Brain and Cognition 84 (2014) 109–117

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Theoretical Integration

Neuroscience, quantum indeterminism and the Cartesian soul

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ARTICLE INFO

Article history:
Accepted 21 November 2013

Keywords:
Quantum theory
Dualism
Soul
Determinism
Heisenbergian uncertainty
Cartesian interactionism

ABSTRACT

Quantum indeterminism is frequently invoked as a solution to the problem of how a disembodied soul might interact with the brain (as Descartes proposed), and is sometimes invoked in theories of libertarian free will even when they do not involve dualistic assumptions. Taking as example the Eccles–Beck model of interaction between self (or soul) and brain at the level of synaptic exocytosis, I here evaluate the plausibility of these approaches. I conclude that Heisenbergian uncertainty is too small to affect synaptic function, and that amplification by chaos or by other means does not provide a solution to this problem. Furthermore, even if Heisenbergian effects did modify brain functioning, the changes would be swamped by those due to thermal noise. Cells and neural circuits have powerful noise-resistance mechanisms, that are adequate protection against thermal noise and must therefore be more than sufficient to buffer against Heisenbergian effects. Other forms of quantum indeterminism must be considered, because these can be much greater than Heisenbergian uncertainty, but these have not so far been shown to play a role in the brain.

1. Introduction

From the very moment of its formulation in the mid 17th C, Descartes' conception of an immaterial *rational soul* (or just *soul*, or *mind*) interacting with the human body-machine has been controversial, but it remained a powerful force in philosophy until well into the 20th century.[1] It subsequently declined owing to serious challenges from both philosophy and neuroscience, but in recent years there have been numerous attempts to promote modified forms of Cartesian dualism (also called *interactionist dualism* or *Cartesian interactionism* or just *interactionism*), motivated often by paranormal phenomena (Kelly, Kelly, & Crabtree, 2006) such as near-death experiences (Carter, 2010; Van Lommel, 2010) or sometimes by metaphysical considerations (Goetz & Taliaferro, 2011; Swinburne, 2013). If the conventional physical forces at work in the brain exerted a control that was completely deterministic, there would be no scope for the postulated nonphysical soul to act, so modern versions of Cartesian interactionism often follow Eccles and Beck (Beck & Eccles, 1992; Eccles, 1986) in invoking quantum indeterminism as a solution to this problem. Such approaches have been cogently criticized (Smith, 2009; Wilson, 1999), but counterarguments are sometimes advanced as is discussed below. I here extend the arguments of Wilson and Smith so as to address the counterarguments, emphasizing quantitative considerations and the inherent resistance of neural function to minor perturbations.

Some writings relating consciousness to quantum theory focus on other aspects of the theory than indeterminism (Penrose, 1994). These are beyond the scope of the present paper, but they have been criticized elsewhere (McKemmish, Reimers, McKenzie, Mark, & Hush, 2009; Smith, 2009; Tegmark, 2000).

1.1. Cartesian mechanism and interactionism

Descartes believed that animals were mindless hydraulic (or more strictly pneumatic[2]) machines. He thought the driving fluids of these machines were the *animal spirits*, which had been invoked by many classical and mediaeval thinkers from Alcmaeon and Plato onwards as being a kind of volatile substance that flowed along nerves, considered (wrongly, of course) to be hollow tubes. Their flow was considered to be controlled by filaments that operated tiny "valvules" in the nerves and in the ventricles of the brain. Descartes attempted to explain reflex movements by the flow of animal spirits. External stimuli would move the skin that would in turn pull on the filaments and hence open valvules to release the flow, ultimately affecting the muscles and producing movement. His idea was not, however, limited to simple movements. He also tried to analyze

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[1] There have been two main notions of soul in western thought. The Platonic (and Augustinian) tradition postulated a separate, interacting soul, whereas the Aristotelian (and Thomistic) tradition postulated an embodied soul, which was thought to be an internal principle inherent in the body, not a separate entity. In postulating a separate, interacting soul Descartes aligned himself with the Platonic tradition. We are here concerned only with the interacting soul postulated by Descartes.

[2] Descartes' model is often described as "hydraulic" but the term 'pneumatic' would be more accurate because he envisaged the driving fluids (the animal spirits) as being more like a gas than a liquid.

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http://dx.doi.org/10.1016/j.bandc.2013.11.008

sensation, and in *Passions of the Soul* (1649) even emotions, as being due to the way animal spirits were induced to flow from the periphery to the brain ventricles as a result of external events.

But Descartes held that *man* was more than a machine. Drawing on the dualistic philosophy that had been so important to many earlier Platonist thinkers on the mind-brain relationship including Galen, he proposed that man was a *soul in a machine.* Human reflex actions and emotions were explained on the same mechanical basis as in animals, but human voluntary thought and behaviour required an interaction between the material automaton and the immaterial, indivisible *rational soul* (or just *soul*), which Descartes considered to lack spatial extension and location. He maintained that the interaction occurred in the pineal gland, where the rational soul redirected small tissue movements so as to regulate the flow of animal spirits, and where the animal spirits could affect the soul. He chose the pineal gland as the site for body-soul interaction because it is a single, unpaired structure appropriate for interaction with a unique soul, and because he believed (incorrectly) that it protruded into the middle (3rd) ventricle and was thus well placed for influencing the movements of the animal spirits.

