S1  The Spectrometer Chip

The spectrometer chip consists of an RF receiver, an RF transmitter, and an arbitrary pulse sequencer, as discussed in the main text (Fig. 2). Here we describe them in details.

S1.1  RF Receiver

Figure S1A shows the RF receiver architecture. The low-noise amplifier (LNA) at the front end consists of three voltage gain stages, with an attenuator inserted between the 2nd and 3rd gain stages. The LNA interfaced with the coil is the most critical building block of the receiver, because the signal is weakest at the front end and thus the LNA determines the noise performance of the entire receiver. Along the same logic, the 1st gain stage at the most front end is the most critical component of the LNA. Hence we will focus on the 1st gain stage in this section. Towards the end of this section, we will also briefly discuss the attenuator, for its role is crucial in preventing the saturation of the receiver.

The 1st gain stage is a differential amplifier [Figure S1B]. Its voltage gain is $g_{m1} R_1$, where $g_{m1}$ is the transconductance of the identical input transistors M1 and M2, and $R_1$ is the identical resistance value of the two load resistors. Minimizing the noise of this 1st gain stage is the most critical design task. We take a few measures. First, to reject extrinsic common-mode noise such as power supply fluctuations and electromagnetic interferences, we use the differential (balanced) topology. Second, to avoid the intrinsic $1/f$ noise, we use pMOS input transistors M1 and M2, whose $1/f$ noise corner is less than 1 MHz, well below the Larmor frequency of $^1$H protons in
the spectroscopy experiments \( f_0 \approx 21.8 \) MHz and in the relaxometry experiments \( f_0 = 12.7 \) MHz. Third, to minimize the intrinsic thermal noise, we use the passive loads \( (R_1) \). Moreover, we minimize the intrinsic thermal noise by optimizing the circuit parameters. The input-referred voltage thermal noise power spectral density (PSD) of the 1st gain stage is

\[
N_{1st-stage}^2 = \frac{8k_BT}{g_{m1}} \left( \frac{1}{g_{m1}R_1} + \frac{2}{3} \right)
\]

\((k_B: \) Boltzmann constant; \( T: \) temperature). We minimize this noise by maximizing \( g_{m1} \) via increasing the channel width of transistors \( M_1 \) and \( M_2 \) and increasing their bias current \( I_1 \). With this minimization of the 1st gain stage noise (along with the less critical noise minimization of subsequent gain stages), the input-referred noise PSD of the entire receiver is reduced to a measured value of \( N_r^2 = 0.82^2 \text{(nV)}^2/\text{Hz} \) at \( f_0 = 21.8 \) MHz (main text, Fig. 2B). In the main text, we described how we maximally exploited this small receiver noise with the coil resonance scheme in order to achieve the very low receiver noise figure of 0.23 dB.
The spin precession signal strength in the coil varies widely with the sample volume or concentration, gyromagnetic ratio, and magnetic field. In our work, for example, the relaxometry experiments deal with a sample 50 times larger than the spectroscopy experiments. A large signal can saturate the receiver, unless the LNA gain is lowered. Therefore, the LNA gain is made adjustable so that the spectrometer chip can be used in a broader variety of experiments, using a tunable voltage attenuator (Fig. S1C). It is a 12-level $R$-$2R$ resistor ladder. After each individual $R$-$2R$ network, the voltage is attenuated by 6 dB, achieving a range of attenuations from 0 dB to 66 dB. An analog multiplexer selects one of the 12 available attenuation levels. Because the attenuator consists of resistors, it generates thermal noise. However, since the signal entering the attenuator has been enhanced substantially by the first two gain stages, the attenuator noise does not significantly affect the overall receiver noise.

S1.2 RF Transmitter

S1.2.1 Multi-phase Generator

The RF transmitter consists of the multi-phase generator driving the power amplifier (PA) (Fig. 2, main text). Figure S2 shows the multi-phase generator architecture, which is based on a delay-locked loop (DLL) (dashed box). The incoming RF signal (frequency: $f_0$) travels down the tunable delay line. The phase frequency detector compares the phases of the delayed RF signal at the end of the line and the original RF signal. Based on this comparison, the charge pump generates a control voltage that tunes the line delay so that the delay through the entire line is kept at one RF period, i.e., at a phase of $2\pi$. The RF signal, $IN_+$, is tapped off of one of the 32 equally-spaced nodes on the line, to select a phase among 32 possibilities, $(2\pi/32) \times k$ where $k = 1, 2, 3, \ldots, 32$ (this node selection is controlled by the arbitrary pulse sequencer). The opposite phase is then set as a phase of a differential RF signal, $IN_-$. These two RF signals drive the PA differentially.

