure 5. 1D ^{1}H NMR spectrum of 167mM cholesterol in deuterochloroform ($CDCl_3$) with TMS as the internal standard. The spectrum was acquired on a Bruker 700 MHz AVANCE III spectrometer equipped with a cryoprobe. (a) Spectrum collected with 32 scans in the homogeneous magnetic field. (b) Spectrum collected with 32 scans in a severely inhomogeneous magnetic field. Spectrum obtained after correcting the spectrum in panel b by using the reference deconvolution method (c) and RH-Unet method (d).

In Figure 5 all of the distorted peaks in the isolate region have been corrected (0.60-1.05 ppm), including those with complex J-coupling. However, some of the distorted peaks in the overlap regions showed a slightly different high-resolution spectrum due to the inhomogeneous field (1.02-2.35 ppm), making it difficult to recognize complex crowed peaks. If the severely distorted peaks superposition the overlapped regions, the find_peaks function [27] may miss some peaks. Therefore, the corrected spectrum may have a slightly different result from the high-resolution spectrum in the overlap regions, while other regions can restore well.

The same conclusion can be drawn from azithromycin sample, and verified the corrected spectrum will not be influenced by the reference peak (e.g., $CDCl_3$ or TMS). In Figure 6, the azithromycin sample shows J-coupling information, and with a broad range of signal intensities. The 1D ^{1}H NMR spectrum of azithromycin acquired in an inhomogeneous field (Figure 6b) corrected by the RH-Unet method, and the reference peak was the residual solvent of $CDCl_3$ (Figure 6d) and TMS (Figure 6e), respectively. The corrected spectral from RH-Unet (Figure 6d and 6e) were similar to that acquired in the homogeneous magnetic field (Figure 6a), shows that the multiple splitting peaks hidden in the broad envelope can be recovered and the redundant stray signals can be effectively suppressed.

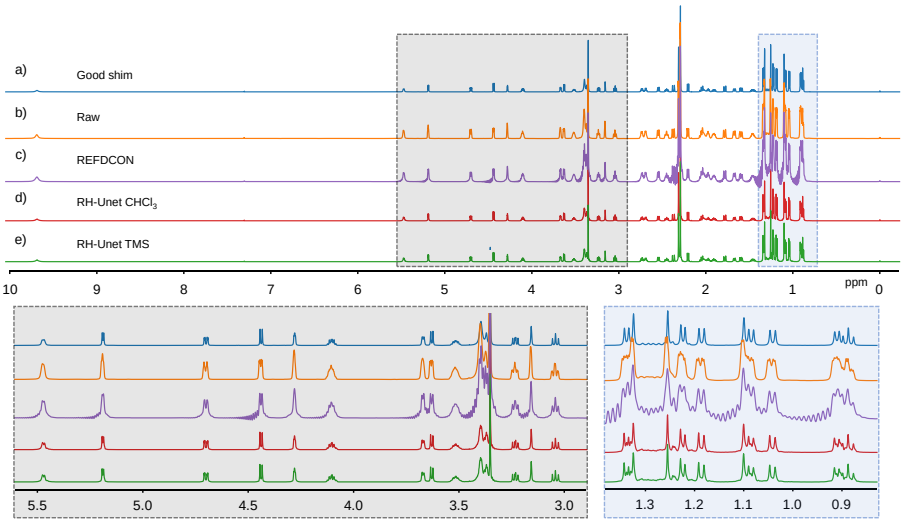

Figure 6. 1D ^{1}H NMR spectrum of 55mM azithromycin in deuterochloroform (CDCl3) with TMS as the internal standard. The spectrum was acquired on a Bruker 700 MHz AVANCE III spectrometer equipped with a cryoprobe. (a) Spectrum collected with 32 scans in the homogeneous magnetic field. (b) Spectrum collected with 32 scans in an inhomogeneous magnetic field. (c) Spectrum obtained after correcting the spectrum in panel b by using the reference deconvolution method. Corrected by the RH-Unet method, and the reference peak was the residual solvent impurities of CDCl3 (d) and TMS (e), respectively.

