Review of: "Catecholaminergic Neuron Electron Transport (CNET): A Neural Signaling Mechanism"

Andrey Schegolev[1]

1 Lomonosov Moscow State University

Potential competing interests: No potential competing interests to declare.

The article "Catecholaminergic Neuron Electron Transport (CNET): A
Neural Signaling Mechanism" is devoted to the analysis and discussing the results of biophysical studies of the mechanisms underlying the CNET theory. The article is written in good scientific language, the topic is more than relevant and very important for modern development and understanding of the hidden mechanisms of the human brain. I definitely recommend the article for further publication.

Before that, however, I would like to get answers to the following questions.

1) In the first part of your work you reasoned that a source of electrons is need to (reason num. 3). Would it be more correct to say here that some chemical compositions (ions, aneons, neurotransmitters, proteins, etc.) with some number of relatively free electrons (I mean electrons in the outer electron shells) are this source of electrons? Only conceptual.

In the second part of your work you answer about this source, I know.

2) Could you please clarify what exactly you mean by adiabatic energy routing in the CNET mechanism? Ishizaki and Fleming in their work of 2012 “Quantum Coherence in Photosynthetic Light Harvesting” also uses this term, but it is not revealed either. I understand that in general, an adiabatic process means that the system does not exchange energy with the environment. Is that implied here as well or are there further clarifications?

If energy routing is a search for a global minimum in the parametric decision space (roughly speaking), then the "rolling" of the system to the next minimum (triggering corresponding action in group of neurons), of course, can be adiabatic in the conventional sense.

3) I think the idea of electron tunneling between different soma is inspired and really has every reason to be true (I hope so). Have you any estimations about how this process can occur (preparatory phase before tunneling) and what the characteristic distance between soma should be and electrons energy?

4) In the 2a you are writing that peroxidase provides a source of high-energy electrons. Have you any quantitative estimations about their energy? And if you do, I think it wouldn't be a problem to write them up.

5) At the end of the last paragraph of part 2, you write that electrons need an electromotive force to make them move. Do you mean that there must be an electrostatic potential between the different somas to make the electrons move towards

the soma membrane for further tunnelling?

6) At the end of the first paragraph in 3b part you mentioned that “Electron tunneling through ferritin would also explain at least part of the mechanism for functional coupling between neurons and glia” with link to relatively old publication of 2000. Also, there are many another work to this theme – coupling between neurons and glia – that explain the relationship without involving additional entities. I do not say that there is no electron tunneling between them - I don’t know for sure, – however, the lack of more recent works investigating this phenomenon is alarming. Or do these works still exist?

7) At the end of 3b it is stated that electrons will be repelled by other electrons or a neuron cell membrane at rest potential of -70 mV, and would be repelled less by neuron cell membrane potentials that are depolarised. Do you think it is possible that when a neuron is activated, there is not only action potential propagation, but also signal transmission between the activated neuron and an unrelated other neuron through electron tunnelling (during the depolarisation stage) and thus performs additional regulatory functions?

8) The first sentence at 4.b. part - citation. “[f] or movement control, dopamine…” - the typo. In original work it is “For movement control, dopamine modulates striatal moment-to-moment activity to mediate action selection. For learning…”

9) I also have a question about electron tunneling mechanism between different somas. As we know in intercellular media there are a lot of different chemical components, for example, neuromediators. How it can be possible that electron can can tunnel from one soma to another bypassing the ever-changing intercellular environment “not getting stuck somewhere in the middle”?

10) In my own opinion, to be sure that the CNET hypothesis is really true it is necessary to obtain evidence of the simultaneous existence of all the mechanisms embedded in the hypothesis, more precisely, evidence that they work together for a specific purpose. You know that there are a lot of examples, when a group of objects or components exhibits properties that are not characteristic of the individual parts of the group - so-called emergent property. Maybe you can suggest a design of an experiment that could close this question?

11) A several months ago I found a discussion of Matthew Fisher's paper on the possibility of the existence of quantum processes in the human brain (Fisher, M. P. (2015). Quantum cognition: The possibility of processing with nuclear spins in the brain. *Annals of Physics*, *362*, 593-602.). The point is that the brain needs some mechanism for long-term storage of quantum information in qubits. Many qubits must be entangled, and this entanglement in some apparently chemical way must affect the way neurons work. There must also be a mechanism for transferring the quantum information stored in qubits throughout the brain. In his paper, Matthew derives the basis for a theory of the emergence of quantum entanglement, at the centre of which he places a "Posner molecule". Fisher presents the Posner molecule as unique, capable of protecting neuronal qubits over large time intervals and thus allowing them to function as a quantum memory. What do you think about it? How this theory can be connected with CNET hypothesis?