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Reply to comment

Reply to criticism of the 'Orch OR qubit' – 'Orchestrated objective reduction' is scientifically justified

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The critical commentary by Reimers et al. [1] regarding the Penrose–Hameroff theory of 'orchestrated objective reduction' ('Orch OR') is largely uninformed and basically incorrect, as they solely criticize non-existent features of Orch OR, and ignore (1) actual Orch OR features, (2) supportive evidence, and (3) previous answers to their objections (Section 5.6 in our review [2]). Here we respond point-by-point to the issues they raise.

Reimers et al.
... For quantum information processing one must have quantum information storage units such as *qubits* ... the involvement of quantum gravity in the manifestation of consciousness would need to be described in terms of how quantum gravity affected the operation of these qubits ...

Stuart Hameroff and Roger Penrose ('H&P')
Basically true. And this is just what we have done. Qubits involve (1) superposition of alternative possible states, and (2) a mechanism by which the possible states reduce, or collapse to definite states.

With regard to point (1), any type of superposed state can, in principle, serve as a qubit, e.g. simultaneous alternative electric charge location, spin, dipole orientation, photon polarization, Fock state, topological pathway ('braid'), or current flow direction (e.g. superconducting Josephson junctions).

In Orch OR, the qubit involves electric dipole orientations in 'quantum channels' within each tubulin (microtubule subunit proteins), and between such tubulins along helical pathways through microtubule lattices. The dipoles occur due to coupled London force attractions among phenyl and indole rings of aromatic amino acids (tryptophan, phenylalanine and tyrosine) which comprise 'quantum channels'. The coupled dipoles oscillate between alternative orientations, and become superpositions of both states to function as qubits (Fig. 1b, and Figs. 5–7 in our review).

This helical dipole pathway version of the Orch OR qubit (akin to a 'topological qubit' [3]) was developed in 2002 [4], after the structure of tubulin was elucidated by electron crystallography [5] to reveal clustered arrays of electron resonance rings ('quantum channels', Fig. 5 in our review) [6]. The helical pathway qubit replaced the earlier notion (1996–1998, Fig. 1a, [7–9]) that oscillating dipoles in individual tubulins were the fundamental qubits. Helical

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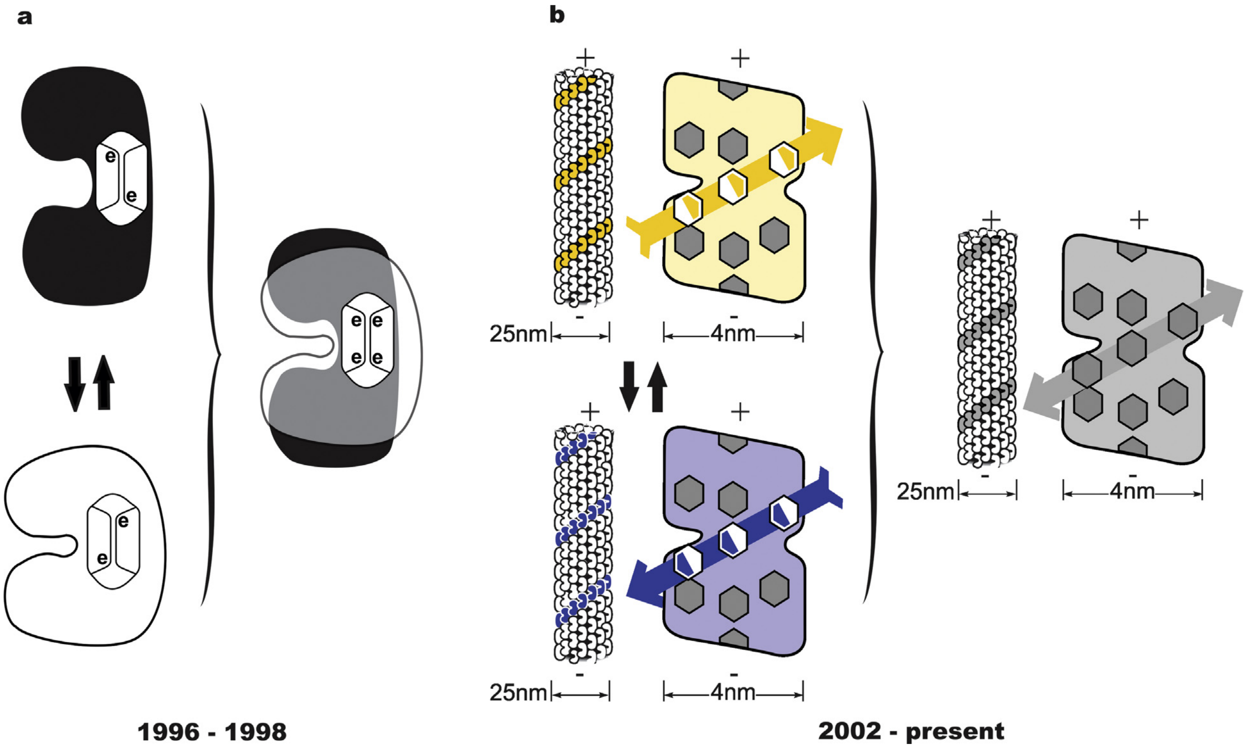

