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Comment on: ‘Experimental indications of non-classical brain function’ 2022 *Journal of Physics Communications* 6 105001

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E-mail: warren.warren@duke.edu**Keywords:** entanglement, intermolecular multiple-quantum coherence, MRI

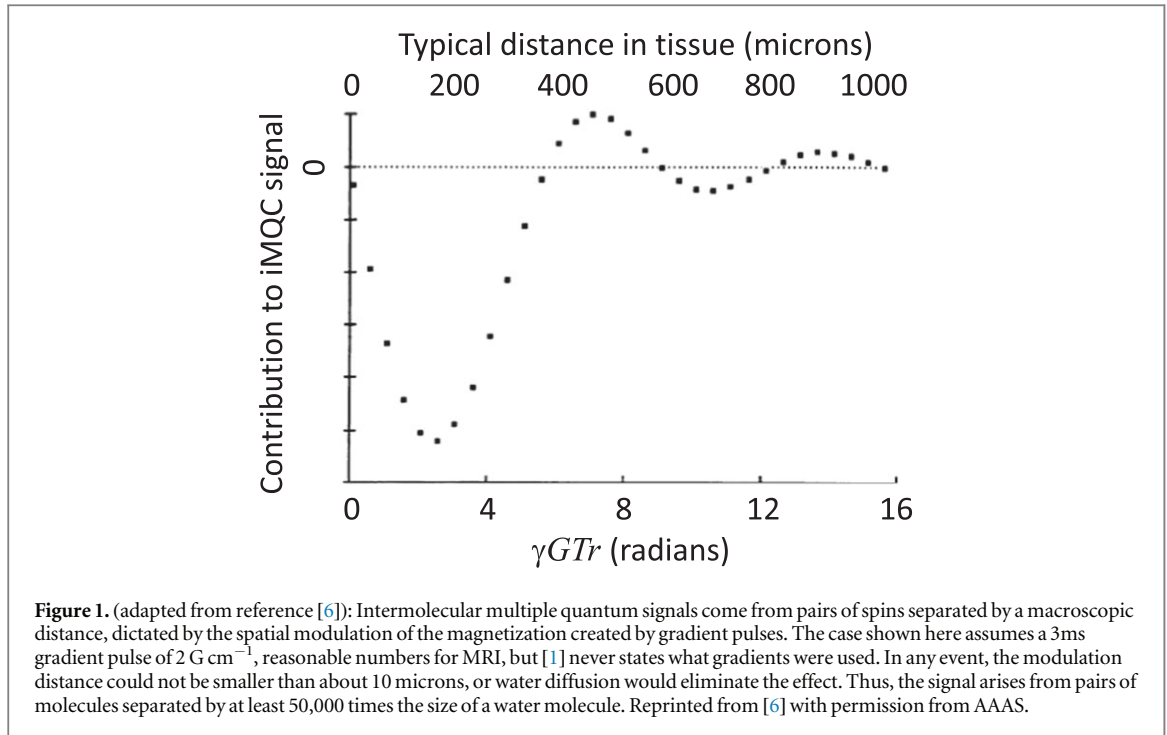
Abstract

A recent paper in this journal presents magnetic resonance imaging (MRI) data on humans which are asserted to ‘suggest that we may have witnessed entanglement mediated by consciousness-related brain functions. Those brain functions must then operate non-classically, which would mean that consciousness is non-classical.’ Unfortunately, the article provides no evidence to justify this claim. In fact, the paper only provides evidence for what we already knew: the brain (and any other living tissue) is complex, multicompartamental, and imprecisely characterized by MRI.

A recent paper in this journal [1] presents magnetic resonance imaging (MRI) data on humans which are asserted to ‘suggest that we may have witnessed entanglement mediated by consciousness-related brain functions. Those brain functions must then operate non-classically, which would mean that consciousness is non-classical.’ The experiments were on done on resting human subjects by imaging intermolecular multiple-quantum coherences (iMQCs) which provide a novel source of image contrast [2–12]. This certainly qualifies as an extraordinary claim, given theoretical derivations that no ensemble of small spin systems near thermal equilibrium at body temperature can ever exhibit entanglement [13]. Such a claim would normally call for extraordinary evidence, particularly because [1] postulates no mechanism, and never even states what might be entangled. Instead, the evidence for ‘non-classical’ behavior presented in reference [1] is the authors’ statement that they were unable to fully simulate their observed signals, plus claims that some signals were larger than they should be in the ‘classical’ limit. This assertion is incorrect, as are other assertions in the paper about magnetic resonance that disagree with decades of published work.

