

## Review of: "Electron Tunneling in Ferritin and Its Potential Influence on Myelin and Cardiomyocytes"

Luminita Labusca<sup>1</sup>

1 National Institute of Research and Development for Technical Physics

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A much-welcomed opinion review (and perhaps an opinion/hypothesis paper at the same time) focusing on quantum biology, particularly on ferritin electron tunneling. A very good point was made regarding the incomplete understanding of the antioxidant-like function of ferritin (and maybe of other iron ion handling/storage proteins) that is almost exclusively discussed in terms of redox chemical reactions and seldom as an effect of electron tunneling. Other proteins such as myoglobin, hemoglobin, the cytochrome C complex proteins could exert similar electron tunneling effects. One point would be understanding the impact of the phenomenon on normal function, aging, and disease, as well as the potentially intricate patterns in which effects interfere with each other and with the surrounding extracellular matrix and biological fluids.

In this perspective, maybe a brief introduction (of several phrases) to the electron tunneling effect in general and to the bases and importance of ferritin-related electron tunneling would be beneficial to readers of multiple backgrounds, including biology.

The manuscript goes on to propose a role for ferritin in impulse transmission across myelin sheets and a possible modality of testing such hypotheses. To note, patch clamp experiments proposed to solve this mystery are quite laborious and prone to multiple confounding variables. Moreover, studies of overexpression and lack of ferritin in respective oligodendrocytes (not oligodendrites), mandatory for proving the causality of such a phenomenon and not mere correlation, would add to complexity (while impeding cell survival in the extremely stressful conditions imposed by patch clamping). Taking into consideration that electron tunneling is supposedly very much environment/cell state dependent, it is with considerable probability that the experimental conditions proposed would modify and even maybe fail to answer the question.

The connection between ferritin expression and inflammation, as well as the response to therapeutic intervention for atrial fibrillation, is not only well known but used in the clinic as routinely as well. The role of ferritin-mediated self-assembled nanolayers proposed here is a hypothesis that merits further careful consideration and appropriate experimental set up for testing.

To note, not only macrophages but many cell types (including stem cells and fibroblasts) have been reported to consistently modify cytoskeletal features (and perhaps a whole range of gene expression related to the cytoskeleton and intercellular communication) when exposed to a magnetic field.



Here again, an experimental setup carefully constructed and interdisciplinary readouts are needed to ascertain whether overexpression of ferritin in cardiac macrophages is causal in producing electron tunneling effects in vivo.

In this reviewer's opinion, more than one biological phenomenon could prove to at least include, if not completely be based on quantum effects. The problem here is not the problem being overlooked by biologists, but rather relies on having the necessary interdisciplinary sound and efficient communication. The setup of appropriate methods of investigation and experiments that could reveal such events without too much disruption to physiological conditions is crucial. The rather static perspective on biology, based on gene expression/protein production/epigenetic fine-tuning, shifting to quantum dynamics and the probabilistic approach to life phenomena, is a consistent change of paradigm. Given its multiple ramifications in the way we approach health, disease, and, most of all, established therapies, it is likely to require consistent effort, willingness, and resources to embark on such a discovery.