It is desired that the multi-phase generator produces the RF signals with a 50% duty cycle for efficient driving of the PA. But the duty cycle can deviate from 50%, as the active devices constituting the delay line exhibit different rise and fall times. To ensure a 50% duty cycle, we implement an auxiliary feedback circuit (Fig. S2, top). It compares the RF signals from the 32nd
Figure S2: Multi-phase generator.

tap and the 16th tap of the line. If the duty cycle is 50%, the two signals are exactly inverted (when one is high, the other is low), and the the phase detector followed by the charge pump in the auxiliary circuit produces no control voltage. However, if the duty cycle is larger [lower] than 50%, the high [low] states of the two signals overlap, which is converted into a control voltage to alter the rise and fall characteristics of the delay line, so as to attain 50% duty cycle.

S1.2.2 Power Amplifier

The NMR coil is driven by the power amplifier (PA), as shown in Fig. S3. In the figure, \( L_c \) and \( R_c \) are the inductance and resistance of the NMR coil, and \( C_c \) is the off-chip tuning capacitance that resonates with \( L_c \) at \( f_0 \), as discussed in the main text. The off-chip inductors, \( L_0 \)'s (\( \sim 22 \) µH), the off-chip \( dc \) blocking capacitors, \( C_0 \)'s (\( \sim 1 \) µF), and the off-chip back-to-back \( pn \)-junction diodes of Fig. S3 were not shown in Fig. 2 of the main text, because these particular components lose much of their meaning in a discussion—as in the main text—that does not involve the details of the PA
The differential RF signals, $\text{IN}_+ \text{ and } \text{IN}_-$, arrive from the multi-phase generator with a particular RF phase selected among the 32 available values. In a transmission mode, the arbitrary pulse sequencer passes the $\text{IN}_+$ and $\text{IN}_-$ signals onto the gates of the PA’s input transistors $M_1$ and $M_2$. Here, $M_1$ and $M_2$ act as switches controlled by their respective RF input signals, $\text{IN}_+$ and $\text{IN}_-$. On the other hand, the two inductors, $L_0$’s, are RF chokes that pass dc currents from the power supply but block RF currents. Thus, when $M_1$ is on with $\text{IN}_+$ high, the current in the inductor $L_0$ on the left of Fig. S3 flows through $M_1$ to ground (transistor $M_3$ acts as an additional conducting path whose resistance can be modulated, as will be discussed shortly); when $M_1$ is off, the current in the inductor $L_0$ on the left is now steered into the NMR coil (as will be explained towards the end of the present section—Sec. S1.2.2—, the back-to-back diodes in the signal path towards the NMR coil provide a simple conducting path in the transmission mode). The $M_2$–$L_0$ pair on the right works in exactly the same way, but with the opposite phase. In this way, the PA injects an RF current into the NMR coil. Transistor $M_3$ [$M_4$] intervening transistor $M_1$ [$M_2$] and

---

1As mentioned in the caption of Fig. S1, the other off-chip dc blocking capacitors, $C_b$’s, for the LNA input were also not shown in Fig. 2 of the main text, as they are simply short-circuited at frequency $f_0$. 

---

**Figure S3**: Power amplifier configuration in our spectroscopy and relaxometry experiments.
the left [right] RF choke \( L_0 \) acts as a resistance, whose value is tuned by the gate voltage set by the arbitrary pulse sequencer; this resistance control can set the amplitude of the RF current injected into the coil [S1].

The NMR coil configuration of Fig. S3 is used for all our NMR measurements. The NMR coil used in the spectroscopy experiments (0.8 \( \mu \)L samples; \( f_0 = 21.8 \) MHz) has \( L_c = 173 \) nH, \( R_c = 0.75 \) \( \Omega \), and \( Q \sim 31.5 \). At the frequency \( f_0 \), the PA sees an effective impedance of \( Q^2 R_c \sim 744 \) \( \Omega \). Into this coil, the PA delivers a measured RF power of 23.7 mW and an RF current with an amplitude of 251 mA; the corresponding \( \pi/2 \)-pulse duration for \(^1\)H protons is 6.3 \( \mu s \). The NMR coil used in the relaxometry experiment (41 \( \mu \)L sample; \( f_0 = 12.7 \) MHz) exhibits \( L_c = 309 \) nH, \( R_c = 0.5 \) \( \Omega \), and \( Q \sim 49.3 \) (a thicker wire is used). In this case, at the frequency \( f_0 \), the PA sees an effective impedance of \( Q^2 R_c \sim 1210 \) \( \Omega \). Into this large coil and with an increased driving, the PA delivers an estimated RF power of 37.6 mW and an RF current with an amplitude of 388 mA; the corresponding \( \pi/2 \)-pulse duration for \(^1\)H protons is 15 \( \mu s \). While more power and more RF current are transmitted into the larger relaxometry coil, the \( \pi/2 \)-pulse duration is larger, because the coil geometry produces a weaker RF magnetic field.

