Psychedelics and the Microtubule: A Conditional Calcium/Tryptophan Exciton Hypothesis and the "Reverse Anaesthetic" Symmetry

Thomas McIver
Independent Researcher, Auckland, New Zealand
tommc9010@gmail.com

Abstract

General anaesthetics bind tubulin and reduce tryptophan-mediated electronic energy migration in microtubules (Kalra et al., 2023), and microtubule stabilisation delays anaesthetic-induced loss of consciousness (Khan et al., 2024). These findings tie loss of consciousness under anaesthesia to contraction of a measurable microtubule photophysical property, and motivate the proposal, within the Orchestrated Objective Reduction (Orch OR) framework, that microtubule quantum processes participate in conscious states. Here we develop the symmetric hypothesis, that classic serotonergic psychedelics (*N*,*N*-dimethyltryptamine, DMT; LSD; and psilocybin/psilocin) act in the opposite direction at the same substrate, expanding rather than contracting microtubule excitonic coherence and thereby producing richer internally generated conscious states. We are explicit that this is a hypothesis, not an established result, and that its central steps are presently unproven. We set out two candidate routes to the microtubule lattice: an indirect receptor-signalling route (5-HT_{2A} $\rightarrow$ intracellular cascade $\rightarrow$ Ca^{2+} $\rightarrow$ perturbation of the tubulin tryptophan network toward coherence-protected subradiant states) and a direct route in which the indole-bearing psychedelic molecule couples to the tryptophan exciton network through its shared chromophore. We discuss how the recent demonstration that 5-HT_{2A}-mediated G_i signalling is essential for hallucinogenic effects (Xu et al., 2026) bears on the signalling route, and why the direct route is partly insulated from it. We give a single decisive, unperformed experiment: the tryptophan-exciton-migration assay of Kalra et al. (2023), run with psychedelics in place of anaesthetics, as the most direct test of the symmetry, and are candid that the bridge from excitonic to conformational coherence, and the involvement of microtubule quantum processes in consciousness at all, remain the framework's load-bearing, unresolved assumptions.

Keywords: Orchestrated Objective Reduction; microtubules; tubulin tryptophan network; excitonic coherence; subradiance; quantum biology; psychedelics; serotonin 2A (5-HT_{2A}) receptor; DMT; LSD; psilocin; consciousness.

1 Introduction

The reversible abolition of consciousness by general anaesthetics is one of the few robust empirical handles on the physical basis of conscious states. A growing body of work locates part of the anaesthetic mechanism not at the synapse but in the neuronal cytoskeleton. Kalra et al. (2023) showed that microtubules support tryptophan-mediated electronic energy migration over distances of approximately 6.6 nm (further than conventional Förster theory predicts) and that the general anaesthetics etomidate and isoflurane measurably reduce this migration length. Khan et al. (2024) showed that pretreatment with the brain-penetrant microtubule-stabilising agent epothilone B delays the onset of anaesthetic-induced unconsciousness in rats. Older work established that microtubule-stabilising agents raise the anaesthetic concentration required to immobilise model organisms (Emerson et al., 2013), and computational modelling has reported that anaesthetic potency correlates with the magnitude of a shift the agents induce in a collective dipole oscillation of tubulin's aromatic residues (Craddock et al., 2017).

Taken together, these results make the Penrose and Hameroff Orchestrated Objective Reduction (Orch OR) proposal (that microtubule quantum processes contribute to conscious moments (Hameroff and Penrose, 2014; Penrose, 1996)) experimentally motivated rather than purely speculative, even though it remains contested on both physical and biological grounds (Section 2.1). The anaesthetic findings supply a directional anchor: the loss of consciousness coincides with the contraction of a measurable microtubule excitonic property.

This paper asks whether the converse holds. If anaesthesia contracts microtubule excitonic coherence, do agents that profoundly *expand* conscious experience (the classic serotonergic psychedelics) act in the opposite direction at the same substrate? We develop this "reverse anaesthetic" idea into a concrete, falsifiable hypothesis. We are deliberately careful about its epistemic status throughout: the symmetry is, at present, strongly evidenced on the anaesthetic side and essentially untested on the psychedelic side. Our central claims are therefore framed as hypotheses and predictions, and we are explicit about which steps are established, which are inferred, and which are unproven. This paper is deliberately confined to the physical substrate; the content and phenomenology of psychedelic experience are treated separately in a companion manuscript, posted concurrently as a preprint.