Fig. 1. Early, and current, versions of the Orch OR qubit. (a) Schematic cartoon version of Orch OR tubulin protein qubit used in Orch OR publications mainly from 1996 to 1998. On left, tubulin oscillates between 2 states with ∼1 nanometer conformational flexing (∼10% tubulin diameter). On right, both states exist in quantum superposition. (Irrespective of the schematic cartoon, the 1 nanometer displacement has never been implemented in Orch OR calculations.) The states are shown to correlate with electron locations (dipole orientations) in two adjacent phenyl (or indole) resonance rings in a non-polar 'hydrophobic pocket'. (b) Schematic cartoon version of the Orch OR qubit developed since 2002 (following identification of tubulin structure by electron crystallography [4,5]). Each tubulin is shown to have 9 rings representing 32 actual phenyl or indole rings per tubulin, with coupled, oscillating London force dipole orientations among rings traversing 'quantum channels', aligning with rings in adjacent tubulins in helical pathways through microtubule lattices. On the right, superposition of alternative tubulin and helical pathway dipole states. There is no conformational flexing. Mechanical displacement occurs at the femtometer level of tubulin atomic nuclei (not shown). Reimers et al. continually, and exclusively, criticize the obsolete, non-implemented version on left (a), and ignore the actual Orch OR dipole pathway qubit version on right (b).

pathway qubits are inherently resistant to decoherence, can couple to natural resonances in microtubule lattices, and associate with alternating current ('AC'). Indeed, Bandyopadhyay's group [10,11] has shown remarkable AC conductance at warm temperature through single microtubules at certain resonant frequencies (e.g. gigahertz, megahertz, and kilohertz). This evidence is consistent with oscillating dipoles extending along helical pathways through microtubules, and thus appears to provide considerable support for Orch OR.

How does the Diosi–Penrose ('DP') gravitational OR scheme influence the operation of Orch OR qubits? We first point out that DP is not really 'quantum gravity' in the normal sense of that term, as explained in our accompanying article [12] in response to Jack Tuszynski ('JT'), and in also our original review article [2]—though Reimers et al. continually use this terminology. This relates to point (2), a mechanism by which the possible states reduce, or collapse to definite states, the so-called 'wavefunction collapse' of the *measurement problem* of quantum mechanics (Section 4.3 of our review). In Orch OR, 'quantum gravity' (DP objective reduction) causes reduction, or collapse, of superpositions to classical states in accordance with $E_G \approx \hbar/\tau$ (Fig. 10 in our review). It may be mentioned that there are current experimental programs aimed at testing the validity of DP, and these ideas have recently become quite popular [13].

So in answer to this question raised by Reimers et al. ("how does quantum gravity affect operation of the qubit?"), Orch OR is very clear: it is the gravitational proposal DP that causes microtubule qubits to reduce, or collapse (in a time $\tau \approx \hbar/E_{\mathrm{G}}$), to definite classical microtubule states (which then regulate brain neurons).

Reimers et al.

In the current review Hameroff and Penrose suggest that the qubit could be either: (a) "interactive dipole states of individual tubulin proteins" . . .

H&P

"Interactive dipole states" YES, "individual tubulin proteins" NO. The Orch OR qubit is a dipole state extending through mesoscopic helical pathways of many tubulins in microtubule lattices (Fig. 1b, and Figs. 6 and 7 in our review). This is a change from early Orch OR theory in which each tubulin was a qubit (Fig. 1a, though without the significant conformational flexing shown there).

Reimers et al.

. . . interactive dipole states . . . such as "London-force dipoles" or (b) magnetic dipoles or (c) nuclear spins. "London force electric dipoles" have been discussed in previous publications but the other two options have been introduced for the first time.