**Figure S4:** Power amplifier configuration for high power delivery.
The RF power in the coil with Fig. S3 is sufficient for our spectroscopy and relaxometry experiments with their respective $\pi/2$-pulse durations being 6.3 $\mu$s and 15 $\mu$s. But we can transmit a larger power by configuring the NMR coil as in Fig. S4. Here $C_t$ in parallel with the NMR coil and two capacitors $2C_m$’s flanking the NMR coil are so chosen that $C_t + C_m$ resonates with $L_c$ at frequency $f_0$; in other words, $C_t + C_m$ is equal to $C_c$ of the previous configuration. Then the PA sees an effective real-valued load impedance $Z_L$ at frequency $f_0$. By increasing $C_m$ and decreasing $C_t$ while keeping $C_t + C_m = C_c$, we lower $Z_L$ so that the PA can deliver more power into the NMR coil. To demonstrate, with the aforementioned coil used in our relaxometry experiment ($L_c = 309$ nH, $R_c = 0.5$ $\Omega$, $Q \sim 49.3$ with $f_0 = 12.7$ MHz), we set $C_t = 440$ pF and $C_m = 72$ pF, yielding $Z_L = 25$ $\Omega$. Due to this lower effective real impedance, a larger measured RF power of 182 mW is now delivered into the coil by the PA.\(^2\)

Finally, let us discuss the role of the back-to-back diodes in Fig. S3.\(^3\) During the transmission mode, due to the large time-varying voltage difference between the OUT$_+$ and OUT$_-$ nodes, one of the two diodes in each back-to-back diode pair is forward biased, providing a conducting path to the NMR coil. On the other hand, during the reception mode, both of the OUT$_+$ and OUT$_-$ nodes are biased at the power supply level, and thus both back-to-back diode pairs are open-circuited (the spin precession signal is too weak to upset this situation). Therefore, the LNA does not feel the effect of the RF chokes, $L_0$’s (and $C_0$’s), including the noise generated by the parasitic resistances of the RF chokes. In this way, during the reception mode, the LNA sees only the NMR coil and the parallel tuning capacitor $C_c$, as discussed in the main text. Note that the main noise mechanism of a pn-junction diode is a shot noise, whose power spectral density is proportional to the diode current; therefore, the back-to-back diode pairs that are open-circuited during the reception mode do not generate noise, which is consistent with the noise discussion of the main text.

\(^2\)Note that in this configuration of Fig. S4, with an additional capacitor $C_m$ at the input of the LNA, in the reception mode, the NMR coil would be still in parallel with $C_t + C_m = C_c$ so that the passive amplification discussed in the main text would be still in effect.

\(^3\)Essentially the same explanation applies to Fig. S4 as well.
S1.3 Arbitrary Pulse Sequencer

The arbitrary pulse sequencer consists of a 4096-bit memory and a digital signal processor [Fig. S5A]. The memory stores a set of codes that describes a specific pulse sequence. To change the pulse sequence, the memory is refreshed with a new set of codes through a serial peripheral interface (SPI). The memory has 64 addresses, with each address storing a single code to specify a segment of an RF pulse sequence, for instance, a single RF pulse and a delay [Fig. S5B]. A single code contains parameters that define the width, amplitude, and phase of a pulse and a delay in order to control the PA and multi-phase generator. The code also dictates whether the receiver should be turned on and connected to the NMR coil to acquire the NMR signal after a pulse.

A pulse sequence can then be defined by a series of codes. For example, the CPMG pulse sequence can be represented by 4 codes, C0-C3 [Fig. S5C]. C0 defines a π/2-pulse followed by a delay. C1 defines a π-pulse and a delay. C2 specifies no pulse (pulse width is set at zero), and signal acquisition during the delay. C3 again specifies no pulse, only a delay. Finally, C1, C2, and C3 are repeated in sequence—each code also includes two parameters, loop start and loop end, whose values can be properly chosen for each code so that a subset of codes is repeated.

A given set of codes in the memory are executed by the digital signal processor consisting of the pulse counter and programmer [Fig. S5A]. The pulse counter accesses the memory addresses one by one. The code in each memory address accessed by the counter is interpreted by the pulse programmer, and is executed by the coordinator to control the PA, multi-phase generator, and receiver. Figure S5D shows the timing diagrams in the example case of the execution of the 4-code CPMG pulse sequence used for our relaxometry experiment.