We make three moves. First (Section 2), we state the proposed substrate and the corrected photophysics: the resource of interest is the long-lived *subradiant* (dark) state manifold of the tryptophan network, not superradiant emission. Second (Sections 3 to 4), we set out two candidate routes by which psychedelics might modulate that manifold: an indirect receptor-signalling route and a direct indole-coupling route, and we treat the qualitative differences between DMT, LSD and psilocin as differences in the temporal envelope of that modulation rather than as a binary difference in receptor signalling bias. Third (Sections 5 to 7), we confront the principal recent complication for the signalling route (Xu et al., 2026) and give the experiments that would test the framework, foremost among them the psychedelic version of the Kalra et al. (2023) exciton-migration assay. Section 8 is a frank account of what the framework cannot do, including the two assumptions

on which everything rests, that microtubule quantum processes are involved in consciousness at all, and that protecting *electronic* coherence in the tryptophan network has any bearing on the *conformational* superpositions that Orch OR requires.

2 The proposed substrate and the subradiance correction

2.1 Orch OR as a conditional, experimentally motivated framework

We situate the hypothesis within Orch OR but do not attempt to prove it. Orch OR proposes that the reduction of a quantum superposition of tubulin conformational (mass) states is an objective physical event, occurring when the gravitational self-energy of the superposition reaches a threshold, on a timescale $\tau \approx \hbar/E_G$ (Penrose, 1996; Hameroff and Penrose, 2014). The proposal is contested. Its most cited difficulty is decoherence: Tegmark (2000) estimated that quantum superpositions in microtubules would decohere in $\sim 10^{-13}$ s, far too fast to be neurophysiologically relevant. Hagan et al. (2002) replied that this estimate used inappropriate parameters and, corrected, obtained a value between $\sim 10^{-5}$ and 10^{-4} s, still orders of magnitude short of the millisecond scales of neural dynamics. We do not regard this gap as closed, and we return to it in Section 8.

What makes the framework worth developing, rather than merely asserting, is that its central biological prediction (that perturbing microtubules should perturb consciousness) has begun to find experimental support specifically in the anaesthetic literature cited in Section 1. That support is real but limited: the epothilone B result (Khan et al., 2024) is a single behavioural study, and its authors themselves note it is compatible with classical mechanisms (a stabilised cytoskeleton could alter membrane-protein trafficking or transport without any quantum interpretation). We treat the anaesthetic evidence as motivating the hypothesis, not as confirming Orch OR.

2.2 The tryptophan exciton network

Tubulin is rich in aromatic residues, and its tryptophans form a network whose ultraviolet transition dipoles can couple. Theoretical work models this network as supporting collective excitonic states (Kurian et al., 2017; Celardo et al., 2019), and Babcock et al. (2024) reported, with supporting experiment, that organised tryptophan mega-networks in microtubule architectures support collective states spanning many orders of magnitude in radiative lifetime: short-lived "bright" (superradiant) states on the scale of hundreds of femtoseconds, and long-lived "dark" (subradiant) states on the scale of tens of seconds. The experimental measurement of Kalra et al. (2023) (a 6.6 nm exciton migration length in microtubules, reduced by anaesthetics) is the most direct evidence that this network sustains functionally relevant energy transport and that anaesthetics act upon it.

We adopt, as an explicit and load-bearing assumption, the proposal that this tryptophan exciton network is a component of the Orch OR-relevant quantum substrate. This identification is *not* established; we defend its status as a hypothesis in Section 8.

2.3 The resource is subradiance, not superradiance

A point of physics must be made precisely, because it is frequently inverted in informal treatments of this topic. The coherence-protecting resource is the *subradiant* manifold, not superradiance. Superradiant states couple strongly to the radiation field and therefore decay rapidly; they emit and are lost. Subradiant (dark) states couple weakly to the field and are correspondingly long-lived: on the tens-of-seconds scale reported by Babcock et al. (2024), and it is precisely this weak coupling that makes them resistant to radiative decoherence. A mechanism that expanded conscious processing by protecting coherence would therefore have to *increase the population and stability of subradiant states*, not drive the system to superradiance. We accordingly describe the relevant transition throughout as entry into a cooperative-coupling regime within which subradiant dark states become populated, and we avoid the phrase "superradiance threshold," which would name the opposite of the intended resource.

3 Two candidate routes from psychedelic to microtubule

A central honest difficulty for any microtubule hypothesis of psychedelic action is the absence, at present, of *any* demonstrated direct interaction between DMT, LSD or psilocin and the tubulin lattice. Every robust link between psychedelics and the cytoskeleton runs through receptor signalling and downstream structural plasticity (Section 3.1). We therefore set out two candidate routes and are explicit that both are, at the microtubule level, hypotheses.

3.1 Route 1: the indirect receptor-signalling route

The first route runs through the canonical pharmacology. A substantial fraction of the neuronal 5-HT_{2A} receptor pool is intracellular rather than surface-expressed; in adult cortical pyramidal neurons the receptor is predominantly intracellular and co-localises with the microtubule-associated protein MAP1A in dendrites (Cornea-Hébert et al., 2002), and the plasticity-promoting action of psychedelics requires this intracellular pool (Vargas et al., 2023). Canonical 5-HT_{2A} signalling proceeds through $G\alpha_q$/phospholipase-C to release intracellular Ca^{2+}.