Descartes' conception of body-soul interaction was strongly critiqued from the very start. The pineal gland as site of body-soul liaison was soon abandoned, but other sites such as the corpus callosum were then proposed (Gaukroger, 1995). More important for our present concerns are early criticisms of the very notion that an immaterial soul could interact with a material body. One of the first protagonists in this debate was the brilliant Princess Elizabeth of Bohemia (oldest daughter of King James VI and I of Scotland and England), who maintained a long correspondence with Descartes. She argued that an immaterial soul could never interact with a material body, and wrote:

> "... *it would be easier for me to concede matter and extension to the soul than to concede the capacity to move a body and to be moved by it to an immaterial thing.*" Princess Elizabeth of Bohemia to Descartes, June 10–20, 1643 (Shapiro, 2007).

This *interaction problem* is the main focus of this paper, but it is by no means the only criticism that can be raised against Cartesian interactionism. To avoid misunderstanding on this point, I now briefly mention other kinds of criticism.

1.2. Modern criticisms of Cartesian interactionism

1.2.1. Criticisms from philosophy

Interactionism has been strongly criticized by philosophers, especially since the 1950s. Linguistic philosophers in the Wittgensteinian tradition such as Gilbert Ryle argued that interactionism was an attempt to solve a non-problem. They claimed that it is an error to ask how mental and biological states fit together, because combining mind language and brain language in the same sentence is a source of confusion. Others, such as U.T. Place and Herbert Feigl argued in the 1950s that the mind and the brain were identical, and their *mind-brain identity* thesis has since become a major position in the philosophy of mind. Still others argue that mind and brain are not so much identical as *complementary aspects* of a single underlying entity (Chalmers, 1996; Murphy & Brown, 2007); this view has a variety of names including *neutral monism* and *dual-aspect theory*. Still others have chosen radical positions according to which either matter does not exist (idealism) or mind does not exist (eliminative materialism). In short, the philosophy of mind is as controversial as ever, but Cartesian interactionism is a minority view. It does however still have some supporters and their number seems to be growing (Goetz & Taliaferro, 2011; Madell, 2010; Swinburne, 2013).

1.2.2. Criticisms from neuroscience

A very strong attack on Cartesian interactionism has come from neuroscience. There is an enormous amount of relevant data, from many different levels of analysis. Cellular neuroscience is providing a detailed mechanistic understanding of how neurons function and communicate with each other. *In vivo* studies are showing how neural circuits analyze visual scenes, pre-programme movements and store memories. And computational studies are testing and refining our understanding of how neural circuits function. It would be beyond our scope to review this vast wealth of data, since most readers of this journal will be well acquainted with it, but it is worth emphasizing two conclusions that can be drawn:

1. Brain activity does not merely parallel mind activity, it causes it, as is shown by the results of brain stimulation.
2. In several cases, as in visual perception or memory storage and retrieval, we understand in some detail how the neural circuits perform operations underlying cognition, without any need for an interacting soul, and can confirm this by simulation.

It is difficult for an interactionist dualist to explain such findings if he believes, as Descartes did, that cognitive functions are performed by the soul and not by the brain.

2. Current day interactionism: a distributed and limited role for the soul or self

The most clearly formulated and most frequently cited modern model for Cartesian dualism is that of Nobel prize-winning neurophysiologist Sir John Eccles (1903–1997), especially the version that he elaborated with physicist Friedrich Beck (Beck & Eccles, 1992; Eccles, 1992, 1995). Recent supporters of Cartesian dualism continue to use this model or ones resembling it (Beck, 2008; Hari, 2008; Stapp, 2009). The model incorporates some but not all aspects of Descartes' original version. Like the latter, it postulates a separate nonphysical self (or soul or mind) interacting bidirectionally with the brain, but it rejects Descartes' notion of a unique site of soul-brain liaison, and instead posits a distributed array of liaison sites. These are postulated to occur in cortical modules, each containing a few thousand neurons, distributed through many parts of the cerebral cortex, particularly in the dominant hemisphere. Eccles generally called the supposed nonphysical interacting entity the "self" or the "mind", because he felt that these terms were more metaphysically neutral than "soul", but he did not object to the term soul. He speculated that the self interacts only with certain modules, which he called "open modules"(Eccles, 1979, 1980). He further suggested that the self is "microgranular", being composed of multiple "psychons", and that within the open modules each psychon would interact with the numerous synapses on a "dendron" consisting of a bundle of apical dendrites belonging to pyramidal neurons (Eccles, 1992). He argued that the open modules must be influenced by the self in situations of conscious volition, and could also be scanned by the self. Thus, the interaction would be bidirectional, self-to-brain and brain-to-self.

Another difference between this model and that of Descartes is that it postulates a much more limited role for the self or soul. To Descartes, almost the whole of cognition was performed by the separate, immaterial soul, not by the brain, but this strong claim is clearly untenable in the light of modern neuroscience. Eccles made only the weaker claim that the "self-conscious mind" (or "self" or "soul" etc.) exerted a "superior interpretative and controlling role...so that there is a unified conscious experience of a global or gestalt character" (lecture 2 in (Eccles, 1980)) and also for intentionality (Beck & Eccles, 1992).

