Ben Cardoen, Timothy Wong, Parsa Alan, Sieun Lee, Joanne Aiko Matsubara, Ivan Robert Nabi, and Ghassan Hamarneh (the authors)

Self-tuning weakly supervised object detection (SPECHT) of sub-diffraction limited caveolae and scaffold and amyloid-beta deposits by super-resolution and confocal microscopy

Identification of objects in fluorescence microscopy is a non-trivial task burdened by parameter-sensitive algorithms, for which there is a clear need for an approach that adapts dynamically to changing imaging conditions. Here, we introduce an adaptive object detection method that, given a microscopy image and an image level label, uses kurtosis-based matching of the distribution of the image differential to express operator intent in terms of recall or precision. We show how a theoretical upper bound of the statistical distance in feature space enables application of belief theory to obtain statistical support for each detected object, capturing those aspects of the image that support the label, and to what extent. We validate our method on 2 datasets : distinguishing sub-diffraction limit caveolae and scaffold by stimulated emission depletion (STED) super-resolution microscopy; and detecting amyloid-beta deposits in confocal microscopy retinal cross-sections of neuropathologically confirmed Alzheimer's disease donor tissue. Our results are consistent with biological ground truth and with previous subcellular object classification results, and add insight into more nuanced class transition dynamics. We illustrate the novel application of belief theory to object detection in heterogeneous microscopy datasets and the quantification of conflict of evidence in a joint belief function. By applying our method successfully to diffraction-limited confocal imaging of tissue sections and super-resolution microscopy of subcellular structures, we demonstrate multi-scale applicability.

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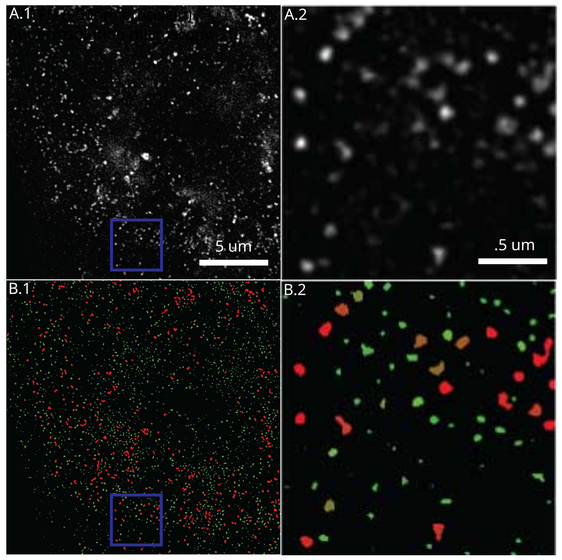
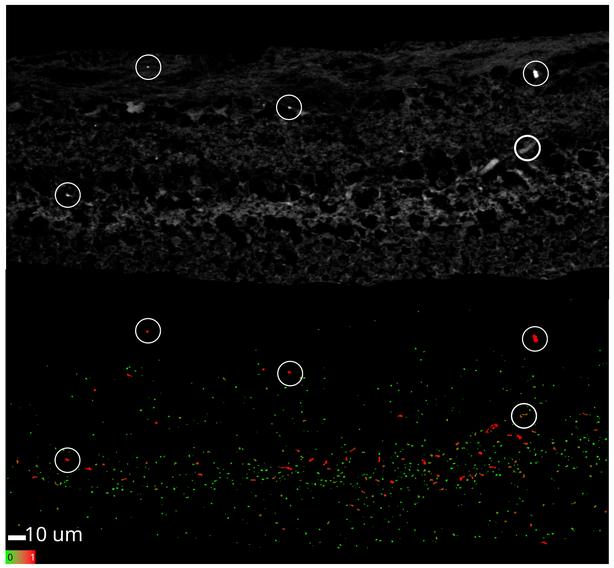
Detecting Caveolae in 2D STED superresolution microscopy



