UNIVERSITY OF TORONTO

VECTOR INSTITUTE

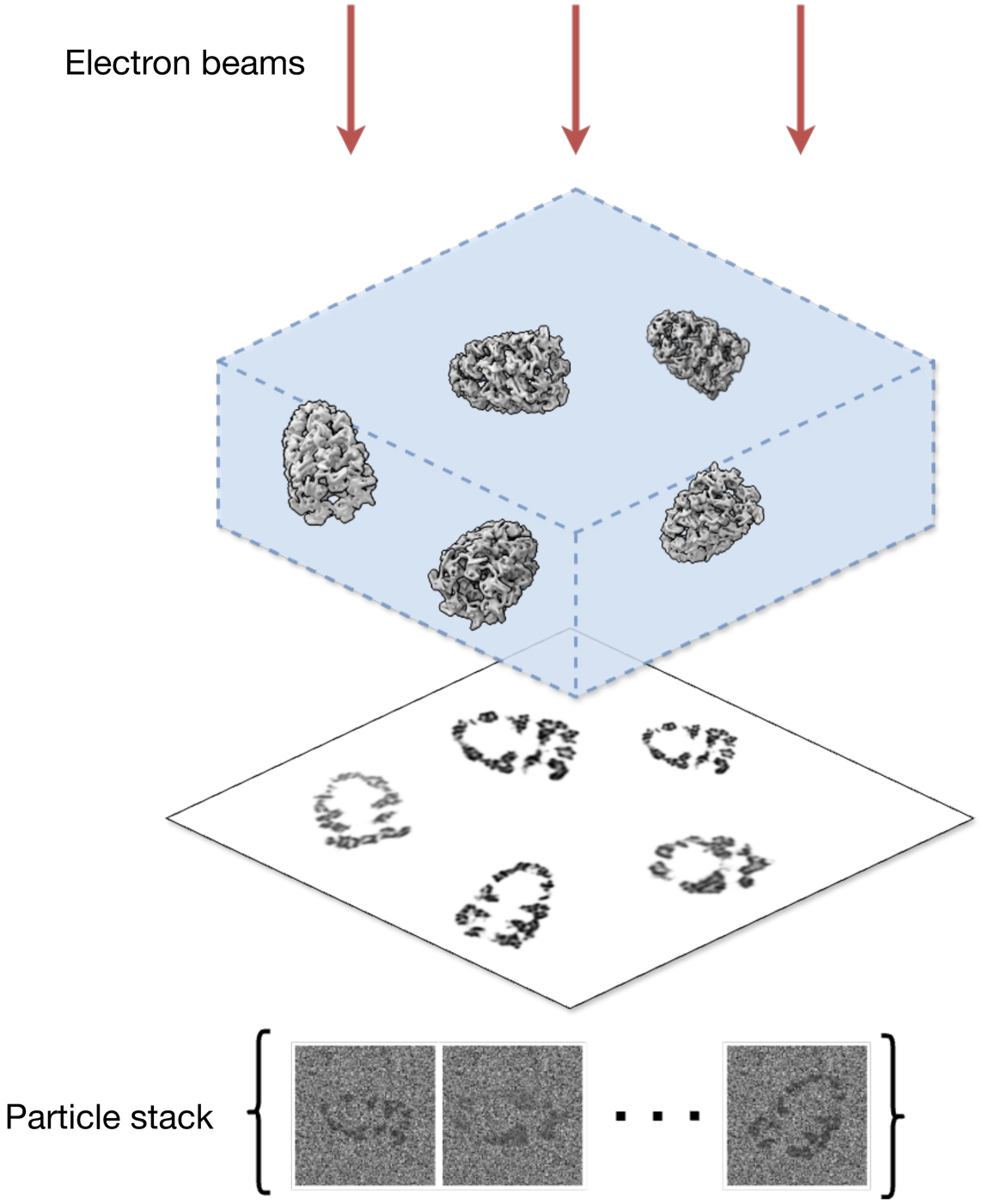
YORK UNIVERSITÉ UNIVERSITY

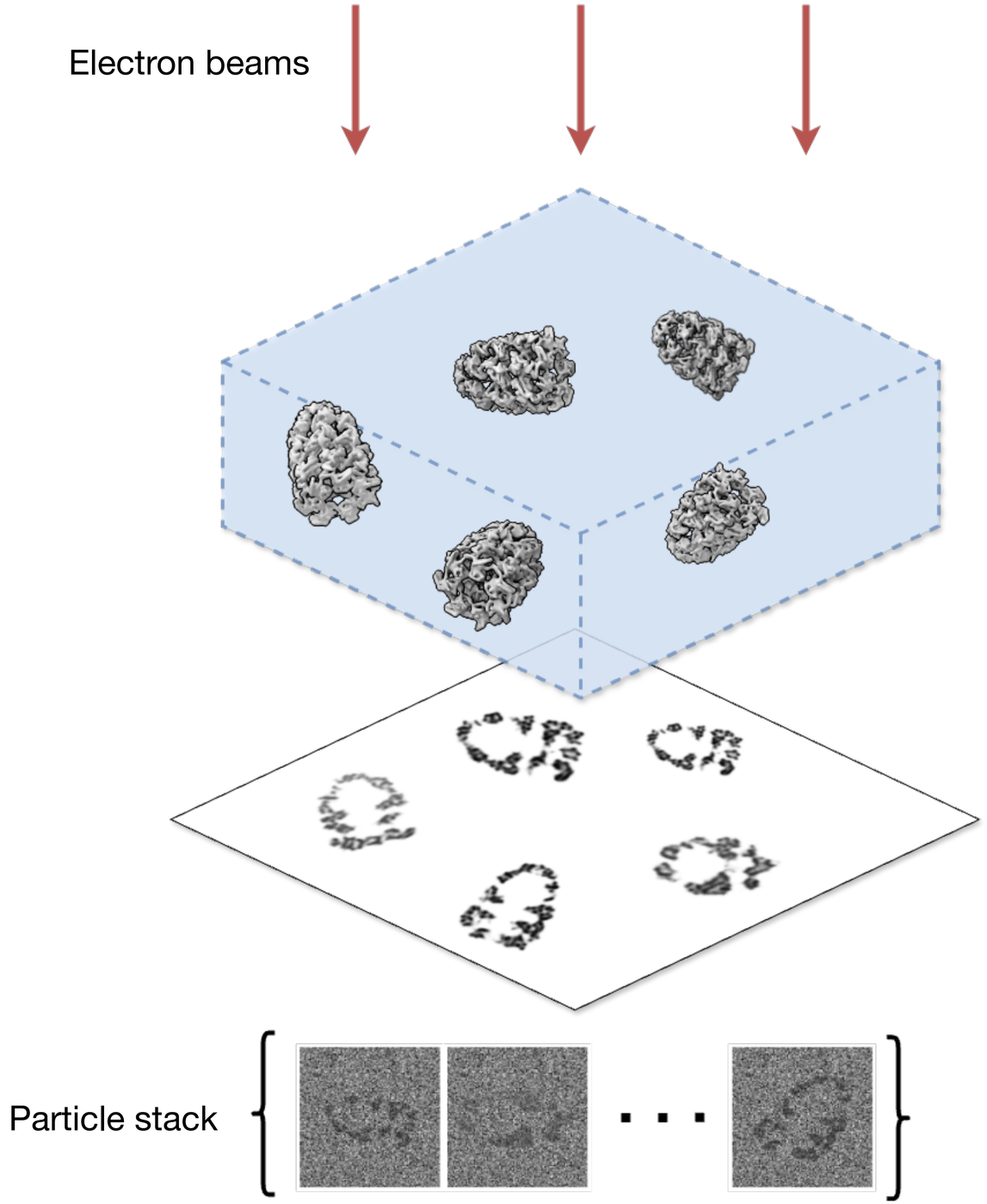
CryoSPIN

Improving Ab-initio Cryo-EM Reconstruction with Semi-Amortized Pose Inference




Project page / Code


Electron beams
Particle stack



Challenges

- Unknown 3D pose
- Low SNR
- Structural variabilities

Pose search

e.g. CryoSPARC, CryoDRGNv2

- Hierarchical pose search with BnB
- Handling pose uncertainty
- Running for each image independently

