Styrene–Dopamine receptor affinity: a Molecular Dynamics study

E De Santis[a], F Stellato[a], GC Rossi[a,b], S Morante[a]

[a]*Department of Physics, University of Rome Tor Vergata and INFN Sezione di Tor Vergata, 00133, Rome, Italy*
[b]*Centro Fermi-Museo Storico della Fisica e Centro Studi e Ricerche "Enrico Fermi", 00184, Roma, Italy*
e-mail: edesantis@roma2.infn.it

Keywords: MD simulations, otoacoustic problems, dopamine receptors, solvent exposure

Styrene is an organic molecule which has several industrial applications. It is extensively used in industrial processes, for example as a reactive diluent in epoxy resins, as an intermediate in the preparation of a variety of agricultural and biological chemicals, cosmetics, surface coatings, treatment of textiles and fibers and as a raw material for the production of phenyl stearyl alcohol in perfume industries.
Significant scientific evidence has been collected in the last decades demonstrating that exposure to styrene, either alone or in concert with noise exposure, has severe ototoxic effects. Occupational medicine studies, performed among workers exposed to this solvent, show a significant decrease of the DPOAE (distortion product otoacustic emissions) levels in styrene exposed ears [1,2,3].
Neurotransmitters such as dopamine have been supposed to be implicated in the mechanism of styrene neurotoxicity. In normal ears, in the outer hair cells membrane proteins able to bind dopamine have been indeed detected. They exist in five variants, known as "dopaminergic receptors" (DR) D1, D2, D3, D4 and D5. Interestingly, D1 and D2 knockout mouse models showed slight, but visible suppression of cochlear responses [4], suggesting a role of these two receptors in the response.
In this work we have used molecular docking to identify the poses on the DRD2 receptor where either styrene or dopamine have the highest binding affinity. We find that the relevant poses are located in the Transmembrane 3, Transmembrane 5 and Transmembrane 6 domains. Our results confirm the data of ref. [5] where the contact loci of dopamine on the DRD2 receptor were identified. We are now performing extensive classical molecular dynamic simulations in order to provide a quantitative evaluation of the binding affinity of styrene as well as dopamine for the D2 dopaminergic receptor.

[1] Lawton, *Int. Arch. Occ. Env. Hea.,* 2 (2006): 93-102.
[2] R. Sisto, *J. Acoust. Soc. Am.,* 134.5 (2013): 3739-3748.
[3] R. Sisto, *Int. J. Audiol.,* 55.9 (2016): 523-531.
[4] Maison, *J. Neurosci.,* 32.1 (2012): 344-355.
[5] Kalani, *PNAS,* 101.11 (2004): 3815-3820.