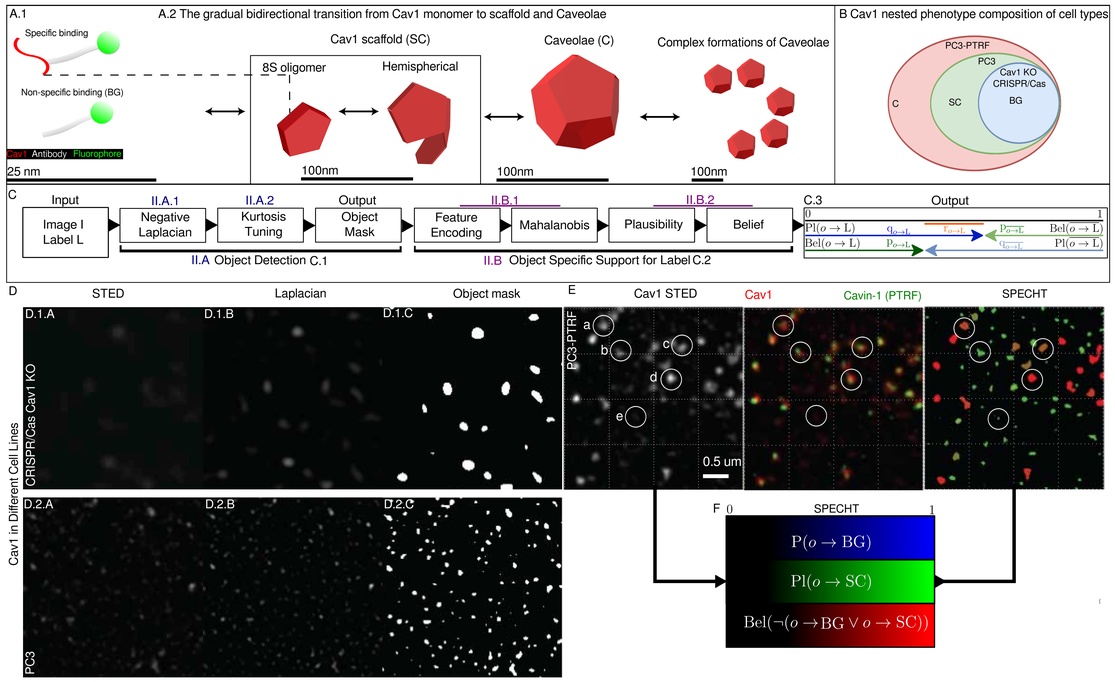
Caveolae are structures composed of Cav1 proteins that enable a cell membrane to withstand stress, and therefore motility. The formation process of Caveolae is thus a critical factor in understanding metastasis in cancer cells. We want to identify in each superresolution image (2D STED, $\sim$ 20nm) if a Cav1 concentration is a Caveolae, background, or scaffold.

Detecting Alzheimer-disease specific amyloid-β in confocal microscopy



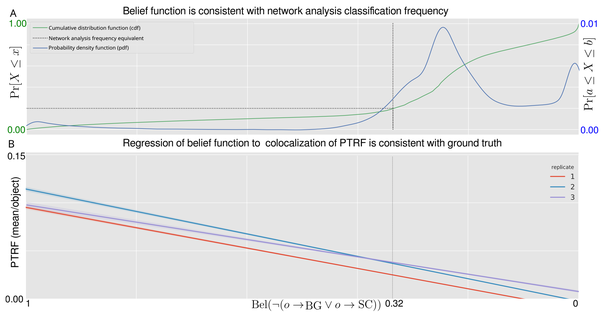
Amyloid-β deposits are associated with Alzheimer disease, but also are present in healthy tissue. We want to identify in retina tissue which AB deposits are indicative of Alzheimer disease, AD+ vs healthy tissue, AD-