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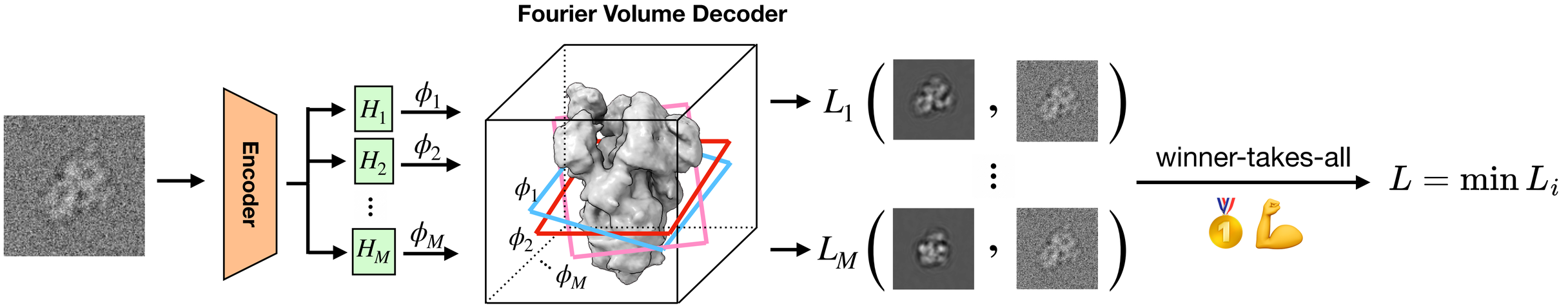
Deep-learning

e.g. CryoPoseNet, CryoAI

- Amortized inference
- A single pose estimate per-image
- Suboptimal pose predictions


