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## Mathematical modelling for autophagosome formation

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Autophagy is an intracellular degradation process mediated by the autophagosome. The membrane dynamics of autophagosome formation is unique and complicated, which involves development of a small membrane cisterna into a cup-shaped structure and a double membrane spherical structure by closing the edge [1].

In this presentation, we discuss the mechanism of autophagosome formation from a physical point of view. A flat cisterna has a highly-curved rim, which is energetically unstable. As increasing the membrane surface, the rim area also increases. In order to reduce the energy, the cisterna is spontaneously curled by decreasing the rim area. Accordingly, a shape transition occurs suddenly due to the first order transition [2].

However, live-imaging experiments have shown that autophagosome formation takes place gradually and sudden closure of a flat membrane is not observed. We hypothesize the presence of protein(s) that stabilize the highly-curved rim, which enables gradual enclosure. Indeed, several autophagy proteins are present at the rim.

Thus, we consider the effects of the rim-stabilizing proteins on the dynamics of autophagosome formation. We show that the proteins localize at the highly-curved rim and stabilize it. As a result, intermediate cup-shape states appear and the closing dynamics becomes moderate similar to that of autophagosome formation *in vivo*.

[1] Mizushima 2017, PMID28186333

[2] Knorr *et al.*, 2012, PMID22427874

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