

# Dense 3D Semantic Segmentation for Biomedical Electron Microscopy

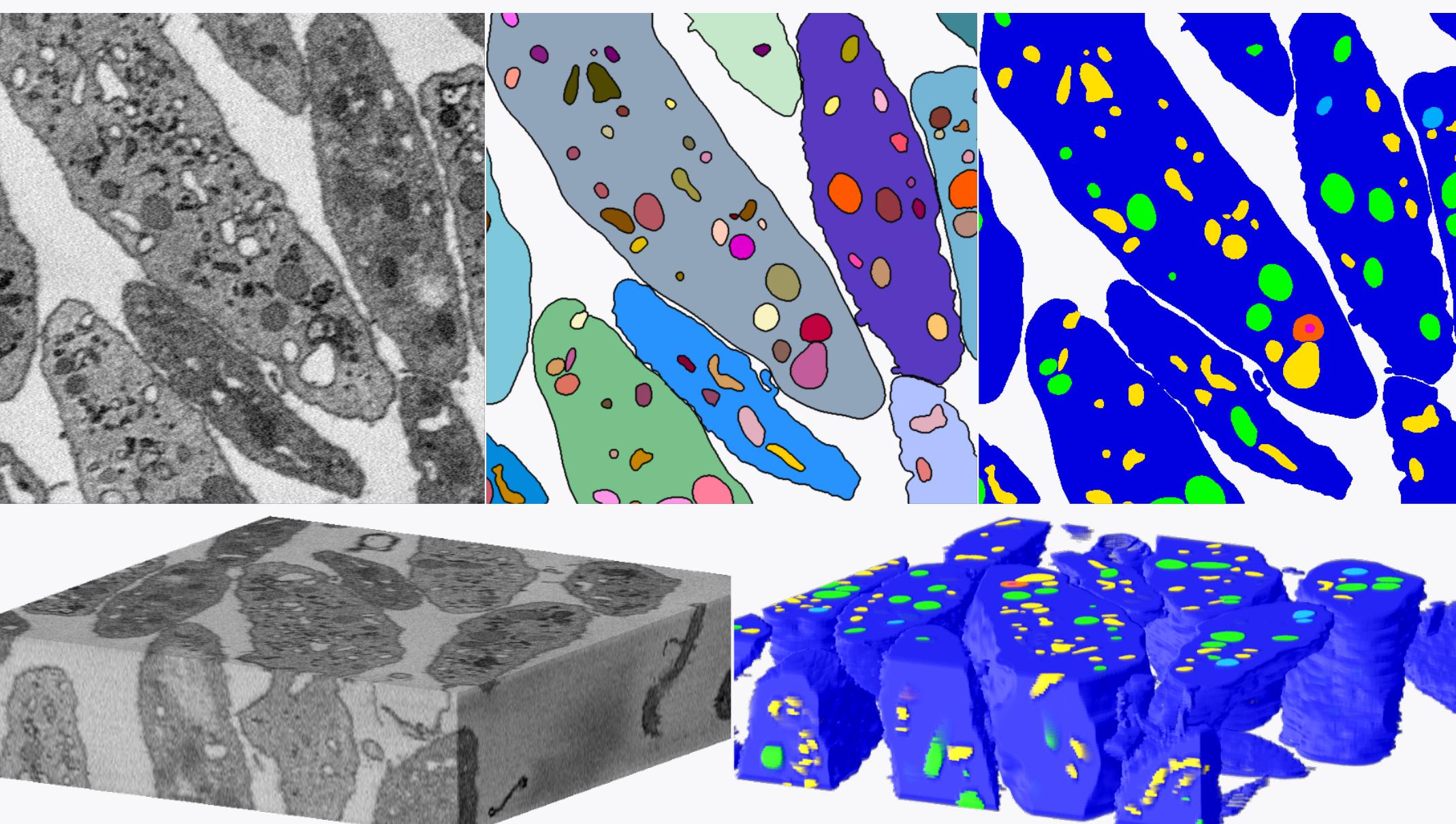
## Board of Scientific Counselors Review