H&P

True. London force 'electric dipoles' remain the primary description for mediating quantum states in tubulin and microtubules, with magnetic dipoles (electron spin), nuclear spins and AC current flow additional, possibly synergistic modes. For example microtubule electron dipoles may induce longer-lived nuclear spin states for short-term memory. As we say in Section 4.6 of our review: "It is to be expected that the actual mechanisms underlying the production of consciousness in a human brain will be very much more sophisticated than what we can put forward at the present time."

Reimers et al.

Previously, Hameroff and Penrose had also proposed that conformational switching could produce coupled electron–vibration qubits but this claim is withdrawn in the current review.

H&P

Not true. There are at least two types of 'conformational switching' to consider in tubulin. The type (1) to which Reimers et al. continually refer was considered and rejected by us in 1996, but implied in cartoon form through 1998, and occasionally thereafter (Fig. 1a). These early Orch OR illustrations showed conformational 'flexing' of entire tubulin proteins (e.g. ∼1 nanometer displacement, ∼10% of tubulin diameter) correlating with discrete information states (and superposition of states). This switching is no longer relevant to Orch OR except historically for the following reason.

In 1996, in attempting to connect brain biology to gravity-induced OR [7], we calculated E_G for superposition separation of three different levels of conformational changes in tubulin: (1) a ∼10% conformational flexing (∼1 nm, 10^{-9} m), as shown in Fig. 1a, (2) movement and separation at the level of atomic nuclei, e.g. carbon atoms (∼5 fm, 5×10^{-15} m), and (3) movement and separation at the level of nucleons, i.e. protons and neutrons (∼ femtometers, 10^{-15} m). The dominant effect was found to be separation of intra-tubulin atomic nuclei (5×10^{-15} m), and all Orch OR calculations have used separation at that level. Nanometer flexing was rejected in 1996, not "withdrawn in the current review". Reimers et al. continually, and exclusively, criticize the obsolete, non-implemented version in Fig. 1a. They ignore the actual Orch OR helical pathway qubit in Fig. 1b as if they never read our review.

Type (2) conformational switching can occur at the aforementioned much smaller level of atomic nuclei, 5×10^{-15} m, femtometers, shown to be optimal for E_G. This is also the calculated displacement of one (e.g. carbon) atomic nucleus caused by a one nanometer shift in nearby electrons by charge and Mossbauer recoil [14,15]. Thus nanometer electron dipoles (London forces) can couple to femtometer nuclear displacements, as needed for E_G in Orch OR.

Slight vibrational displacements at the level of atomic nuclei are likely to be associated with (e.g. megahertz) AC electronic resonances discovered by Bandyopadhyay's group in piezoelectric microtubules, e.g. mediated by London force dipole oscillations. London repulsive forces (Pauli exclusion when electron clouds get too close and overlap) are 100 times stronger than attractive forces, likely to promote nonlinear mechanical vibrations in microtubules with displacement at the level of atomic nuclei.

Reimers et al.

The London force is of quantum-mechanical origin. An instantaneous fluctuation of the electronic distribution creates a dipole in one molecule that in turn induces a dipolar response in a neighbouring molecule. This leads to a net attractive force.

H&P

True. Quantum-mechanical London ('dipole dispersion') force attractions are precisely how anesthetic gas molecules bind (e.g. in brain microtubules; Fig. 6 in our review) to disperse quantum dipoles and selectively erase consciousness (sparing non-conscious neuronal brain activities [16–19]). London forces are weak, but numerous and influential, and able to govern protein function [20].

Reimers et al.

The key feature is that these electric dipoles are *fluctuations*, not *states*. Individual *states* are needed to construct a qubit, and the review makes no attempt at specifying how qubit states could be associated with these London fluctuations.

H&P

Not true, as Fig. 1b (and 7 in our review) demonstrate. London force dipoles can couple, and 'fluctuate' collectively ('oscillate') between two alternative orientation states, with quantum superposition of both states. The London force-mediated shifts themselves are indeed instantaneous, but lifetimes of particular states following each shift are finite, e.g. up to 10^{-4} s as shown in microtubule resonances by Bandyopadhyay's group [10,11]. The evidence appears to be in support of our contention.

It is somewhat gratifying to note Reimers et al. have dropped their previous misguided criticism that electrons within a phenyl or benzene ring are delocalized, and therefore cannot constitute a switch [21]. As we show in Section 5.6 in our review, this would apply only to single phenyl rings, not coupled rings or contiguous arrays of such rings, as exist in tubulin.

