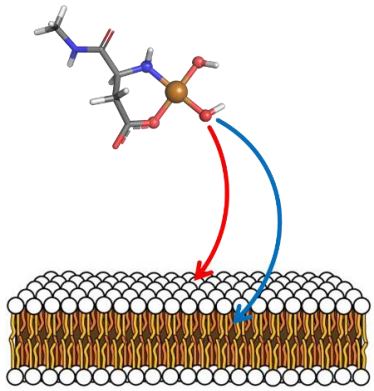
Membrane damages induced by Cu(II)-Aβ·OH radical species. OH propagation toward polar head groups and lipid tails of membrane phospholipid bilayers at DFT level.

Luca Bertini[a], Alberto Rovetta[a], Laura Carosella[a], Federica Arrigoni[a], Luca De Gioia[a], Jacopo Vertemara[a], Giuseppe Zampella[a].

[a] Department of Biotechnologies and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy

luca.bertini@unimib.it

The Oxidative stress [1] appears to be one of the major determinants of the pathogenesis and progression of Alzheimer's disease (AD). According to the oxidative stress hypothesis in AD, the interactions of redox active Cu(II) ions with Aβ peptide is linked to production of toxic reactive oxygen species (ROS). While the Cu(II)-Aβ ascorbate assisted OH radical production is well characterized, less is known about the following OH propagation processes.



The product that comes from the O2 ascorbate-assisted reduction cycle is the Cu(II)-Aβ·OH species in which one OH radical is coordinated to Cu(II). Besides intramolecular Aβ oxidative processes [4], OH radical can propagates oxidizing polar head groups and lipid tails of phospholipid belayers in brain membranes.

We investigate at Density Functional Theory level [2-4] the OH propagation of Cu(II)-Aβ·OH model coordinations exploring 1) Cu(II)-Aβ·OH/phosphocholilne polar head non-bonding interaction; 2) breaking mechanism of the $-CH_2-N(CH_3)_3^+$ C-N and glycerol C-O bonds in phosphocholilne upon impact of an Cu(II)-Aβ·OH radical; 3) The lipid peroxidation initiation step considering a selection of fatty acids singled out among the most abundant in human brain membranes. The results obtained can be useful to elucidate some aspects of the binding and the reactivity of the Cu(II)-Aβ·OH in connection with oxidative stress and copper dyshomeostasis in AD.

References

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