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Article

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High-Fidelity Control of Spin Ensemble Dynamics via Artificial Intelligence: From Quantum Computing to Imaging

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ABSTRACT

High-fidelity control of spin ensemble dynamics is essential to many fields, spanning from quantum computing to optical, coherent, and nuclear magnetic resonance (NMR) spectroscopy and imaging (MRI). However, attaining robust and high-fidelity quantum spin operations remains an unmet challenge. Using a combination of an evolutionary algorithm and artificial intelligence, we designed time-optimal, radio frequency (RF) pulses with tunable spatial or temporal field inhomogeneity compensation and fidelity for unitary operations up to 0.9999. As a benchmark, we constructed a spin entanglement operator and a programmable quantum state creator for a weakly-coupled two-spin-1/2 system. We achieved high-fidelity transformations under multiple inhomogeneity sources. The newly designed RF pulses are more robust and less prone to imperfection than the commonly used shapes for basic liquid-state NMR experiments and reduce RF artifacts in MRI. This new strategy will enable the design of efficient quantum computing operators as well as new spectroscopic and imaging techniques.

Keywords: High Fidelity RF pulses, Spin Entanglement, Genetic Algorithm, Artificial Intelligence, NMR Spectroscopy, Magnetic Resonance Imaging.
INTRODUCTION

High-fidelity control of quantum spin systems is at the foundation of many applications such as quantum computing, coherent and optical spectroscopies, as well as nuclear magnetic resonance (NMR) spectroscopy and imaging (MRI)\(^1\)-\(^4\). Spin operations such as excitation, inversion, refocusing, etc. are central to these techniques and are achieved by applying radiofrequency (RF) pulses of finite length and amplitude. However, the RF and external field inhomogeneities and finite pulse width effects make the coherent manipulation of spin ensemble dynamics rather challenging\(^5\). The latter affects quantum operations' fidelity, such as gates, on-demand entangled state generation, and coherent control \(^1\),\(^6\),\(^7\). MRI and NMR at high- and ultra-high fields are also affected by these experimental errors as they require high operational fidelity levels for coherent and high-efficiency control of heterogeneous spin ensembles \(^8\),\(^9\). Moreover, these imperfections accumulate in multi-pulse experiments, leading to low fidelity operations and sizable signal losses\(^10\). Although advanced computational techniques have been instrumental for designing compensated RF pulses such as composite, adiabatic, and numerically-optimized pulses \(^5\),\(^11\)-\(^17\),\(^18\), the fidelity and compensation levels for instrumental inhomogeneities achieved are still inadequate to perform spin operations for reliable quantum computing.

Here, we introduce a novel strategy to achieve high fidelity control of spin ensemble dynamics with a high-level compensation for inhomogeneity and offset effects, reaching an unprecedented level of fidelity for several spin operations. We combined an evolutionary algorithm with artificial intelligence to accomplish this task, generating a family of time-optimal phase shapes with constant amplitude to reach an operational fidelity higher than 0.9999. These RF shapes display a smooth profile and are symmetric for all universal flipping operations with high tolerance against random noise. We demonstrated our approach's versatility by designing several spin operations for selected applications, including the generation of quantum spin entanglement, liquid-state NMR spectroscopy, and magnetic resonance imaging.
RESULTS

We combined an evolutionary algorithm with artificial intelligence into a new software, GENERator of Triply Compensated pulses via Artificial Intelligence or GENETICS-AI, to design new highly compensated spin operations. The overall architecture of GENETICS-AI is reported in the Methods (Extended Data Fig. 1). The core module of the algorithm consists of a network of interconnected optimization routines, including an iterative forward search (IFSA) and iterative self-correcting algorithms (ISCA), which search the RF phase space and generate an Optimal Phase Surface (OPS) through an iterative evolution of the solutions. Once the OPS library is built, a neural network (PhaseNET) is trained on this library to predict new RF shapes with customizable flip angles, bandwidth (BW, i.e., the range of frequencies irradiated by an RF pulse with a specified fidelity), RF inhomogeneity compensation, and operational fidelity. The standout feature of GENETICS-AI is the multiple bidirectional validation of each RF shape through an optimization network, where each solution is connected to its neighbor as a generator or corrector. A few example outputs of high-fidelity RF shapes designed using GENETICS-AI are shown in supplementary Figs. 1-2. These universal π/2 and π pulses cover a bandwidth of 40 kHz with pulse lengths less than 200 μs and an average operational fidelity of 0.9999. The RF amplitude ($\omega_1 = \gamma B_1/2\pi$, where $\gamma$ is the gyromagnetic ratio) of these operations has a constant value of 25 kHz. Supplementary Fig. 3 shows a comparison of GENETICS-AI broadband universal π pulses with RF inhomogeneity compensation for different bandwidth values.

*Characteristics of GENETICS-AI pulses.* All GENETICS-AI pulses are constant amplitude and possess a smooth, symmetric phase shape, reducing the amplitude or phase switching errors associated with RF transmitters and amplifiers. These shapes' smoothness is attributable to the IFSA and ISCA optimization network that generates the OPS in which each shape is connected to a family of shapes by iterative forward or reverse search schemes. The smoothness of phase shape can be estimated by calculating the average phase difference (APD):
\[ \text{APD} = \frac{1}{n-1} \sum_{j=1}^{n-1} |\varphi_j - \varphi_{j+1}| \]  

(1)

