Supporting Information

Rapid Estimation of Repetition Time (T_r) for Quantitative Nuclear Magnetic Resonance

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Supporting Information I: An example Python script

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.optimize import curve_fit
# Given experimental data (Tr in seconds, intensity I)
Tr_values = np.array([0.1, 1, 10])  # Time points
Intensity_values = np.array([10, 80, 99.9])  # Signal intensities
# Define the exponential saturation function
def exponential_saturation(Tr, I0, T1_star):
    return I0 * (1 - np.exp(-Tr / T1_star))
# Fit the curve
params, _ = curve_fit(exponential_saturation, Tr_values, Intensity_values, p0=[100, 1])
# Extract fitted parameters
I0_fitted, T1_star_fitted = params
# Generate fitted curve for visualization
Tr_fit = np.linspace(0, 15, 200)
Intensity_fit = exponential_saturation(Tr_fit, I0_fitted, T1_star_fitted)
# Calculate Tr value for 99.99% of max intensity
target_fraction = 0.9999
Tr_9999 = -T1_star_fitted * np.log(1 - target_fraction)
# Plotting
plt.figure(figsize=(8, 5))
plt.scatter(Tr_values, Intensity_values, color='red', label='Experimental Data')
plt.plot(Tr_fit, Intensity_fit, color='blue', label='Fitted Curve')
plt.axvline(Tr_9999, color='green', linestyle='--', label=f'Tr @ 99.99% = {Tr_9999:.2f} s')
plt.xlabel("Tr (Repetition Delay Time, s)")
plt.ylabel("Signal Intensity")
plt.title("Exponential Saturation Fit and Tr at 99.99% Recovery")
plt.grid(True)
plt.legend()
plt.tight_layout()
plt.show()
# Print the result
print(f'Repetition delay Tr to reach 99.99% of maximum intensity: {Tr_9999:.4f} s")
```

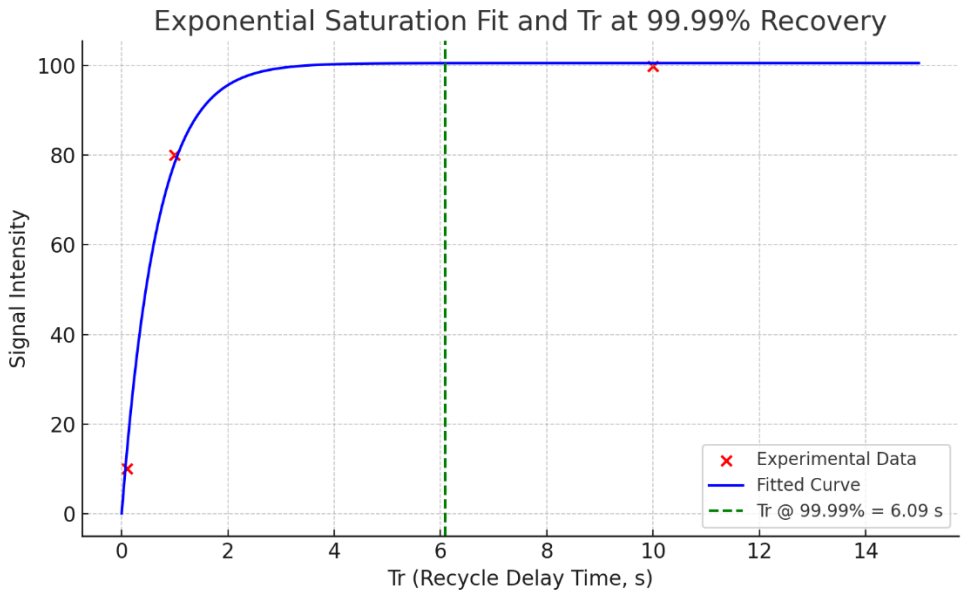

Fig. S1. Plot of the Python Script by ChatGPT 4o. Note: This curve can also be calculated and fitted by ChatGPT 5 (T_r = 6.09 s), Copilot (T_r = 6.09 s), Gemini (T_r = 6.09 s) and Claude (T_r = 6.09 s).