CryoSPIN: **S**emi-Amortized **P**ose **In**ference

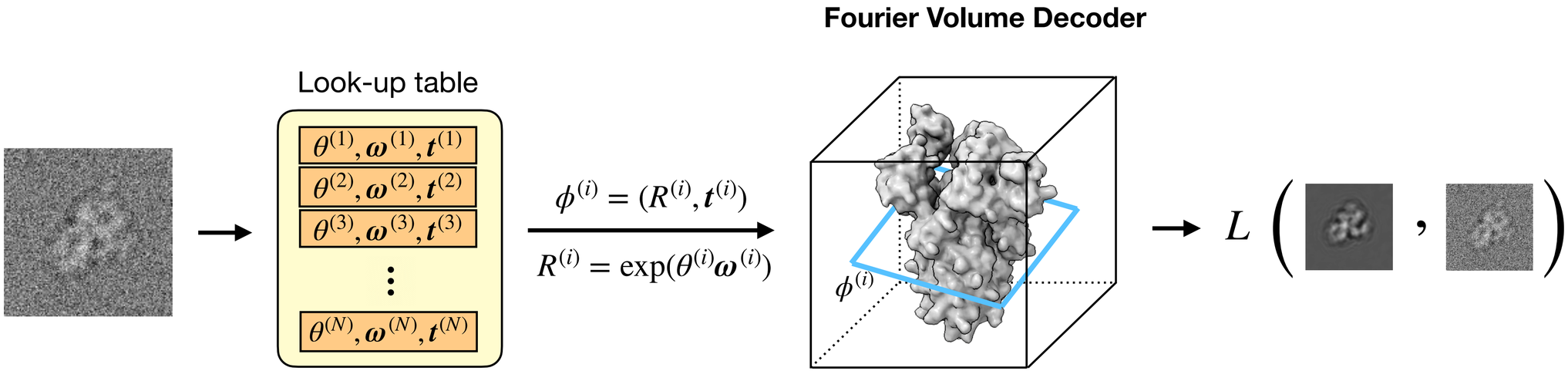

Multi-choice Amortized Inference



👍 **Multi-head** encoder can handle multi-modal pose posterior

👎 Limited pose encoding: yielding **sub-optimal** predictions

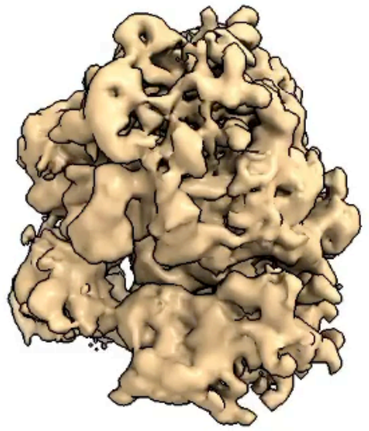
Auto-decoding



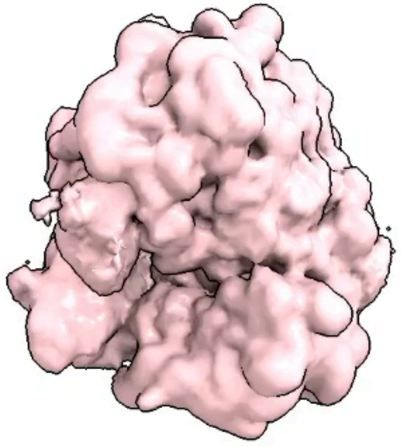
👍 More **flexible** direct per-image pose optimization

👍 **Accelerates** convergence to more **accurate** pose estimates

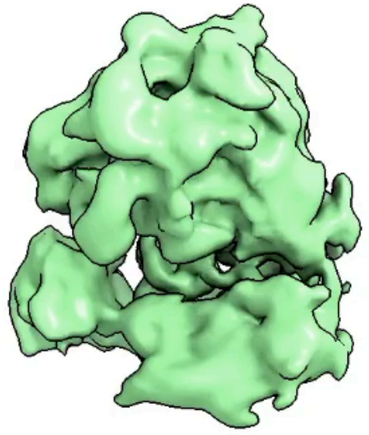
CryoSPARC



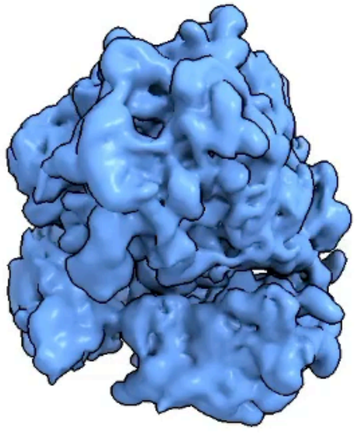
CryoDRGN



CryoAI



CryoSPIN (Ours)



