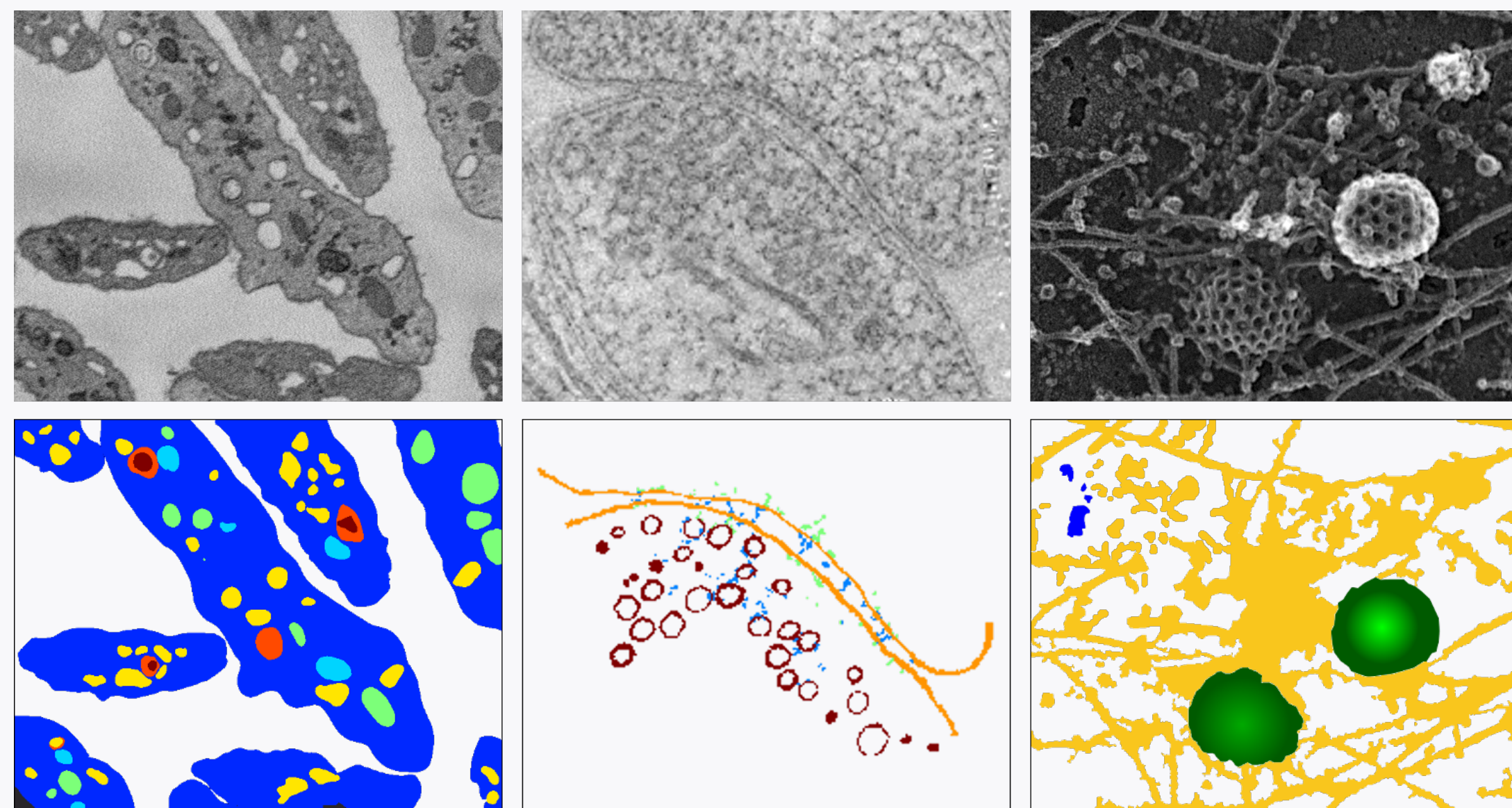


# Neural Segmentation Algorithm Design for Biomedical Electron Microscopy

## Introduction

- Biomedicine uses **electron microscopy** (EM) to study biological matter at the nanoscale.
- New electron microscopes can acquire large datasets quickly.
- 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 by repeated cutting and scanning.
- **Systems biology** will greatly benefit from high-throughput EM, but data analysis is challenging.
- Major bottleneck is **image segmentation**: grouping image voxels together according to image content.
