

## Interaction of $\alpha$ -tocopherol with a polyunsaturated lipid studied by MD simulations

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Polyunsaturated phospholipids are essential components of neural membranes and their effect on membrane architecture is proposed to be the molecular origin of a myriad of health benefits. A downside of polyunsaturated phospholipids is that they are highly susceptible to oxidation due to the presence of multiple double bonds.  $\alpha$ -Tocopherol is the most biologically active component in a family of phenolic compounds that comprise vitamin E, which is the major lipid soluble antioxidant in cell membranes. To investigate whether  $\alpha$ -tocopherol preferentially interacts with polyunsaturated phospholipids to optimize protection against oxidation, we performed MD simulations on 1-stearoyl-2-docosahexaenoylphosphatidylcholine (SDPC, 18:0-22:6PC) and 1-stearoyl-2-oleoylphosphatidylcholine (SOPC, 18:0-18:1PC) bilayers containing  $\alpha$ -tocopherol. SDPC with a docosahexaenoyl sn-2 chain is polyunsaturated, while SOPC with an oleoyl sn-2 chain serves as a monounsaturated control. The simulations were run under constant pressure for 200 ns on a system that comprised 80 phospholipid molecules, 20  $\alpha$ -tocopherol molecules and 2165 water molecules. We discovered significant differences between the two systems. Analysis of the simulations indicates that the  $\alpha$ -tocopherol has a strong interaction with the polyunsaturated fatty acid. The flip-flop of  $\alpha$ -tocopherol across the bilayer is also much faster in SDPC than in SOPC. Solid state NMR, neutron scattering and complementary experiments are now underway to test the predictions from the MD simulations.

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