These results in above figures demonstrated that the proposed RH-Unet method effectively restores and corrects distortion spectrum caused by different inhomogeneous magnetic fields. These corrected spectra are highly accurate and compare well with carefully shimmed field NMR spectra.

To stop the training and obtain an acceptable corrected spectrum, a discussion was

held regarding the choice of a threshold value for evaluation metrics in *SI*. The value of the threshold was set to 0.05. And the comparison of the RH-Unet with different layers are shown in the SI, with a threshold value to 0.05.

CONCLUSIONS

In this study, we proposed a data post-processing method called RH-Unet, which combines an encoder-decoder architecture with a convolutional neural network (CNN) to restore and correct distorted NMR spectra that have been acquired in different inhomogeneous magnetic fields. The real singlet peak region of the reference and standard Lorentz lineshape were used as basic peak pattern to construct feature-label pair. The training results showed that the RH-Unet model was suitable for diverse solvent systems and was not affected by the reference. The RH-Unet method is universal to all experimental samples and NMR platform data, and can be processed quickly on a personal computer. It provides a relatively economical and rapid method for obtaining high-resolution NMR spectra in inhomogeneous magnetic fields. The RH-Unet method showed excellent ability in corrected the distortion spectrum caused by inhomogeneous magnetic fields, with a performance that surpasses that of the reference deconvolution (REFDCON) method incorporated in Bruker Topspin software. The excellent performance of the RH-Unet method in obtaining high-resolution NMR spectra in inhomogeneous magnetic fields will greatly promote the application of high-resolution NMR.

ACKNOWLEDGMENTS

This work was supported by the National Key Research and Development Program of China (2018YFA0704002, 18YFE0202300), and National Natural Science Foundation of China (21991081, 21921004, 21974149).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Du, F.F., et al., *Structure elucidation of nanoparticle-bound organic molecules by H-1 NMR.* Trac-Trends in Analytical Chemistry, 2009. **28**(1): p. 88-95.
2. Iarocz, L.E.B. and M.S. Silva, *Nuclear magnetic resonance chiral discrimination of fipronil and malathion agrochemicals: A case study.* Chirality, 2021. **33**(9): p. 528-534.