The proposed terminal step is that this Ca^{2+} transient perturbs the tubulin tryptophan network. Two features of tubulin calcium handling constrain this. Tubulin presents a single high-affinity Ca^{2+} site ($K_d \approx 3.2$ μM) and approximately sixteen low-affinity sites ($K_d \approx 280$ μM) (Solomon, 1977), and calcium-induced microtubule depolymerisation is a high-micromolar-to-millimolar effect (O'Brien et al., 1997). Physiological IP_3-evoked transients (of order 0.1 to 1 μM) therefore produce only graded, sub-saturating occupancy of the high-affinity site and never approach the depolymerising regime; on this route the calcium-induced perturbation is monotonic and lies entirely within the polymer-stabilising window. The proposed physical channel for the perturbation is a cation/π interaction between Ca^{2+} and the indole rings, such interactions are known to dislocate the indole HOMO charge density and shift its electronic transition (Juszczak and Eisenberg, 2017), although that work concerns amine and alkali cations and the demonstration for Ca^{2+} specifically has not

been made. A supporting consideration is that Ca^{2+} is redox-inactive and so, unlike transition-metal cations, cannot quench tryptophan by photoinduced electron transfer; a cation/π-driven conformational perturbation is therefore the only plausible channel by which it could act on the indole electronic state. That such a perturbation *redistributes excitonic population into subradiant states* is the novel and unproven claim; it is the central prediction of Section 7, not an established finding. We note that no published study links a calcium-induced change in inter-tryptophan geometry to a change in collective sub- or super-radiant state populations.

3.2 Route 2: the direct indole-coupling route

The second route is more speculative but has a feature that makes it worth stating: it does not depend on the receptor-signalling cascade at all, and is therefore insulated from the G_i/G_q question discussed in Section 5. Its premise is structural. Tryptophan's chromophore is the indole ring, and DMT, psilocin and LSD all contain an indole moiety. A molecule sharing the network's chromophore could, in principle, couple to the tryptophan exciton network directly, as an additional chromophore that participates in, and thereby alters, the collective excitonic states.

This possibility has been examined computationally. Colbourne et al. (2026) docked a library of substituted tryptamines to tubulin and incorporated the bound ligands as additional chromophores in a tight-binding model of the tryptophan exciton network, concluding that tryptamine binding can modify the excitonic landscape in a ligand-dependent manner. We flag one caution: this is static-docking plus isolated-ligand excited-state theory, not a wet-lab measurement, and the spectroscopic test remains undone. Importantly for the symmetry hypothesis, their result for LSD specifically was a *localised* ligand-centred state with negligible reorganisation of the tryptophan manifold, that is, in that model LSD did *not* strongly enhance delocalisation. If borne out, this would mean the direct route does not support the reverse-anaesthetic symmetry for LSD, even if it does for the smaller tryptamines DMT and psilocin, whose indole structures are closer to tryptophan itself. We return to this as a potential second axis of DMT/LSD divergence in Section 4.

4 DMT, LSD and psilocin as distinct temporal envelopes

The most direct recent pharmacology bears on what does *not* distinguish the classic psychedelics: a systematic comparison found that the tested classic psychedelics are unbiased partial 5-HT_{2A} agonists, with a threshold level of G_q-signalling efficacy, rather than bias between transducers, separating psychedelic from non-psychedelic activity among this class (Wallach et al., 2023). The same study also engineered deliberately β-arrestin-biased 5-HT_{2A} ligands that block psychedelic-like effects, showing that biased signalling can independently produce non-hallucinogenic outcomes in purpose-built compounds: so bias is not irrelevant in general, only among the naturally occurring classic psychedelics themselves. We therefore do not attribute the qualitative differences between the classic compounds to a binary difference in signalling bias. On the indirect route (Section 3.1), the compound-specific variable is instead the *temporal envelope* of the calcium signal, set by receptor

residence time; on the direct route (Section 3.2), it is the compound-specific way each indole couples to the network.

DMT. In behavioural studies, the relevant 5-HT$_{2A}$-mediated effects of *N*-methyltryptamines are arrestin-independent in vivo (Schmid and Bohn, 2010); we therefore describe DMT as arrestin-independent in vivo rather than as "Gα_q-biased." DMT binds and dissociates rapidly, consistent with a brief, high-amplitude calcium transient on the indirect route. DMT also regulates sigma-1 receptors (Fontanilla et al., 2009) and increases neuronal differentiation markers through sigma-1 (Morales-García et al., 2020), but its sigma-1 affinity is orders of magnitude below its 5-HT$_{2A}$ affinity, so we treat sigma-1 as a modulator rather than the core route.

