Questions for Professor Jennifer Lippincott-Schwartz

Q: Your data on single molecule tracking of VAPB on MAMs is exciting. Any idea for an approach to study the actual membrane remodelling processes at MAMs closer, especially during intracellular homeostatical changes.

This is a good question. To watch the membrane remodelling events at MAMs during homeostatic changes, we will need to image these sites over hours at superresolution, as the homeostatic changes take time to occur and can only be visualized by superresolution approaches. That said, looking at these sites before and after the homeostatic change can set the groundwork for setting up hypotheses for what remodeling events may be occurring.

Q: Your 3D images illustrate how extremely crowded the intracellular milieu is. In that vein, do you think it is possible that the morphology of some membrane-bound organelles (like vesicles) is defined by purely physical phenomena such as diffusion-limited aggregation, or Hele-Shaw flow, (https://en.wikipedia.org/wiki/Diffusion-limited_aggregation) rather than by purposeful, active morphogenesis?

This is a great question. My own view is that much of the morphologies of membrane-bound organelles is driven by organelles interacting with each other (and the cytoskeleton). For example, in our FIB-SEM datasets, you often see ER spreading itself up against a mitochondria (perhaps to increase its contact site surface). The ER's flattened shape at these contact sites is controlled by contact site tethering proteins. Regarding your specific question about Hele-Shaw flow, I don't have an answer since the fluid mechanics in a cell may operate differently than outside cells. This is because membrane organelles (which would be the parallel plates) are themselves fluid entities.