3. Ziarek, J.J., D. Baptista, and G. Wagner, *Recent developments in solution nuclear magnetic resonance (NMR)-based molecular biology.* Journal of Molecular Medicine, 2018. **96**(1): p. 1-8.
4. Schwalbe, H., *Editorial: New 1.2 GHz NMR Spectrometers— New Horizons?* Angewandte Chemie International Edition, 2017. **56**(35): p. 10252-10253.
5. Kovacs, H., D. Moskau, and M. Spraul, *Cryogenically Cooled Probes — A Leap in NMR Technology.* Progress in Nuclear Magnetic Resonance Spectroscopy, 2005. **46**: p. 131-155.
6. Novakovic, M., et al., *Heteronuclear transfers from labile protons in biomolecular NMR: Cross polarization, revisited.* Journal of Magnetic Resonance, 2021. **333**: p. 12.
7. Salnikov, O.G., et al., *N-15 NMR Hyperpolarization of Radiosensitizing Antibiotic Nimorazole by Reversible Parahydrogen Exchange in Microtesla Magnetic Fields.* Angewandte Chemie-International Edition, 2021. **60**(5): p. 2406-2413.
8. Vuister, G.W. and A. Bax, *Resolution enhancement and spectral editing of uniformly 13C-enriched proteins by homonuclear broadband 13C decoupling.* Journal of Magnetic Resonance (1969), 1992. **98**(2): p. 428-435.
9. Pervushin, K., et al., *Attenuated T-2 relaxation by mutual cancellation of dipole-dipole coupling and chemical shift anisotropy indicates an avenue to NMR structures of very large biological macromolecules in solution.* Proceedings of the National Academy of Sciences of the United States of America, 1997. **94**(23): p. 12366-12371.
10. Michal, C.A., *Magnetic field homogeneity: A new approach to orthogonalizing and optimizing shim gradients.* Journal of Magnetic Resonance, 2007. **185**(1): p. 110-117.
11. Chen, Z., et al., *High-resolution NMR spectroscopy in inhomogeneous fields.* Progress in Nuclear Magnetic Resonance Spectroscopy, 2015. **90-91**: p. 1-31.
12. Pelupessy, P., E. Rennella, and G. Bodenhausen, *High-Resolution NMR in Magnetic Fields with Unknown Spatiotemporal Variations.* Science, 2009. **324**(5935): p. 1693-1697.
13. Perlo, J., et al., *High-Resolution NMR Spectroscopy with a Portable Single-Sided Sensor.* Science, 2005. **308**(5726): p. 1279-1279.
14. Shapira, B. and L. Frydman, *Spatial encoding and the acquisition of high-resolution NMR spectra in inhomogeneous magnetic fields.* Journal of the American Chemical Society, 2004. **126**(23): p. 7184-7185.
15. Morris, G.A., *Compensation of instrumental imperfections by deconvolution using an internal reference signal.* Journal of Magnetic Resonance (1969), 1988. **80**(3): p. 547-552.
16. Metz, K.R., M.M. Lam, and A.G. Webb, *Reference deconvolution: A simple and effective method for resolution enhancement in nuclear magnetic resonance spectroscopy.* Concepts in Magnetic Resonance, 2000. **12**(1): p. 21-42.
17. Morris, G.A., H. Barjat, and T.J. Home, *Reference deconvolution methods.* Progress in Nuclear Magnetic Resonance Spectroscopy, 1997. **31**(2): p. 197-257.
18. Kirillov, A., et al. *Segment Anything.* 2023. arXiv:2304.02643 DOI: 10.48550/arXiv.2304.02643.
19. Ouyang, L., et al., *Training language models to follow instructions with human feedback.* ArXiv, 2022. **abs/2203.02155**.
20. Wu, K., et al., *Improvement in Signal-to-Noise Ratio of Liquid-State NMR Spectroscopy via a Deep Neural Network DN-Unet.* Analytical Chemistry, 2021. **93**(3): p. 1377-1382.

21. Qu, X., et al., *Accelerated Nuclear Magnetic Resonance Spectroscopy with Deep Learning.* Angewandte Chemie International Edition, 2020. **59**(26): p. 10297-10300.
22. Luo, J., et al., *Fast reconstruction of non-uniform sampling multidimensional NMR spectroscopy via a deep neural network.* Journal of Magnetic Resonance, 2020. **317**: p. 106772.
23. Becker, M., et al., *Acquisitions with random shim values enhance AI-driven NMR shimming.* Journal of Magnetic Resonance, 2022. **345**: p. 107323.
24. Ronneberger, O., P. Fischer, and T. Brox *U-Net: Convolutional Networks for Biomedical Image Segmentation*. 2015. arXiv:1505.04597 DOI: 10.48550/arXiv.1505.04597.
25. Willemink, M.J., et al., *Preparing Medical Imaging Data for Machine Learning*. Radiology, 2020. **295**(1): p. 4-15.
26. Dong, N.Q. and E.P. Xing. *Domain Adaption in One-Shot Learning*. in *European Conference on Machine Learning and Principles and Practice of Knowledge Discovery in Databases (ECML PKDD)*. 2018. Dublin, IRELAND: Springer International Publishing Ag.
27. Virtanen, P., et al., *SciPy 1.0: fundamental algorithms for scientific computing in Python.* Nature Methods, 2020. **17**(3): p. 261-272.
28. Du, P., W.A. Kibbe, and S.M. Lin, *Improved peak detection in mass spectrum by incorporating continuous wavelet transform-based pattern matching.* Bioinformatics, 2006. **22**(17): p. 2059–2065.
29. Couturier, R., G. Perrot, and M. Salomon. *Image Denoising Using a Deep Encoder-Decoder Network with Skip Connections*. in *25th International Conference on Neural Information Processing (ICONIP)*. 2018. Siem Reap, CAMBODIA: Springer International Publishing Ag.