In the spectroscopy experiments of the main text, the 1D spectroscopy employs 1-code sequences, J-resolved spectroscopy and COSY both use 2-code sequences, HSQC uses 7-code sequence for the 1H channel and 5-code sequence for the 13C channel, and HMQC uses 3-code sequence for the 1H channel and 4-code sequence for the 13C channel.
Figure S5: (A) Architecture of the arbitrary pulse sequencer. (B) A code and its parameters to represent an RF pulse. (C) A set of codes in the example case of the CPMG pulse sequence. (D) Timing diagram associated with the arbitrary pulse sequencer, with the CPMG pulse sequence as an example.

S1.4 Temperature-Compensated Design

Circuit performance generally varies with temperature. In our spectrometer chip, the transmitter is quite immune to temperature variation, because the multi-phase generator is a negative feedback circuit and the PA uses transistors as switches. The arbitrary pulse sequencer is also quite
insensitivity to temperature, for it is a digital circuit whose temperature-dependent behaviors can be appreciable only in the GHz range. In contrast, the analog receiver is sensitive to temperature, and it can even fail to work at a high temperature (e.g., 150 °C). Therefore here we focus on the receiver.

We first consider the temperature-insensitive design of the LNA, in particular, its front-end 1st stage discussed in Sec. S1.1 and shown on the left of Fig. S6, along with a current bias circuit [S2] on the right of the figure. By applying the basic circuit theory to the bottom two n-MOS transistors M₃ and M₄, the bias current \( I_b \) generated by the bias circuit can be evaluated as

\[
I_b = \left[ 2\mu_n C_{ox} (W/L)_4 R_b^2 \right]^{-1}
\]

where \( \mu_n \) is the electron mobility, \( C_{ox} \) is the per-unit-area gate oxide capacitance, \( (W/L)_4 \) is the channel width-to-length ratio of M₄, and \( R_b \) is the resistor shown in Fig. S6. The bias current \( I_1 \) of the 1st gain stage is proportional to \( I_b \) because of the current mirroring, specifically,

\[
I_1 = (W/L)_t (W/L)_5 \times I_b
\]

where \( (W/L)_t \) is the channel width-to-length ratio of the tail transistor of the 1st gain stage, and \( (W/L)_5 \) is the identical channel width-to-length ratio of the top two transistors M₅ and M₆ of the bias circuit. The transconductance of the two identical input p-MOS transistors M₁ and M₂ is given by

\[
g_{m1} = \left[ 2\mu_p C_{ox} (W/L)_1 I_1 \right]^{1/2}
\]

where \( (W/L)_1 \) is the identical channel width-to-length ratio of M₁ and M₂, and \( \mu_p \) is the hole mobility. Putting all these results together, we obtain
\[ g_{m1}(T) = \frac{1}{R_b(T)} \times \sqrt{\frac{\mu_p(T)}{\mu_n(T)}} \times \sqrt{\frac{(W/L)_1(W/L)_t}{(W/L)_5(W/L)_4}} \propto \frac{1}{R_b(T)}. \] (S2)

This expression makes temperature-dependent parameters explicit. In attaining the last expression, we have dropped the temperature-independent factors, along with the approximation that \( \mu_p \) and \( \mu_n \) have the same temperature dependency. Therefore, the voltage gain \( g_{m1}R_1 \) of the 1st stage is

\[ g_{m1}(T)R_1(T) \propto \frac{R_1(T)}{R_b(T)}. \] (S3)

Since both \( R_b(T) \) and \( R_1(T) \) made of the same materials have the same temperature dependency, the gain is temperature independent. The key here is to arrange \( g_{m1} \) to have exactly the inverse temperature dependency of \( R_1 \). We use the same scheme in the 2nd and 3rd gain stages to make their gains temperature independent as well.

The later stages of the receiver are more immune to temperature variations. As the mixers are configured in the switching topology, their conversion gain is temperature independent to the first order. The low-pass filters are a feedback circuit built around an operational amplifier, and its gain is the ratio of two resistors in the feedback loop, whose temperature dependencies cancel out. In the measurements, the gain of the entire RF receiver varies only by 4 dB across 25 °C to 150 °C.