This idea that the soul's role might be limited to certain aspects of cognition, including intentionality, was shared by another eminent neuroscientist, Wilder Penfield, whose experiments stimulating the human brain provided an enormous wealth of information on the mind-brain relationship. He switched from monism to dualism towards the end of his career, because he never found a "place in the cerebral cortex where electrical stimulation will cause a patient to believe or to decide" (Penfield, 1975, p75). But the situation has since changed, because, in awake humans, stimulation of the supplementary motor area at intensities too weak to produce a movement has occasionally evoked an irrepressible desire to move (Fried et al., 1991), and stimulation of areas BA-39 and BA-40 in the parietal cortex reliably triggers a desire to move (Desmurget et al., 2009). These findings undermine Penfield's motivation for adopting dualism, but I do not think they are rigorously incompatible with the Eccles model.

In fact, the distributed, limited form of interactionism assumed in this model is difficult to refute directly. Its most outrageous prediction is that physical causality is incomplete in dendrons when they are affected by mind, but the authors make no proposals as to how this might be tested. Eccles conjectures that the changes will be "slight" (p47 of (Eccles, 1980)) and at the minuscule level of Heisenbergian uncertainty (Beck & Eccles, 1992). To detect such minute changes, or prove their absence, would involve identifying the "open" dendrons (but how?) and all their thousands of inputs, calibrating the strengths of each input with extraordinary precision, and then performing an exquisitely detailed and accurate input–output analysis by recording from the dendrons and separately from all their inputs, and all this in awake humans! This is a very long way beyond what is currently possible, but I am in fact glossing over numerous additional technical difficulties, such as the presence of synaptic noise (due to thermal noise) in the neurons being studied, and the subtle effects of glia on neurotransmission.

But, even though the hypothesized interaction is difficult to investigate directly, a strong case can be made against its occurrence by challenging its mechanism, as is explained in the next section.

3. The interaction problem

Ever since the time of Descartes, his opponents (beginning with Elizabeth of Bohemia) have raised doubts as to whether an immaterial mind/soul could affect the brain, because it would seem to violate numerous laws of (classical) physics including the conservation of energy and of momentum. Only two ways have been proposed for answering this objection. One (unpopular) has been to suggest that the mind/soul has physical powers. The other has been to suggest ways in which a non-physical soul might be free to interact with the physical world without violating any physical laws.

3.1. A mind/soul with physical powers?

The idea that the mind/soul might have physical powers has never been popular. This would entail that the soul was in a sense physical, which might seem incompatible with the immaterial soul postulated by Descartes, although many notions of modern physics such as electro-magnetic or gravitational fields would have seemed suspiciously immaterial in the 17th C, and this was in fact considered a problem with Newton's theory of gravitation well into the 18th C. So might a mind/soul be physical in some sense? Belief in a physical soul has occasionally been supported by people who attempted to estimate its mass by weighing the body before and after death and one such attempt was published in a medical journal (MacDougall, 1907). The paper was criticized because of the limited sample size, variable results and inadequate precision of the weighing procedure, and following a debate in the New York Times, the author admitted that the experiments would need to be confirmed. I know of no published confirmations, although there are some informal claims on the web. I know of no convincing evidence for a physical soul.

3.2. Mind-brain interaction without violation of physical laws

3.2.1. Early proposals for mind-brain interaction

Far more popular is the suggestion that a mind (or self, will or soul etc.) could influence brain-function without violating physical laws. Various proposals have been put forward. For example, Descartes himself (according Leibniz – (McLaughlin, 1993)) suggested that the soul might affect the direction of motion of the animal spirits, but not the absolute quantity of motion. This would have seemed to Descartes to solve the problem, because the vectorial form of the law of conservation of momentum (*quantité de mouvement* in French) was not then understood, and he thought the conserved quantity was the absolute (non-directional) value |mv|. We now, of course, know that this is untrue. Then, in the early 20th C, the dualist philosopher C.D. Broad, who believed that all synapses were electrical, suggested that the mind might influence brain activity by changing the electrical resistances of the synapses (Broad, 1925). He argued that this could occur without violation of the conservation of energy, but it is nowadays realized that this would still violate the laws of physics.[3]

Far more popular, since the 1930s, has been the idea of mind-brain interaction through the subtle mysteries of quantum physics. Two related issues were involved, and both were raised as early as 1932: the notion that quantum physics provided an important insight into the mystery of *consciousness* (Von Neumann, 1932/1955), and the notion that quantum indeterminism might open the way for *free will* (Jordan, 1932) (for review of this early literature see (Walter, 2001)). At the semi-popular level these issues have become a veritable industry. I cannot fully review this vast field, but will here focus on the publications on mind-brain (or soul-brain etc.) interaction that seem to me the most serious. Top of the list must surely come the publications of Eccles in collaboration with physicist Friedrich Beck (Beck & Eccles, 1992; Eccles, 1992). Further developments along the same lines continue to be proposed (e.g. Schwartz, Stapp, & Beauregard, 2005; Stapp, 2009).

3.2.2. Quantum physics

The fundamental equation of quantum physics is Schrödinger's wave equation, which is a linear second order partial differential equation whose dependent variable is called "the wave function". The wave function (represented by ψ, which is a solution to the Schrödinger equation) is considered to be the most complete and fundamental description possible of a physical system. It can be interpreted as a probability amplitude, and its values are in general complex numbers (with real and imaginary parts).