LSD. LSD is distinguished structurally by an extracellular-loop "lid" that traps it at the receptor and produces an exceptionally slow off-rate (Wacker et al., 2017), consistent on the indirect route with a prolonged, lower-amplitude calcium envelope rather than an acute flash. That LSD's subjective and neural effects are 5-HT$_{2A}$-mediated is established by ketanserin blockade, which abolishes the subjective response when given before LSD (Preller et al., 2017) and shortens and attenuates it when given afterward, without altering LSD pharmacokinetics (Becker et al., 2023).

Psilocin. Psilocin (the active metabolite of psilocybin) sits between DMT and LSD in receptor kinetics and is expected, on the indirect route, to produce an intermediate calcium envelope. Its position can be read quantitatively from comparative signalling kinetics (Wallach et al., 2023).

A possible second axis of divergence. If the direct route (Section 3.2) contributes, then the structural difference between the simple tryptamines (DMT, psilocin) and the ergoline LSD provides a second, signalling-independent reason the compounds might differ: the computational result of Colbourne et al. (2026) suggests LSD couples to the tryptophan network in a qualitatively different (localised) way. We present this as a hypothesis to be tested, not a result.

For the systems-level contrast, we note only that psychedelics are proposed to broadly increase measures of cortical entropy and global integration, per the entropic-brain framework (Carhart-Harris et al., 2014), the macroscopic opposite of the anaesthetic state; we do not treat this as microtubule-level evidence. The companion preprint develops signal diversity of this kind as a candidate proxy for the amount of experience; we do not put it to that use here.

5 Reconciling the signalling route with G$_i$-dependent hallucinogenesis

The indirect route as stated routes through Gα_q-driven calcium release, and a recent finding complicates this. Xu et al. (2026), using in vitro and in vivo approaches and five cryo-EM structures of 5-HT$_{2A}$/G protein complexes (including psilocin- and DOI-bound 5-HT$_{2A}$-G$_i$ complexes), reported that 5-HT$_{2A}$-mediated non-canonical G$_i$ signalling is essential for the hallucinogenic effect,

and identified a G_q-biased compound (DOI-NBOMe) that produced therapeutic-like effects in mice *without* hallucinogenic effect. We take this finding seriously and do not attempt to explain it away.

Three observations frame how it bears on the present hypothesis. First, it stands in tension with the report that G_q efficacy predicts psychedelic potency (Wallach et al., 2023); the field is not settled, and we present our framework as one position within a live dispute rather than as resting on a closed question. Second, and most consequentially for the indirect route, the canonical route to intracellular calcium (and hence to the tubulin perturbation of Section 3.1) runs through $G\alpha_q$, not G_i. If hallucinogenesis is G_i-dependent and the G_q-driven calcium arm is dispensable for hallucination (Xu et al., 2026), then a calcium-to-microtubule mechanism would, on that evidence, track the *therapeutic* (G_q) axis of psychedelic action rather than the *hallucinogenic* (G_i) one. This is a substantial qualification: it suggests the indirect route, if real, may be more relevant to the plasticity-related and therapeutic effects of psychedelics than to the generation of altered perceptual phenomenology. Third, the direct route (Section 3.2) is largely insulated from this complication, because it does not pass through any G protein.

We therefore state the position of the indirect route conditionally and modestly: it proposes a G_q/calcium-linked microtubule-modulating arm of psychedelic action that may contribute to therapeutic and plasticity-related effects, and we do not claim it is sufficient for, or even necessarily central to, hallucinogenesis. Whether microtubule modulation contributes to the perceptual effects is left to the direct route and to experiment.

6 Calcium-dependent excitonic redistribution as a prediction

The claim that a physiological calcium transient redistributes tubulin tryptophan excitons into long-lived subradiant states is, to our knowledge, untested. We make it explicit as a prediction with a defined direction. Precedent establishes only the weaker components, that tubulin tryptophan fluorescence reports conformational state (Guha et al., 1996), that calcium binds tubulin at defined affinities (Solomon, 1977; O'Brien et al., 1997), and that cation/π contact perturbs indole electronics (Juszczak and Eisenberg, 2017). The step from these to a change in collective subradiant-state population is the hypothesis. Section 7 gives the spectroscopic signatures that would confirm or falsify it.

7 Experimental predictions

We separate the decisive near-term experiment from supporting predictions, and we mark those that are conditional on the still-unproven redistribution step of Section 6.