where \( n \) is the number of points in the phase shape, and \( \varphi_j \) is the phase's \( j^{\text{th}} \) point. To demonstrate the smoothness of GENETICS-AI pulses, we calculated the APD values for a series of 500-point universal \( \pi \) pulses, which are tolerant to changes in RF amplitude up to \( \pm 10\% \) (Supplementary Figs. 4a-b). As expected, the APD value increases with the bandwidth, indicating higher geometrical complexity of the phase shape at larger bandwidth. For a 500-point phase shape with random numbers, the APD value is 120°, whereas the GENETICS-AI pulses designed for NMR spectroscopy the APD value is less than 10°. In addition to their smooth shapes, GENETICS-AI pulses are highly tolerant of random noise on phase or amplitude shape, which dramatically affects the operational fidelity. To test the robustness to these imperfections, we added random numerical noise to the amplitude and phase of a GENETICS-AI pulse and evaluated changes in its operational fidelity. Supplementary Figs. 4c-e shows a universal \( \pi \) pulse with a bandwidth of 100 kHz and RF amplitude (\( \omega_1 \)) of 25 kHz that performs spin operations with a fidelity of 0.999 in the absence of noise. Upon addition of noise, with an amplitude of 5 kHz (20%), the fidelity drops by only 0.014 (i.e., 0.985), demonstrating a high tolerance to random sources of noise. A similar scenario is anticipated for simultaneous errors in amplitude and phase shape. To assess the refocusing pulses' performance obtained with GENETICS-AI, we compared several of these shapes to best-performing pulses reported in the literature \(^{15,16,19-23} \). We tested the length, operational bandwidth, and average fidelity of these pulses (Supplementary Fig. 5 and supplementary Table 2). For all the shapes tested, the GENETICS-AI pulses show higher fidelity and shorter duration. The new pulses are time-optimal and tunable for any operational fidelity and, which enables one to perform refocusing operations up to 220 kHz bandwidth, with a pulse length of 4 ms and a maximum RF amplitude of 10 kHz. Note that when using higher resolution RF shapes, the maximum bandwidth can be further improved.
**Creation of High fidelity spin entanglement.** The creation and preservation of High fidelity spin entanglement are central to quantum computing and are crucial for several applications such as Shor’s factoring algorithm, quantum teleportation, and dense coding. The generation of entanglement from a pure state (e.g., $|\alpha\alpha\rangle$) involves applying a Hadamard gate on one spin followed by a Controlled-NOT (C-NOT) gate. A reliable physical implementation of entangling two quantum systems requires unitary operations, which compensate for instrumental inhomogeneity within an experimentally feasible range. For NMR, dipolar/scalar coupled spin-$\frac{1}{2}$ nuclear spins (such as $^1$H and $^{13}$C in $^{13}$CHCl$_3$) form a two-qubit (quantum bit) quantum computer. RF and external field inhomogeneities as well as errors in the determination of the coupling constant lower the fidelity level of the quantum gate or final state. Though NMR quantum computer is a quantum statistical mechanics system with ensemble-averaged measurements, it is a testbed for quantum algorithms and quantum simulations. Therefore, using GENETICS-AI, we created a robust entangling operator (GEN-Entangler) for a weakly coupled two-spin-$1/2$ system (Fig. 1a). We designed the GEN-Entangler with triple compensation, i.e., minimizing inhomogeneities of RF field amplitude ($\Delta\omega$), offset ($\Omega$) as well as the zz-type of interactions (i.e., weak scalar coupling, $\Delta J$). The modular nature of the GEN-Entangler makes it possible to individually customize the level of compensation for $\Delta\omega$, $\Omega$, and $\Delta J$. In this framework, the J-coupling compensation level is controlled by the number of spin-echo (SE) elements ($n$). For $n = 1$, the pulse sequence consists of a single SE element with three global pulses and a J-coupling compensation level up to $\pm 10\%$ (Fig. 1b). For $n = 2$, the tolerance increases to $\pm 30\%$, and for $n = 4$ to $\pm 50\%$. For the demonstration of GEN-Entangler, we have used the pulse sequence with $n = 2$ and RF pulses with inhomogeneity compensation levels of $\pm 20\%$ and $\pm 2$ kHz for $\Delta\omega$ and bandwidth, respectively (Fig. 1c). We created a $|\alpha\alpha\rangle$ pseudo-pure state (Mitra et al.) using the $^{13}$C-$^1$H spin pair of neat CHCl$_3$. Subsequently, starting from a $|\alpha\alpha\rangle$ state and using the pulse sequence shown in Fig. 1a (Supplementary Table 1), we created a maximally entangled state, $1/\sqrt{2} (|\alpha\alpha\rangle + |\beta\beta\rangle)$, between $^1$H and $^{13}$C spins of
CHCl$_3$ (Figs. 1d). As a metric for robustness, we simulated a 0.99 fidelity iso-surface of GEN-Entangler for the simultaneous triple compensation of $\Delta \omega_1$, $\Omega$, and $\Delta J$, and compared it with a standard C-NOT entangler with rectangular pulses (Fig. 1f). We then experimentally generated six entangled states by detuning the pulses' calibrated optimal values and performed the quantum state tomography. The yellow outer iso-surface in Fig. 1f represents the fidelity volume obtained with the GEN-Entangler for $n = 2$. In contrast, the inner red surface represents the fidelity volume corresponding to the standard C-NOT entangler using rectangular RF pulses. Considering the maximum levels of inhomogeneity for all three parameters, the fidelity volume obtained by GEN-Entangler is approximately 100 times larger than the corresponding rectangular shape pulse. For an iso-surface fidelity of 0.98, the volume ratio, $V_{\text{GEN}}/V_{\text{RECT}}$, increases up to 200 times (Fig. 1g), demonstrating that the new entangler has a significantly higher tolerance for experimental errors. Note that the GEN-Entangler sequence is ~62% shorter than the $\Delta J$ compensated Controlled-NOT gate sequence by Jones et al. $^{31}$; therefore, it has an additional advantage in terms of time duration.
Creation of High fidelity broadband pulses with a generalized flip angle. Generalizing broadband (BB) operations for an arbitrary flip angle is quite challenging, as it requires individual optimization for the desired flip angle or final state. Nonetheless, GENETICS-AI was able to create high fidelity BB pulses for any arbitrary flip angle or final state. Our algorithm generated an optimal phase surface (OPS) with smooth phase shapes vs. flip angle transitions (Figs. 2a-b). The neural network trained on this OPS library created BB RF shapes for any flip angle with a fidelity greater than 0.9999. We implemented this RF pulse generator in two different ways: as a programmable single qubit quantum state creator and a quantum gate generator. The former assumes an initial state \( |\alpha\rangle \), whereas the latter consists of a BB universal flipping operation (Figs. 2a-b). Notably, the pulse length is independent of the flip angle or spin state. This feature is critical for quantum computing as these pulses’ fixed-length removes any inhomogeneity associated with changes in
time duration. Bloch sphere trajectories of a few example pulse operations with various flip angles are shown in Figs. 2c-d. As an example, Figs. 2e-f show the RF shape and fidelity profile of a 113.5° flip angle pulse. These high fidelity single-qubit operations and the GEN-Entangler form a complete set of operations for universal quantum computing.