The temperature-compensated design of the LNA described above also helps make the receiver noise less dependent on temperature. Since the entire receiver noise performance is dominated by the noise of the 1st gain stage, let us take a look at Eq. (1)—rewritten right below—that expresses the input-referred noise PSD of the 1st gain stage:

\[ N_{1\text{st-stage}}^2 = \frac{8k_B T}{g_{m1}} \left( \frac{1}{g_{m1}R_1} + \frac{2}{3} \right). \]

The factor in the parenthesis is temperature independent, because \( g_{m1}R_1 \) has been made so. Also as \( g_{m1} \propto 1/R_b \) has been arranged, with increasing temperature, \( R_b \) made up of poly-silicon goes down, thus \( g_{m1} \) goes up. So in the factor outside the parenthesis, the increase of the numerator
with increasing temperature is somewhat compensated by the increasing denominator. Thus the receiver noise too has been made less dependent on temperature; in simulation, the input referred noise of the receiver increases by only 25%, as temperature changes from 25 °C to 150 °C.

S2 Calibration of Magnetic Field Fluctuation

The field of the NdFeB magnet used for our spectroscopy has a considerable temperature dependency (−1200 ppm/K). Therefore, as the ambient temperature varies, the Larmor frequency drifts. Imagine an analyte with $N$ NMR-active nuclear spins, where individual spins are indexed by $k$ (1, 2, · · ·, $N$). The magnet’s field, $B_0 + \Delta B_0(t)$, consists of intended field $B_0$ and temporal fluctuation $\Delta B_0(t)$ ($\ll B_0$). The angular Larmor frequency $\Omega_k(t)$ for the $k$-th spin is then $\Omega_k(t) = \gamma (1 + \delta_k) \cdot (B_0 + \Delta B_0(t)) + \epsilon_k$, where $\gamma$ is the gyromagnetic ratio, $\delta_k$ is the chemical shift, and $\epsilon_k$ is the $J$-coupled frequency offset. This can be approximated to the first order as

$$\Omega_k(t) \approx \gamma B_0 (1 + \delta_k) + \epsilon_k + \gamma \Delta B_0(t),$$

where $\Omega_{0,k}$ is the intended Larmor frequency and $\Delta \Omega(t)$ is the drifting frequency component. $\Delta \Omega(t)$ is identical among all spins to the first order. The NMR signal from a given scan is then given by

$$s(t) = \exp \{i \Delta \Omega(t) t\} \times \sum_{k}^N c_k \exp \{(i \Omega_{0,k} - \lambda_k) t\},$$

where $c_k$ is the complex amplitude representing the signal strength and phase, and $\lambda_k$ is the exponential decay rate corresponding to relaxation. Note the definition of $s_0(t)$ and $w(t)$. In 1D spectroscopy that has only the acquisition phase, only $w(t)$ reflects the effect of $\Delta \Omega(t)$. In 2D spectroscopy, the $\Delta \Omega(t)$ effect is imprinted, during the evolution phase, onto $s_0(t)$ via the complex amplitude $c_k$, while $w(t)$ still reflects the effect of $\Delta \Omega(t)$ during the acquisition phase. We describe how to estimate $\Delta \Omega(t)$ and how to subsequently remove its effect from $s(t)$. 
S2.1 Estimation of $\Delta \Omega(t)$

Consider a general multiple scan experiment. The field drift is typically slow as compared to a single scan period. Therefore, $\Delta \Omega(t)$ of a given scan may be written as $\Delta \Omega(t) = \Delta \Omega_0 + \Delta \Omega_1 t$. The constant term $\Delta \Omega_0$ is the frequency drift accumulated over the prior scans; the time-varying term $\Delta \Omega_1 t$ is the ongoing frequency drift in the given scan. Both $\Delta \Omega_0$ and $\Delta \Omega_1$ vary from scan to scan. Here we describe how to estimate $\Delta \Omega_0$ and $\Delta \Omega_1$ from the measured signal $s(t)$. To this end, let $S(\omega)$ be the Fourier transform of $s(t)$ that can be written out as

$$s(t) = \exp \{i \Delta \Omega_0 t\} \times \exp \{i \Delta \Omega_1 t^2\} \times \sum_k c_k \exp \{(i \Omega_{0,k} - \lambda_k) t\}, \quad (S6)$$

and we define $P_S(\omega) \equiv |S(\omega)|^2 / \int |S(\omega)|^2 df$, which is a probability density function that captures the distribution of Larmor frequencies.