Prediction 1 (decisive; the psychedelic mirror of the anaesthetic experiment). The experiment of Kalra et al. (2023) (measurement of tryptophan exciton migration length in stabilised microtubules) has never been run with psychedelics. We predict that DMT and psilocin, applied

directly to microtubule preparations, will *increase* the exciton migration length above the ∼6.6 nm baseline, mirroring the decrease to ∼5.6 to 5.8 nm that anaesthetics produce. This is the most direct possible test of the reverse-anaesthetic symmetry. A null result or a decrease would substantially weaken the hypothesis. Because this assay uses microtubule preparations rather than intact signalling, a positive result would also support the *direct* route (Section 3.2); running it with and without intact receptor signalling would begin to separate the two routes. We note that the computational result of Colbourne et al. (2026) predicts a weaker or absent effect for LSD specifically, which this experiment would test directly. Separately, the companion preprint notes that the same assay, read with an additional spectroscopic observable, bears on a downstream question: whether any expanded dark-state population is *recruitable* into reduction or *inert*, a question that lies beyond the substrate claim made here.

Prediction 2 (subradiant signature). If the mechanism is subradiant-state population rather than bright-state enhancement, then under conditions that increase migration length the tryptophan ensemble should show *reduced* steady-state fluorescence yield (population moved into dark states) together with a *lengthened* fluorescence lifetime and slowed anisotropy decay. A simple increase in bright-state emission would be evidence *against* the proposed mechanism.

Prediction 3 (microtubule dependence of the psychedelic response). Mirroring Khan et al. (2024) and Emerson et al. (2013), microtubule-stabilising agents (e.g. epothilone B) and destabilising agents should modulate any microtubule-linked optical/coherence marker of psychedelic action, and (more speculatively) should modulate the behavioural psychedelic response, with appropriate 5-HT_{2A} controls.

Prediction 4 (calcium concentration window; conditional). On the indirect route, agents that prolong or buffer the sub-micromolar phase of the calcium transient without changing its peak should modulate the optical/coherence marker differently from agents that change the peak amplitude. This follows from the two-site calcium model (Solomon, 1977) and distinguishes the proposed mechanism from a simple "more calcium, more effect" account.

Prediction 5 (route dissociation via G_i/G_q; conditional). If, following Xu et al. (2026), hallucinogenesis is G_i-dependent while the microtubule-modulating arm is G_q/calcium-linked, then G_q-biased and G_i-biased compounds should dissociate: a G_q-biased, non-hallucinogenic compound (e.g. DOI-NBOMe) should still produce the microtubule optical/coherence signature, whereas behavioural hallucinogenic potency should track G_i engagement. Observing this dissociation would support the modest, therapeutic-arm framing of Section 5; failing to observe it would require revising the indirect route.

Prediction 6 (compound-specific envelopes; conditional). On the indirect route, the temporal envelope of any optical/coherence marker should differ across compounds in the manner

predicted by their receptor kinetics: a brief, high-amplitude response for DMT; a prolonged, lower-amplitude response for LSD; an intermediate response for psilocin.

Prediction 7 (compound-specific coupling; conditional on the direct route). If the direct route contributes, the simple tryptamines (DMT, psilocin) and the ergoline LSD should differ in how they alter the tryptophan exciton network, with LSD producing a more localised perturbation (Colbourne et al., 2026). This is testable by the same spectroscopic methods as Prediction 1.

8 Limitations and unresolved gaps

We state the framework's principal weaknesses plainly, because an honest account of them is more useful than a polished one that conceals them.

Orch OR is not established. The proposal that microtubule quantum processes participate in consciousness is a minority position and is not proven. This paper does not prove it; it assumes it conditionally and asks what would follow. If Orch OR is false, the systems-level and consciousness-related interpretation of the present hypothesis falls away, although the narrower, testable claim (that psychedelics alter microtubule tryptophan photophysics) could still hold and remain worth testing in its own right.

The exciton-to-conformation bridge is not derived. This is the deepest gap. The coherence-protecting resource we invoke is *electronic* (the tryptophan exciton manifold), whereas the objective reduction of Orch OR acts on *conformational* (mass) superpositions of tubulin. These are distinct physical degrees of freedom, and no derivation in the literature connects protection of the former to extension of the latter. We do not supply one. We note only that electronic and conformational coordinates are vibronically coupled in real molecules, so the relationship is in principle a question of coupling magnitude rather than of category; quantifying it, an explicit coupling constant linking exciton, phonon and conformational degrees of freedom for the tubulin lattice, is a decisive theoretical requirement that remains outstanding. The strongest existing attempt to bridge electronic/dipolar and conformational dynamics, via coherent Fröhlich condensation, was argued to be physically untenable in the biological regime (Reimers et al., 2009), and we do not rest the bridge on it.

The calcium-to-subradiant step is a prediction, not a finding. As stated in Sections 3.1 and 6, no study demonstrates that a calcium transient redistributes tubulin tryptophan excitons into subradiant states. This is the central empirical claim of the indirect route and is presently unproven.

No psychedelic has been shown to act directly on microtubules. The direct route (Section 3.2) rests on a single computational study (Colbourne et al., 2026), whose LSD result in fact

points against the symmetry for that compound. The decisive wet-lab experiment (Prediction 1) has not been performed.