High fidelity Broadband RF pulses for liquid-state NMR at high magnetic fields. We also explored the phase space for typical RF pulse operations used in high-resolution liquid-state NMR spectroscopy. For quantum computing achieving the highest fidelity of pulse operations is critical, on the other hand, for liquid-state NMR spectroscopy, it is crucial to tune the fidelity to match the
spin systems’ relaxation features and maximize the signal-to-noise ratio (S/N). The intrinsic flexibility of the IFSA and ISCA modules of GENETICS-AI enables one to tune RF shapes for any given operational fidelity. To demonstrate this feature, we generated several OPS libraries with fidelities varying from 0.9 to 0.99999. The OPS for BB inversion pulses for different cutoff fidelities is shown in supplementary Fig. 6a. Using numerical fitting, we obtained an empirical relationship between the operational fidelity ($\tilde{\varphi}$) of the RF pulse with total nutation angle ($\Theta$):

$$\Theta \approx S \times -\log(1 - \tilde{\varphi}) + G$$  \hspace{1cm} (2)

where $S$ and $G$ are the slope and intercept functions that depend on the bandwidth (BW), RF amplitude, and compensation level. As shown in equation 2, the total nutation angle, $\Theta$, increases linearly with $-\log(1 - \tilde{\varphi})$. This empirical relationship still holds for universal $\pi$ pulses; however, it may significantly deviate from the linear response at higher bandwidth due to the RF pulses’ digital resolutions (Supplementary Fig. 6b). It is possible to avoid this issue by increasing the number of points in the pulse shape. For BB inversion pulses with a bandwidth of 100 kHz and RF amplitude, $\omega_1 = 25$ kHz, we achieved an unprecedented fidelity of 0.99999 with a pulse length of 274 $\mu$s. Of course, if the pulse length becomes a problem, the same operation can be achieved using a 57.5 $\mu$s pulse with a fidelity of 0.9, which avoids signal losses for fast relaxing spin systems. The simulated offset responses and time evolution of the z magnetization component at fidelities 0.9, 0.95, 0.99, 0.999, 0.9999, and 0.99999 are shown in supplementary Figs. 7a-b. The IFSA and ISCA optimization modules explore the phase space of any operation up to the limit imposed by the digital resolution of a specific shape, i.e., the number of points ($n$) used to faithfully represent a given shape. For example, we performed multiple optimizations of BB inversion pulses with digital resolutions $n = 16$, 26, 50, 76, and 100. The IFSA/ISCA optimization progress for these operations are shown using the ‘$\Theta$-Bandwidth’ plot, where $\Theta$ is the total nutation angle (Supplementary Fig. 8). In this case, we observed a linear relation between $\Theta$ and bandwidth, indicating that the bandwidth increase is constant for a unit change in pulse length or amplitude.
At higher bandwidth, the relationship is no longer linear. The slope of the curve decreases, as shown in supplementary Fig. 8a, which significantly increases the RF power requirement to excite the specific bandwidth. The linearity holds up to BW$_{\text{max}}$ (maximum bandwidth) and increases with the shape's digital resolution (Supplementary Fig. 8b). As the bandwidth increases, the shape's geometrical complexity increases and requires more shape points for its faithful representation. The ‘$\Theta$-bandwidth’ plot for ultra-broadband universal π and inversion pulses are shown in supplementary Fig. 8c. Supplementary Fig. 9 shows the increased geometrical complexity of RF shape with bandwidth for the universal π and inversion pulses. To achieve a bandwidth of 20 $\times$ $\omega_1$ for a universal π operation, it is necessary to increase the shape resolution to 2000 points. In supplementary Fig. 10, we report an ultra BB excitation pulse of 500 points, which can excite a bandwidth of 22 $\times$ $\omega_1$. This pulse is equivalent to an in-phase excitation bandwidth of 550 kHz using a 440 $\mu$s pulse duration ($\omega_1 = 25$ kHz). We experimentally tested this BB pulse by recording a proton 1D spectrum of uniformly $^{15}$N labeled K48C mutant of ubiquitin (U-$^{15}$N UBI$^{K48C}$) with an RF amplitude of 0.5 kHz on an 850 MHz spectrometer. The excitation bandwidth of the pulse is $22 \times 0.5$ kHz = 11 kHz, sufficient for the full excitation of the $^1$H resonances in a protein. A comparison between a rectangular pulse with $\omega_1$ of 16.67 kHz and the BB pulse of 0.5 kHz is reported in supplementary Fig. 10c. As expected, we observed a loss of signal intensity for the ultra BB pulse due to the relaxation during the pulse execution. Nonetheless, the power required for these BB pulses is only 6.57 mW, while a corresponding rectangular shape pulse would need 7.3 W to excite the same bandwidth.

We also tested the compatibility of our new pulses with multi-pulse NMR experiments. Specifically, we implemented RF inhomogeneity-compensated BB π/2 and π pulses into the 2D [$^1$H-$^{15}$N] Heteronuclear Single Quantum Correlation (HSQC) experiment, a central building block for biomolecular liquid-state NMR spectroscopy $^{34-36}$. Fig. 3a shows the new RF phase shapes designed to compensate inhomogeneity in RF amplitude up to ±20% and an excitation bandwidth.
covering the full chemical shift range of $^1$H and $^{15}$N for a Larmor frequency up to 1.2 GHz, which
is the highest magnetic field commercially available. The relatively short length of these pulses (~
500 μs for $\omega_1 = 12.5$ kHz for $^1$H and 5.8 kHz for $^{15}$N) makes them a robust alternative for the most
widely used sensitivity enhanced version of HSQC at magnetic fields at a Larmor frequency
greater than 1.2 GHz.