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### Introduction

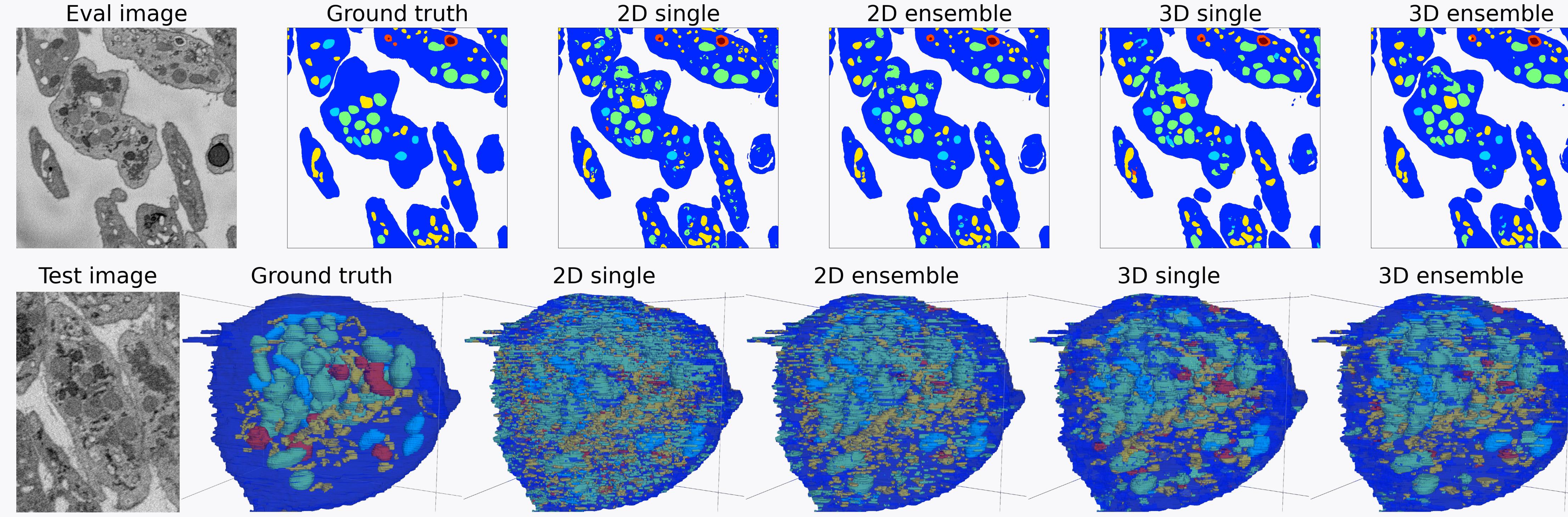
- Biomedicine uses **electron microscopy** (EM) to study biological matter at the nanoscale.
- Serial block-face scanning electron microscopy (**SBF-SEM**): Image up to  $1 \text{ mm}^3$  biological samples at  $\sim 5 \times 5 \times 25 \text{ nm}$  resolution - giga/teravoxel datasets possible.
- **Systems biology** will greatly benefit from high-throughput EM, but data analysis is challenging.
- **Dense semantic segmentation**: Create rich 3D structural models of all (most) cells and organelles in sample, as opposed to just parts.
- Challenging for computers, slow and challenging for humans.
- **Computer vision** (CV) algorithms use neural nets to predict segmentations from 3D image volumes.



2D and 3D views of an SBF-SEM platelet dataset and a semantic model of its cells and organelles.

### Challenges

- Training **label generation** is tedious, and experts may disagree.
- Lack of **3D benchmark datasets** makes it hard to compare and share tools for biomedical computer vision.
- Automated segmentation is still **not accurate enough** for dense semantic segmentation of interesting biological EM datasets.
- **Goal:** Better **neural architectures** for more useful CV algorithms.
- **Goal:** Better **software infrastructure** to turn CV algorithms into useful tools for microscopists.
- **Goal:** Release high-quality **3D benchmark datasets** to spur community development.