To simplify matters slightly, let us consider a particular example, the use of Schrödinger's equation for predicting the position of a single particle (it can also be used to predict other variables, e.g. the momentum). The wave function ψ contains information about the probability of the particle being found at a particular position if we were to measure it, and *the square of the wave function's*

[3] Much more recently, Collins has argued that a mind-brain interaction without exchange of energy or momentum may be possible, on the grounds that the quantum correlations in Bell's theorem do not involve energy exchange. Collins (2008) Modern Physics and the Energy-Conservation Objection to Mind-Body Dualism. *Am Philos Quart*, 45, 31–42.

absolute value ($|\psi|^2$) is interpreted to represent the probability function for the particle's position. Thus, even though Schrödinger's equation is deterministic at the micro-level, its implications for the macro-level are probabilistic.

How, then, should this mysterious transisition from the micro-level to the macro-level be understood? Various interpretations have been proposed (Genovese, 2010), and the question is still controversial, but we shall consider only one of the most widely accepted interpretations, which is called the Copenhagen interpretation after the city where it was formulated (by Niels Bohr and Werner Heisenberg). According to this interpretation, the measuring process *collapses* the wave function from a distribution (multiple) to a point function (unique). This may seem rather strange, because it seems to be saying that before measurement the electron was in several places at once! In fact, strictly speaking, the Copenhagen interpretation sidesteps (though arguably does not solve) this problem by asserting that before a measurement is performed one cannot meaningfully speak about the position. Why the wave function should collapse is unclear, but its cause is considered to be the interaction with an observer or apparatus external to the quantum system being studied. Some specialists maintain that the collapse is dependent on the subjectivity of a conscious observer (Stapp, 2009), but others deny this (Yu & Nikolic, 2011).

The above account of quantum physics is simplified, but adequate for our present purposes. The important point is that the probabilistic nature of the wave function implies a degree of indeterminacy, that I shall call *quantum indeterminacy*. We now need to go into more details about the nature of the indeterminacy.

3.2.3. Heisenberg's uncertainty principle

One of the direct consequences of the wave nature of quantum physics is Heisenberg's uncertainty principle. This states that there is a limit to the precision with which certain pairs of variables can be known. Considering position (x) and momentum (p), if the uncertainty in the position is Δx and the uncertainty in the momentum is Δp, then the product of these must obey the inequality $\Delta p \cdot \Delta x \geqslant h/4\pi$ where h (Planck's constant) = 6.63 $\times 10^{-34}$ J.s. Other versions exist, applying to different pairs of variables, and we shall later make use of a version involving energy (E) and time (t): $\Delta E \cdot \Delta t \geqslant h/4\pi$. Since h is very small indeed, Heisenbergian uncertainty is of no relevance to macroscopic objects such as apples or ants; but it is very relevant to microscopic entities such as electrons and photons.

The imprecision in Heisenberg's principle is not just a measurement problem, but is a fundamental limitation to knowledge since it can be derived directly from the Schrödinger wave equation (the fundamental equation of quantum mechanics). Many people go a step further, and say that it is a fundamental statement about existence itself. In other words, electrons and other very small particles do not just appear fuzzy, but really are fuzzy. In philosophical terms, the indeterminism is considered to be not just epistemological but ontological.

When these ideas were introduced in the 1920s, they were revolutionary. The (then) new notion that physics, on a very fine scale, is not strictly deterministic went against the rigorous determinism that had been accepted since the time of Isaac Newton. This led to considerable debate, most famously between Albert Einstein, who believed that the fuzziness of quantum physics is merely a reflection of our ignorance, and Niels Bohr, who believed it reflected the fundamentally probablilistic nature of reality. Einstein believed that there must be a more fundamental law of physics underlying quantum mechanics that is truly deterministic. Such a view has been supported by David Bohm and others, and the debate goes on. Many physicists and philosophers agree with Bohr that the indeterminism is ontological, but there is still plenty of disagreement (El Naschie, 2007; Genovese, 2010; Hiley & Peat, 1991; Hodgson, 2002).

4. Theories involving quantum effects

Even while the Einstein-Bohr debate was continuing in the 1930s, the notion that Heisenbergian uncertainty might provide fundamental indeterminacy for brain function was seized upon by the physicists Eddington and Jordan, who proposed it as a basis for brain indeterminism and hence for free will (Walter, 2001). Many others followed suit, and similar ideas continue to be proposed by scientists (Beck, 2001, 2008; Glimcher, 2005; Schwartz et al., 2005; Stapp, 2009) and philosophers (Balaguer, 2010; Kane, 1996; Lucas, 1970; Taliaferro, 1994). However, others have followed Schrödinger (Schrödinger, 1945) in arguing that the scale of Heisenbergian uncertainty was two small for it to have a significant effect on living organisms or on their cells. It is generally accepted that Schrödinger was correct with respect to biology as a whole (Hoffmann, 2012) and I shall argue that this general conclusion is valid even for brain function.

4.1. Quantum effects at the synapse

If Heisenbergian uncertainty is relevant to brain function, what are the critical cellular locations where this applies? The one most commonly invoked by dualists is the synapse, as was proposed by Eccles from as early as 1953 (Eccles, 1953). One reason for postulating the synapse as the liaison-site was that he postulated the self/mind to influence conscious decision-making directly, which implies a site directly involved in the generation or control of neural activity (Eccles, 1986).

Eccles' aim was to make Cartesian dualism compatible with physics, but to do this he had to deny what most physicists believe, that Heisenbergian uncertainty is random. On Eccles' view, the uncertainty is more like a cloud cover that hides the *directed* influence of the self/mind.