Fig. 3 | RF inhomogeneity compensated high-resolution multi-pulse NMR experiment. a, GENETICS-AI shapes for universal $\pi$ and $\pi/2$ pulses for $^1$H (blue) and $^{15}$N (red) channels. RF amplitudes were constant at 12.5 and 5.8 kHz for $^1$H and $^{15}$N channel, respectively. The pulse lengths for $\pi/2$ and $\pi$ pulses were 488.6μs and 509.8μs for $^1$H and 483.8μs and 524μs for $^{15}$N. b, Simulated fidelity profiles for $^1$H (blue) and $^{15}$N (red) for the pulse shapes in a. The inner contour level indicates a fidelity of 0.99. c, GENETICS-AI version of the HSQC (GEN-HSQC) spectrum of $^{15}$N labeled K48C mutant of Ubiquitin recorded using calibrated amplitude values for $^1$H (12.5 kHz) and $^{15}$N (5.8 kHz) channels on a Bruker 850 MHz spectrometer at 300K. The insets show the intensity comparison of the standard ‘hsqceuotf3gpsi2’ version ($I_{RECT}$) and GEN-HSQC ($I_{GEN}$) at different RF amplitudes for selected residues. Left y axis shows the normalized peak intensities of standard (blue) and GEN-HSQC (red) relative to the calibrated reference spectra ($I_{RECT}$ and $I_{GEN}$), whereas the right y axis represents the normalized intensity of standard HSQC (blue) with respect to $I_{GEN}$.

For comparison, we used the classical HSQC experiment with pulse field gradient (PFG) coherence
selection and the corresponding version with the BB GENETICS-AI pulses (GEN-HSQC).

We acquired the amide fingerprint spectra of U-^{15}N UBI^{K48C} \cite{37}. Fig. 3c shows the 2D GEN-HSQC
spectra recorded on U-^{15}N UB\textsuperscript{K48C} with calibrated RF amplitudes of 12.5 and 5.8kHz for \textsuperscript{1}H and \textsuperscript{15}N, respectively. To assess the BB pulses' tolerance for RF amplitude inhomogeneity on both \textsuperscript{1}H and \textsuperscript{15}N channels, we scaled the RF pulse amplitudes in steps of 5\% up to ±20\% while keeping their length constant. The insets of Fig. 3c show the comparison of representative resonance intensities of the GEN-HSQC spectrum ($I_{GEN}$) vs. the standard HSQC experiment ($I_{RECT}$). Overall, the spectrum acquired with the GEN-HSQC sequence displays a higher S/N ratio, with a significantly higher tolerance for RF inhomogeneity. Remarkably, the relative intensity of the GEN-HSQC is higher than the classical HSQC, even at fully calibrated RF amplitudes. The gain in sensitivity observed with the GEN-HSQC sequence can be attributed to the combination of high-fidelity pulse operation and RF inhomogeneity compensation. For HSQC with standard rectangular-shaped pulses, the intensity for residues near the \textsuperscript{1}H carrier frequency is ~0.8 and drops to ~0.5 for off-resonance irradiation relative to GEN-HSQC. For an attenuation of ±20\% of the hard pulses, the amide peaks are barely observable, whereas the signal intensities for the GEN-HSQC show a constant response. We also tested the performance of GEN-HSQC on the catalytic subunit of cAMP-dependent protein kinase A (PKA-C, Supplementary Fig. 11). For this larger protein (42 kDa), the GEN-HSQC spectrum shows a higher S/N ratio and detects additional amide peaks that are not observable with the standard HSQC experiment. The dramatic drop in peak intensities observed in the standard HSQC experiment is due to the accumulation of pulse imperfections over multiple pulses on both channels, \textit{i.e.}, ten pulses for \textsuperscript{1}H and seven for \textsuperscript{15}N.

Finally, we demonstrated the ultra-high RF inhomogeneity compensation of GENETICS-AI pulses by Spin Echo imaging, where we simulated the effect of RF inhomogeneity by scaling the RF pulse amplitudes up to ±100\%, keeping the pulse length constant. Fig. 4a shows a RF inhomogeneity-compensated SE sequence (GEN-SE) used to image a phantom constituted by two 4mm glass beads immersed in a 5mm Shigemi NMR tube filled with 10\% D\textsubscript{2}O and 90\% H\textsubscript{2}O (Fig. 4b).
The 1D image of the phantom along the z-direction using the SE sequence with standard rectangular-shaped pulses is shown in Fig. 4c. The pulse shapes and their fidelity profiles are shown illustrated in Supplementary Fig. 13. The intensity of the image acquired with the standard rectangular pulse version of SE becomes significantly lower with RF amplitude scaling (Fig. 4d). In contrast, the GEN-SE generates high-quality images with less artifacts, even at $\omega_1$ inhomogeneity of ±80% (Fig. 4e).

**DISCUSSION**

**Fig. 4 | Spin Echo Imaging at ultra-high RF inhomogeneity.** a, Spin-echo (SE) pulse sequence used for imaging. The $\pi/2$ and $\pi$ pulses are replaced with GENETICS-AI pulses for GENETICS version of SE sequence. The amplitude of the pulses are constant (16.67 kHz) and pulse lengths for $\pi/2$ and $\pi$ pulses are 437 μs and 567 μs, respectively. The maximum RF amplitude tolerance level ($\Delta \omega_1^{\text{max}}$) of these pulses were ±80%. The gradient strengths ($G_1$ and $G_2$) for all the experiments were set at 50% (3.3 G/cm). b, Diagram of phantom and coil geometry. The phantom consists of two glass beads of 4 mm diameter in a 5 mm Shigemi tube filled with 10% D$_2$O and 90% H$_2$O. c, 1D image of the phantom using the pulse sequence in a. d, RF inhomogeneity response of 1D imaging using standard rectangular shaped pulses of amplitude 16.67 kHz. e, Same as d using GENETICS-AI pulses. The RF shapes and their fidelity profiles are shown in supplementary Fig. 13. The experiments were performed in a Bruker 900 MHz NMR spectrometer.
The combination of a novel evolutionary algorithm and artificial intelligence presented here enables the optimization of spin operations with high fidelity in the presence of different sources of inhomogeneity. The operational fidelity, bandwidth, RF inhomogeneity compensation, and flip angle are customizable to meet various applications' requirements. The latter is achieved via the forward and reverse optimization coupled with a neural network that generates time-optimal phase shapes in a few milliseconds. The fast generation of the RF pulse is of paramount importance for building a programmable quantum compiler. As an example, we created a high-fidelity operator for spin entanglement with an unprecedented simultaneous triple compensation of experimental inhomogeneities. Unlike previous methods\textsuperscript{38}, the modular design of the new spin entangler makes it possible to tune the individual parameters to match the instrumental inhomogeneity profiles. Although demonstrated for a heteronuclear spin system, the experimental implementation for homonuclear spin system is straightforward as all GEN-Entangler pulses are applied globally. Entangling nuclear spins has been previously demonstrated for two and three qubits in NMR\textsuperscript{6,39,40}. Also, high fidelity entanglement has been previously realized for other quantum systems, including electrons in two proximal nitrogen-vacancy centers of diamond with fidelity $> 0.82$\textsuperscript{7}, and between two superconducting qubits\textsuperscript{41}. Our GEN-Entangler may contribute to improving these methodologies with higher compensation and fidelity.

