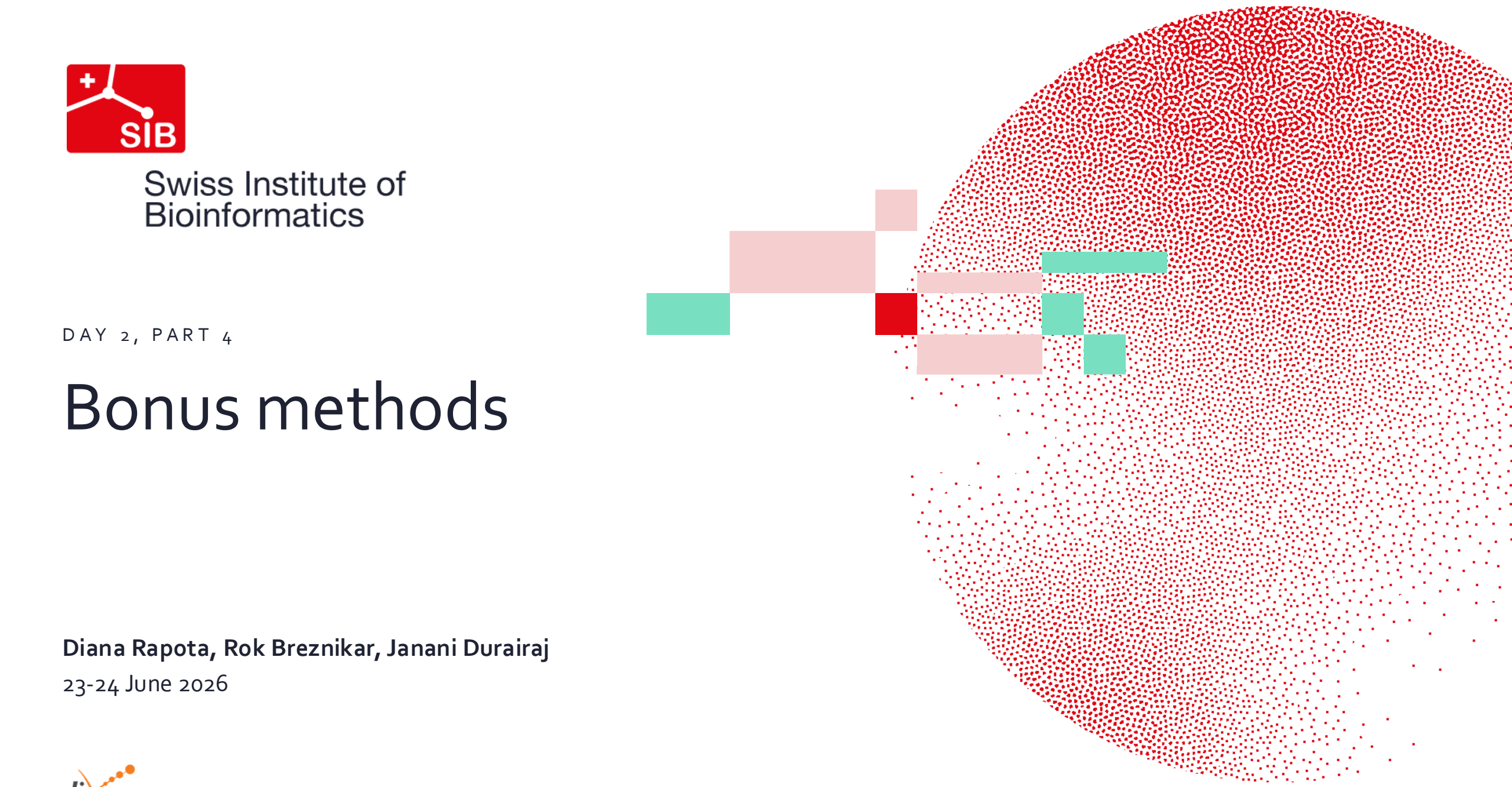


Swiss Institute of Bioinformatics

DAY 2, PART 4

Bonus methods

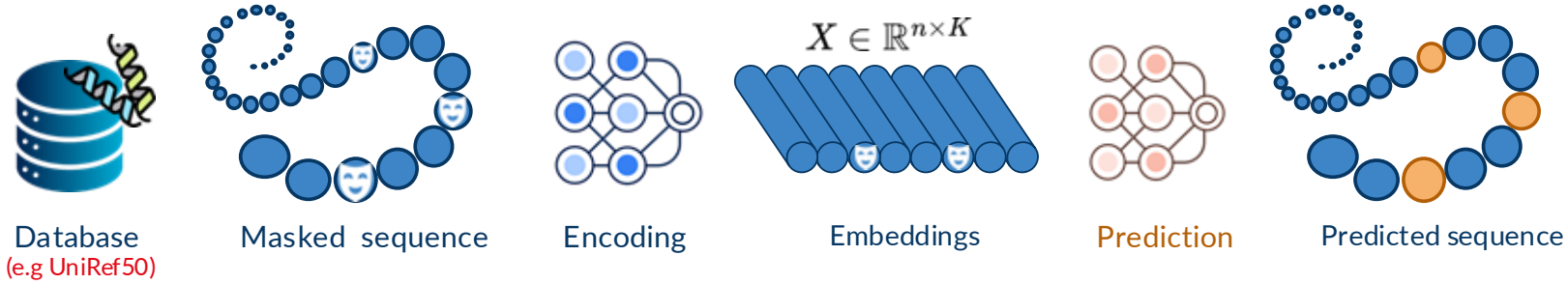
Diana Rapota, Rok Breznikar, Janani Durairaj

