Modeling ER morphologies

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The peripheral endoplasmic reticulum (ER) forms different morphologies composed of tubules and sheets. Proteins such as the reticulons shape the ER by stabilizing the high membrane curvature in cross-sections of tubules and sheet edges. Here, we show that membrane curvature along the edge lines is critical for determining the specific ER morphologies. We demonstrate computationally, that arc-like proteins can scaffold membranes into edges with different spontaneous curvature of the edge line. We then describe a model that explains virtually all observed ER morphologies based on two types of curvature-stabilizing proteins that either generate straight or negatively curved edge lines (R- and L-type proteins). Dependent on the concentrations of R- and L-type proteins, tubules, sheets, fenestrations, and sheet stacks with helicoidal connections can be generated. R-type proteins, including reticulon 4a/b, favor tubules and outer edges of sheets, whereas L-type proteins, such as lunapark, promote junctions between tubules and sheets, including three-way junctions, i.e. small sheets with concave edges. The model agrees with experimental observations and explains how curvature-stabilizing proteins determine ER morphology.