Supporting Information II: Aripiprazole as an example to demonstrate the RSD calculation using selected signal responses

Table S1. RSD(%) calculation based on selected signal responses in the NMR spectrum of aripiprazole solution

	Chemical shifts (ppm)	9.97	7.28; 2.29	7.12	7.03	6.43; 6.48	3.91	1.64
	Number of ^{1}H	1H	2H	1H	1H	2H	2H	4H
Experiment #1	Absolute integral	9158.51	18292.49	9213.59	9127.90	18249.02	18353.44	36654.60
	Integral-per-^{1}H	9158.51	9146.245	9213.59	9127.90	9124.51	9176.72	9163.65
	RSD (%)	0.33						
Experiment #2	Absolute integral	9156.25	18293.17	9206.67	9113.97	18205.25	18366.47	36647.39
	Integral-per-^{1}H	9156.25	9146.59	9206.67	9113.97	9102.625	9183.24	9161.85
	RSD (%)	0.37						
Experiment #3	Absolute integral	9180.74	18289.57	9186.85	9123.76	18222.79	18371.01	36644.61
	Integral-per-^{1}H	9180.74	9144.785	9186.85	9123.76	9111.40	9185.51	9161.15
	RSD (%)	0.34						

Supporting Information III: qNMR spectra of test samples

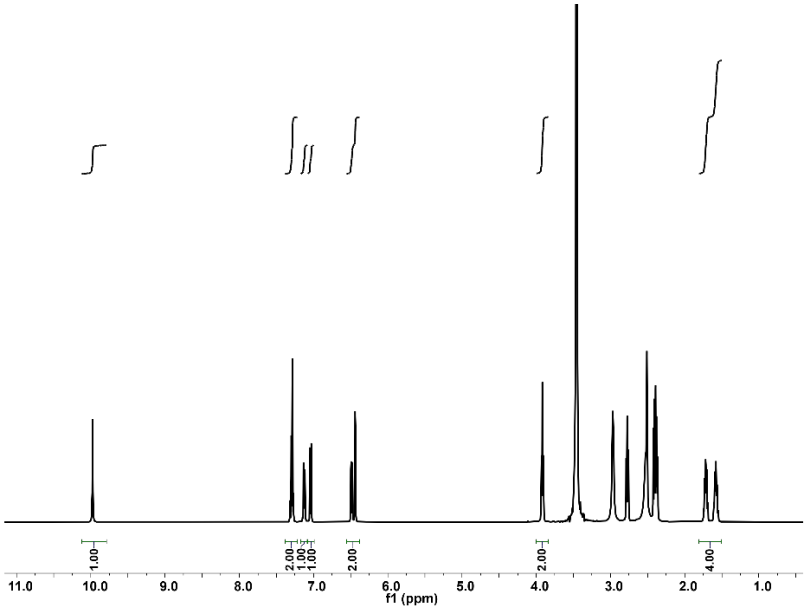

Fig. S2. An example of qNMR analysis using an aripiprazole solution in DMSO-d_6, in which the signal responses between 2.0 and 3.0 ppm were excluded due to solvent-related interference. The longest T_1 value was acquired based on the signal response at 7.30 ppm.

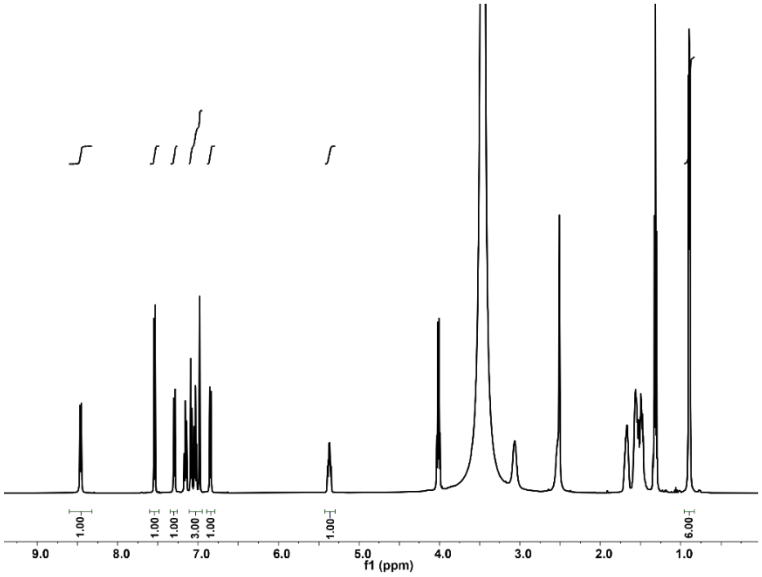

Fig. S3. An example of qNMR analysis using a repaglinide solution in DMSO-d_6, in which the signal responses between 2.0 and 4.5 ppm were excluded due to solvent-related interference, and the signal response at 7.16 ppm was excluded due to potential impurity interference. The longest T_1 value was acquired based on the signal response at 7.55 ppm.