23-24 June 2026

elixir SWITZERLAND

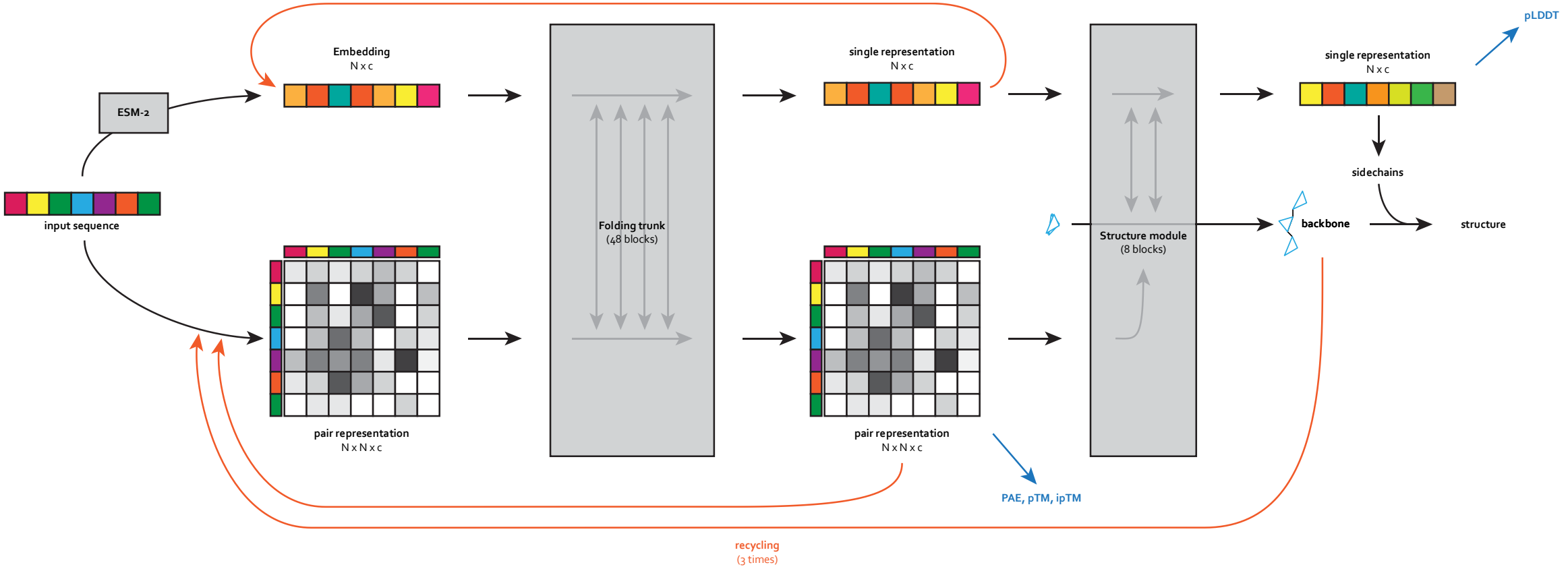
ESM-2

- Protein language model (pLM)
- Trained on 65 million sequences
  (compared to billions of sequences AlphaFold2 has access to when constructing an MSA)