The high fidelity for spin operations ($> 0.99999$) with a customizable RF inhomogeneity compensation and flip angle of GENETICS-AI enables the design of broadband spin operations for high and ultra-high fields, which are notoriously arduous to achieve for spectroscopy\textsuperscript{5,42}. A similar level of control can be achieved for liquid-state NMR experiments, which involve large ensembles of nuclear spin quantum processors in a highly mixed state. The new GENETICS-AI pulses show an increased sensitivity for multi-pulse NMR experiments that will improve their performance at ultra-high magnetic field strength (see supplementary Fig. 14).
Deep reinforcement learning or simple neural network have been used in specific pulse optimization cases\textsuperscript{43} or for predicting multidimensional RF pulses for imaging\textsuperscript{44,45}; however, GENETICS-AI is the first implementation of artificial intelligence for the design of general spin operations. The neural network built into GENETICS-AI is trained by an extensive library of realistic RF pulse shapes and performance profiles to generate pulses with smooth phase shapes and constant amplitude. These features improve the experimental fidelity by reducing pulse transient effects\textsuperscript{46}.

In conclusion, the combination of genetic algorithm and artificial intelligence showed that it is possible to control the spin dynamics of heterogeneous spin ensemble with a fidelity up to 0.99999 by evolving the phase shape of RF pulse. The robust spin entangler and programmable quantum compiler originated by GENETICS-AI will have an immediate application for quantum information processing. Moreover, the customizable bandwidths, inhomogeneity compensation levels, and fidelity of the operation will perform highly sensitive biomolecular NMR experiments at ultra-high fields (> 1.2 GHz).

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METHODS

Architecture of GENETICS-AI. The architecture of GENETICS-AI is reported in Extended Data Fig. 1.

Extended Data Fig. 1 | Schematic of GENETICS. The top layer represents the front-end of GENETICS-AI with user inputs of pulse specifications, trained neural network and optimal shape output. The middle layer consists of contour indexing algorithm and various optimal phase surfaces. The 'deep layer' consists of IFSA/ISCA algorithm and generation of 'optimal phase surfaces'.

Input module: The first module consists of a customizable input interface in which the user defines the specific problem to be solved. The input parameters are:

1) **Operator type**: desired pulse operation, i.e., excitation, inversion, universal π, π/2, π/3 and π/4 pulses.
2) **Maximum RF amplitude**: maximum allowed peak amplitude of the shape.
3) **Operational bandwidth**: desired bandwidth for the pulse operation (kHz).
4) **RF amplitude compensation level**: amount of RF inhomogeneity/miscalibration to be compensated.
5) **Average fidelity for the operation**: average fidelity for the pulse, where the average is calculated over the range of specified bandwidth and/or amplitude compensation level.
Iterative Forward Search and Self Correction Algorithms (IFSA-ISCA): generation of Optimal Phase Surfaces (OPS). The first part of the algorithm consists of novel iterative optimization algorithms called IFSA (Iterative Forward Search Algorithm) and ISCA (Iterative Self Correction Algorithm) that perform optimal conversion of a resource into a target variable, generating a family of solutions, i.e., optimal phase surface or OPS. The resource variable provides the range of maximum RF amplitude or pulse length for the IFSA-ISCA to explore. In contrast, the target variable is set according to the problem type, such as operational bandwidth, fidelity, and compensation levels for various inhomogeneities. The individual solutions in OPS are interconnected through the iterative forward and backward optimization network of IFSA-ISCA. These algorithms' primary objective is to maintain a minimum fitness value for the optimization network by altering the variable's value outside the optimal space and performing further optimization.

For the broadband (BB) pulse design, the operational bandwidth (BW) and total nutation angle (Θ) are the target and resource variables. Θ is the time integral of RF amplitude shape over the pulsing time. IFSA initializes these variables using the standard rectangular-shaped pulse bandwidth and nutation angle, which is the minimum possible value for the resource variable. After initialization, IFSA performs an adiabatic perturbation of the target variable, which results in a loss of the fitness value. IFSA maintains a minimum fitness value through an iterative loop by increasing the resource variable, followed by an optimization step. IFSA increases the degree of optimization through an iterative perturbation-evolution process and finds optimal solutions virtually impossible to reach using a standard optimization algorithm. The iterative evolution process is always monitored to check the solutions' integrity and time optimality, and a backward evolution is initiated if necessary. This perturbation-evolution process with forward and backward searches connects each family's solution either as a generator or corrector.
To illustrate IFSA-ISCA protocol, let's consider the case of a 100-point BB inversion pulse design (Extended Data Fig. 2a). ISCA optimization is initialized with bandwidth (BW) and $\theta$ of a standard rectangular $\pi$ pulse. The algorithm performs the first iteration by perturbing the BW by $\epsilon$. The small increase in bandwidth reduces the fitness value of the RF shape. At this point, IFSA tries to maintain the fitness of the shape by increasing $\theta$, a step which is followed by Broyden–Fletcher–Goldfarb–Shanno (BFGS) $^{47}$ or a Genetic Algorithm (GA) optimization $^{48}$. This optimization step evolves the RF shape to a new 'perturbed' BW and updates the fitness value. Once IFSA-ISCA

Extended Data Fig. 2 | Schematic of IFSA-ISCA Algorithm. a, Algorithmic steps for calculating the optimal phase surface (OPS) of a broadband universal $\pi$ pulse. b, $\theta$ – BW plot of the IFSA-ISCA optimization. The arrows indicate the trajectory of the optimization. The arrows pointing toward increasing values of the bandwidth are generated by IFSA, while those pointing down are generated by ISCA.
attains a cutoff fitness value, bandwidth will be perturbed again and undergoes the same optimization process. The evolution of broadband pulse is monitored by ‘Θ – BW’ plot (Extended Data Fig. 2b). The forward search of IFSA is coupled with a self-correction protocol that initiates an ISCA to keep the time-optimal trajectory. Once initiated, ISCA performs reverse iterations by reducing Θ in small steps. As in the IFSA case, the system compensates for the loss in fitness by reducing bandwidth by ε. Once the system reaches the fidelity cutoff, the iterative reverse search continues until the reverse trajectory meets the forward (Extended Data Fig. 2b). This adiabatic transition of optimal RF shape from low to high bandwidth continues until the IFSA-ISCA reaches the maximum bandwidth imposed by the digital resolution of the pulse shape (Supplementary Fig. 8a). The self-correcting protocol is based on a simple philosophy that if the nth step's fidelity is more than expected, the previous steps may not be time-optimal. Therefore, the self-correcting protocol is triggered when IFSA detects an increase in fitness, typically 20% close to the maximum from cutoff in one optimization step. The latter indicates a possible correction in the trailing trajectory, and ISCA updates this with a higher slope trajectory (Extended Data Fig. 2b).