In the course of this project, we tested many configurations of 2D and 3D segmentation networks and ensembles. This figure shows results from the best 2D and 3D individual networks and ensembles. (**Top**) Comparison of 2D segmentation cross-sections on the evaluation dataset. (**Bottom**) Comparison of 3D renderings on one of the test cells from another platelet sample than the one used for training. Testing networks on the same tissue system but a different physical sample helps gauge how robust they are to image variations.

### Methods

- **Data:** Two SBF-SEM platelet volumes with 6 label classes: Cell, mitochondrion, alpha granule, canalicular system, dense granule, dense core.
- **2D-3D network:** Large 2D segmentation module forms intermediate predictions which are input to a smaller 3D segmentation module. Memory efficient, better observed results than 3D alone.
- Run architecture generation experiments on **Biowulf** to compare net design choices.

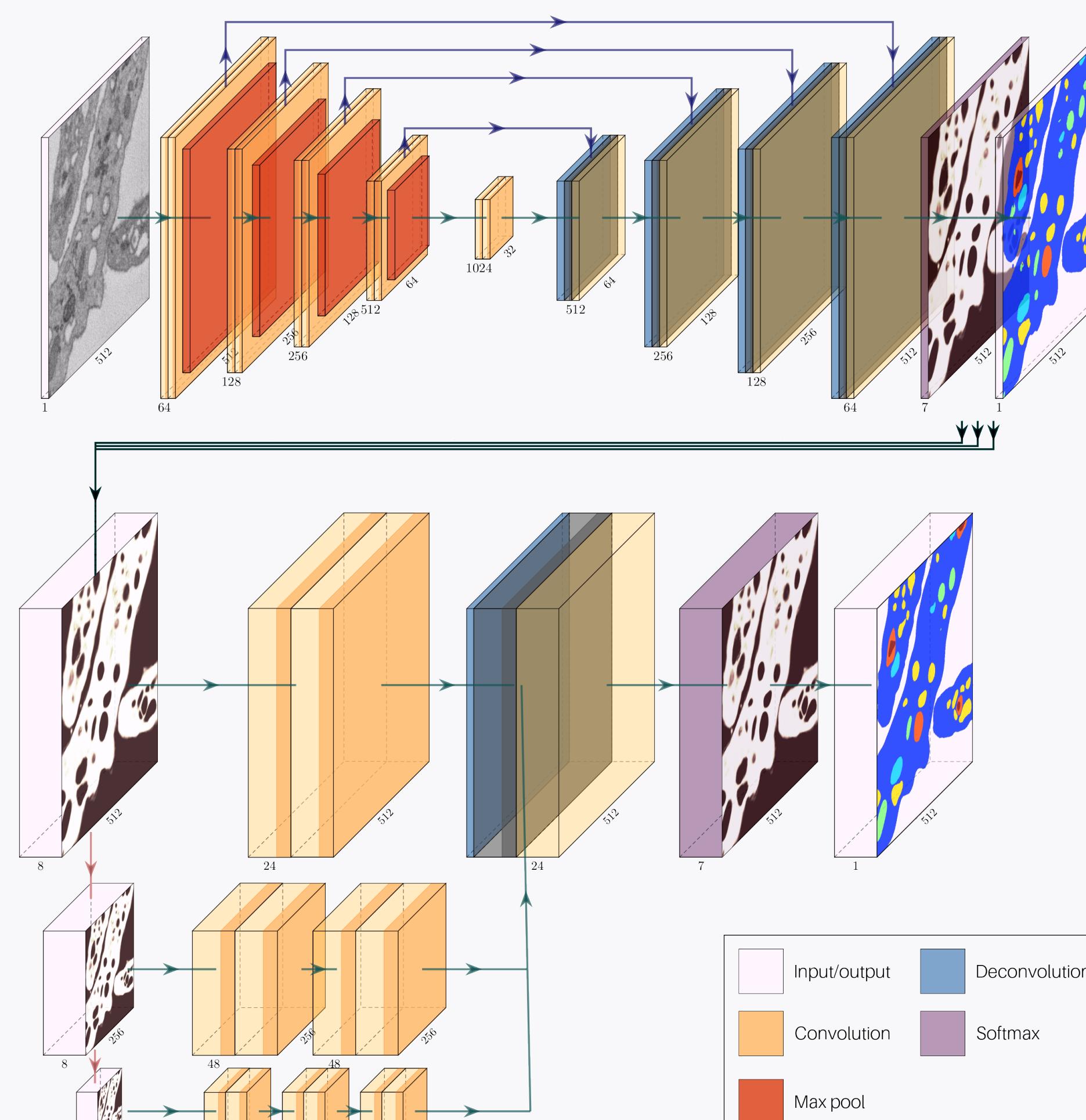


Diagram of a typical 2D-3D network. A 2D (+3x3x3) encoder-decoder feeds class probabilities from successive 2D image windows into a 3D spatial pyramid module to produce a final segmentation prediction.

### Results

- Overall, a **2D-3D+3x3x3** ensemble performs best on the test dataset, the best indicator of generalization ability.
- 3x3x3 ablation better on eval. Difference is not significant compared with same-net variations between training sessions.
- 3D nets better than 2D nets. Ensembles better than individual nets.
- All LCIMB nets perform much better than existing baselines like DeeplabV3, DeepVess, and MedicalNet when trained on our segmentation task.

Architecture	Eval MIOU	Test oMIOU
Ens. 2D-3D+3x3x3 4	0.686	<b>0.553</b>
Ens. Abl. 3x3x3 Convs 5	<b>0.690</b>	0.520
Ens. 2D-3D 4	0.688	0.470
2D-3D+3x3x3	0.665	0.547
2D-3D	0.650	0.477
Abl. 3x3x3 Convs	0.667	0.466
Abl. Multi-Loss	0.652	0.467
Abl. 3D Pyramid	0.646	0.487
Ens. Abl. Multi-Loss 3	0.633	0.445
Ens. Abl. 3D Pyramid 3	0.681	0.533

