α-Tocopherol is well designed to protect polyunsaturated fatty acids

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Polyunsaturated fatty acids (PUFA) are an influential constituent in cell membranes, but are extremely vulnerable to oxidation. The presumptive role for α-tocopherol (α-toc), the molecular form of vitamin E retained by the human body, is to protect PUFA-containing lipids from oxidation. To investigate whether α-toc preferentially interacts with PUFA in support of this function, we performed MD simulations on lipid bilayers composed of 1-stearoyl-2-docosahexaenoylphosphatidylcholine (SDPC, 18:0-22-6PC) and 1-stearoyl-2-oleoylphosphatidylcholine (SOPC, 18:0-18:1PC) in the presence of α-toc. SDPC with docosahexaenoic acid (DHA) for the sn-2 chain is polyunsaturated, while SOPC with oleic acid (OA) for the sn-2 chain serves as a monounsaturated control. The simulations were run at 37 °C under constant pressure for 200 ns on a system that comprised 80 phospholipid molecules, 20 α-toc molecules and 2165 water molecules. In qualitative agreement with our results from solid state ^{2}H NMR and neutron scattering experiments, the simulations show that α-toc increases order inside the bilayer and that the chromanol headgroup sits near the surface in both SDPC and SOPC. Analyses of the density distribution of the lipid chains relative to α-toc show that the α-toc's chromanol headgroup, the part of the molecule that protects against oxidation, would have more chance to interact with PUFA chains than saturated chains. A major prediction from our simulations is that α-toc undergoes flip-flop across the bilayer and that the rate is an order of magnitude greater in SDPC than SOPC. This is a remarkable finding that reveals a possible mechanism by which the chromanol group would not only wait at the membrane surface but would also patrol the membrane interior to meet lipid radicals and terminate the chain reaction by which lipid peroxidation proceeds.