Every BFGS/GA optimization initiate with an RF shape obtained from the previous iteration of both forward and reverse searches. This initial guess considerably speeds up the optimization procedure and maintains a smooth transition of the shape with the target variable. As shown in Extended Data Fig. 3, we obtained a smooth phase surface for a 200-point universal π pulse and inversion pulse. This semi-continuous solution surface with increasing bandwidth is the OPS. OPS’s geometric features increase with operational complexity, bandwidth, average fidelity, and RF amplitude (ω₁) compensation level (Supplementary Fig. 6). OPS for 1000-point inversion and 2000-point universal π pulse for higher bandwidths are shown in Supplementary Fig. 9.
The fitness function ($\bar{\mathcal{F}}$) used in IFSA-ISCA is defined as the average operational fidelity of a given RF shape, and is calculated over a range of offset and $\Delta \omega_1$:

$$\bar{\mathcal{F}} = \frac{1}{N_{BW} N_{\Delta \omega_1}} \sum_{BW} \sum_{\Delta \omega_1} \text{Trace}(U_{\text{tar}} \times U_{\text{plat}}^\dagger)$$

where $U_{\text{tar}}$ is the target unitary operator, $U_{\text{plat}}$ is the unitary operator of the RF shape, $N_{BW}$ is the number of offset values from -BW/2 to +BW/2 used in the averaging, and $N_{\Delta \omega_1}$ is the number of RF amplitudes from $(\omega_1 - \Delta \omega_1/2)$ to $(\omega_1 + \Delta \omega_1/2)$ used in the averaging. Even though higher values of $N_{BW}$ and $N_{\Delta \omega_1}$ improve the fitness, smaller values are generally preferred as they are less computationally expensive. An example target unitary operator for universal $\pi$ pulse is $U_{\text{tar}} = e^{-i \pi I_z}$.

The fitness function given in eqn. 1 is used for operator optimization, where the operator type is a unitary operator. The fitness function for a state preparation (such as excitation and inversion) pulse design is given by,

$$\mathcal{F} = \frac{1}{N_{BW} N_{\Delta \omega_1}} \sum_{BW} \sum_{\Delta \omega_1} \text{Trace}(\rho_{\text{tar}} \times U_{\text{plat}} \times \rho_{\text{ini}} \times U_{\text{plat}}^\dagger)$$

where $\rho_{\text{ini}}$ and $\rho_{\text{tar}}$ are the initial and target states, respectively. For inversion pulse, the initial state corresponds to $\rho_{\text{ini}} = I_z$, and the target state is $\rho_{\text{tar}} = -I_z$. 

**Extended Data Fig. 3 | Optimal Phase surfaces of broad band pulses.** a, 200-point universal $\pi$ pulse and b, inversion pulse with bandwidths from $2\omega_1$ to $5\omega_1$. The IFSA cutoff fidelity for these pulse designs are 0.999.
Neural Network (PhaseNET): generation of new optimal solutions from the OPS library.

Once IFSA-ISCA generates the OPS, all the shapes are indexed using a novel ‘Contour Indexing Algorithm’ (CIA). CIA evaluates all the possible rectangles fit within the various contour levels of the ‘offset- $\Delta \omega_1$’ pulse profile as shown in Extended Data Fig. 4a. The index values of each RF shape (CIA files) and the corresponding shape used for training the neural network (PhaseNET), which predicts new RF shapes that are not directly available in the OPS. To accomplish this task, we used the traincgp function provided in MATLAB (Conjugate gradient back-propagation with Polak-Ribiére updates). A schematic of PhaseNET is reported in Extended Data Fig. 4b.

Extended Data Fig. 4 | Schematic of CIA and PhaseNET. a, Contour Indexing of 100-point universal $\pi$ pulse. 2D high resolution fidelity profile is generated and iteratively identified all the unique rectangles fitted within a contour and saved the dimensions to cia file. The process looped up to a maximum contour value of 0.99999. b, Architecture of the neural network used in "PhaseNET".

All GENETICS-AI algorithms are written in MATLAB® (R2018a) and executed on a personal computer with Intel® Core™ i7-7700K processor. The generation of a single OPS of 100 points takes approximately 12 hours of calculation on a single core. For a 500-point shape, the calculation time grows exponentially to approximately a week of computer time. We have implemented up to
2000-point RF shape, generating a database with more than 200,000 RF shapes for various operators, bandwidths, and RF amplitude compensation levels.

Solution NMR Sample Preparations.

Recombinant expression and purification of U-\(^{15}\)N ubiquitin K48C mutant (Ubi\(^{K48C}\)) was carried out as described previously\(^{49}\). The sample consisted of 0.80 mg of U-\(^{15}\)N Ubi\(^{K48C}\) was solubilized in 10 mM sodium acetate buffer (pH 6.0) and 100 mM NaN\(_3\). The final concentration of the sample was 300 µM. The expression and purification of the catalytic subunit of protein kinase A (PKA-C) was carried out as reported by Masterson et al.\(^{50}\) The NMR sample consisted of 200 µM 90%-\(^2\)H, and U\(^{15}\)N-labeled human PKA-C\(_\alpha\) (isoform II) saturated with 60X excess of ATP\(_\gamma\)N (12 mM) in 20 mM KH\(_2\)PO\(_4\), 90 mM KCl, 10 mM MgCl\(_2\), 10 mM DTT, and 1mM NaN\(_3\). The final pH was 6.5.

Data availability

The data that support the findings of this study are available from online version of the manuscript and the corresponding author upon reasonable request.