The decoherence gap is unclosed. Even the most favourable corrected estimate of microtubule coherence times (Hagan et al., 2002) falls orders of magnitude short of neural timescales, and the long-lived states we invoke (Babcock et al., 2024) are a property of organised tryptophan networks under specific modelling assumptions whose in vivo realisation is unconfirmed. The historical precedent of long-lived electronic coherence in photosynthesis (Engel et al., 2007) has itself been reinterpreted as predominantly vibrational (Duan et al., 2017), and cannot be transferred uncritically.

The G_i finding qualifies the signalling route. As discussed in Section 5, Xu et al. (2026) implies the G_q/calcium arm may be more relevant to therapeutic than to hallucinogenic effects, which constrains how much of psychedelic phenomenology the indirect route can claim to address.

DMT polypharmacology. DMT's sigma-1 and other receptor interactions (Fontanilla et al., 2009) mean that even its 5-HT_{2A}-linked effects are not cleanly isolated.

The molecule-to-experience gap. Finally, we do not claim that any microtubule-level mechanism explains the *content* of psychedelic experience. There is no principled mapping from the state space of a chromophore network to perceived form, in the way that the retinocortical map grounds the cortical theory of geometric visual hallucinations (Bressloff et al., 2001; Ermentrout and Cowan, 1979; Klüver, 1966). Connecting molecular coherence to phenomenology is unsolved, and we do not present the present hypothesis as solving it. A companion preprint takes up precisely this gap, separating the amount of an experience from its form: it assigns the geometric structure of visual phenomenology to the classical cortical model cited above and leaves the non-visual remainder explicitly open. We do not pursue that layer here.

9 Discussion

The contribution of this paper is narrow and, we hope, correspondingly defensible. The anaesthetic side of the proposed symmetry rests on real measurements: anaesthetics bind tubulin, reduce tryptophan exciton migration (Kalra et al., 2023), and microtubule stabilisation opposes anaesthetic action (Khan et al., 2024; Emerson et al., 2013). The psychedelic side is, at present, a hypothesis, that these indole-bearing molecules act in the opposite direction at the same substrate: supported by structural plausibility and one computational study, and not yet by any direct measurement. We have tried to state the symmetry where it is strongest (as a directional, substrate-level contrast anchored in the anaesthetic data) and to be candid where it is weakest (the unmeasured psychedelic effect, the underived exciton-to-conformation bridge, and the unproven involvement of microtubule quantum processes in consciousness).

The framework's value, if it has any, is that it is falsifiable and that the decisive experiment is feasible with existing apparatus. Running the Kalra et al. (2023) assay with DMT, psilocin and LSD would, in a single well-precedented measurement, either reveal the predicted mirror-image increase in exciton migration or fail to, and a failure would be as informative as a success. The two-route structure also makes a sharper experimental program possible: the same assay, performed with and without intact receptor signalling, begins to separate a direct chromophore-coupling mechanism from an indirect calcium-mediated one, and the G_i/G_q dissociation of Prediction 5 connects the framework to the most current pharmacology (Xu et al., 2026). We regard the most likely outcome, on present evidence, to be that any psychedelic/microtubule effect is partial and compound-specific (plausibly weaker for LSD, whose computed coupling to the tryptophan network is localised rather than delocalising (Colbourne et al., 2026), than for the simple tryptamines, which that computation did not examine) and more relevant to therapeutic and plasticity-related effects than to perceptual phenomenology. That would be a more modest result than the "reverse anaesthetic" slogan suggests, but it would be a real one, and it is the version the evidence can currently bear.

10 Conclusion

General anaesthetics contract a measurable microtubule excitonic property as they abolish consciousness. We have asked whether classic psychedelics expand the same property, and have set out a conditional, falsifiable hypothesis, with two candidate routes to the microtubule, a corrected subradiant-state mechanism, an explicit reconciliation with G_i-dependent hallucinogenesis, and a decisive unperformed experiment, while being explicit that the psychedelic half of the symmetry is presently untested and that the framework's deepest assumptions (the involvement of microtubule quantum processes in consciousness, and the bridge from electronic to conformational coherence) remain unresolved. The strongest claim the present evidence supports is not that psychedelics are reverse anaesthetics, but that they *might* be, at the level of the tubulin tryptophan network, and that a single feasible experiment would tell us whether to take the possibility further.

Funding

This research received no external funding.

Conflict of Interest

The author declares no conflict of interest.

References

Babcock, N. S., Montes-Cabrera, G., Oberhofer, K. E., Chergui, M., Celardo, G. L., and Kurian, P. (2024). Ultraviolet superradiance from mega-networks of tryptophan in biological architectures. *The Journal of Physical Chemistry B*, 128(17):4035–4046.

