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Self-organized molecular sorting

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Eukaryotic cells maintain their internal order through a hectic process of sorting and distillation of molecular factors taking place on their lipid membranes. A similar sorting process is implied in the assembly and budding of enveloped viruses. We have proposed a theoretical model of the process, in which molecular sorting emerges from the coupling of phase separation and membrane bending. Localized sorting domains form by phase separation on lipid membranes and grow by ab- sorbing laterally diffusing molecules. The domains induce membrane bending and the nucleation of a lipid vesicle. Since the newly generated vesicle is enriched in the biochemical factors of the engulfed domain, this results in a natural distillation process. We found that sorting efficiency is optimal at intermediate values of the aggregation strength, where the number of sorting domains is minimized and simple scaling laws hold. Experimental data suggest that living systems may have evolved to exploit these optimal conditions. In this context, a natural parameter controlling the efficiency of molecular distillation is the critical size of sorting domains. In the experiments, sorting domains are classified into unproductive—characterized by short lifetimes and low proba- bility of extraction—and productive—those that evolve into vesicles that are ultimately extracted. This observation is in agreement with the predictions of classical nucleation theory for subcritical and supercritical phase separated domains. Simple estimates suggest that a large pool of distinct molecular species can be sorted in parallel without significantly interfering with each other, par- ticularly when their homotypic affinities are comparable. However, the mean time spent by sorted molecules on the membrane increases with the heterogeneity of the pool. Overall, these findings provide a unifying perspective on molecular sorting in biological membranes and offer broader insights into cellular organization and viral assembly.

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