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Authors Contributions

G.V., M.V.S., and MG conceived and directed all research, along with helping with data analysis and writing the manuscript. M.V.S., K. P., and M.M. coded GENETICS-AI and carried out the NMR high-resolution and imaging experiments.

Competing Interests

G.V. and M.V.S. filed a provisional patent on the design of RF pulses using AI. “System and method for producing radiofrequency pulses in magnetic resonance using an optimal phase surface” Appl. UMN #20170394.
SUPPLEMENTARY INFORMATION

High-Fidelity Control of Spin Ensemble Dynamics via Artificial Intelligence: From Quantum Computing to Imaging

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**Supplementary Figure 1 | Broadband universal π/2 pulse.** a, Phase shape of a GENETICS-AI universal π/2 pulse of bandwidth 40 kHz. Amplitude is constant at 25 kHz. b, Offset response of the pulse for input states Mx, My and -Mz. c, Bloch sphere trajectories for a range of chemical shifts approximately on-resonance for initial state Mz. d, Time evolution of all the magnetization components during the pulse.
Supplementary Figure 2 | Broadband universal π pulse. a, Phase shape of a GENETICS-AI universal π pulse of bandwidth 40 kHz. Amplitude is constant at 25 kHz. b, Offset response of the pulse for input states Mx, -My, and -Mz. c, Bloch sphere trajectories for a range of chemical shifts approximately on-resonance for initial state Mz. d, Time evolution of all the magnetization components during the pulse.
Supplementary Figure 3 | 2D fidelity profiles for universal π pulses. a, Standard rectangular π pulse of 20 μs and GENETICS-AI π pulses with bandwidths b, 20 kHz (90 μs). c, 30 kHz (124 μs). d, 40 kHz (189 μs). e, ~500 kHz (1360 μs). The RF amplitude for all the pulses are constant (25 kHz).
Supplementary Figure 4 | Characteristics of GENETICS-AI shape. a, Variation of average phase difference with bandwidth for a 500-point universal π pulses (RF compensation of ±10%). b, Example of RF shapes with various average phase differences. c, Amplitude and phase shape of broadband universal π pulse with a bandwidth of 100 kHz (for ω₁ = 25 kHz, pulse length = 244 μs). d, Average inversion or refocusing response of Mx (‘square’), My (‘circle’), and Mz (‘triangle’) magnetizations with different noise levels on amplitude (blue), phase (green), and on both simultaneously (red). The average response for each magnetization was evaluated by keeping the same magnetization as the initial state and calculated the average frequency response of the GENETICS-AI pulse over 100 kHz bandwidth and 1000 different noise profiles at the same noise amplitude. Starting with an initial state of Mx, the universal π pulse (with phase x) keeps the magnetization along the same direction, whereas the My and Mz initial states are inverted. e, Amplitude and phase shapes with noise modulation of 20% in RF amplitude and 20° in phase shape.
Supplementary Figure 5 | Comparison of GENETICS-AI refocusing pulses with previously published shapes. a, Plot of the ‘Refocusing bandwidth-pulse length’ for best performing GENETICS-AI pulses vs. published refocusing pulses. Refocusing bandwidth of each pulse is calculated by averaging the offset responses of Mx -> Mx and My -> -My operations with a cutoff operational fidelity of 0.95. Each pulse is labeled with a short form and color coded for the same family. Supplementary Table 2 shows the full names and relative reference for each pulse analyzed. The size of each dot represents the average operational fidelity of the pulse. b to k, are the selected pulse shapes and corresponding offset responses for selected RF shapes. All RF shapes are available for download at http://veglia.chem.umn.edu/software-downloads.
Supplementary Figure 6 | Fidelity and pulse length of inversion and universal $\pi$ pulses. 

**a**, OPSs of 100-point broadband inversion pulses. The cutoff fidelities of the surfaces from the top right to the bottom are 0.9, 0.95, 0.99, 0.995, 0.997, 0.999, 0.9995, 0.9997, and 0.99995. With increase in fidelity, geometric features of optimal phase surface increases. 

**b**, Change in total nutation angle ($\Theta$) with fidelity ($F$) for the inversion pulses in **a**. The color gradient from blue to red indicates the variation of the bandwidth for the pulses ranging from $2x\omega_1$ to $5x\omega_1$. As the bandwidth increases, the $\Theta$ increases linearly. The digitization effect of the RF shape adds nonlinear behavior to the fidelity response at higher fidelity or bandwidth.

**c**, OPSs of 200-point broadband universal $\pi$ pulses. The fidelities of OPSs from the top right to the bottom are 0.9, 0.99, 0.9999, and 0.99999. 

**d**, Change in total nutation angle ($\Theta$) with fidelity ($F$) for inversion pulses in **c**. The color gradient from blue to red indicates bandwidth of the pulses varying from $2x\omega_1$ to $5x\omega_1$. 

Supplementary Figure 7 | Performance of the inversion pulses with different operational fidelities. 