In an early version, Eccles applied the Heisenbergian uncertainty to the position and velocity of synaptic vesicles (Eccles, 1970), but the calculations were criticized by Wilson who showed that the vesicles were many orders of magnitude too large for Eccles' theory to work (Wilson, 1976). Subsequently, Eccles teamed up with physicist Beck and they presented a model according to which quantum tunneling of "quasiparticles"[4] between the lipid bilayers of the synaptic vesicle and the presynaptic membrane would affect vesicular fusion and hence neurotransmitter release, thereby influencing the activity of the postsynaptic cell, and hence more generally brain activity (Beck, 2001; Beck, 2008; Eccles, 1992, 1995). Since this view was first proposed, some of the biological details of the model have turned out to be incorrect; e.g. Beck and Eccles assumed that transmitter release involves the transition of a paracrystalline presynaptic grid to a metastable state, which is no longer accepted. It has become clear that the movement of vesicles to the cell membrane and their fusion with it are rigorously controlled by a complex of many different proteins, and that the final fusion is only possible when one of these proteins (a member of the *synaptotagmin* family) changes its conformation as a result of interaction with calcium (Jahn & Fasshauer, 2012). In addition to these problems, the quantitative aspects of the model were criticized by neurophysiologist David Wilson using an alternative formulation of Heisenberg's principle in which the variables are energy and time rather than position and momentum (Wilson, 1999). Wilson further argued that it would be more plausible (or at least less implausible) to postulate

[4] A quasiparticle is a multipartite system treated as though it were a single-particle; Eccles and Beck do not specify further.

Heisenbergian effects on the control of presynaptic calcium concentration rather than on the movement of synaptic vesicles (Wilson, 1999). The following argument, which resembles that of Wilson, indicates that Heisenbergian effects are too small even for this improved version.

As a specific example, we consider whether a fluctuation within the limits of Heisenbergian uncertainty could affect the presynaptic calcium concentration by permitting a chemical bond to be modified in an ion channel in the presynaptic membrane, as has been proposed by recent supporters of the Eccles approach (Schwartz et al., 2005; Stapp, 2009). This could be a calcium channel, influencing calcium concentration directly, or a sodium channel that would influence it indirectly through a prior change in presynaptic electrical potential. I shall here focus on calcium channels.

The process of calcium influx has been well studied. When an action potential reaches the synaptic terminal, this causes calcium influx through voltage-dependent calcium channels in the membrane of the terminal. The channels are very narrow (about 1 nm) and the calcium ions go through in single file, moving progressively from binding site to binding site within the channel. The calcium concentration around a given synaptotagmin molecule depends on calcium influx through a small number (perhaps 2–5) nearby channels. Several calcium ions can bind to a synaptotagmin molecule. (Schneggenburger, Han, & Kochubey, 2012; Sudhof, 2004). We need to consider whether Heisenbergian effects could modify the influx of calcium through channels and hence affect the availability of calcium to synaptotagmin molecules.

According to Heisenberg's principle, there is a limit to the precisions of energy (E) and time (t) given by $\Delta E{\cdot}\Delta t \geqslant h/4\pi$ where $h = 6.63 \times 10^{-34}$ J.s. In other words, an energy change ΔE can be "hidden" for a time Δt providing ΔE is of the order of $h/4\pi\Delta t$. According to current views on synaptic function Δt would need to be at least 10 ms to have even a minimal effect on the presynaptic calcium concentration, probably much more, because this concentration builds up gradually over the much longer period of about 500 ms (Sudhof, 2004). Substituting this conservative value of $\Delta t = 10$ ms gives a ΔE of approximately 5.2×10^{-30} J, which is about 200,000 times too small to disrupt even a single Van der Waals interaction, the weakest kind of chemical bond ($E = 1 \times 10^{-24}$ J).

Even if quantum phenomena could occasionally affect calcium flow through channels, it seems very unlikely that this could have a significant effect on synaptic transmission, because the numbers of calcium ions involved are sufficiently large to swamp any quantum effects. Smith has argued this in a detailed discussion of the possibility of quantum effects at synapses, stating that the number of ions involved is 10^{18}–10^{19} (Smith, 2009). The numbers going through a given channel at a single opening are much smaller, of the order of one thousand (Smith, 2009), but this would still be enough to swamp the effects of a 10 ms change in the channel due to quantum fluctuations.

Alternative sites for quantum effects than synapses have been proposed, including gap junctions, because these are known to play an important role in the synchronisation of gamma oscillations, which is an important correlate of consciousness (Hameroff, 2012). However, Δt would still need to be at least 10 ms for there to be a minimal effect, so the above calculation still applies yielding as above a ΔE of about 5.2×10^{-30} J, which is far too small to disrupt even a Van der Waals interaction.