Becker, A. M., Klaiber, A., Holze, F., Istampoulouoglou, I., Duthaler, U., Varghese, N., Eckert, A., and Liechti, M. E. (2023). Ketanserin reverses the acute response to LSD in a randomized, double-blind, placebo-controlled, crossover study in healthy participants. *International Journal of Neuropsychopharmacology*, 26(2):97–106.

Bressloff, P. C., Cowan, J. D., Golubitsky, M., Thomas, P. J., and Wiener, M. C. (2001). Geometric visual hallucinations, Euclidean symmetry and the functional architecture of striate cortex. *Philosophical Transactions of the Royal Society B*, 356(1407):299–330.

Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E., Chialvo, D. R., and Nutt, D. (2014). The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience*, 8:20.

Celardo, G. L., Angeli, M., Craddock, T. J. A., and Kurian, P. (2019). On the existence of superradiant excitonic states in microtubules. *New Journal of Physics*, 21(2):023005.

Colbourne, M. T., Gassab, L., and Craddock, T. J. A. (2026). Effects of substituted tryptamines on the excitonic structure of the tubulin tryptophan network. *Photonics*, 13(7):636.

Cornea-Hébert, V., Watkins, K. C., Roth, B. L., Kroeze, W. K., Gaudreau, P., Leclerc, N., and Descarries, L. (2002). Similar ultrastructural distribution of the 5-HT2A serotonin receptor and microtubule-associated protein MAP1A in cortical dendrites of adult rat. *Neuroscience*, 113(1):23–35.

Craddock, T. J. A., Kurian, P., Preto, J., Sahu, K., Hameroff, S. R., Klobukowski, M., and Tuszyński, J. A. (2017). Anesthetic alterations of collective terahertz oscillations in tubulin correlate with clinical potency: Implications for anesthetic action and post-operative cognitive dysfunction. *Scientific Reports*, 7:9877.

Duan, H.-G., Prokhorenko, V. I., Cogdell, R. J., Ashraf, K., Stevens, A. L., Thorwart, M., and Miller, R. J. D. (2017). Nature does not rely on long-lived electronic quantum coherence for photosynthetic energy transfer. *Proceedings of the National Academy of Sciences*, 114(32):8493–8498.

Emerson, D. J., Weiser, B. P., Psonis, J., Liao, Z., Taratula, O., Fiamengo, A., Wang, X., Sugasawa, K., Smith III, A. B., Eckenhoff, R. G., and Dmochowski, I. J. (2013). Direct modulation of microtubule stability contributes to anthracene general anesthesia. *Journal of the American Chemical Society*, 135(14):5389–5398.

Engel, G. S., Calhoun, T. R., Read, E. L., Ahn, T.-K., Mančal, T., Cheng, Y.-C., Blankenship, R. E., and Fleming, G. R. (2007). Evidence for wavelike energy transfer through quantum coherence in photosynthetic systems. *Nature*, 446(7137):782–786.

Ermentrout, G. B. and Cowan, J. D. (1979). A mathematical theory of visual hallucination patterns. *Biological Cybernetics*, 34(3):137–150.

Fontanilla, D., Johannessen, M., Hajipour, A. R., Cozzi, N. V., Jackson, M. B., and Ruoho, A. E. (2009). The hallucinogen N,N-dimethyltryptamine (DMT) is an endogenous sigma-1 receptor regulator. *Science*, 323(5916):934–937.

Guha, S., Rawat, S. S., Chattopadhyay, A., and Bhattacharyya, B. (1996). Tubulin conformation and dynamics: A red edge excitation shift study. *Biochemistry*, 35(41):13426–13433.

Hagan, S., Hameroff, S. R., and Tuszyński, J. A. (2002). Quantum computation in brain microtubules: Decoherence and biological feasibility. *Physical Review E*, 65(6):061901.

Hameroff, S. R. and Penrose, R. (2014). Consciousness in the universe: A review of the 'orch or' theory. *Physics of Life Reviews*, 11(1):39–78.

Juszczak, L. J. and Eisenberg, A. S. (2017). The color of cation-π interactions: Subtleties of amine–tryptophan interaction energetics allow for radical-like visible absorbance and fluorescence. *Journal of the American Chemical Society*, 139(24):8302–8311.

Kalra, A. P., Benny, A., Travis, S. M., Zizzi, E. A., Morales-Sánchez, A., Oblinsky, D. G., Craddock, T. J. A., Hameroff, S. R., MacIver, M. B., Tuszyński, J. A., Petry, S., Penrose, R., and Scholes, G. D. (2023). Electronic energy migration in microtubules. *ACS Central Science*, 9(3):352–361.