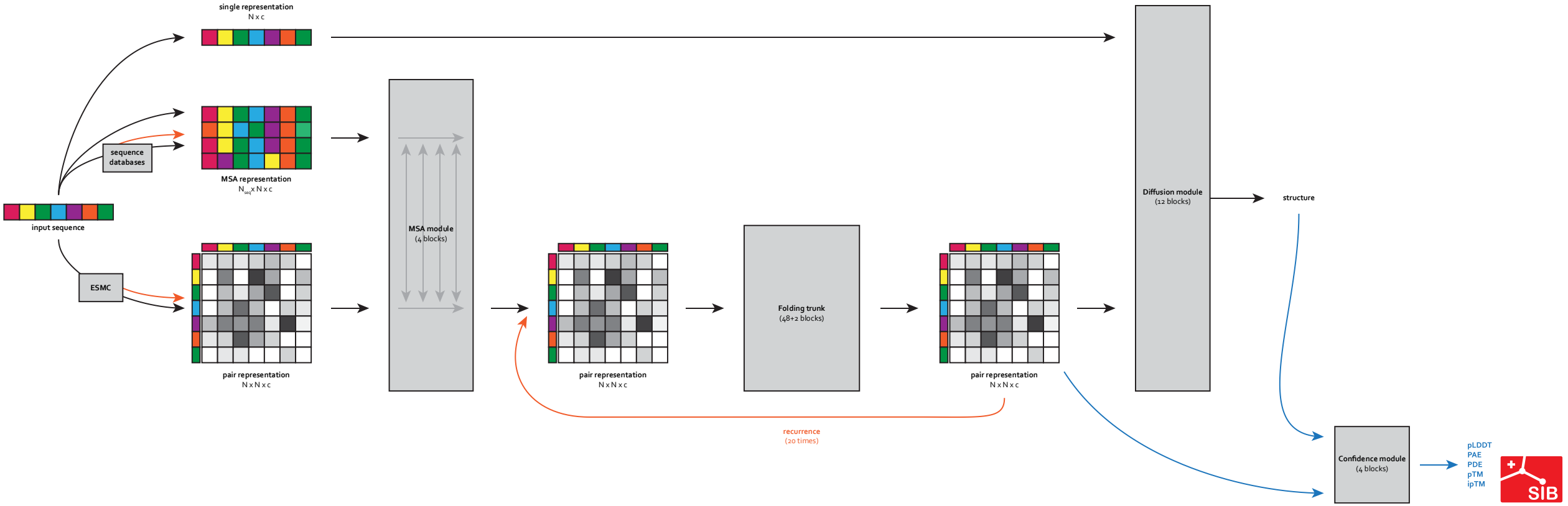
ESMFold

- Similar architecture as AlphaFold2,
  no templates and ESM-2 embedding instead of MSA → fast
- Doesn't perform as well as AlphaFold2



