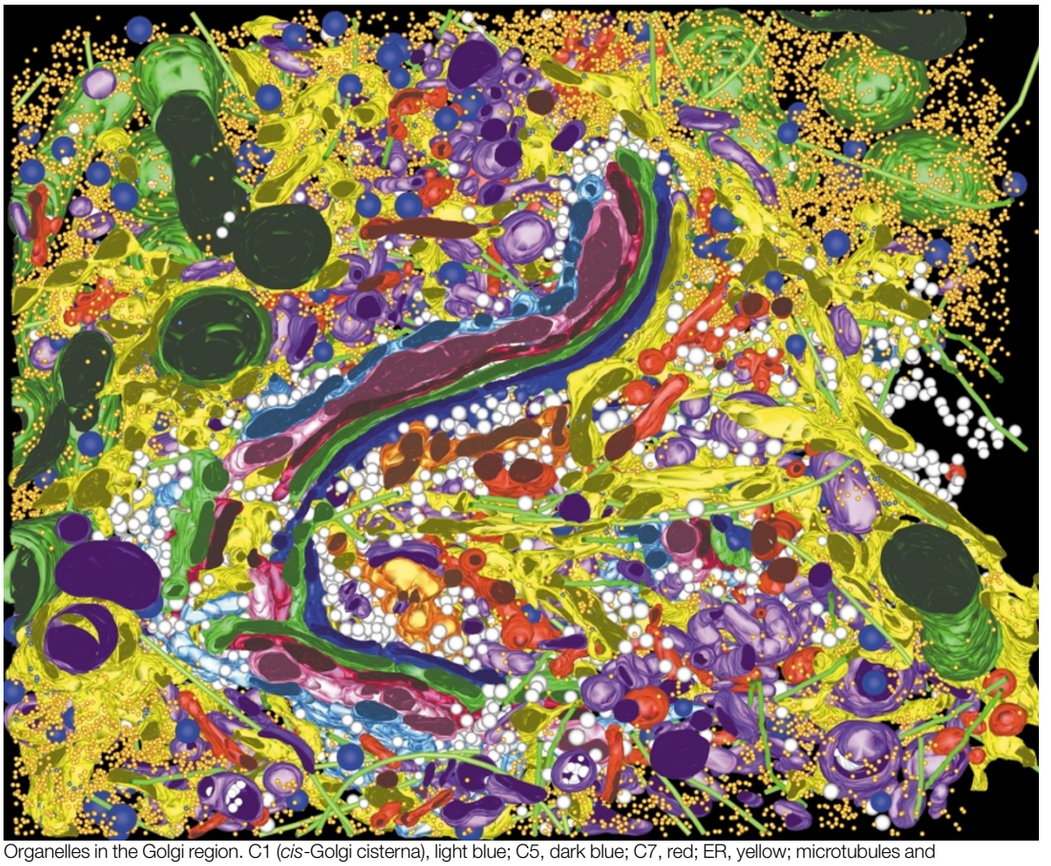

Organelles in the Golgi region. C1 (*cis*-Golgi cisterna), light blue; C5, dark blue; C7, red; ER, yellow; microtubules and mitochondria, green; dense core vesicles, blue; clathrin-negative vesicles, white; clathrin-positive vesicles and compartments, red; clathrin-negative compartments, purple; free ribosomes, orange. Reproduced with permission from National Academy of Sciences © (2001).

TECHNIQUE

The visible cell project . . .

Pancreatic β-cells (HIT-T15) were put to death through high-pressure freezing and freeze-substitution, cut into ribbons of serial 400-nm-thick sections and studied by electron tomography. Marsh and colleagues collected 480 images of three serial sections by tilting the grid that holds the specimen by 1.5° over a range of 120° about two orthogonal axes. They then combined all these images to produce a single, high resolution three-dimensional reconstruction of a $3.1 \times 3.2 \times 1.2\ \mu m^3$ area around the Golgi apparatus of a cell. You would think this is a lot of work for a single image, but just look at the result!

The freezing procedure immobilized all cellular activity within milliseconds, so the final image probably reflects the situation found in a live cell. In addition to being incredibly pretty, this snapshot of the cell also gives us some insights into the organization of organelles around the Golgi.

There were not many surprises about the structure of the Golgi itself, which is here made up of seven cisternae (C1 to C7, going from *cis* to *trans* Golgi). One interesting observation is that the endoplasmic reticulum (ER) seems to traverse the Golgi stack through aligned openings in the cisternae. There are close contacts between the ER and the C5, C6 and C7 cisternae, which might point to direct exchange between these organelles instead of vesicular transport. Following up on these observations might shed some light on the relationship between the ER and the Golgi, which has been controversial over the past years.

Microtubules seem to follow closely the membranes of the C1 cisterna of the Golgi and of endosomal compartments. However, the ER seems to be anchored along microtubules at a few points only. Here again, this observation could provide a lead for further investigation into the interaction of organelles with microtubules.

The technique is not only qualitative but also provides a means to quantify organelles *in situ* in three dimensions, and to measure accurately their physical associations with other organelles. For example, at first sight, you might get the impression that the Golgi region is very crowded, but Marsh and colleagues calculated that only about 34% of the volume is taken up by organelles, the rest being made up of cytoplasmic matrix.

Although many of the findings in this study are not truly novel or revolutionary, being able to see organelles in three dimensions in their natural cellular context should have high impact on how we imagine life in the cell.

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References and links

ORIGINAL RESEARCH PAPER Marsh, B. J. *et al*. Organellar relationships in the Golgi region of the pancreatic beta cell line, HIT-T15, visualized by high resolution electron tomography. *Proc. Natl Acad. Sci. USA* **98**, 2399–2406 (2001)

WEB WATCH

… and the virtual cell project

The Virtual Cell is described by its creators as "a general computational framework for modelling cell biological processes". Access to this software is available over the internet through a JAVA-based interface, and although there is no charge for academic use of the Virtual Cell, users are required to register.

So what is the Virtual Cell? It has been developed at the National Resource for Cell Analysis and Modeling (NRCAM), a US-based resource centre supported by the National Center for Research Resources. Those behind it claim that the technology links biochemical and electrophysiological data with experimentally derived microscopic images showing the subcellular localizations of the molecules involved. In this way, they say, "physiological results can be simulated within the empirically derived geometries, thus facilitating the direct comparison of model predictions with experiment".

There are two interfaces to the Virtual Cell — one biologically orientated, the other mathematical. The biological interface has been designed to allow users to define cellular geometry, create models and simulations, and to analyse the results of such simulations.

For those unfamiliar with the technology or software there's a 'User's Guide', backed up by a tutorial designed to work in conjunction with it, and a 'User Discussion' page for troubleshooting. There are also examples of what the site can do — the applications shown include use of the Virtual Cell to study diffusion processes in mitochondrial cristae, and a simulation of a calcium wave in neuroblastoma cells. Movies are provided with some of the examples, although more explanation would enhance their value.

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