4.2. Quantum indeterminism beyond Heisenberg

As mentioned briefly above, Heisenbergian uncertainty is not the only form of quantum indeterminism. Heisenberg's principle specifies only a lower bound to the indeterminism, which means that if a physicist attempted to measure the position and momentum (or energy and time, etc.) of a particle, even if she had perfect equipment there would be a scatter to p and x such that $\Delta p.\ \Delta x$ would be at least as great as $h/4\pi$. This leaves open the possibility that in some cases quantum indeterminism might be much greater (Brownnutt, 2012). To illustrate this, Brownnutt gives the well understood example of certain superposition states of a calcium ion, showing that in this case there could in principle be almost 10^{16} times greater indeterminism than predicted by Heisenbergian uncertainty. This kind of situation (a trapped ion in a superposition state) is much too fragile to apply in the warm, wet environment of a biological organism, as Brownnutt admits, but he draws attention to some remarkable situations where nonheisenbergian quantum effects can apparently occur in biological situations. These involve photosynthesis (Lee, Cheng, & Fleming, 2007; Mohseni, Rebentrost, Lloyd, & Aspuru-Guzik, 2008) and magnetic field sensititivity (Gauger, Rieper, Morton, Benjamin, & Vedral, 2011), both involving the phenomenon of quantum coherence, which refers to situations where the wave-like properties of the elements of a system have a constant relative phase. This is thought to be rare in biology, or exceedingly brief, because molecular noise in living cells tends to destroy the coherence. But, remarkably, the paper on avian magnetic-field sensitivity claims coherence lasting for many tens of microseconds (Gauger et al., 2011). A few other examples of quantum effects in biology have been reported, and this new field is gaining momentum, but some of the data are controversial and it is too early to know how widespread these phenomena will turn out to be (Ball, 2011; Bordonaro & Ogryzko, 2013). To date there is no evidence that such quantum processes are involved in neuron-to-neuron communication or brain function.

The hypothesis that quantum coherence may play a role in brain function has in fact been debated intensely for more than 20 years following the proposal by Roger Penrose that human conscious thought requires the brain to work like a quantum computer (Penrose, 1989, 1994) and the proposal of Stuart Hameroff's group that microtubule networks can perform computations (Lahoz-Beltra, Hameroff, & Dayhoff, 1993). Their intention was not to argue for quantum indeterminism or any kind of soul-body interactionism, but the considerable debate that followed their hypothesis is relevant to the question of quantum coherence in the brain. Microtubules are very fine tubes, about 20 nm in diameter and up to 25 μm long, that occur in virtually all cells except prokaryotes (bacteria and archea). They play several different roles in cells, of which the most important and well established are to maintain cell structure, to form mitotic spindles for cell division, and to provide platforms for intracellular transport. In neurons, networks of microtubules run down the insides of axons and dendrites, and are involved in transporting proteins and other molecules from the cell body to the axonal or dendritic tip or vice versa. But Penrose and Hameroff attributed to them another completely different function, proposing that water molecules in different microtubules may exist in a state of quantum coherence and that the resulting nonlocally correlated changes could have rapid effects in the neural networks of the brain. This theory attracted considerable attention, perhaps because of Penrose's prestige, but also strong criticism (Tegmark, 2000). The weight of scholarly opinion is currently rather strongly against the microtubule hypothesis (McKemmish et al., 2009; Smith, 2009).

Taking all of this together, it seems to me that the postulate of substantial indeterminism, much greater than the Heisenbergian $h/4\pi$, remains extremely speculative.

5. Amplification of Heisenbergian uncertainty by chaos or other means

An alternative strategy for trying to rescue the relevance of quantum indeterminism has been to propose that Heisenbergian uncertainty might somehow be amplified. By far the most frequently proposed amplification mechanism is chaos. The most important criterion of a chaotic system is that it must be extremely sensitive to initial conditions or perturbations. A consequence of this property is that chaotic systems (like the weather) are in practice unpredictable over a long period, even though they are deterministic. The proposed idea is that deterministic chaos, when combined with quantum theory, would become indeterministic. The behaviour of chaotic systems has been analysed extensively by mathematicians and computational modellers, and chaos is believed to occur in numerous different situations in physics, chemistry and biology.

Of particular relevance to our present concerns, chaos has been claimed to occur in the electric activity of the brain. Since the 1980s, numerous electrophysiological studies of action potentials in various brain regions have been interpreted as evidence for chaotic processes (Kozma & Freeman, 2008). It is technically difficult (perhaps impossible) to test rigorously whether a series of action potentials or waves recorded from the brain is truly chaotic, but there is sufficient evidence to convince most specialists that chaos does often occur in brain activity (Battaglia & Hansel, 2011; Korn & Faure, 2003; Tsuda & Fujii, 2007). The relevance of this to mind-brain interactionism is that chaos is sometimes claimed to provide a means of amplifying the tiny indeterminism available from quantum theory (Hobbs, 1991; Hong, 2003; Kane, 1996; King, 1991). The chaos responsible for the amplification could be in the electrical activity of brain neural networks (as discussed above) or at an intracellular level, where chaos is likewise claimed to occur (Houart, Dupont, & Goldbeter, 1999). But despite the intuitive appeal of the amplification hypothesis, it suffers from at least four major problems.

5.1. Difficulties with quantum chaos

First, the combination of chaos with quantum theory is problematic. Surprisingly, even though q*uantum chaos* has been studied for more than two decades and is the subject of numerous papers every year, its very existence is debated (Bishop, 2008). This is because of the mathematically predicted "quantum suppression of chaos"; if the equations of a chaotic system are combined with Schroedinger's equation, the chaos is suppressed. The causes of this seem to be only partly understood, but have been linked to the fractal nature of chaotic attractors, to the fact that quantum systems cannot display classical trajectories on a finer scale than that of Planck's constant, and to the fact that Schrödinger's equation gives solutions that are periodic or quasi-periodic and hence incompatible with chaos, which is inherently aperiodic (Hobbs, 1991; Koperski, 2000). Hobbs (1991) argued that the problem of quantum suppression might be solvable, but his arguments have been criticized by Bishop, who provides a nuanced discussion of this problem (Bishop, 2008). A further complication is that the quantum suppression of chaos can in some but not all situations be suppressed by another quantum effect, the phenomenon of *decoherence* caused by interaction between the quantal system and its environment (Berry, 2003; Zurek, 1998). All in all, this casts serious doubts on the hypothesized amplification of indeterminism by chaos, without refuting it decisively. But there are other problems.