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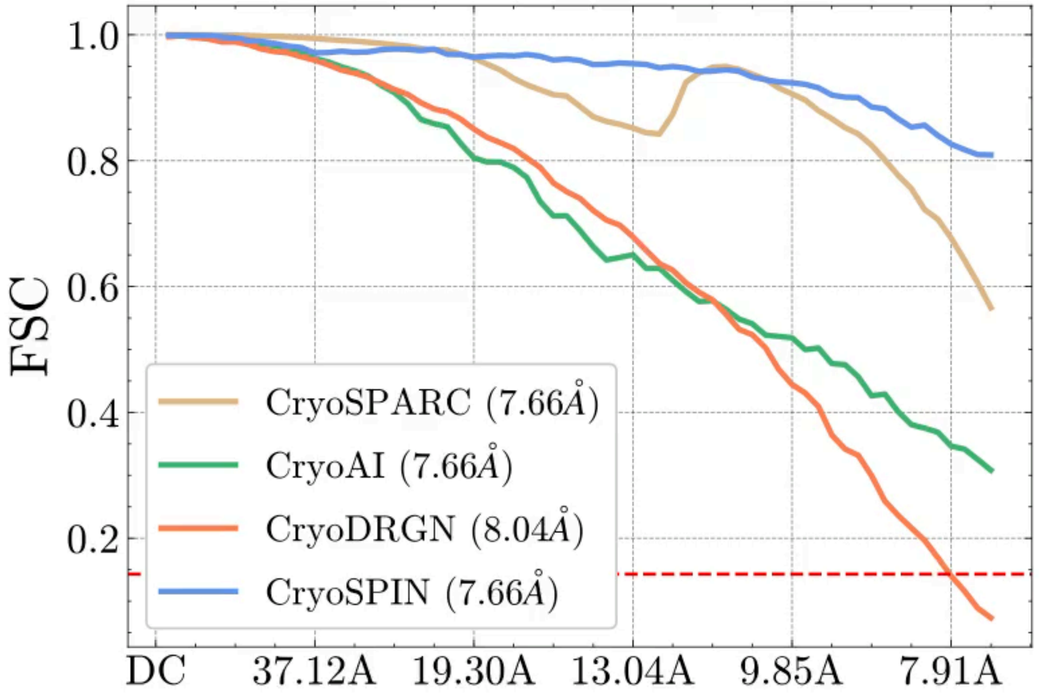
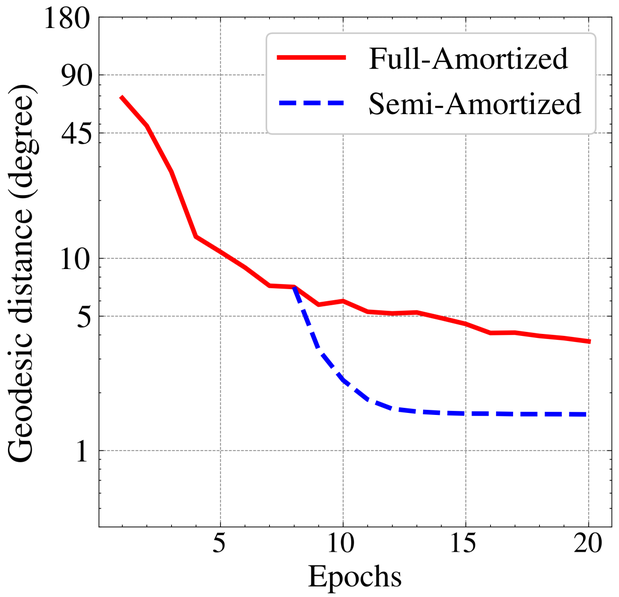
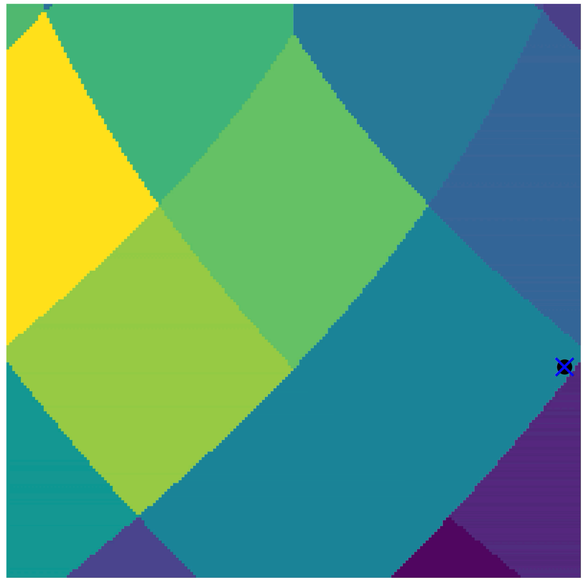
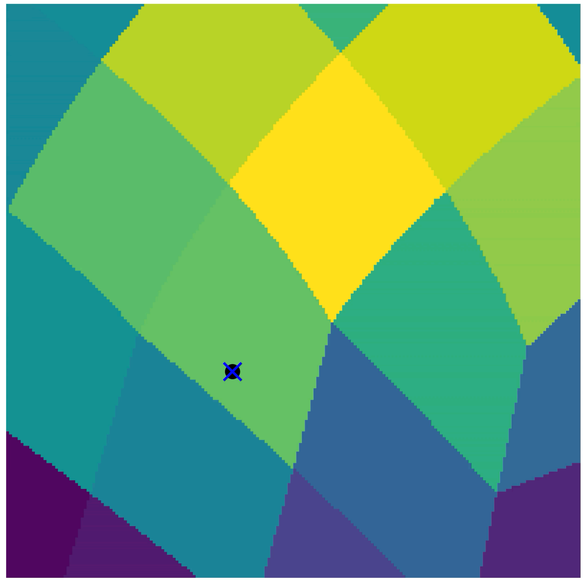