Reimers et al.

No model of Orch OR can be treated seriously without the following: (i) a precise description of the quantum states of the qubit.

H&P

In an explorative work of this nature, where there remain many unknown factors, it is unreasonable to demand great precision at this stage. Nevertheless, we have provided a plausibly precise description (see above), as dipole states mediated by London forces in resonance rings aligned in helical pathways through microtubule. Reimers et al. ignore this, appearing not to have read or understand our review, criticizing, instead, an obsolete cartoon. If Reimers et al. are asking for, say, a Hamiltonian operator as a precise description for a microtubule quantum state, see our suggestions below.

Reimers et al.

... (ii) a description of the mechanism through which the wavefunctions representing these states become entangled.

H&P

Orch OR has always linked qubit entanglement to Fröhlich-type coherence, or condensation, akin to laser-induced entanglement in technological quantum systems.

Reimers et al.

... including specification of the basis in which measurements of the qubit's properties are performed in situ, ...

H&P

"Measurement" of microtubule qubits is taken to occur by the DP proposal for gravitational OR. Reimers et al. appear to have missed the key point.

Reimers et al.

(iii) a means of achieving quantum coherence over the required time scale.

H&P

The non-polar, hydrophobic environment within ‘quantum channels’ shields quantum coherence from polar environmental interactions. This is the solubility phase in which anesthetics act, and the likely origin of consciousness. Ambient energy, electric fields and mechanical vibrations pump coherence (as occurs in photosynthesis, and as suggested by Fröhlich). Most importantly, apparent quantum coherence up to 10^{-4} s has been shown by Bandyopadhyay’s group [10,11] to occur in single microtubules at warm temperature, which may be sufficient for Orch OR.

Reimers et al.

Hameroff and Penrose provide only a vague set of qubit possibilities. By not specifying the qubits in the current review they fail to provide a means by which the postulated links between quantum gravity and conscious behaviour could be assessed.

H&P

As remarked upon above, to ask for too much precision in our suggested mechanisms is, at this stage, an unreasonable request. Nevertheless, we have clearly specified our proposal for an Orch OR qubit, as the Orch OR helical dipole pathway that Reimers et al. appear to ignore.

Unlike previous proposals for a physical basis for consciousness, Orch OR provides a detailed, testable, falsifiable and moderately rigorous theory, not only for consciousness, but also for microtubule dynamics. It is a broadly based scheme, addressing areas of molecular biology, neuroscience, quantum physics, pharmacology, philosophy, quantum information theory, and even aspects of quantum gravity. Orch OR has been repeatedly challenged but, in our view, remains to be seriously threatened.

Reimers et al.

In previous versions of Orch OR, they *did* define a qubit that at the time might have been considered a reasonable proposition to advance and test. They proposed that conformational switching produced a coupled electron–vibration qubit that interacted with the cellular environment through associated large changes in microtubule structure and with quantum gravity via the significant mass displacement associated with the vibration.

H&P

We have addressed these issues in our comments above.

Reimers et al.

Coupled electron–vibration qubits are indeed considered as possibilities for use in modern quantum information technologies [22–24]. Quantum coherence was postulated to be provided by Fröhlich condensation [25–27] a predicted but unobserved macroscopic quantum effect. The original proposal thus contained a critical testable hypothesis.

H&P

Fröhlich condensation remains in Orch OR, and we consider Bandyopadhyay’s gigahertz, megahertz and kilohertz resonance in microtubules to be clear evidence *for* Fröhlich condensation, e.g. mediated by oscillating London force dipoles (Section 4.5 in review).

Reimers et al.

We tested this hypothesis and found two fatal shortcomings, resulting in it being withdrawn from Orch OR in this current review.

H&P

It is not withdrawn (Section 4.5), and the supposed ‘fatal shortcomings’ missed the mark entirely. In Orch OR, Fröhlich condensation is alive and well in Bandyopadhyay coherence.

Reimers et al.

First, we showed the conformational-switch was not a vibration, as is required for the qubit, but instead involves an irreversible chemical reaction [21].

H&P

There is no requirement of a qubit that it be a vibration. But Reimers et al. again refer to the long-rejected (and non-existent, in terms of underlying calculations) nanometer flexing of tubulin (Fig. 1a), instead of femtometer (6 orders of magnitude smaller) displacement at the level of atomic nuclei. We agree that coherent tubulin nanometer flexing would require significant chemical energy in the form of GTP hydrolysis and is not feasible (nor did we ever propose such an idea). Fröhlich condensation is pumped by ambient energy and mitochondrial electric fields [2].

