1. Stacked endoplasmic reticulum sheets are connected by helicoidal membrane motifs
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M. Terasaki, T. Shemesh, N. Kasthuri, R. W. Klemm, R. Schalek, K. J. Hayworth, A. R. Hand, M. Yankova, G. Huber, J. W. Lichtman, T. A. Rapoport, and M. M. Kozlov

2. Terasaki spiral ramps in the rough endoplasmic reticulum
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J. Guven, G. Huber, and D. M. Valencia

Recommended with a commentary by Thomas R. Powers, Brown University

The endoplasmic reticulum is involved in several critical cell functions, such as protein synthesis, lipid synthesis, calcium regulation, and the folding and transport of newly synthesized proteins. This membranous organelle consists of sheets and tubules, and is also connected, somewhat mysteriously, to the nuclear membrane. Typically the sheets are depicted in biology textbooks as a stack of pancakes, with an aqueous region, the lumen, inside each pancake. It is has been strongly suspected that the lumina of different sheets are connected, but until recently the nature of the connection was unclear since it is difficult to discern the three-dimensional structure from two-dimensional electron micrographs of thin slices of the cell (left panel, Fig. 1). Recently, Terasaki and collaborators [1] used electron

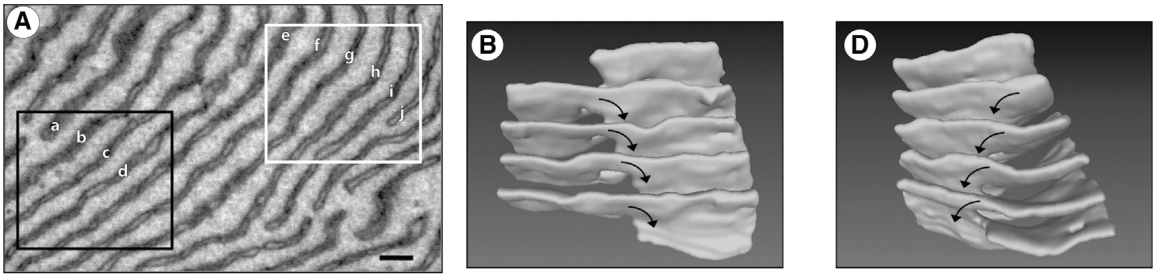

Figure 1: Left panel: Electron micrograph showing a cross-section of endoplasmic reticulum sheets in a cell in a mouse salivary gland. Thin sections (40 nm) are scanned serially and then used to reconstruct the three-dimensional structure. The scale bar is 200 nm. The middle panel shows the 3d reconstruction of the left-handed structure corresponding to the black box in the left panel, and the right panel shows the 3d reconstruction of the right-handed structure corresponding to the white box in the left panel. Figure adapted from [1].

scanning microscopy to deduce the three-dimensional shape of the endoplasmic reticulum. Electron micrographs are created from a thin section of the cell, but since the sections are typically thicker than the approximately 50 nm thickness of a sheet, it is difficult to resolve the details of how nearby sheets are connected. By adapting a technique that was first introduced to map out the connections between neurons [2], the authors generated a series of 30–40 nm thin slices, with each successive slice originating at a slighter greater depth in the cell.

Three-dimensional reconstructions of the endoplasmic reticulum from two nearby regions of a mouse cell are shown in the central and right panel of Fig 1. The reconstructions make clear that the sheets and the lumen in each region are continuous. The structure is that of a spiral ramp in a parking garage, with the layers roughly parallel and with the inner boundary of the sheet tracing out a helical shape. The core of this so-called "Terasaki ramp" is a highly curved section of the bilayer membrane on the cytosolic side of the organelle. Note that the two ramps shown in Fig. 1 are of opposite handedness. Unlike the other famous helices of molecular biology, the authors observe left- and right-handed ramps in roughly equal proportion throughout the endoplasmic reticulum.

The authors also put forth a model based on the mechanics of membranes to explain the observed structure, and this model is extended by Guven, Huber, and Valencia [3]. The high curvature of the membrane at the edge of a ramp is thought to be stabilized by curvature-inducing membrane proteins such as reticulon and DP1/Yop1p proteins that localize to the helical sheet edges [4]. The rest of the membrane is governed by the Helfrich energy, which gives an elastic energy cost for bending. The full governing equations are nonlinear and complicated, but they show that there are solutions which are minimal surfaces, i.e. surfaces that have zero mean curvature. Using the small deflection approximation to make analysis possible, Guven and collaborators show that while a single isolated ramp has a high energy that diverges logarithmically with lateral size, a dipole consisting of a right-handed ramp next to a left-handed ramp has finite energy. The structure of the ramp dipole is consistent with electron microscopy data. The authors also propose a mechanism for dipole formation at a 3-way tubular junction. The insights garnered by these observations and theoretical models should lead to continued progress in understanding the intricate structures of the cell.

References

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