Khan, S., Huang, Y., Timuçin, D., Bailey, S., Lee, S., Lopes, J., Gaunce, E., Mosberger, J., Zhan, M., Abdelrahman, B., Zeng, X., and Wiest, M. C. (2024). Microtubule-stabilizer epothilone b delays anesthetic-induced unconsciousness in rats. *eNeuro*, 11(8):ENEURO.0291–24.2024.

Klüver, H. (1966). *Mescal and Mechanisms of Hallucinations*. University of Chicago Press, Chicago.

Kurian, P., Obisesan, T. O., and Craddock, T. J. A. (2017). Oxidative species-induced excitonic transport in tubulin aromatic networks: Potential implications for neurodegenerative disease. *Journal of Photochemistry and Photobiology B: Biology*, 175:109–124.

Morales-García, J. A., Calleja-Conde, J., López-Moreno, J. A., Alonso-Gil, S., Sanz-SanCristobal, M., Riba, J., and Pérez-Castillo, A. (2020). N,N-dimethyltryptamine compound found in the hallucinogenic tea ayahuasca, regulates adult neurogenesis in vitro and in vivo. *Translational Psychiatry*, 10:331.

O'Brien, E. T., Salmon, E. D., and Erickson, H. P. (1997). How calcium causes microtubule depolymerization. *Cell Motility and the Cytoskeleton*, 36(2):125–135.

Penrose, R. (1996). On gravity's role in quantum state reduction. *General Relativity and Gravitation*, 28(5):581–600.

Preller, K. H., Herdener, M., Pokorny, T., Planzer, A., Kraehenmann, R., Stämpfli, P., Liechti, M. E., Seifritz, E., and Vollenweider, F. X. (2017). The fabric of meaning and subjective effects in LSD-induced states depend on serotonin 2A receptor activation. *Current Biology*, 27(3):451–457.

Reimers, J. R., McKemmish, L. K., McKenzie, R. H., Mark, A. E., and Hush, N. S. (2009). Weak, strong, and coherent regimes of fröhlich condensation and their applications to terahertz medicine and quantum consciousness. *Proceedings of the National Academy of Sciences*, 106(11):4219–4224.

Schmid, C. L. and Bohn, L. M. (2010). Serotonin, but not N-methyltryptamines, activates the serotonin 2A receptor via a β-arrestin2/Src/Akt signaling complex in vivo. *Journal of Neuroscience*, 30(40):13513–13524.

Solomon, F. (1977). Binding sites for calcium on tubulin. *Biochemistry*, 16(3):358–363.

Tegmark, M. (2000). Importance of quantum decoherence in brain processes. *Physical Review E*, 61(4):4194–4206.

Vargas, M. V., Dunlap, L. E., Dong, C., Carter, S. J., Tombari, R. J., Jami, S. A., Cameron, L. P., Patel, S. D., Hennessey, J. J., Saeger, H. N., McCorvy, J. D., Gray, J. A., Tian, L., and Olson, D. E. (2023). Psychedelics promote neuroplasticity through the activation of intracellular 5-HT2A receptors. *Science*, 379(6633):700–706.

Wacker, D., Wang, S., McCorvy, J. D., Betz, R. M., Venkatakrishnan, A. J., Levit, A., Lansu, K., Schools, Z. L., Che, T., Nichols, D. E., Shoichet, B. K., Dror, R. O., and Roth, B. L. (2017). Crystal structure of an LSD-bound human serotonin receptor. *Cell*, 168(3):377–389.e12.

Wallach, J., Cao, A. B., Calkins, M. M., Heim, A. J., Lanham, J. K., Bonniwell, E. M., Hennessey, J. J., Bock, H. A., Anderson, E. I., Sherwood, A. M., Morris, H., de Klein, R., Klein, A. K., Cuccurazzu, B., Gamrat, J., Fannana, T., Zauhar, R., Halberstadt, A. L., and McCorvy, J. D. (2023). Identification of 5-HT2A receptor signaling pathways associated with psychedelic potential. *Nature Communications*, 14:8221.

Xu, Z., Wang, H., Yu, J., Deng, Y., Tian, X., Ni, R., Xia, F., Yang, L., Xu, C., Zhang, L., Luo, R., Chen, P., Zhang, X., Liu, Y., Hou, J., Zhang, M., Chen, S., Su, L., Sun, H., He, Y., Chen, D., Chen, X., Miao, Z., Xie, J., Liu, X., Zhao, J., Ke, B., Tian, X., Zeng, L., Zhang, L., Tang, X., Yang, S., Liu, J., Wang, X., Yan, W., and Shao, Z. (2026). Psychedelics elicit their effects by 5-HT2A receptor-mediated Gi signalling. *Nature*, 651:829–837. A Publisher Correction was issued (Nature 651, E5, 2026; doi:10.1038/s41586-026-10249-5), correcting typographical superscript errors only; it does not affect the reported findings.