Reimers et al.

Second, we examined the postulate that Fröhlich condensation could deliver unprecedented quantum coherence in a qubit involving electronic motion [28]. Whilst Fröhlich proposed that the coupled nonlinear equations that he solved would show *Bose–Einstein*-like behaviour, we found that instead a Fröhlich condensate would be *extremely incoherent*.

Further, we showed that significant *classical* effects of Fröhlich condensation did not manifest unless the system was very far from thermal equilibrium, with component parts needing to be at temperatures in excess of 500 K for room-temperature operation. Fröhlich condensation could not sustain quantum coherence in biological systems and could not support Orch OR.

H&P

The calculations behind these criticisms have nothing to do with Orch OR, microtubules or biology.

In the paper to which they refer [28], Reimers et al. applied the Wu–Austin Hamiltonian to "a linear chain of coupled oscillators *as envisaged in the Orch OR proposal*." This is false. Orch OR does ***not*** envisage microtubules as a 1-dimensional chain of oscillators. We envisage microtubules as 3-dimensional crystalline cylindrical lattices with Fibonacci geometry and gigahertz, megahertz and kilohertz resonances.

Moreover, the Wu–Austin Hamiltonian is suspect, as it lacks a lower bound, doesn't converge, and is therefore considered 'unphysical' [29]. Moreover it addresses rigid, polar, alpha helical intra-protein regions rather than non-polar 'quantum channels'. Using a different Hamiltonian, Samsonovich et al. [30] simulated microtubules as 2-dimensional lattice planes with toroidal boundary conditions (approximating 3-dimensions). They found strong Fröhlich coherence in super-lattice patterns on a simulated microtubule which precisely match experimentally-observed attachment sites for microtubule-associated proteins (MAPs).

Reimers et al.

We also note that the observed decoherence times for quantum processes involving electronic motion are usually in the range of 10 fs to 30 ps. A qubit with dynamics even slightly coupled to electronic motion would not retain quantum coherence on the 25 ms timescale required for Orch OR which Hameroff and Penrose suggest in this current review. This has consequences for all proposed qubits.

H&P

This, at last, is a reasonable objection, but an anticipated one. Bandyopadhyay's findings of gigahertz, megahertz and (as low as) 10 kilohertz resonances indicate microtubule 'decoherence times' (duration for which decoherence is avoided, i.e. 'coherence times') for microtubules can persist as long as 10^{-4} s. This same 'coherence time' of 10^{-4} s was also calculated based on Orch OR stipulations [31], but is indeed 250 times briefer than the 25 ms we invoked for Orch OR events, e.g. correlating with (40 Hz) gamma synchrony EEG.

In a supplemental modification, we suggest in our review that Orch OR events occur at much higher frequencies (e.g. megahertz) than previously proposed (e.g. at 40 Hz), and that interference between sets of coherent microtubule vibrations (e.g. in megahertz) results in much slower 'beat frequencies', e.g. at 40 Hz gamma synchrony. Indeed, electro-encephalographic (EEG) rhythms (whose origins have never been understood) may actually be 'beats' of much faster megahertz Orch OR events in intra-neuronal microtubules. Moreover, recently-observed very high frequency (kilohertz) EEG [32], too fast for membrane depolarizations, may reflect intra-neuronal microtubule dipole oscillations.

By $E_G \approx \hbar/\tau$, 10 MHz Orch OR ($\tau = 10^{-7}$ s) would have a much greater E_G (compared with 40 Hz gamma synchrony Orch OR), and involve microtubules in an estimated 10^9 neurons, one percent of the brain (Section 5.2 in our review). This also suggests that decoherence need be avoided for only 10^{-7} s. Bandyopadhyay's group has already shown decoherence time 100 times longer, at 10^{-4} s, so Orch OR is on more solid ground with respect to decoherence.

Orch OR has some support from experimental evidence and is a scientifically justified proposal. The riddle of how EEG is generated (including kilohertz EEG [32]) may also perhaps be solved in terms of Orch OR.

Reimers et al.

In an effort to perpetuate their model they now include "electron-cloud dipoles (London forces)", magnetic spin dipoles and nuclear spins in a list of possible qubits, without suggesting how any of these phenomena could in fact be used to make a relevant qubit.