- **Semantic** segmentation: Assign a “class” to each voxel in an image (cell, organelle, etc.). Main focus of this poster.
- **Instance** segmentation: Assign a unique tag to each object in an image.



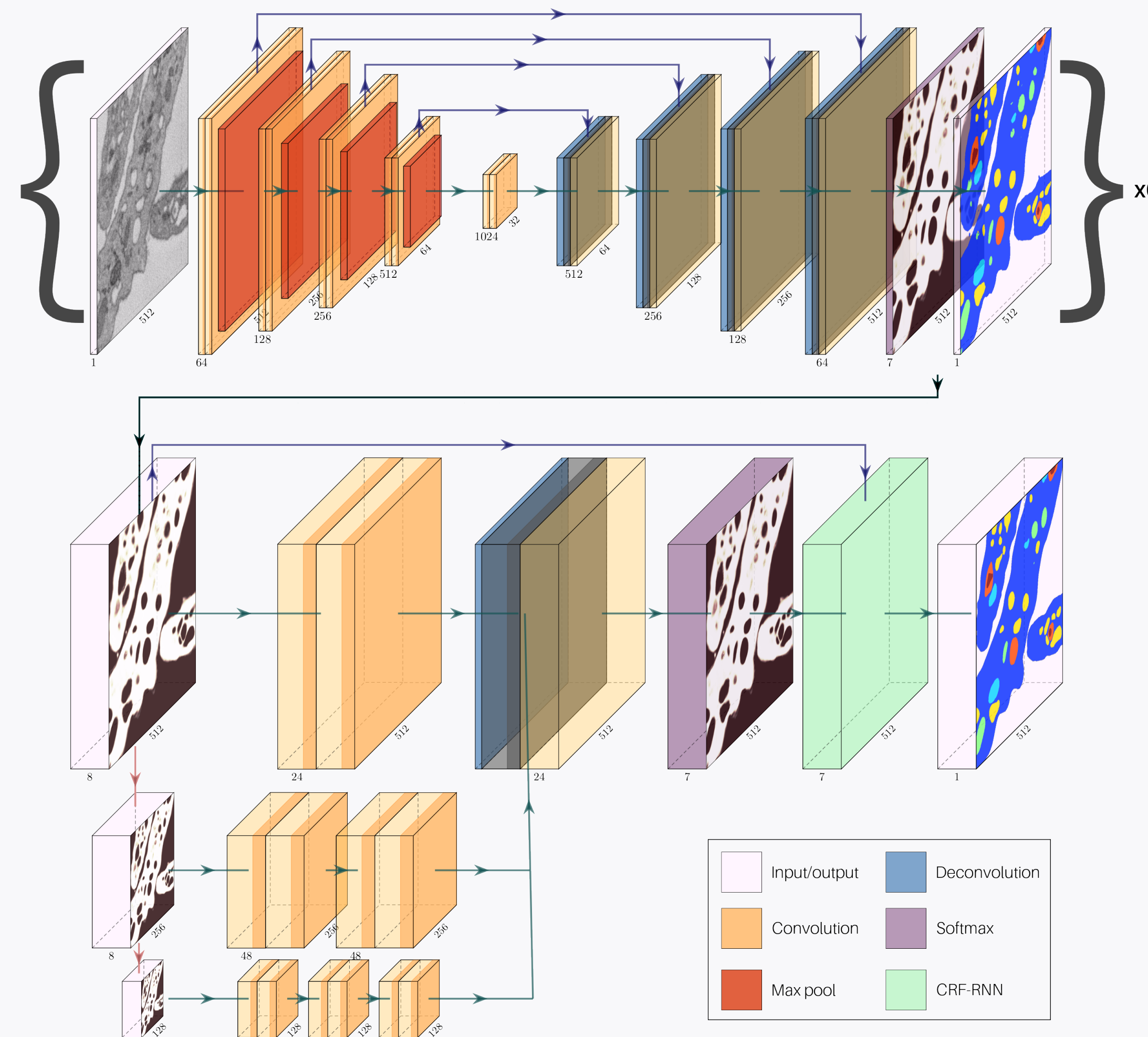
Sample EM images, and their semantic segmentations. **Left**: SBF-SEM image of platelet cells. **Center**: TEM tomographic image of synaptic tissue, courtesy of NINDS Laboratory of Neurobiology. **Right**: Platinum-replica TEM tomographic image of a HeLa cell wall, courtesy of the NHLBI Taraska Lab.

