

Editorial

Special Issue: microtrabecular concept of the cytoplasm revisited

We know the cell is filled with proteins, macromolecular complexes, nanomachines, filaments, tubules and organelles, but we still lack a clear understanding of the spatial organization, mutual interactions and interactions of all these cellular components.

Over 20 years ago, at the University of Colorado in Boulder, Keith Porter pushed the limits of the High Voltage Electron Microscope (HVEM) to probe the organization of cell cytoplasm. Porter and his collaborators examined whole cells -- fixed, frozen-dehydrated, or freeze-substituted. They became convinced that the cytoplasm contained a lattice of anastomosing microtrabecular structures, a sort of "cytoplast" surrounding all organelles and cytoskeletal elements. Porter's 1981 description of the microtrabeculae given in full in John Heuser's piece in this special issue starts with "The microtrabecular lattice is continuous throughout the cell; it divides the cytoplasm into a 'protein-rich' polymerized phase and an excluded 'water-rich' fluid phase".

Today the words macrotrabeculae and cytoplast have almost disappeared from textbooks and biology journals because nobody could put names of specific molecules on such cytoplasmic structures. Also, it became increasingly obvious that fixations and even the best fast-freezing techniques had artifactual consequences that created empty regions in the cytoplasm.

Twenty years later, John Heuser asks "Whatever happened to the 'microtrabecular concept'?". The author displays in startling red-green anaglyphs for 3D viewing, the most striking micrographs and conceptual drawings generated by Porter and his students, post-docs, collaborators and visitors during the microtrabecular years in Boulder.

Heuser himself pushed high resolution observations of the cell further by using alternative strategies for preparing samples such as fast-freezing and deep-etching. This has allowed Heuser and his associates to visualize cellular structures at the level of constituting macromolecules -- cell cortex, axomemes, trafficking organelles, synapses, etc. Some of these spectacular structures are displayed in 3D anaglyphs in the following pages. Heuser, who challenged Porter's view of the microtrabecular lattice, recounts the evolution of our ideas about the structure of the cytoplasm since Ramon Y Cajal made his histological discoveries of organelles a century ago. The saga of the discovery of microtrabeculae and its present status is also commented on in 2

letters by John Wolosewick and Mark McNiven who participated in the microtrabecular research and recount Porter's unique way of leading the adventure.

In this issue Heuser reexamines the substructure of the cytoplasm using fast-freezing and deep-etching, and compares it with the substructures obtained in the 80's by Porter's HVEM observations. Using various cells as well as concentrated protein solutions, Heuser finds that there is no clear evidence for the presence of a cytoplasmic microtrabecular network, but that the cytoplasm substructure consists of an intricately woven cytoskeletal scaffold and its multiple associated macromolecular structures. Of course this may be just a matter of semantics. The tightly woven meshwork of actin filaments, intermediate filaments and microtubules, and the cohorts of associated proteins, ribosomes and other nanomachines coating them, may form some kind of microtrabecular network. We may wonder, as Porter did, whether protein-rich networks surrounding cytoskeletal elements and organelles reorganize in a coordinated fashion under various physiological conditions. High resolution probing of cytoplasmic reactions and interactions *in situ* with confocal microscopy is one way to approach this question in the living cell. But we need to get closer. John Heuser's fascinating electron micrographs of motors, spokes, and microtubules in the axoneme show how important molecular resolution is to our understanding of cellular structures and their mechanics.

Now that knowing the cell's proteome and its dynamic behavior is a reachable goal, it remains to be seen at the highest possible resolution how these proteins interact, and how they assemble and disassemble into substructures in the cytoplasm of cells. As in Porter's time, we need new ways to probe the cell using the most powerful techniques of our days.

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