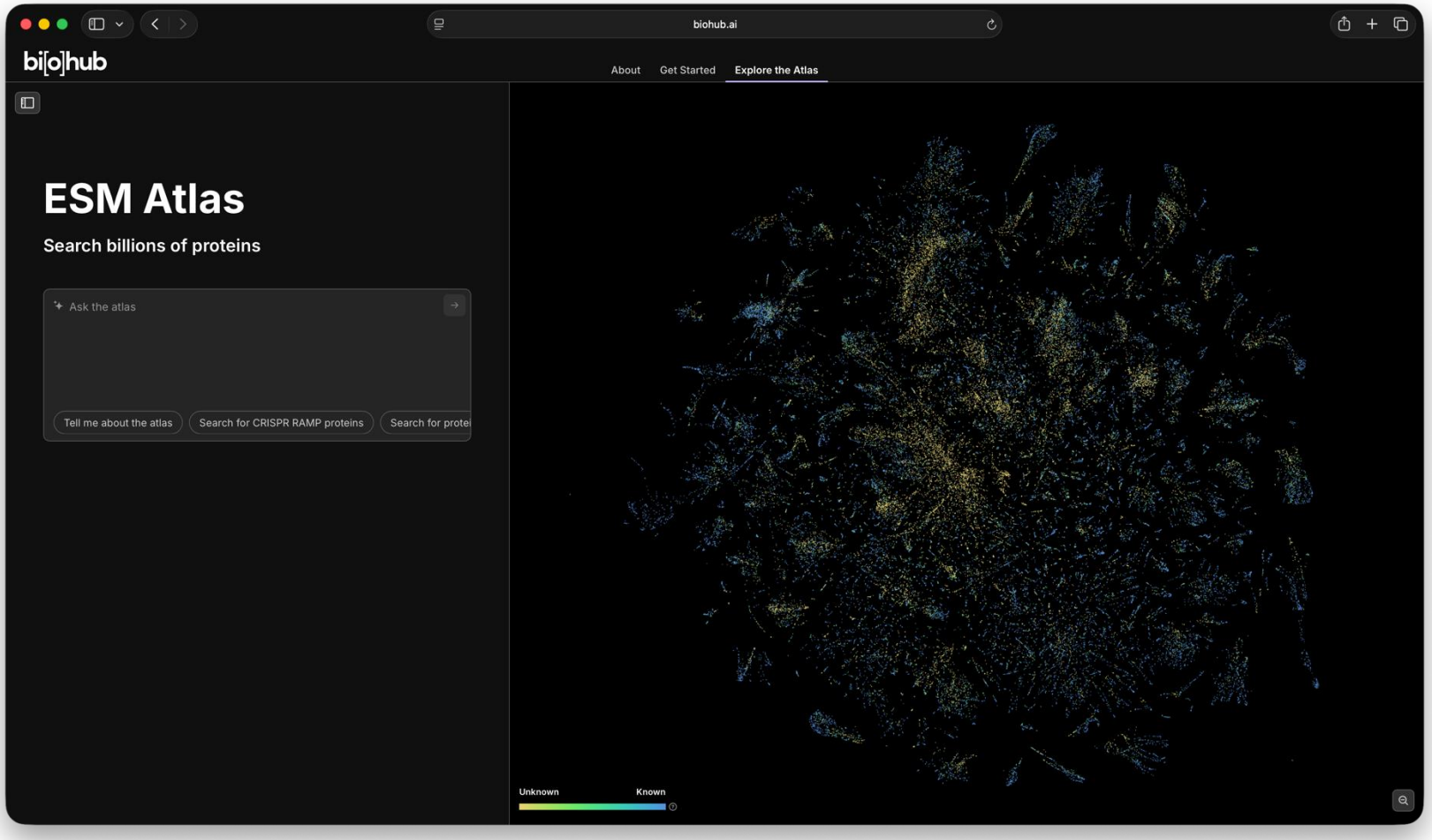
ESMC, ESMFold2

- Protein language (ESMC) trained on 2.8 billion sequences
- Different folding architecture (ESMFold2)
- Better at antibodies and protein-protein interactions; there is also a fast version