## Segmentation Challenges

- Training **label generation** is tedious, and experts may disagree.
- Different EM hardware + sample combinations create **many image types**.
- Segmentation automation difficulty is highly **problem-dependent**.
- **Goal**: A **reproducible workflow** for effective neural segmentation architecture discovery, training, and usage.
- **Goal**: Use that workflow to design **problem-specific segmentation algorithms**.

## Network Architecture Design

- Segmentation networks use combinations of **multi-scale convolutional** modules.
- Common modules: pooled convolution blocks, dilated convolution blocks, encoder-decoders, spatial pyramid pooling units, more.
- **Architecture design**: Construction of a computation graph which contains the variables trained during learning.
- Segmentation network architecture design is a combinatorial search with a **large state space** and **expensive evaluations**.



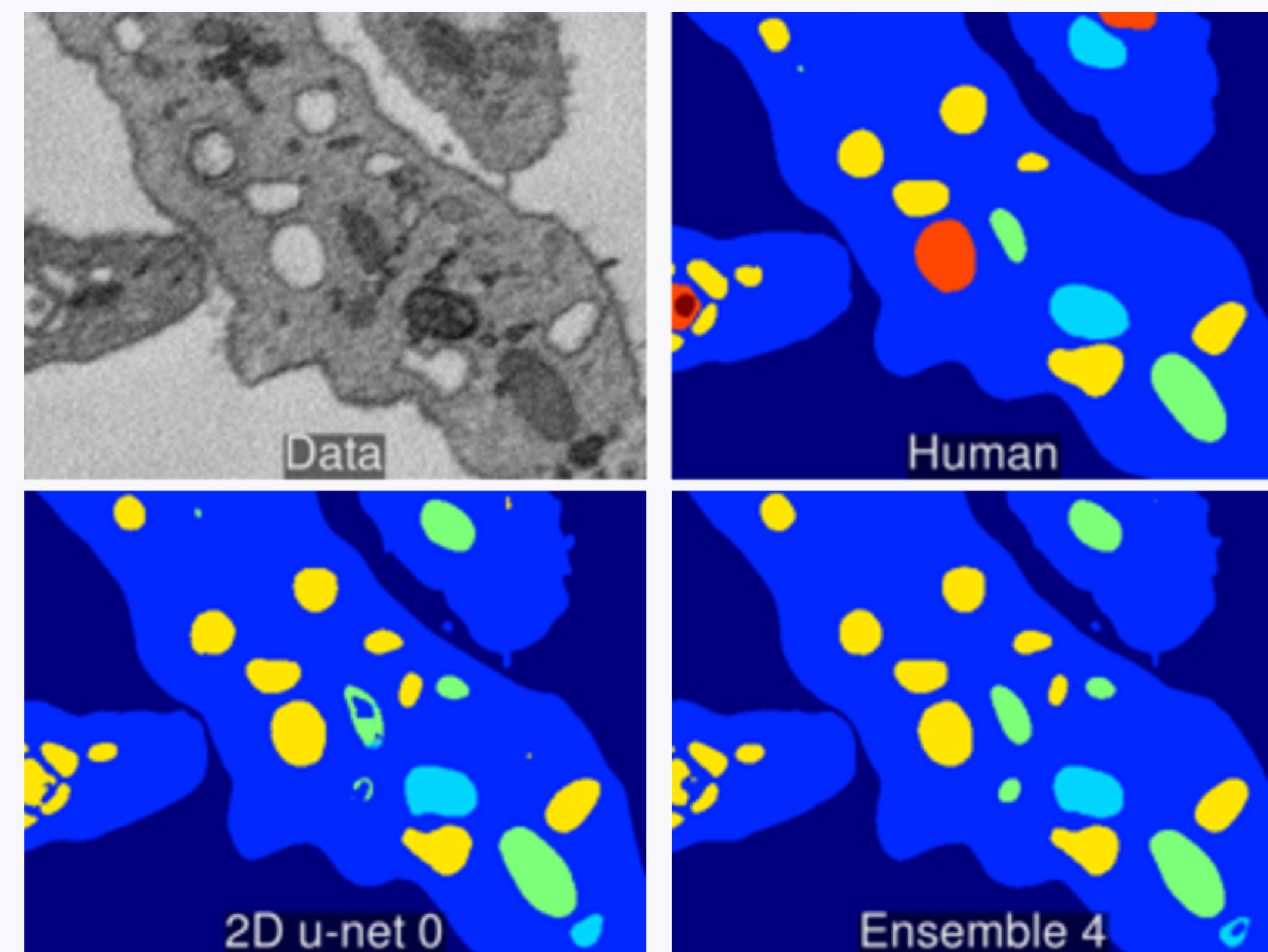
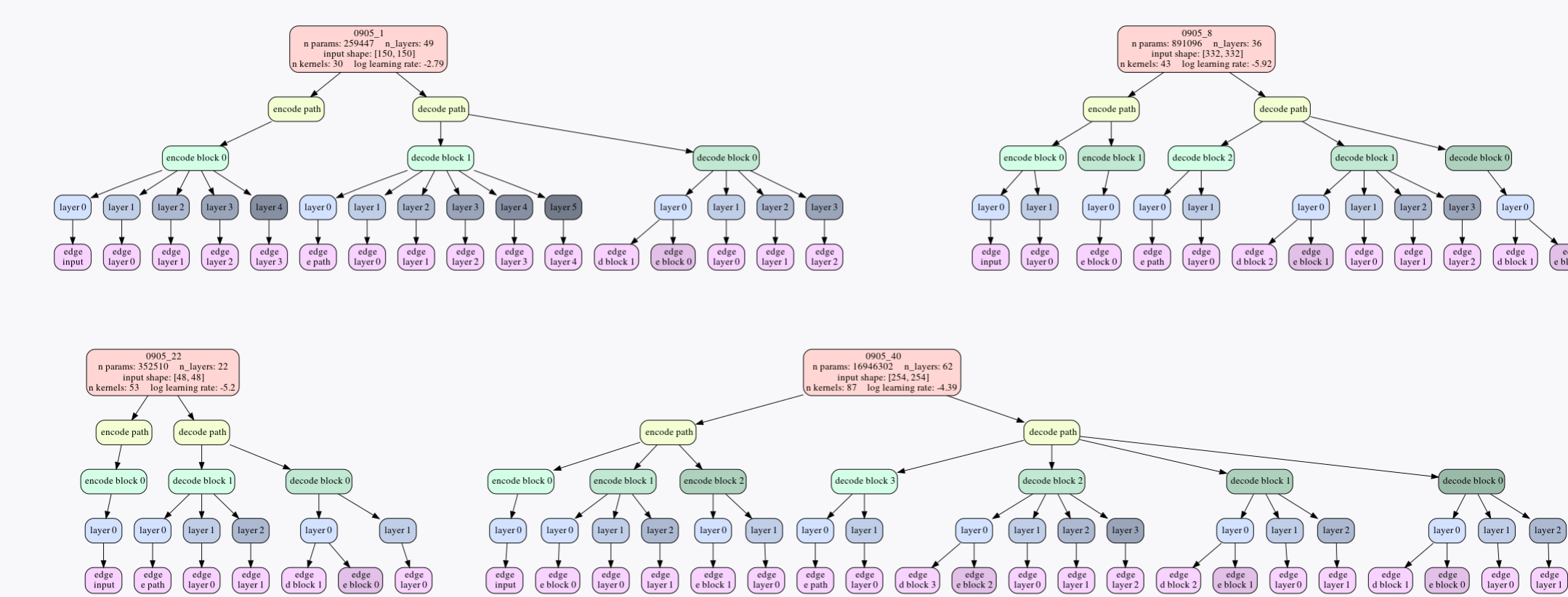
Example of a hybrid-3D + CRF-RNN segmentation network, of the type found most effective on 3D SBF-SEM data so far. More info in the next box.