S2.1.1 $\Delta \Omega_1$ Estimation

The estimation of $\Delta \Omega_1$ of a given scan with a signal $s(t)$ is done with that stand-alone data $s(t)$ with no reference to other scans. As can be seen from Eq. (S6), the effect of $\Delta \Omega_1$ is to distort the line shape of $S_0(\omega)$, the Fourier transform of $s_0(t)$ (whereas the effect of $\Delta \Omega_0$ is to translate the peak positions of $S_0(\omega)$ by $\Delta \Omega_0$). Due to the line shape distortion by $\exp\{i \Delta \Omega_1 t^2\}$, the entropy of $P_S(\omega)$ is larger than the entropy of $P_{S_0}(\omega)$. Therefore, if we define $u(t) \equiv \exp\{-i \Delta \Omega_1 t^2\} s(t)$ with $\Delta \Omega_1$ being a variable, the entropy of $P_U(\omega) - U(\omega)$ is the Fourier transform of $u(t)$—will be minimized when the variable $\Delta \Omega_1$ is equal to $\Delta \Omega_1$. Formally speaking, we estimate $\Delta \Omega_1$ by finding $\Delta \Omega_1$ that minimizes the entropy

$$H(\Delta \Omega_1) = - \int P_U(\omega) \ln P_U(\omega) df. \quad (S7)$$

\(^4\)Note that the unit of $\Delta \Omega_1$ is not angular frequency.
**S2.1.2 \( \Delta \Omega_0 \) Estimation**

The effect of \( \Delta \Omega_0 \) is to translate the peak positions of the spectrum. To estimate \( \Delta \Omega_0 \) of each scan, we *randomly* choose one specific scan among the multiple scans, and use it as a reference scan. This reference scan is not from an extra reference material such as TMS, but is the very data attained from the sample under test. Let the signals of the given scan and the reference scan be \( s(t) \) and \( r(t) \); their Fourier transforms are \( S(\omega) \) and \( R(\omega) \). Then, the estimation of \( \Delta \Omega_0 \) of \( s(t) \) is done in a relative sense, in that \( \Delta \Omega_0 \) here is interpreted as the amount of the translation of the peak positions of \( S(\omega) \) from the peak positions of \( R(\omega) \). If we consider a variable \( \hat{\Delta} \Omega_0 \), the peak positions of \( S(\omega + \hat{\Delta} \Omega_0) \) will align with those of \( R(\omega) \), when \( \hat{\Delta} \Omega_0 \) is equal to \( \Delta \Omega_0 \), bringing the statistical distance between \( P_S(\omega + \hat{\Delta} \Omega_0) \) and \( P_R(\omega) \) to the (or a near) minimum\(^5\). Formally speaking, we can estimate \( \Delta \Omega_0 \) by finding \( \hat{\Delta} \Omega_0 \) that minimizes the statistical distance, for which we choose the Hellinger distance [S3]:

\[
D(\hat{\Delta} \Omega_0) = \left[ 1 - \int \left\{ P_S(\omega + \hat{\Delta} \Omega_0)P_R(\omega) \right\}^{1/2} df \right]^{1/2}. \tag{S8}
\]

**S2.2 Calibration**

**S2.2.1 1D NMR**

After we estimate \( \Delta \Omega_0 \) and \( \Delta \Omega_1 \) for a given scan using the technique of Sec. S2.1, we multiply \( \exp\{-i\Delta(\Omega(t)t\} = \exp\{-i(\Delta \Omega_0 t + \Delta \Omega_1 t^2)\} \) to the measured \( s(t) \) of the scan. This calibrates out \( w(t) \) and yields the desired signal \( s_0(t) \):

\[
s_0(t) = \exp\{-i\Delta \Omega(t)t\} \times s(t) = \sum_{k} c_k \exp\{i(\Omega_{0,k} - \lambda_k)t\}. \tag{S9}
\]

\(^5\)In 1D NMR, since the spectral line shape is identical from scan to scan (after first estimating the shape-altering \( \Delta \Omega_1 \) and calibrating it out), the statistical distance is indeed brought to the minimum after the alignment. In 2D NMR, even after removing the effect of \( \Delta \Omega_1 \), the spectral peak heights will not be exactly identical from scan to scan, due to \( c_k \) in Eq. (S6) that is affected by the field fluctuation. In this case, the statistical distance will not necessarily brought to the exact minimum after the alignment. Nonetheless, it will come close to the minimum, and thus the procedure described here estimates \( \Delta \Omega_0 \) quite well, as seen later with the actual data.
S2.2.2 2D NMR

A single scan in 2D NMR consists of an evolution phase of a fixed time duration \( t_1 \), followed by an acquisition phase running in time \( t_2 \). Thus for 2D NMR, Eq. (S5) can be rewritten as

\[
s(t_2) = \exp \{ i \Delta \Omega(t_2) t_2 \} \times \sum_{k} c_k(t_1) \exp \{ i(\Omega_{0,k} - \lambda_k) t_2 \}. \tag{S10}
\]