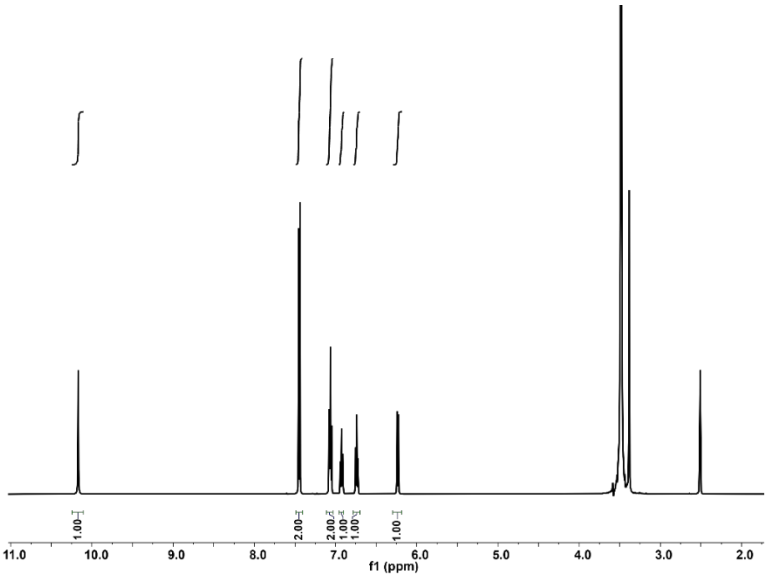

Fig. S4. An example of qNMR analysis using a diclofenac sodium solution in DMSO-d_6. The longest T_1 value was acquired based on the signal response at 7.45 ppm.

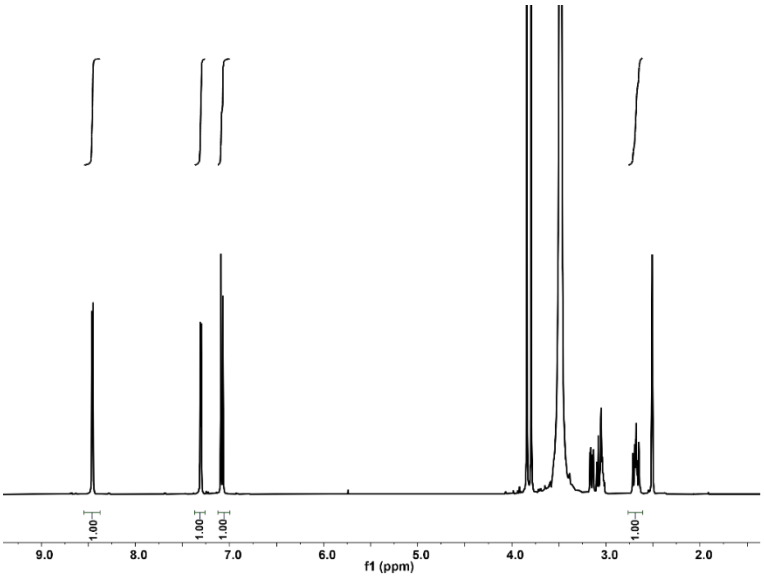

Fig. S5. An example of qNMR analysis using a donepezil impurity C solution in DMSO-d_6, in which the signal responses between 3.0 and 4.0 ppm were excluded due to solvent-related interference. The longest T_1 value was acquired based on the signal response at 8.44 ppm.

