Interplay of lipids and proteins in membrane domain formation

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We developed a mathematical model of lateral diffusion of lipids and proteins in cellular membranes. The movement of lipids and proteins along the membrane surface is modelled as stochastic displacement on a triangular lattice governed by nearest neighbor interactions. The three lipid species used in our model (phosphatidylcholine, sphingomyelin and cholesterol) may switch between two alternative ordering states characterized by different mobilities. Minimization of the ordering energies between nearest neighbors may result in the formation of lipid domains subdividing the membrane in two phases: A liquid ordered (Lo) or liquid disordered (Ld) phase. Parameterization of the model was performed such that experimentally determined diffusion rates and phases in ternary lipid mixtures of model membranes were correctly recapitulated. The contact energies properties of the considered model proteins species were chosen such that they have a high affinity to either the Ld or Lo phase. The mobility of proteins was fitted to experimental data for different protein densities. Our simulations show that proteins are able to induce the formation of Lo domains in membranes that in the absence of protein would not show a phase separation. It is also shown that under physiological conditions proteins may prevent the lipid domains from growing to larger size that would make them detectable by means of optical microscopy. Both findings contribute to the ongoing debate about the mechanisms underlying the formation of lipid rafts.