In the evolution phase of duration \( t_1 \), the fluctuation effect is imprinted onto the complex amplitude of \( c_k(t_1) \), yielding the fluctuation-affected \( s_0(t_2) \). In the acquisition phase, \( w(t_2) \) develops with the field fluctuation. Just like in the 1D NMR calibration case, the 2D NMR calibration also starts by using the technique of Sec. S2.1 to estimate \( \Delta \Omega_0 \) and \( \Delta \Omega_1 \), and subsequently calibrates out \( w(t_2) \), attaining:

\[
s_0(t_2) = \sum_{k} c_k(t_1) \exp \{ i(\Omega_{0,k} - \lambda_k) t_2 \}. \tag{S11}
\]

But this is only the acquisition phase calibration, or \( f_2\)-domain calibration. We now have to perform a \( f_1\)-domain calibration to correct \( c_k(t_1) \) or ultimately \( s_0(t_2) \). \( c_k(t_1) \) including the effect of the frequency drift \( \Delta \Omega_0 \) can be written as\(^6\)

\[
c_k(t_1) = \sum_{j} d_{jk} \cos \{ (\Omega_{0,j} + \Delta \Omega_0) t_1 + \phi_{jk} \} \tag{S12}
\]

where \( j \) and \( k \) are spin indices, \( d_{jk} \) and \( \phi_{jk} \) are respectively complex and real numbers dependent upon the pulse sequence, and the cosine modulation can be set by a particular RF phase of any pulse sequence. While we have already estimated \( \Delta \Omega_0 \) from the \( f_2\)-domain calibration, \( \Delta \Omega_0 \) appears in the argument of cosine, thus is not simply removed. But another scan with the same evolution time of \( t_1 \) but with sine-modulated complex amplitude \( c_k'(t_1) \)—which is necessary for frequency discrimination—resolves this issue. For this scan, again we first perform the \( f_2\)-domain calibration

\(^6\)We ignore the effect of \( \Delta \Omega_1 \) here, because the evolution phase is typically short and line-shape quality is not important issue in 2D NMR [S4].
with an estimated frequency drift $\Delta \Omega'_0$ and obtain

$$s'_0(t_2) = \sum_k c'_k(t_1) \exp \{ (i\Omega_{0,k} - \lambda_k) t_2 \}; \quad (S13)$$

with $c'_k(t_1) = \sum_j d_{jk} \sin \{ (\Omega_{0,j} + \Delta \Omega'_0) t_1 + \phi_{jk} \}$. \quad (S14)

Since the $s_0$-signal free of field fluctuation is expressed as the following, using the complex amplitude free of fluctuation,

$$s_{0,\text{cal}}(t_2) \equiv \sum_k c_{k,\text{cal}}(t_1) \exp \{ (i\Omega_{0,k} - \lambda_k) t_2 \}; \quad (S15)$$

$$c_{k,\text{cal}}(t_1) \equiv \sum_j d_{jk} \exp \{ i(\Omega_{0,j} t_1 + \phi_{jk}) \}, \quad (S16)$$

we can see that

$$\left. \frac{c_k(t_1) \cdot \exp (-i\Delta \Omega'_0 t_1) + c'_k(t_1) \cdot i \exp (-i\Delta \Omega_0 t_1)}{\cos \{ (\Delta \Omega_0 - \Delta \Omega'_0) t_1 \}} \right| = c_{k,\text{cal}}(t_1), \quad \text{or,} \quad (S17)$$

$$\left. \frac{s_0(t_2) \cdot \exp (-i\Delta \Omega'_0 t_1) + s'_0(t_2) \cdot i \exp (-i\Delta \Omega_0 t_1)}{\cos \{ (\Delta \Omega_0 - \Delta \Omega'_0) t_1 \}} \right| = s_{0,\text{cal}}(t_2). \quad (S18)$$

Since we have already estimated $\Delta \Omega_0$ and $\Delta \Omega'_0$ and measured $s_0(t_2)$ and $s'_0(t_2)$, we can evaluate the left hand side of Eq. (S18), thus correcting $s_0(t_2)$ and $s'_0(t_2)$ into $s_{0,\text{cal}}(t_2)$. We call this $f_1$-domain calibration approach Method 1.

An alternative $f_1$-domain calibration approach exploits the following identify:

$$s_0(t_2) \cdot \exp (-i\Delta \Omega_0 t_1) + s'_0(t_2) \cdot i \exp (-i\Delta \Omega'_0 t_1) = s_{0,\text{cal}}(t_2) + [f_1 \text{ noise floor}], \quad (S19)$$

where the noise-floor term is given by

$$\sum_k \sum_j d_{jk} \sin (\Delta \Omega_0 - \Delta \Omega'_0) t_1 \cdot \exp \left[ -i \left\{ \left( \Omega_{0,j} + \Delta \Omega_0 + \Delta \Omega'_0 \right) t_1 - \phi_{jk} + \frac{\pi}{2} \right\} \right] \cdot \exp \{ (i\Omega_{0,k} - \lambda_k) t_2 \}. $$
Since we have already estimated $\Delta \Omega_0$ and $\Delta \Omega'_0$ and measured $s_0(t_2)$ and $s'_0(t_2)$, we can evaluate the left hand side of Eq. (S19), which approximates the fluctuation-free $s_0$-signal, $s_{0,\text{cal}}(t_2)$. This is an approximation due to the noise-floor term on the right hand side of Eq. (S19); we cannot determine this noise floor term due to hitherto unknown $d_{jk}$ and $\phi_{jk}$. In fact, the noise term does not yield deterministic peak patterns, but only raises the background noise in $f_1$ domain. We call this approach **Method 2**.