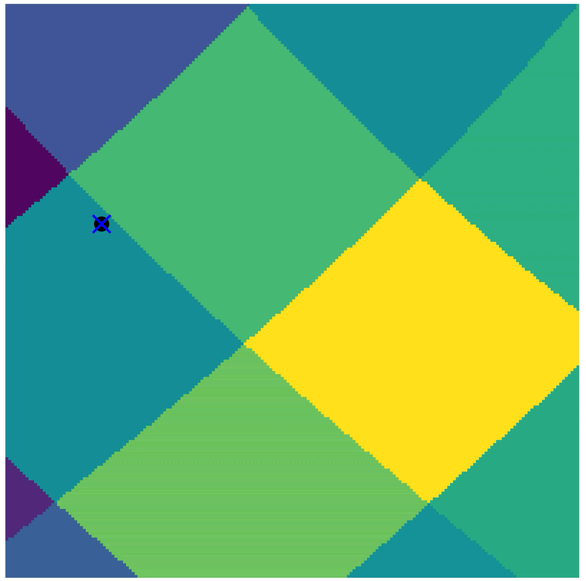
Spike Protein

Trajectories of pose estimates overlaid on the log-posterior heatmap (zoomed-in around GT)

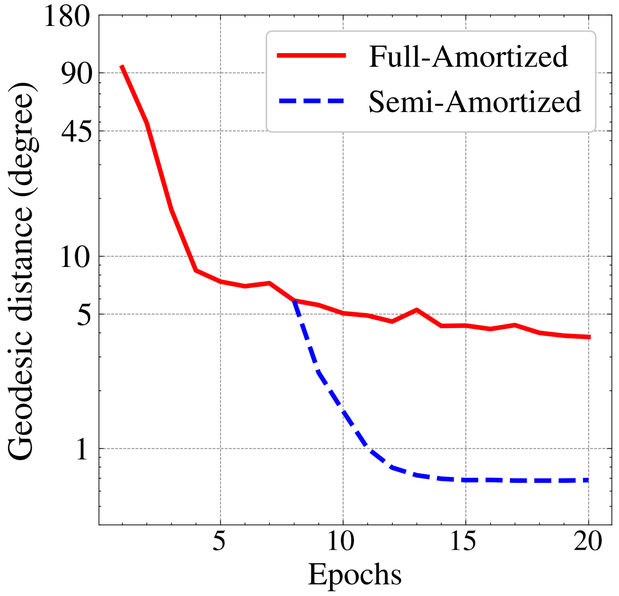


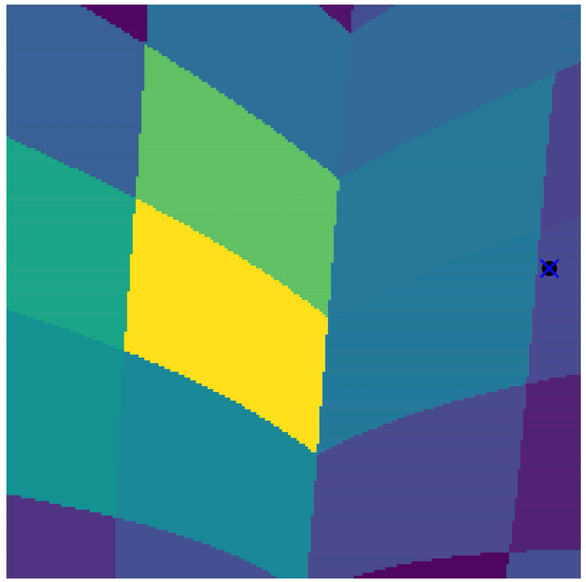


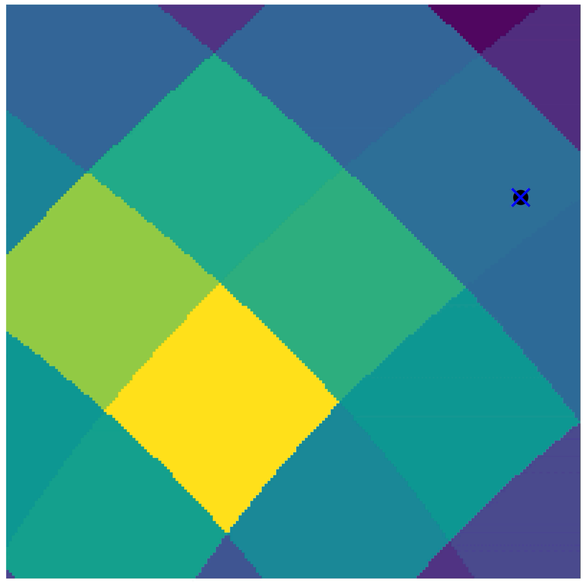


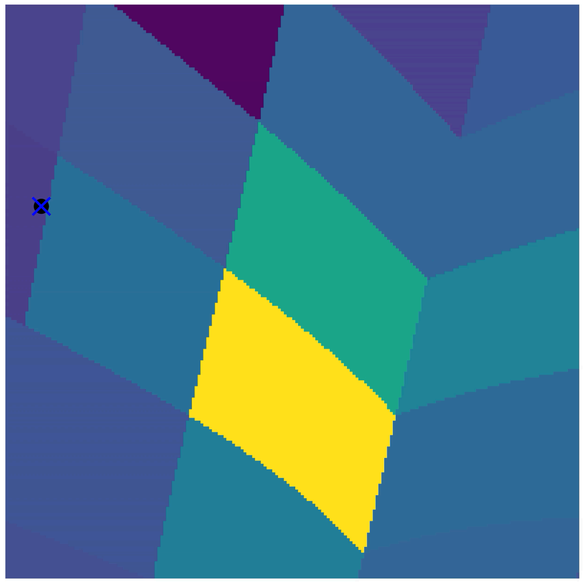


Spliceosome



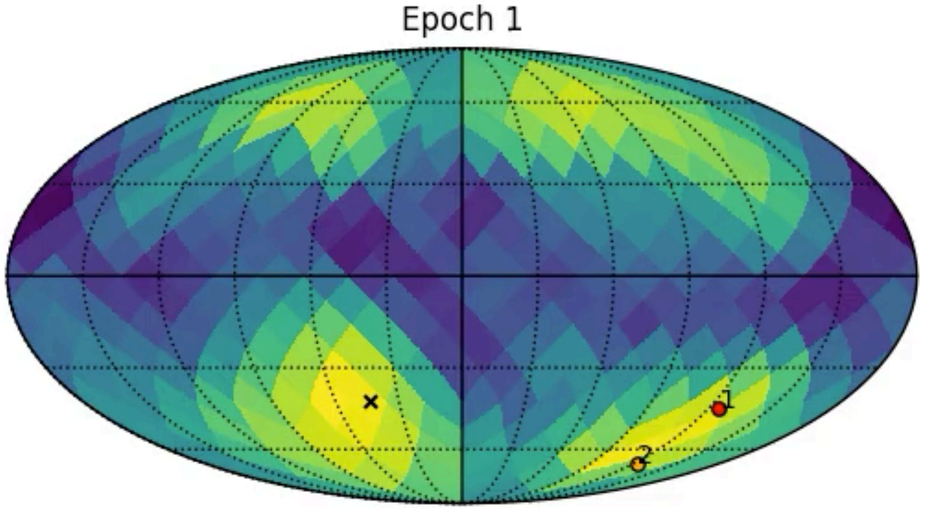