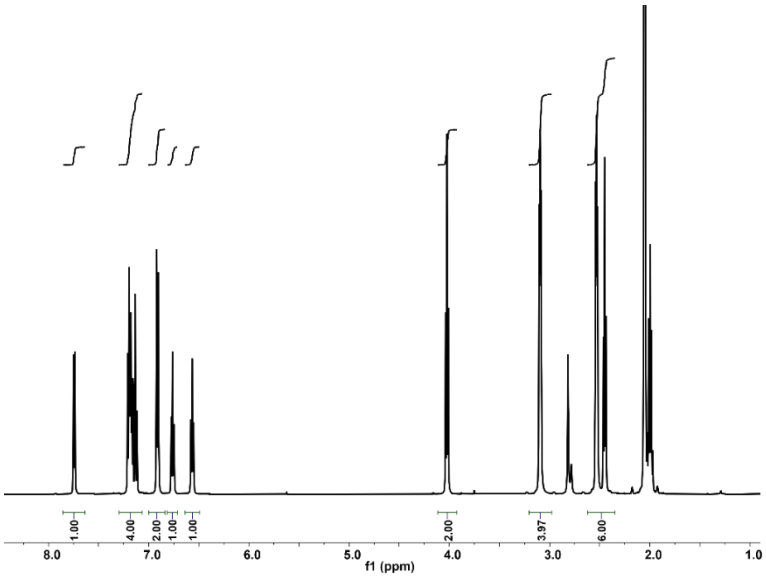

Fig. S6. An example of qNMR analysis using a trazodone hydrochloride impurity B solution in acetone-d_6, in which the signal responses around 2.0 ppm and 2.7 ppm were excluded due to solvent-related interference. The longest T_1 value was acquired based on the signal response at 7.76 ppm.

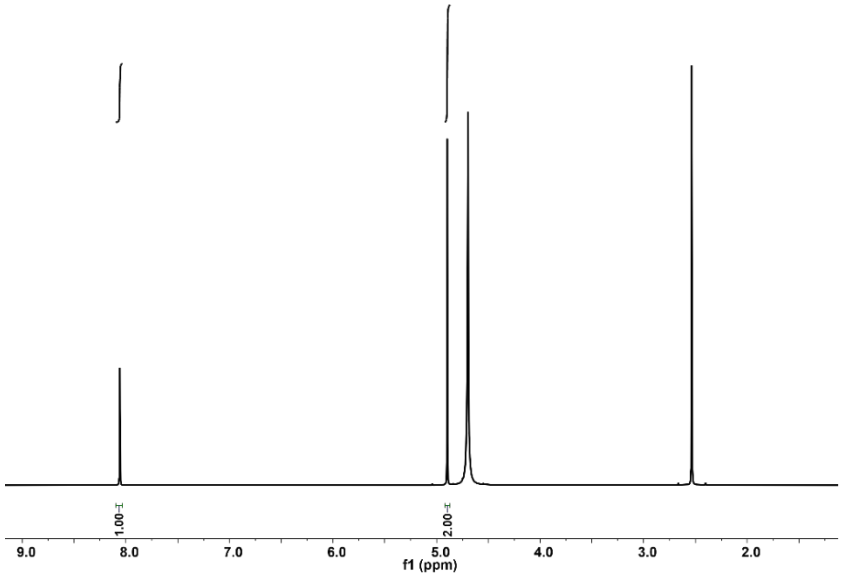

Fig. S7. An example of qNMR analysis using a pyridoxine hydrochloride solution in D_2O. The longest T_1 value was acquired based on the signal response at 8.02 ppm.

Supporting Information IV: *"Intermediate precision"* test

This experiment is primarily designed to evaluate whether the proposed approach remains effective under different scenarios. Specifically, we used four different compounds and conducted both T_1 measurements and T_r predictions using JEOL ECZL500G SPA (JEOL Ltd., Tokyo, Japan) equipped with a cryoprobe. T_1 was analyzed using software Delta 6.1.0 (ver). For T_r prediction, absolute integration was calculated using Mnova 15.1.0. The results can be found in **Table S2**, and they are generally consistent with our conclusions. Notably, all predicted T_r values fall within the "sweet spot" range. This indicates that the proposed method for T_r prediction remains reliable.

Table S2. T_r-based on measured T_1 vs. predicted T_r at $I_{max}^{99.99\%}$ for compounds in different instruments and by a different analyst

Chemical	Solvent	Measured T_r (s)			Predicted T_r (s) When AQ=4 s
		$5\times T_1$	$7\times T_1$	$10\times T_1$	
Lactic acid	MeOD-d_4	25.7	35.9	51.4	37.4
Potassium gluconate	D_2O	11.5	16	23	21
Sodium benzoate	D_2O	25	35	50	47
Capecitabine	ACN-d_3	13.1	18.3	26.2	25.4