3D network results summary. Mean intersection-over-union (MIOU) on eval data and organelle MIOU (oMIOU) on test data. 2D experiments and baselines not shown. *Abl.* short for ablation, *Ens.* short for ensemble. The test dataset contains only a small number of labeled cells among unlabeled ones; restricting the MIOU stat to the labeled region invalidates cell class statistics, hence the use of oMIOU.

### Future Work

- **Robust segmentation:** Train a single segmentation model that works across multiple datasets. May involve:
  - Transfer learning of networks or network modules between datasets.
  - **Hierarchical semantics:** Predict a hierarchy of both broad and narrow classes to better deal with unknown structures.
- **Panoptic segmentation** for biological EM: Combining semantic and instance segmentation to generate 3D object meshes and semantics from images.
- **Expand benchmark dataset:** Currently assembling a collection of annotated EM image volumes for release to the machine learning community: <https://bio3d-vision.github.io/>.
- Use a **correction-training feedback loop** to produce large amounts of labeled training data. Requires integrating machine learning tools with established in-lab analysis software.
- **Active learning:** Develop algorithms to determine which data is most *informative*.
- **Intramural collaboration** to build a biological microscopy scientific computing + machine learning team with the size necessary to address research and applications in their full scope.

### References

- [1] M. Guay, Z. Emam, A. Anderson, and R. Leapman, "Designing deep neural networks to automate segmentation for serial block-face electron microscopy," in *15th IEEE International Symposium on Biomedical Imaging, ISBI 2018, Washington, DC, USA, April 4-7, 2018*, pp. 405–408, 2018.
- [2] M. Guay, Z. Emam, and R. Leapman, "Problems and progress in automating electron microscopy segmentation," *Microscopy and Microanalysis*, vol. 24, no. S1, pp. 508–509, 2018.

### Acknowledgements

- This work made use of the computational resources of the **NIH HPC Biowulf cluster**.
- Data for this project was acquired in collaboration with Professor Brian Storrie's lab at UAMS ([link](#)).
- View this poster online at <https://leapmanlab.github.io/bsc-2019/poster.pdf>.