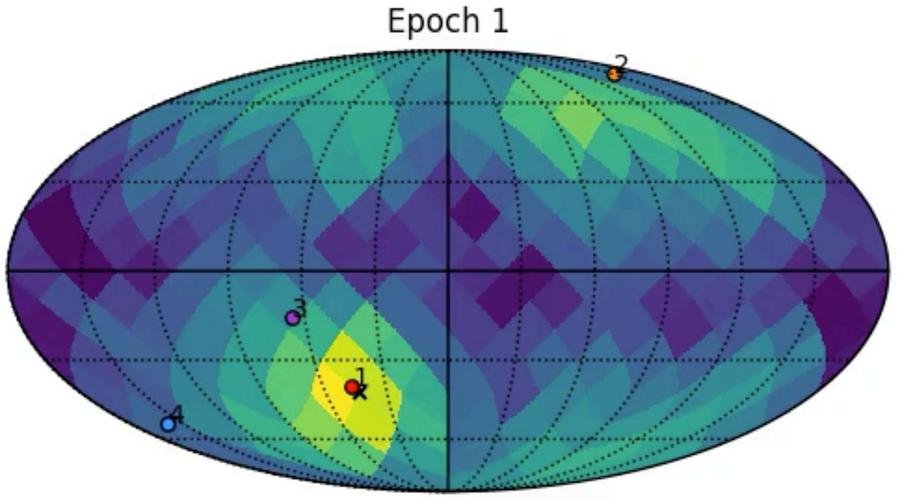


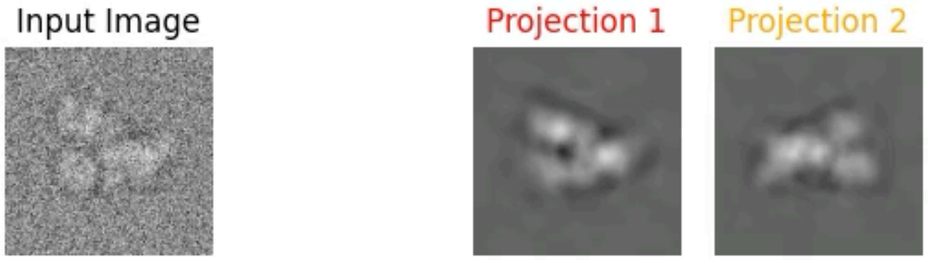


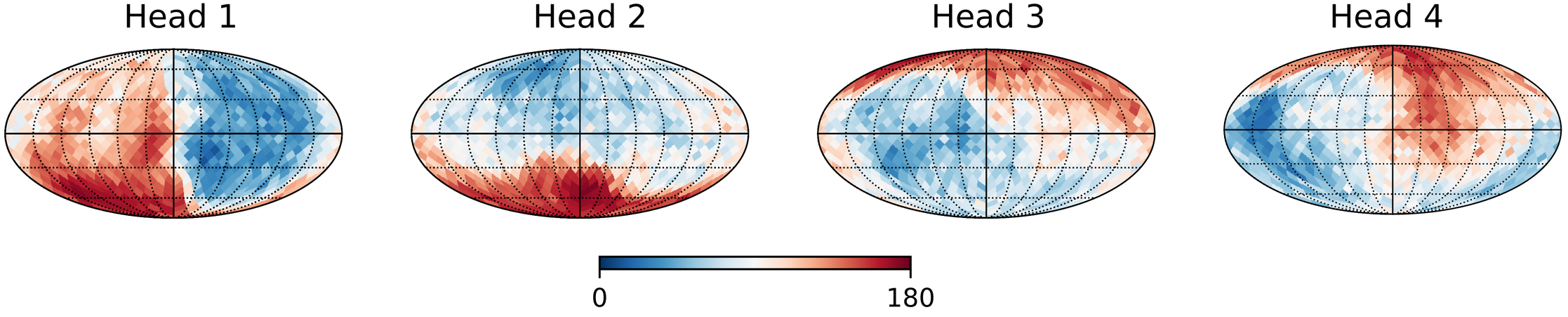
CryoAI encoding

Multi-head encoding









Conclusion

Developing a new **multi-head encoder** which returns multiple plausible candidates to mitigate **pose ambiguity**.

A new objective “**winner-take-all loss”**, which enables diversity and **specialization**.

Semi-Amortized pose inference, which begins with amortized pose inference, followed by direct per-particle pose optimization that **stabilizes** convergence to **accurate** poses.

CryoSPIN, our semi-amortized method, achieves higher-resolution on synthetic and experimental datasets in ab-initio reconstruction.

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