

Review of: "[Review] The Studies of Lipid Phase Polymorphism in Model Membranes"

Arun John Peter¹

¹ University of Fribourg

Potential competing interests: No potential competing interests to declare.

The mini review by Han & Gasanoff gives a brief overview on lipid phase polymorphisms and proteins that induce the transitions from lamellar to non-bilayer states. The review is interesting and informative but for a biologist not specialized in this topic, there are parts of the review which a bit difficult to follow. Therefore, simplifying the content a bit further will enable a wider audience to understand and appreciate this review better.

Major comments:

1. First of all, it will be very useful to the reader if the authors add a figure in the beginning that depicts clearly a lamellar phase, a non-bilayer lipid phase and show processes like intermembrane lipid exchange, the biogenesis of lipid droplets, membrane fusion/fission that are associated with non-bilayer states. Something like Fig 2 but in a simplified manner.
2. There are a number of terms in the review that need simplification or an explanation of what they mean so that a naïve biologist is readily able to follow. For instance, in this sentence "Formation of the body-centered cubic phase and hexagonal phase is..", the authors could explain what a body-centered cubic phase and hexagonal phase mean or depict these in Fig1. Similarly, HII phase needs explanation and abbreviations like TM, IMM should be expanded at least once in the text.
3. There are many instances where some of the statements or comparisons could be followed by a statement of consequence. For example, there is a sentence "Both cytotoxins phenocopy membranotropic properties of C8 subunit of the F0 sector in bovine ATP synthase [43][34]." It is unclear to me why this comparison is made. The other statement "1P- and 1H-NMR spectroscopy studies of the large unilamellar liposomes made of either PC+10mol% CL or PC+10mol% PS and treated with either CTI or CTII have shown that CTII induces formation of non-bilayer structures and increases membrane permeability of both PC+10mol% CL and PC+10mol% PS liposomes, while CTI induces formation of non-bilayer structures and increases membrane permeability only in PC+10mol% CL liposomes (Figure 1)" could end like, "suggesting that (the whole point of the observed difference could be explained)." Another example "CTII decreases angular anisotropy of the spin label EPR spectral signals in lipid films enriched with acidic phospholipids". I am not sure what to interpret here and probably readers who are not familiar with EPR might have the same issue. If the authors could guide with their interpretations, it will help the readers to grasp the content readily. Please look at other instances where comparisons or statements do not have conclusions and address them if possible.

Minor comments:

1. Page 3, there is a typo. "Disfunction" should be corrected to "Dysfunction."
2. Page 5, I am not sure what the authors mean by "short-changed alcohols".
3. Perhaps the NMR spectra in Figure 1 could be explained even further and simpler if possible.