5.2. A more general problem with the amplification hypothesis

The second problem is more general, applying to any kind of amplification of quantum effects, whether by chaos or by other means. As Bishop has argued in detail, the validity of such a notion depends crucially on the particular interpretation of quantum mechanics that is being employed (Bishop, 2008). Taking a simple chaotic system as an example (a chaotic pendulum), he discusses the difficulties of the amplification hypothesis in relation to various different models of quantum mechanics. But here I am obliged to simplify. A naïve version of the amplification hypothesis might assume that two systems that are identical (i.e. have identical sets of initial conditions) at time T_0, apart from tiny differences due to Heisenbergian uncertainty (quantum fluctuations), will diverge due to amplification so that a measurement at time T_1 will show much larger differences than existed at time T_0. This is however problematic for at least two reasons. First, it implies the existence of precise initial conditions before the time of measurement, whereas some interpretations of quantum mechanics deny that this has any meaning. Second, even if we accept the meaningfulness of initial conditions before the time of measurement, the notion of quantum fluctuations before measurement is also problematic, because in standard interpretations of quantum mechanics, quantum indeterminism does not exist at the quantum level but arises only in the transition between the quantum level description and the macroscopical one. In this example, at least, the indeterminism arises after the amplification process, and so it will not be amplified. Bishop's more detailed analysis (Bishop, 2008) indicates that the amplification hypothesis may still be tenable with particular assumptions about quantum mechanics, but the situation is far from clear.

5.3. Specificity requirement of the indeterminism

The third problem concerns the *specificity* of the indeterminism. With or without amplification, the step from indeterminism to soul-mediated control requires the unconventional interpretation that Heisenbergian uncertainty is not true indeterminism, but, as is mentioned above, a kind of cloud cover permitting the soul or mind to *determine* brain activity unnoticed. Thus, we are asked to accept, without evidence, that what everybody believed was random is in fact directed and meaningful, and further that the directedness is maintained even after enormous amplification by processes such as chaos whose ability to conserve specificity is unclear.

5.4. The brain's noise-resistance

The fourth problem with the amplification hypothesis relates to the efficacy of the brain's noise-resistance mechanisms. Every cell in the body is constantly subject to thermal noise – thermally driven molecular movements - and is resistant to its effects. Thermal noise causes significant fluctuations in many cellular events including transcription and translation ("gene expression noise"), ion channel permeability ("channel noise") and synaptic function ("synaptic noise"). Individual cells and brain function as a whole both have numerous inbuilt noise-resistance mechanisms including mass action, negative feedback and frequency-selective feedback, as I have discussed in detail in a recent review (Clarke, 2012). Thermal noise can be considered random in the sense that it is not biologically controlled or coordinated in any way with cellular function, but is on a sufficiently large scale to be describable by classical (deterministic) physics. This constitutes a fundamental problem for hypotheses of soul-mind interaction based on quantum-scale phenomena, because a neuron (or neural circuit etc.) whose function is resistant to thermal noise should *a fortiori* be resistant to the much smaller perturbations of quantum phenomena. The implications of this problem are very general. They apply whether or not the uncertainty is amplified, are valid for any kind of amplification system, and extend beyond quantum indeterminism to other conceivable sources of very small physical uncertainty such as the finitude of the Planck length, which has been proposed as an alternative possible source of ontological indeterminism (Lewis & MacGregor, 2006). I here compare the magnitudes of thermal noise and Heisenbergian uncertainty.

The energy of thermal noise is given by:

$E_{th} = 0.5$ kB T.n, where n is the degrees of freedom = 3; kB is Boltzmann constant = 1.38×10^{-23} J/K; T is the 310K.

Whence $E_{th} = 6.4 \times 10^{-21}$ J (about 10^9 times larger than the value of $\Delta E \sim 5.2 \times 10^{-30}$ J calculated in Section 7.2, assuming that $\Delta t = 10$ μs).

Thus, the thermal energy of the molecules is 9 orders of magnitude greater than the energy change that can be hidden by Heisenbergian uncertainty. But the functioning of neurons has to be resistant to thermal noise. And if the Heisenbergian uncertainty is amplified by chaos or in other ways, the far greater fluctuations due to thermal energy will presumably be amplified as well. Beck and Eccles understood this clearly and drew attention to the problem (Beck & Eccles, 1992), and Beck has continued to do so (Beck, 2001, 2008). Indeed, the quantitative conclusions of Beck and Eccles are similar to mine: that the Heisenbergian $\Delta E \cdot \Delta t \geqslant h/4\pi$ can only provide a physiologically relevant ΔE if Δt is exceedingly small, in the picosecond range or still faster (e.g. electron transfer). The main difference between us is that Beck & Eccles think that such rapid events may affect brain functioning, whereas I think this most unlikely. In a subsequent paper, Beck cites evidence for a picosecond range effect involving electron transfer in the response of photobacteria to light (Beck, 2001), but there appears to be no evidence for such an effect in relation to brain function. I actually agree with Beck that the most plausible (or least implausible) target for a quantum effect on synaptic function would be electron transfer, but I know of no theoretical or experimental evidence that this could be important in brain function.