## Hybrid-3D Networks

- **2D vs 3D** tradeoffs: spatial context vs. memory usage, dealing with anisotropy along  $z$  axis.
- **Hybrid-3D network**: Large 2D convolutional encoder-decoder module forms intermediate predictions. Concatenated 2D predictions form input to a small 3D convolutional spatial pyramid module.
- A 3D **CRF-RNN** (conditional random field as recurrent neural network) module can be used as well.
- Hybrid-3D + CRF-RNN architecture is currently the best performer.

## Architecture Design Algorithms

- **Algorithmic** architecture design: automatically search the architecture design space.
- Observation: Segmentation networks form hierarchical **module trees**: A tree of modules built up from repeated, simpler modules.
- **Random sampling** of module hierarchy trees finds effective segmentation architectures with modest computational resources.
- Combine with other **black box optimization** tools to improve parameters that do not alter the module hierarchy.
- Run architecture search on NIH's **Biowulf** using new distributed evaluation tools.
- Diverse high-performing architectures are combined into **ensembles** for improved prediction.



(**Top**) A collection of randomly-generated module trees for 2D encoder-decoder networks. Each module forms part of a final computation graph. (**Bottom**) Importance of ensembling for segmentation algorithms. Data and human ground-truth labelings are compared with the single best network and the best network ensemble from 100 random 2D encoder-decoder networks.

## Conclusion

- We built **high-performing 3D EM segmentation** algorithms with a new architecture which combines 2D and 3D convolutional processing modules.
- Module architecture design made use of **random module tree** sampling followed by **black box** optimization.
- Random sampling strategy produces high-performance segmentation networks and requires little machine learning expertise.
- New scripting tools enable efficient, fault-tolerant distributed architecture search on Biowulf.
- Resulting segmentation algorithms **accelerate segmentation** for lab research workflows.
- Challenges:
  - **End-to-end** training of large networks with model-parallel multi-GPU.
  - Deal with **anomalies** in datasets not found in training data.

## Future Work

- **Robust segmentation**: Train a single segmentation model that works across multiple datasets. Requires transfer learning but also more.
- **New public dataset**: Currently assembling a collection of annotated EM image volumes for release to the machine learning community.
- Use a **correction-training feedback loop** to produce large amounts of labeled training data.
- Combine **instance and semantic** segmentation algorithms to increase usefulness of segmentation tools for researchers.
- Work with collaborators to **improve segmentation software** from preprocessing through data visualization.

## Acknowledgements

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- **View this poster online** at (<https://leapmanlab.github.io/umd2019.pdf>).