**a**, Offset response of broadband ($BW = 100 \text{ kHz}$, $\omega_1 = 25 \text{ kHz}$) inversion pulses with fidelities varying from 0.9 to 0.99999. **b**, Time evolution trajectories of the Mz magnetization component for all inversion pulses. Three different bandwidth regions are shown with different color coding. For pulses with different fidelity, spins follow different trajectories to reach the final state.
 Supplementary Figure 8 | Limit imposed by the digitization of shapes on operational bandwidth. a, $\Theta$-bandwidth response of IFSA-ISCA optimization of broadband inversion pulses with different digital resolution of the shapes. Average operational fidelity is set to 0.999. The linear response of bandwidth breaks at $BW_{\text{max}}$. b, $BW_{\text{max}}$ as a function of the number of points. c, $\Theta$-bandwidth of 1000-point inversion and 2000-point universal $\pi$ pulse. The OPS of the IFSA-ISCA optimizations are shown in supplementary Fig. 9.
Supplementary Figure 9 | High resolution OPSs. a, OPS of 1000 point inversion operation, and b, 2000-point universal $\pi$ pulse. The region inside the white rectangle is expanded on right hand side to show continuous geometric features of the OPS.
Supplementary Figure 10 | Ultra-broad excitation pulse for high-resolution NMR spectroscopy. a, RF amplitude and phase shape of ultra-broadband in-phase excitation pulse. b, Excitation profile, and c, 1D spectrum of U-15N ubiquitin K48C using GENETICS-AI ultra-broad band excitation pulse (red, \( \omega_1 = 0.5 \) kHz). The high-power rectangular pulse version is shown in blue. The lower sensitivity is due to the relaxation during the low power excitation pulse, which does not occur for an RF amplitude of 16.67 kHz. An excitation sculpting pulse scheme was used for water suppression with 2 ms selective pulses.
Supplementary Figure 11 | Application of GEN-HSQC to large enzymes. GEN-HSQC spectra of 200 μM $^{15}$N labelled catalytic subunit of protein kinase A (42 kDa). The figure insets compare the intensity of various resonances recorded using GEN-HSQC (red) and standard ‘hsqctefp3gpsi2’ version (blue) of the HSQC experiment. Both experiments are recorded on a Bruker 850 MHz spectrometer at 273K using 128 complex indirect points were acquired with 16 scans per FID and 1.5s relaxation delay. Maximum RF amplitudes were 16.67 kHz for $^1$H and 7.7 kHz for $^{15}$N.
Supplementary Figure 12 | Refocusing response of composite chirp pulse and GENETICS-AI π pulse. Amplitude and phase shapes of a, composite chirp pulse and b, GENETICS-AI π pulse. The experimental offset responses of c, composite chirp pulse and d, GENETICS-AI π pulse for refocusing operation with transverse magnetization, Mxy. The offset response of phase (red) of refocused signal is shown in right y axis. The maximum RF amplitude of both pulses are fixed at 25 kHz. Experiments were performed using ¹H signal from a H₂O+D₂O sample on a 600 MHz Bruker spectrometer.
Supplementary Figure 13 | RF shapes used in the SE imaging sequence of glass bead phantom (Fig. 4). Amplitude and phase shape of a, $\pi/2$ pulse and b, $\pi$ pulse. c, 2D fidelity profile of $\pi/2$ pulse shown in a and d, 2D fidelity profile $\pi$ pulse shown in b. The pulse lengths of $\pi/2$ and $\pi$ pulse are 437μs and 567μs respectively with constant RF amplitude shape of $\omega_1 = 16.67$ kHz.
Supplementary Figure 14 | RF pulses for biomolecular NMR experiments in a hypothetical 5 GHz spectrometer. a, Universal π/2 pulse and b, universal π pulse for ¹H channel with RF amplitude constant at 16.67 kHz. The operational bandwidth of these RF pulses was ~100 kHz. c, Universal π/2 pulse. d, Universal π pulse for ¹³C channel with RF amplitude constant at 16.67 kHz. The operational bandwidth of these RF pulses was ~250 kHz. e, Universal π/2 pulse. f, Universal π pulse for the ¹⁵N channel with RF amplitude constant at 5 kHz. The operational bandwidth of these RF pulses was ~20 kHz. The offset responses are shown for initial states Mx(red), My(blue) and Mz(black). The average fidelity of these operations are 0.999.
Supplementary Table 1 | Pulse and delay values for the GEN-Entangler pulse sequence for \( n = 1, 2, \) and \( 4. \) The pulse and delay parameters were obtained by an iterative optimization process starting from a single spin-echo element (\( n = 1 \)) and three global pulses. The time-optimal pulse and delay parameters were evaluated for a state conversion problem, where the initial state was \( |\alpha\alpha\rangle \) and the final state \((1/\sqrt{2})(|\alpha\alpha\rangle + |\beta\beta\rangle)\) for a range of \( J \) coupling values (\( \Delta J \)). In the second iteration, the algorithm increases \( \Delta J \), until the average fidelity stays within the cutoff (0.999). Once the iteration process reaches the maximum \( \Delta J \) for a single spin echo, the process is repeated for 2 spin-echo elements. The entire optimization process is scripted in MATLAB and took around 2 hours of computation on a PC laptop with Core -i7 processor.

| \( n \) | \( \theta_0 \) | \( \phi_0 \) | \( \theta_i \) | \( \phi_i \) | \( \tau_i \times 1/J \) |
|------|------|------|------|------|---------|
| 1    | 1.5708 | 3.1416 | 0    | 2.0944 | 0.6155  | 0.25, 0.25 |
| 2    | 1.5708 | 1.3090 | 0.7854, 0.7854 | 1.0472, 1.5708 | 1.8326, 1.3090 | 0.2491, 0.2491, 0.4982, 0.4982 |
| 4    | 1.5708 | 1.5725 | 2.0106, 0.2042, 3.0247, 1.3422 | 1.9356, 0.6266, 2.4976, 0.6248 | 0.8954, 2.9479, 1.4748, 1.6703 | 0.2470, 0.2470, 0.4939, 0.4939, 0.4946, 0.4946, 0.4944, 0.4944 |
Supplementary Table 2 | RF pulses and references used for the comparison in supplementary Fig. 5.

| Pulse Label   | Name               | Reference          |
|---------------|--------------------|--------------------|
| ReBurp        | ReBurp             | 1                  |
| Q3            | Q3-Gaussian Cascade| 2,3                |
| RSnob         | RSnob              | 4,5                |
| IVega         | IVega              | 6                  |
| Crp100comp.4  | Crp100comp.4       | 7                  |
| Crp80comp.4   | Crp80comp.4        | 7                  |
| Crp60comp.4   | Crp60comp.4        | 7-9                |
| T1 to 2       | Tycko-Cho-Schneider-Pines | 10               |
| S1 to 6       | Shaka-Pines        | 9,11               |
| B1 to 2       | Borneman1 -2       | 12                 |
| TPG           | Tycko-Pines        | 13                 |
| W             | Waugh              | 14                 |
| Burbop1 to 4  | Burbop1 to 4      | 15                 |
| G5            | G5                 | 16                 |
| Gen-1 to 16   | GENETICS-AI pulses | This manuscript    |
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Figures

Figure 1

Nuclear spin entanglement. Please see manuscript .pdf for full caption.

Figure 2
Broadband high-fidelity arbitrary flip angle pulses generated with GENETICS-AI. Please see manuscript .pdf for full caption.

Figure 3

RF inhomogeneity compensated high-resolution multi-pulse NMR experiment. Please see manuscript .pdf for full caption.
Spin Echo Imaging at ultra-high RF inhomogeneity. Please see manuscript .pdf for full caption.