6. Living without a quantum-based Cartesian soul

The above considerations indicate that attempts based on quantum indeterminism to explain how a disembodied soul might influence the brain are not encouraging. This does not refute quantum-based interactionism conclusively, because new and unexpected phenomena might always be discovered, but it does make quantum-based interactionism rather implausible. How serious is this philosophically?

Philosophers defending quantum-based Cartesian dualism have mostly been motivated by the conviction that reductionist materialism is inadequate to account for conscious thought (Dilley, 2004; Goetz & Taliaferro, 2011; Madell, 2010; Taliaferro, 1994) and by the desire to draw out the full implications of quantum physics for the philosophy of mind (Stapp, 2009). There has also been a recent surge of enthusiasm for quantum-based dualism because of increased interest in paranormal phenomena (Kelly et al., 2006) including near-death experiences (Carter, 2010; Van Lommel, 2010).

A further motivation for some philosophers, although not discussed in this review, has been concern about the implications of neural *determinism*. Many (most?) philosophers argue that neural determinism is in fact compatible with free will, or at least with “the varieties of free will worth wanting” to quote Dennett’s famous subtitle (Dennett, 1984). These *compatibilists* argue that free will should be defined as *freedom from compulsion*, not freedom from determinism. Compatibilism has long enjoyed widespread support among philosophers, but the contrary view of *incompatibilism* also has its advocates. For an incompatibilist, acceptance of neural determinism would require us to deny the existence of free will, and this stark view, known as *hard determinsism* has some defenders (Honderich, 1988; Pereboom, 2001). Other incompatibilists accept free will and argue that there must therefore be indeterminism in brain function. These *libertarians*, as they are called, need to identify a plausible source for the ontological indeterminism that is required by libertarian theories of free will (Balaguer, 2010; Doyle, 2011; Kane, 1996). Some libertarian philosophers invoke a Cartesian soul (Goetz & Taliaferro, 2011; Swinburne, 2013) and postulate a quantum-based soul-brain interaction mechanism of the kind that I have criticized above, but other libertarians explicitly reject Cartesian dualism but still invoke quantum indeterminism in the neural decision process (Kane, 1996) or in idea-generating neural processes prior to the decision process (Doyle, 2011). Behavioural psychologists interested in the survival value of unpredictability have likewise invoked quantum indeterminism (Glimcher, 2005).

The present arguments apply also to these other types of indeterminism. In some ways the latter are even harder to defend than quantum-based Cartesian dualism, because the dualist has the advantage of being able to invoke a synchronous coordinating action of the soul, which might help to raise the tiny quantum-level influences above the noise level, whereas the other approaches have no such trump card. Thus, my arguments raise problems for all such quantum-based approaches.

What are the implications of this for our conception of humanity? Rejecting Cartesian dualism would not require the acceptance of reductionistic materialism because many “soft materialist” positions can be defended that lie between the extremes of Cartesian dualism and reductionistic materialism. These include a cluster of related positions that are variously called neutral monism or dual-aspect theory or nonreductive physicalism, that can be linked to a compatibilist account of free will (Chalmers, 1996; Murphy & Brown, 2007). In my opinion they are fully compatible with human dignity, rooted in conscious thought that is integrated with brain function and dependent on it, but not reducible to it.[5]

7. Concluding remarks

The present paper raises problems for attempts to ground notions of a Cartesian soul (or self etc.) or free will on Heisenbergian uncertainty, because the uncertainty is too small in absolute terms and – even more importantly – in relation to the deterministic, but biologically uncontrolled, disruptions due to thermal noise. Moreover neurons and neural circuits have a built-in resistance to the thermal noise, and it seems unlikely that the smaller effects of Heisenbergian uncertainty could overcome the powerful noise-resistance mechanisms. Various authors have suggested that these difficulties might be solved if Heisenbergian uncertainty were amplified by chaos or by other means, but there are several difficulties with this view. Recent results in the new field of quantum biology raise the question of whether quantum effects greater than Heisenbergian uncertainty might provide a solution, but this remains speculative since such effects have never been shown in neural circuits. Finally, the foundational assumption of ontological indeterminism that underlies all attempts to base soul-brain interaction or neural indeterminism on quantum indeterminism is far from being universally accepted.

Even though I raise difficulties for attempts to ground notions of a Cartesian soul (or self) and free will in quantum indeterminacy

[5] Also, Cartesian dualism is not an essential component of religious belief. While it is true that most religions have a notion of a soul, this does not have to be a disembodied soul of the Cartesian variety. For example, Christianity, Judaism and Islam have all been influenced by two different philosophical traditions rooted in classical Greek thought. One of these, stemming from Plato, does indeed postulate a disembodied soul, but the other, stemming from Aristotle, postulates an embodied soul, a principle within the body, not a separate thing outside it.

(Heisenbergian or other), I do not consider that rejection of this particular grounding need undermine the notions of selfhood and free will, because moderate versions of physicalism such as dual aspect theory, and a compatibilist approach to free will provide alternative groundings.

Acknowledgments

I am grateful to Michael Brownnutt for comments on the manuscript, and to an anonymous reviewer for very detailed criticism of the most helpful kind.

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