ESM Atlas

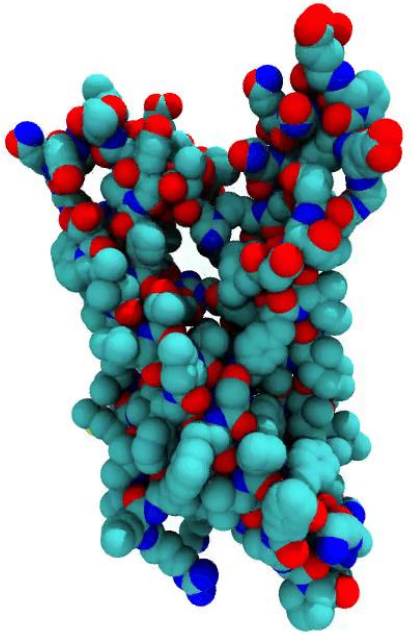
- 1.1 billion structures
- Using ESMFold2



Language Modeling Materializes a World Model of Protein Biology (2026)

BioEmu

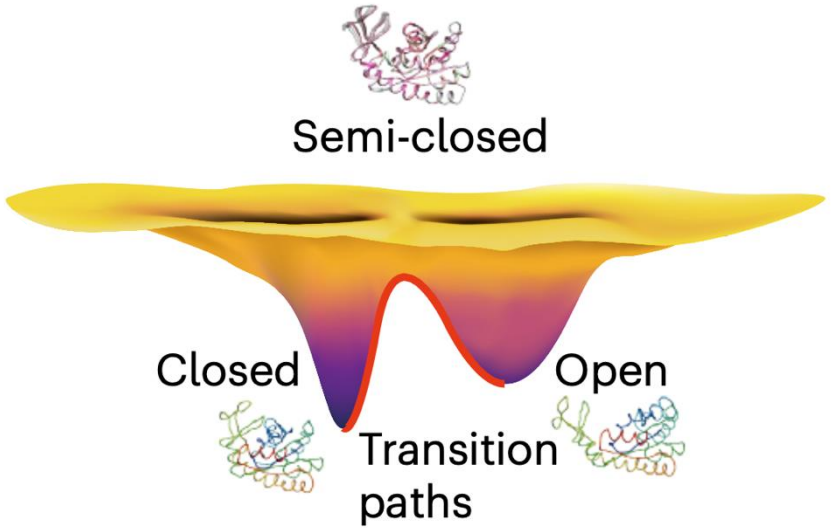
- AlphaFold is trained to predict only one conformation (crystal structure)
- Proteins are very dynamic in their native environment (solution, temperature, concentration)
- Methods to simulate protein dynamics:
  - MD – Molecular dynamics (physics based, takes a lot of time to simulate a few microseconds)



BioEmu

- Similar architecture to AlphaFold2
  - Replaces the structure module with a denoising diffusion model

- Trained to predict ensembles of conformations
  - Static structures, MD simulations, equilibrium distributions



Predicting equilibrium distributions for molecular systems with deep learning (Nature Machine Intelligence, 2024)
Scalable emulation of protein equilibrium ensembles with generative deep learning (Science, 2025)

Useful links

AlphaFold: A practical guide from EMBL-EBI:

https://www.ebi.ac.uk/training/online/courses/alphafold/

AlphaFold 3 guide:

https://www.ebi.ac.uk/training/online/courses/alphafold/

AFDB tutorial:

https://www.ebi.ac.uk/training/events/accessing-and-interpreting-predicted-protein-structures-alphafold-database/

ColabFold guide:

https://doi.org/10.1038/s41596-024-01060-5