Phosphatidylserine (PS) is an essential phospholipid present in all mammalian cellular membranes, and it is especially abundant at the plasma membrane inner leaflet.

PS is involved in many important cellular events. It is synthesised only in the endoplasmic reticulum (ER) (and a specialised region of ER called MAM, mitochondria-associated membrane), but it is needed in all cellular membranes. Therefore, translocation of PS from the site of synthesis to other locations in the cell must take place. In addition, the concentration of PS varies among cellular organelles, being highest in the plasma membrane. Also the distribution of PS molecular species differs between organelles. How is intracellular PS translocation mediated without perturbing the distinct lipid contents of organelles? Possible lipid translocation mechanisms include transfer mediated by lipid transfer proteins, vesicular transfer, spontaneous diffusion via cytoplasm and lateral diffusion via membrane contacts.

In this thesis and the original publications, results are presented indicating that spontaneous diffusion has an important role in intracellular PS translocation. It was shown that from PS synthesised in the ER/MAM, the less hydrophobic species are rapidly translocated to mitochondria and decarboxylated therein to PE, while more hydrophobic ones are translocated much more slowly. As a result, the PS species remaining in the ER/MAM are, on the average, more hydrophobic than those initially synthesised. Many of these obviously incorporate to exocytic vesicles and are transported to the plasma membrane. It was also shown that PS translocation from the plasma membrane to mitochondria is much slower for the more hydrophobic PS species. Therefore the hydrophobic PS species, once arrived into the plasma membrane, may not be prone to efflux from the membrane, which could be crucial for the maintenance of a high concentration of PS in the inner leaflet of the plasma membrane.