Learning to look *beyond* what we can see

Leveraging statistical learning to improve scientific discovery from fluorescence microscopy

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Statistical and computational learning answer cellular biology questions with a clinical impact
Reducing false positives and false negatives in 3D single molecule localization microscopy (SMLM).

SMLM: 2D image sequence to 3D point cloud

3000 nm

2D acquisition

3D labelled microtubules, ~ 100nm diameter.
Reducing false positives and false negatives in 3D single molecule localization microscopy (SMLM).

SMLM: 2D image sequence to 3D point cloud

High density can induce artifacts
Accurate density prediction can reduce reconstruction errors.

With density known, **Reconstruction** can approximate **emitters** more accurately.
Belief theory enables weakly supervised object detection in fluorescence microscopy

### Belief theory principles

<table>
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<th>A3</th>
<th>Statistical Support</th>
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<tbody>
<tr>
<td>P(α → L)</td>
<td>Pl(α → L)</td>
<td>Bel(α → L)</td>
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<td>P(α → L)</td>
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- **A.2**: Plausibility and belief are each other's complement
  - Pl(α → L) → Bel(α → L)

- **A.3**: Weak evidence, maximum certainty
  - P(α → L) → Bel(α → L)

- **A.4**: Strong evidence, high certainty
  - P(α → L) → Bel(α → L)

- **A.5**: Strong evidence, medium certainty
  - P(α → L) → Bel(α → L)

- **A.6**: No evidence, maximum uncertainty, 'ignorance'
  - P(α → L) → Bel(α → L)
Detecting Alzheimer-associated amyloid-β deposits in confocal retinal tissue.

Alzheimer incidence is rising **quickly**, detection is often **too late to reverse/treat**.

Can we detect Alzheimer signature in retinal tissue?

Amyloid-β deposits in confocal microscopy of retinal cross-sections (neuro pathologically confirmed Alzheimer’s disease donor tissue).

Amyloid-β is essential for **healthy cells**, we need to detect which deposits are **markers** for Alzheimer’s disease.
Identifying key stages of the formation process of protein complexes in the cell membrane.

Caveolae are ~100 nm spherical invaginations that buffer the cell membrane against shock.

Scaffolds combine into caveolae

Formation process is largely unknown, therefore key to capture and quantify
Capturing mitophagy in live cells.

Mitophagy removes damaged or dysfunctional mitochondria from the cell.

Mitophagy in a cancer cell (fibrosarcoma) recorded over time