The concepts of coherence, correlation, and entanglement are easily confused, and can lead to a variety of misinterpretations [14]. A coherence is an off-diagonal element of the density matrix when it is written in the Hamiltonian eigenbasis. It is an intermolecular multiple-quantum coherence (iMQC) when the connected states involve flipping multiple spins on different molecules. In the early 1990s, two-dimensional NMR experiments [15] observed spectral peaks with all of the theoretical properties of iMQC transitions, between spins *typically separated by many microns or even millimeters*. The idea that such iMQCs would be observable also was an extraordinary claim in the early 1990s (they were called CRAZED sequences for a good reason), but the experiments were trivial to reproduce on any of thousands of existing spectrometers-including, for example, observation of coherences between molecules in different tubes [5]. Eventually, a full theoretical interpretation evolved [6, 16, 17]; the effects also manifest in simpler form as multiple spin echoes in solid ^3He [18] and in water [19].

The theoretical interpretation [6, 16] showed that these effects arise because of a limitation in the canonical expansion for the Boltzmann equilibrium density matrix for N nuclear spins in a high field:



$$\rho_{eq} = \frac{e^{-(\hbar\omega_0/kT)\sum_i I_{zi}}}{Tr(e^{-(\hbar\omega_0/kT)\sum_i I_{zi}})} \approx 2^{-N} (E + (\hbar\omega_0/kT)\sum_i I_{zi})$$

$$= \{ +(\hbar\omega_0/kT)^2 \sum_{i,j} I_{zi} I_{zj} / 2 + \dots \} \quad (1)$$

where ω_0 is the nuclear spin Larmor frequency (800 Mrad s⁻¹ in the 3T magnet used in [1]), E is the unit (identity) matrix, and the matrix I_{zi} is diagonal in the usual (Zeeman) basis set, returning +1/2 if spin i is up (α) and -1/2 if spin i is down (β). At body temperature, $\hbar\omega_0/kT \approx 2 \times 10^{-5}$ for ¹H nuclei at 3T. In the traditional treatment, the term in {brackets} in equation [1] is then assumed to be small and is omitted, leaving only one-spin operators at equilibrium. As discussed extensively in [16], the problem is that there are N operators in the last saved term (where $N \approx 10^{26}$ for a human brain) but N^2 operators in the first omitted term, and even more in later terms in the expansion. This matters because the dipole-dipole interaction between *distant* water molecules (separated by many microns) is not eliminated by liquid diffusion on an NMR timescale, and these two-spin couplings can convert multispin operators (such as the ones created by rotating the term in brackets using an rf pulse) into observable magnetization.

Because the dipole-dipole interaction averages to zero over a spherical surface, large signals are only produced by breaking spin symmetry, most commonly with gradient pulses. The simplest case is the pulse sequence {rf pulse, flip angle 90°}- {gradient pulse, length T , gradient strength G }- {rf pulse, flip angle 45°}- delay τ). During the second delay both the longitudinal (z -axis) magnetization and the transverse magnetization are modulated with a spatial period $2\pi/\gamma GT$ which is typically 5–500 μ m (about a million times larger than a water molecule). In that case, a large signal can be recovered which is a sum of an astronomically number of very small terms, each reflecting a pair of spins separated by roughly the ‘correlation distance’ $\pi/\gamma GT$, half the spatial period (figure 1) [6].

Specific properties of iMQCs are readily predicted. For the zero-quantum coherences (iZQCs) observed in [1], they are independent of the phase of the exciting pulse and of the resonance offset, but have a well-defined dependence on the correlation gradient direction, as was observed. The maximum signal for the sequence above is 41% of the bulk magnetization [4], vastly larger than anything measured in [1].

It is important to note that in structured media, such as tissue, the contrast (both theoretically and experimentally) is not a simple combination of conventional image contrasts [20]. In a typical application, the decay of an iZQC signal will reflect the distribution of resonance frequency differences between spins separated by the correlation distance. This is *not* the same as the distribution of resonance frequency differences over the size of an MRI image voxel (which samples a volume thousands of times larger) that gives conventional contrast such as T_2^* relaxation. Thus, while a quantitative signal calculation is completely possible for a simple sample, such as a spherical ball of water, the expected signal is very sensitive to details of the precise structure of the magnetization at the micron level [21] which is of course unknown *in vivo*. This is, of course, why iMQC imaging is useful-it extracts information.

