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Ubiquitin and adaptor protein dynamics on mammalian peroxisome membranes

Peroxisomes are membrane-bound organelles within eukaryotic cells that post-translationally import folded proteins into their matrix. Matrix protein import involves a shuttle receptor protein, usually PEX5, which is ubiquitinated during the import process. The translocation of the cargo protein into the matrix is not well understood, and its energetics remain controversial. We stochastically model different ways AAA ATPase-driven removal of PEX5 could couple with cargo translocation. We find that translocation coupling involving more than one PEX5 produces a qualitatively distinct ubiquitin signal. Recent work has shown that ubiquitin on mammalian peroxisome membranes can lead to selective degradation by autophagy, i.e. 'pexophagy.' Our results indicate that low cargo traffic could lead to a natural disuse signal enhancing pexophagy. Adaptor proteins couple ubiquitin to the autophagy machinery. One such adaptor protein for peroxisomes is NBR1, which both sticks to membranes and self-interacts. To understand factors other than ubiquitin leading to selective pexophagy, we model NBR1 dynamics on peroxisomes. We consider individual NBR1 clusters on peroxisomes growing and shrinking and find their coarsening behaviour depends upon the radius distribution of peroxisomes in the system. The radius distribution can change both the power law for cluster growth as well as cluster size distributions. We find that clusters evaporate from small peroxisomes first, concentrating adaptor proteins on larger peroxisomes, independent of the sphere size distribution. This suggests a cellular mechanism for using self-interacting adaptor proteins to bias degradation towards larger organelles.