H&P

Here's how. Any type of superposition corresponds to separated spacetime geometry and gravitational self-energy E_G which will undergo OR at time $\tau \approx \hbar/E_G$.

The Orch OR proposal is aimed at perpetuating truth and scientific knowledge. If it were to be shown invalid, we would drop the model and acknowledge accordingly. But we believe that, so far, it has survived the many extensive criticisms, such as those by Reimers et al. (see Section 5.6 in our review).

Nevertheless, as said earlier, and in accordance with scientific principles, we have tried to improve and adapt the theory when the need arises, and when new information has come forth (though 'electron cloud London force dipoles' have always been key components). For example quantum channels, helical pathway qubits, and faster (megahertz) Orch OR events with EEG beat frequencies are adaptations based on new knowledge of tubulin structure and Bandyopadhyay coherence. Magnetic spin dipoles and nuclear spin are indeed also suggested in this review, and for good reasons. Quantum (magnetic) spin transfer through phenyl rings is increased with temperature [33], and likely to be important biologically. Oscillating spin currents, or spin flips, may propagate through quantum channels as easily as electric (London force) dipoles, or together, synergistically, along with nuclear spin and displacement. Longer-lived nuclear spin may encode short-term memory. Reimers et al. do not even recognize or address these developments.

Reimers et al.

The review is thus neither self-consistent or scientifically coherent and violates the basic tenants of good scientific practice [34].

H&P

Orch OR is self-consistent, scientifically coherent and increasingly supported by evidence. Reimers et al. accuse us of a lack of good scientific practice. Their reference [34] describes "Seven deadly sins", e.g. "using pretty pictures instead of solid science". Presumably they refer to conformational flexing as shown in Fig. 1a (developed before tubulin structure was known), which is unrelated to the underlying scientific calculations based on atomic nuclear displacement, and the helical dipole qubit. Fig. 1b more closely describes the present Orch OR helical pathway qubit, but is a simplification, e.g. showing 9 rings per tubulin rather than the actual 32 rings per tubulin. These rings within tubulin also are where anesthetic gas molecules bind and act to erase and prevent consciousness.

With regard to the use of "pretty pictures" instead of solid science, Fig. 1 in Reimers' et al. original Orch OR criticism [28] depicts individual coupled oscillators (presumably tubulins) floating in a bath, the cell as "minestrone soup". Tubulins and microtubules do not float, but exist as solid state crystalline lattices. By their own criteria, Fig. 1 in Reimers' et al. [28] violates basic tenants of good scientific practice. However their "minestrone soup" picture emphasizes a critical point raised by Jumper and Scholes [35] in their constructive commentary:

Jumper and Scholes [35]

"... what do we really know about the fundamental nature and properties of the biological environment? The concept of "warm, wet & noisy" is put forth when one imagines the complex components and workings of a biological system to be ... a messy business, incapable of supporting 'delicate' quantum processes .... Should we reconsider the premise that living entities are founded on uncorrelated and chaotic machinery? [Why] do we expect incoherence in biology? ... On the contrary, it appears that living systems are governed by cycles and correlations, requiring massive cooperation across a large range of time and length scales."

Reimers et al.

The specification of the quantum qubit should be the centrepiece of the proposal. All other aspects of the Orch OR proposal are only relevant in terms of how they affect the qubits. Without a viable qubit specification there is no connection between the proposal and the observations of Bandyopadhyay and others. Without a qubit there is no connection to postulated effects of quantum gravity. Without a qubit there is no testable hypothesis linking together the phenomena of quantum gravity, elementary biochemical function, and consciousness, and no basis on which "Orch OR theory" can be considered as a proposal worthy of further consideration.

H&P

We agree. That's why we have defined an Orch OR qubit based on oscillating London force dipoles in resonance rings in helical pathways through microtubule lattices. The oscillations occur in gigahertz, megahertz and kilohertz frequency ranges, may interfere to cause slower 'beats' seen as EEG rhythms, and appear to be in line with Bandyopadhyay's findings. Reimers et al. ignore our specified qubit and solely criticize an irrelevant cartoon.

We believe that Orch OR is a detailed, testable, falsifiable and reasonably rigorous approach to a theory of consciousness, and microtubule function. Supportive evidence for Orch OR from microtubules (Bandyopadhyay coherence [10,11], Eckenhoff anesthetic effects [36–38], quantum channels [6]) is of a kind not yet found in other relevant theories. Orch OR has been repeatedly challenged, but we do not feel that it has yet been seriously threatened.

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