Intermolecular multiple-quantum coherences in solution are, however, essentially classical in nature, meaning that it is also possible to use a modified Bloch equation picture to visualize them [6, 16, 17]. Thus, they are absolutely not a witness to entanglement. In fact, they do not even reflect any correlation between the spins, meaning that for any operators $I_{\alpha 1}$, $I_{\beta 2}$ ($\alpha, \beta = x, y$, or z) and spins 1, 2

$$\langle I_{\alpha 1} I_{\beta 2} \rangle = \text{Tr}(\rho I_{\alpha 1} I_{\beta 2}) = \langle I_{\alpha 1} \rangle \langle I_{\beta 2} \rangle \quad (2)$$

This follows because the initial N -spin equilibrium density matrix is separable into a direct product of $N 2 \times 2$ matrices σ_i , each one of which specifies the state of only one spin:

$$\rho = \sigma_1 \otimes \sigma_2 \otimes \sigma_3 \dots \otimes \sigma_n \quad (3)$$

At equilibrium the individual states have the form $\sigma_i = E/2 + (\tanh(\hbar\omega_i/2kT))I_{zi}$; the spin operators can be rotated in a pulse sequence, but the very small, distant dipolar couplings in solution never create significant terms that break this separability.

As discussed in detail in [16, 22] couplings between spins within the same molecule *can* create correlations (meaning the equalities in equations (2)–(3) can be violated), and (intramolecular) multiple quantum coherences have been used in many applications, including a variety of simulations of quantum computation. However, what [1] claims is evidence suggesting entanglement, which is a still more stringent concept than correlation. As discussed in reference [23], a system is by definition not entangled if its density matrix can be written as an average of separable density matrices, with nonnegative weights p_i that sum to 1:

$$\rho = \sum_i p_i \rho_i = \sum_i p_i (\sigma_{1,i} \otimes \sigma_{2,i} \otimes \sigma_{3,i} \dots \otimes \sigma_{n,i}) \quad (4)$$

Reference [13] showed that, starting from any density matrix that is ‘sufficiently close’ to the completely mixed state $2^{-N}E$, every possible matrix must be expressible in this form. For the case of pairs of coupled spins, sufficiently close would be any temperature above about 10 mK. This and related arguments [24] are also the reason that NMR quantum computation is not scalable to large systems, and is not being actively pursued. Entanglement does exist in spin ensembles, but only in very special cases such as large magnetization (tens of thousands of times higher than in [1]), or in parahydrogen gas (because the nuclear degrees of freedom are coupled to rotation).

With this in mind, what was measured in reference [1] The short answer is that it is impossible to tell from the paper. The pulse sequence is only sketched out in their figure 2; the methods section disagrees with their figure 2; and critical parameters such as the strength of the gradient used to give the iZQC signal are not included. It is impossible to reproduce the experiment. Even if we knew the exact sequence, the magnetization is very highly modulated because saturated magnetization is created and allowed to partially relax, and the brain is structured at a level of detail far finer than the voxel size of an MR image. This implies it would be impossible to do an accurate calculation, and makes it preposterous to assert that a signal difference would not have a classical explanation.

They never state what they think might be ‘entangled.’ Water has two spins, and entangled states of water exist (very far from room temperature thermal equilibrium), but they would disappear within milliseconds in bulk tissue because water protonates and deprotonates [25]. The signal detected in [1] is detected by dipolar interactions (as proven by the experimental dependence on gradient direction), which again is only sensitive to pairs of spins many microns apart.

The paper contains additional astonishing claims, such as ‘Consciousness-related or electrophysiological signals are unknown in NMR’ This ignores over three decades of work in functional MRI (fMRI) [26], which has been used in thousands of studies to monitor brain activity (including functional MRI with iMQCs) [7, 27, 28]. However, this claim is needed to justify assigning ‘entanglement’ to the difference between awake and sleeping brain scans—a difference which, in any event, is also the subject of hundreds of papers on resting state fMRI [29].

It is nearly impossible to prove a negative in science. I cannot disprove the assertion that a contribution to the difference between two complex experiments is because of entanglement. I also cannot disprove the assertion that a contribution to the difference is because of active intervention by aliens from Alpha Centauri. I don’t believe the latter explanation, because I know of no evidence for it, but either explanation is equally consistent with what is presented here.

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Data availability statement

No new data were created or analysed in this study.

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