Each of the two methods has its own limitation. In **Method 1**, the denominator of the left hand side of Eq. (S18) approaches zero as $(\Delta \Omega_0 - \Delta \Omega'_0) t_1$ approaches $\pi/2 \times (\text{odd integer})$. In this case, the background noise is significantly amplified. Therefore, **Method 1** is effective when $(\Delta \Omega_0 - \Delta \Omega'_0) t_1$ is reasonably different from $\pi/2 \times (\text{odd integer})$, or when the signal-to-noise ratio is high enough to tolerate amplified noise. The limitation of **Method 2** is the noise floor term of Eq. (S19). Thus depending on the calibration situation, we select the appropriate method.

### S2.3 Demonstration

We first demonstrate our calibration technique using 1D ethanol NMR spectroscopy [Fig. S7]. Sixteen free induction decay signals are collected from an ethanol sample (a single scan/wait time of 6 seconds). We first perform the $\Delta \Omega_1$ calibration for each of the 16 scans to correct its line shape. Figure S7A shows the pre- and post-calibration data for the 15th scan as an example. The estimated $\Delta \Omega_1$ via the entropy minimization is $2\pi \times 15.6$ Hz [Fig. S7B]. Using this estimated value, we remove the effect of $\Delta \Omega_1$ in the 15th scan, repairing the line shape (Fig. S7A). The estimated $\Delta \Omega_1$ for each of the 16 scans is shown in Fig. S7F.

After the $\Delta \Omega_1$ calibration for each of the 16 scans, we perform the $\Delta \Omega_0$ calibration to align their spectra. Before we perform this $\Delta \Omega_0$ calibration, the spectrum averaged over the 16 scans [Fig. S7C, left] lacks the fine feature, because the 16 scans are not aligned. We estimate $\Delta \Omega_0$ for each scan by finding the minimum Hellinger distance with respect to the 1st scan as a reference scan. For example, for the 15th scan, the distance is minimized with $\Delta \Omega_0 = 2\pi \times 16.7$ Hz [Fig. S7D]. The averaged spectrum, after estimating $\Delta \Omega_0$ for each scan and aligning the 16 spectra, exhibits the fine feature [Fig. S7C, right]. The estimated $\Delta \Omega_0$ for each of the 16 scans is shown in
Figure S7: 1D ethanol spectrum calibration. (A) Spectrum of the 15th scan before and after the $\Delta \Omega_1$ calibration. (B) The entropy of the 15th scan vs. estimation variable $\hat{\Delta \Omega}_1$. (C) Spectrum averaged over the 16 scans before and after the $\Delta \Omega_0$ calibration (the $\Delta \Omega_1$ calibration has been already performed for each spectrum). (D) The Hellinger distance between the 15th and 1st reference scan as a function of estimation variable $\hat{\Delta \Omega}_0$. (E,F) Estimated $\Delta \Omega_0$ and $\Delta \Omega_1$ for each of the 16 scans.

Fig. S7E.

The calibration of 2D ethanol COSY spectrum using our technique was already presented in Fig. 6 of the main text (Method 1 and Method 2 both were used). Figure S8 shows yet another demonstration of our calibration technique, now using 2D toluene ($C_6H_5CH_3$) COSY.
Figure S8: 2D toluene COSY spectrum calibration. (A) Raw spectrum. (B) Spectrum after the $f_2$-domain calibration. (C) Spectrum after both $f_1$ and $f_2$-domain calibration.

Before calibration, the spectrum does not bear any peak feature (Fig. S8A). After the $f_2$-domain calibration, peaks and valleys appear vertically around $f_2$ of 7 ppm and 2 ppm (Fig. S8B). After a subsequent $f_1$-domain calibration using Method 2, the correct spectrum emerges (Fig. S8C), exhibiting two expected diagonal-peaks, corresponding to the $^1$H chemical shifts of the CH$_3$ and C$_6$H$_5$ groups. Cross-peaks do not shown because of the weak coupling between the two groups.

References


