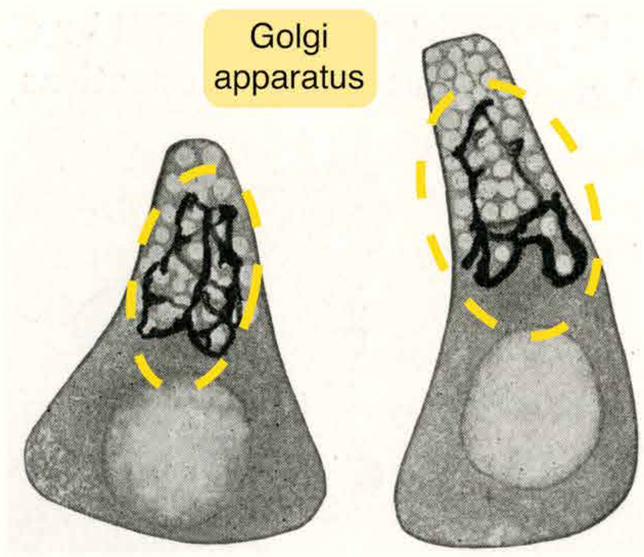
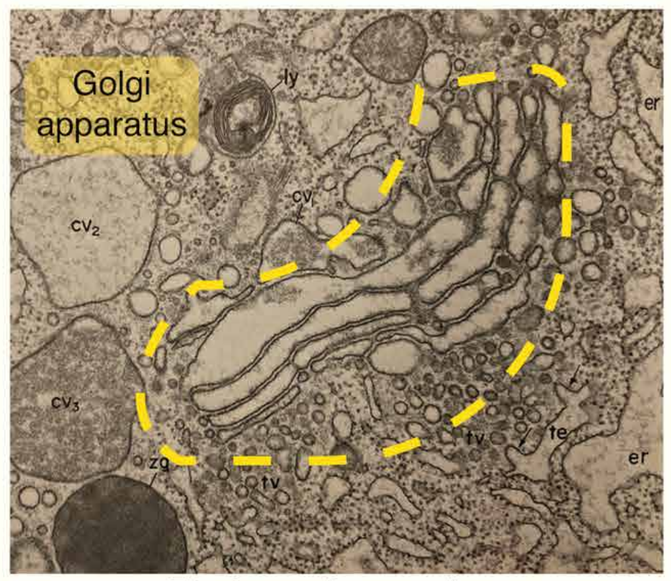
RESOLVING THE INSIDE OF CELLS

Before 1900, it was not clear which structures that appeared to exist inside cells were real and meaningful for the cell. Maybe some were artifacts of the way the cells had to be prepared for observation with the light microscope. And maybe other things existed that were not visible microscopically.



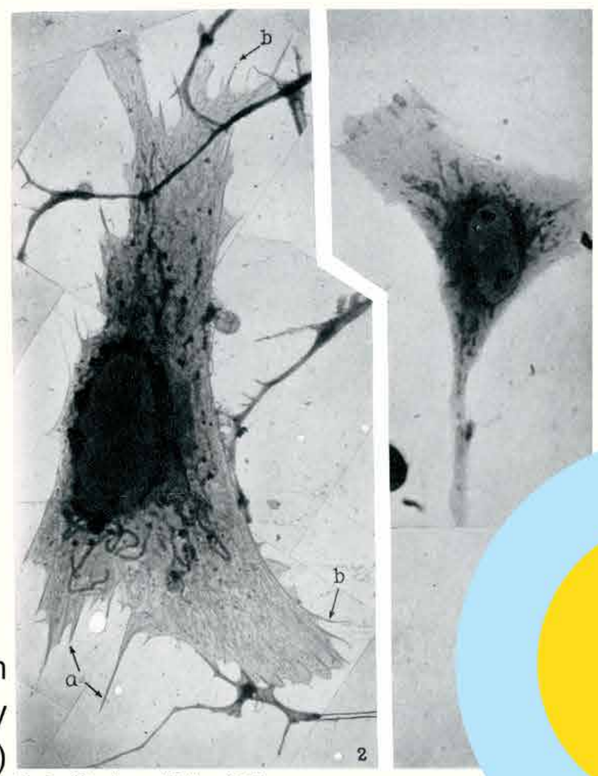
Light micrograph *Cowdry 1924*



Electron micrograph *Farquhar & Palade 1981*

In the 1930s and 1940s, use of the electron microscope (EM) in biology generated new ways to access cellular anatomy. EM made it possible to see more by seeing differently. The greatly increased resolution compared to light microscopy helped researchers visualize the internal parts, or organelles, in much finer detail and to discover new structures in what had been previously deemed the "optically empty" part of the cytoplasm.

With EM, the American Keith Porter, alongside colleagues Albert Claude and Ernest Fullam, saw previously invisible strands in the cytoplasm, later called the endoplasmic reticulum.

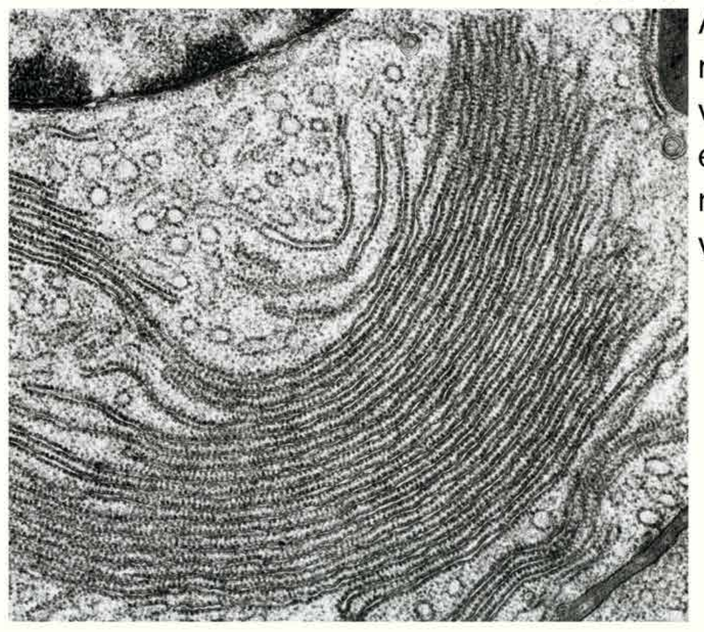


Light micrograph could not resolve the structure of the endoplasmic reticulum (right)

Electron micrograph resolving previously invisible structures (left)

Porter, Claude, and Fullam 1945

Fawcett 1981



A highly magnified view of the endoplasmic reticulum via EM

Further improvements in electron microscopy resulted in even more magnified and detailed images, which influenced theories about organelle function. EM brought new revelations and questions, while also producing exciting new images that required interpretation.

Yet EM, like most light microscopy, required killing the cell by chemical fixation, followed by dehydration, embedding, sectioning, and staining. Cytologists asked: can we observe living cells as they change over time?