Adaptive object detection and belief theory based contrastive learning algorithm



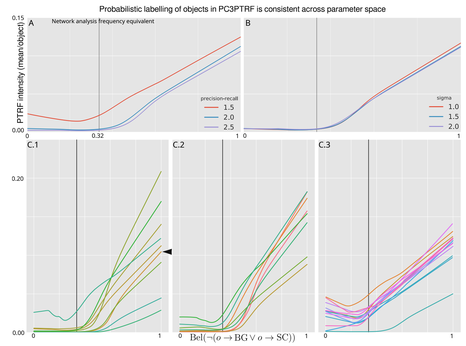
Outline of our method [1]. A: The formation process of Caveolae. B: Genotype alteration allows us to build a 3-valued belief label. C: The control flow of our algorithm (SPECHT) details the individual steps from self-tuning object detection to belief theory based labelling. D: The need for self-tuning object detection becomes clear as we contrast the intensity and object diversity in Cav1 knock-out (D.1.A), PTRF-KO (D.2.A), and the unaltered cells (E). E.Specht: An example of an annotated (inset) of a prostate cancer cell. We observe high (expected) colocalization with PTRF for objects labelled as Caveolae, PTRF is necessary for the formation of Caveolae.

Results are consistent SMLM-based Caveolae frequency.



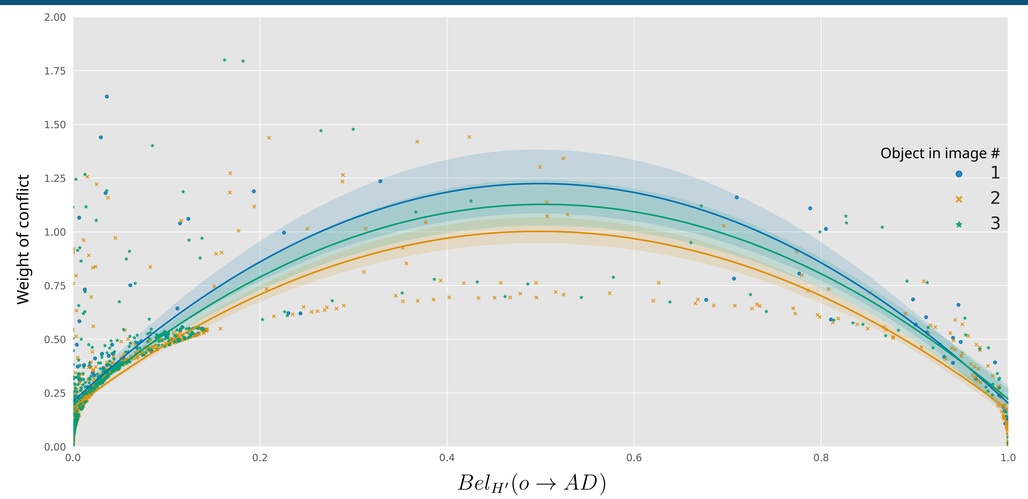
Cav1 requires PTRF to form Caveolae. Caveolae in PC3-PTRF cells is reported at a 20% [2] frequency. Our belief label (X-axis) is consistent with both. Observe how the 20% frequency coincides with a clear elbow point in the cdf and pdf curves.

Results are consistent with PTRF colocalization.



LOESS regression of the belief label (X-axis): colocalization of PTRF with Cav1 is consistent across cells and coincides with the elbow point of the cdf curve.

Conflict computation between heterogeneous models



Example of conflict (Y-axis, $\sim$ disagreement) between individual object labels when SPECHT is modelled on 2 distinct datasets. A higher Y-value indicates higher disagreement, each marker represents a single object in an image. The X-axis denotes the belief label. Minimum conflict is highest where the belief label is around .5.

[1] Ben Cardoen et al. "SPECHT: Self-tuning Plausibility Based Object Detection Enables Quantification of Conflict in Heterogeneous Multi-scale Microscopy". In: (Sept. 2020). DOI: 10.36227/techrxiv.12971051.v1.

[2] Ismail M Khater et al. "Super resolution network analysis defines the molecular architecture of Caveolae and Caveolin-1 scaffolds". In: *Scientific Reports* 8.1 (2018), pp. 1–15.

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