NMR-AI powered Drug Discovery

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CEEC Mee 2025

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AIffinity
MOLECULAR DESIGN

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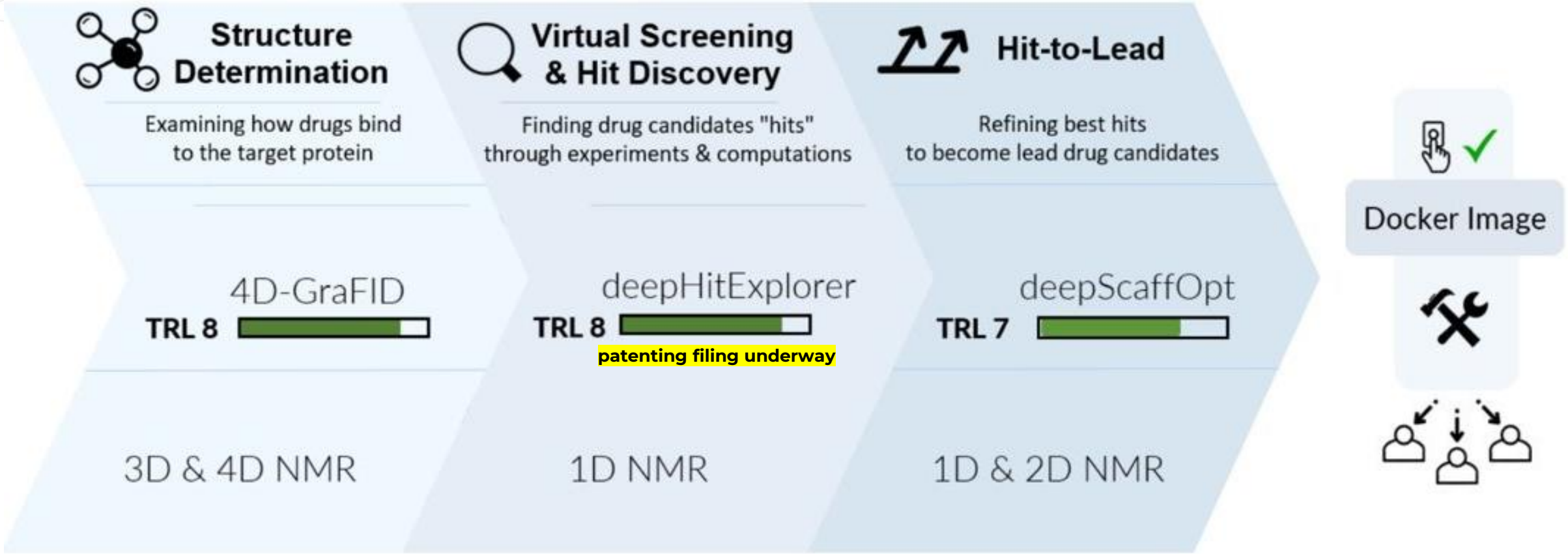
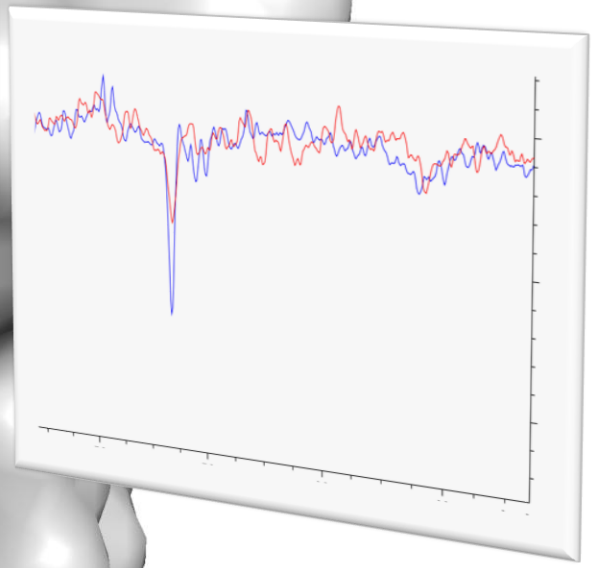
Our solution: NMR-AI Integrated platform for Streamlined Target-to-Lead Process

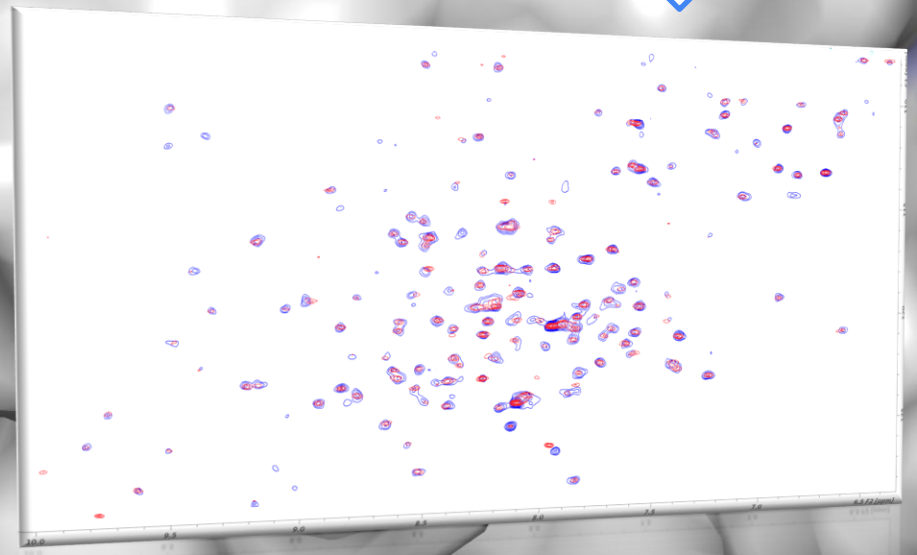


Ultra-Fast NMR Experiments

Ligand interactions



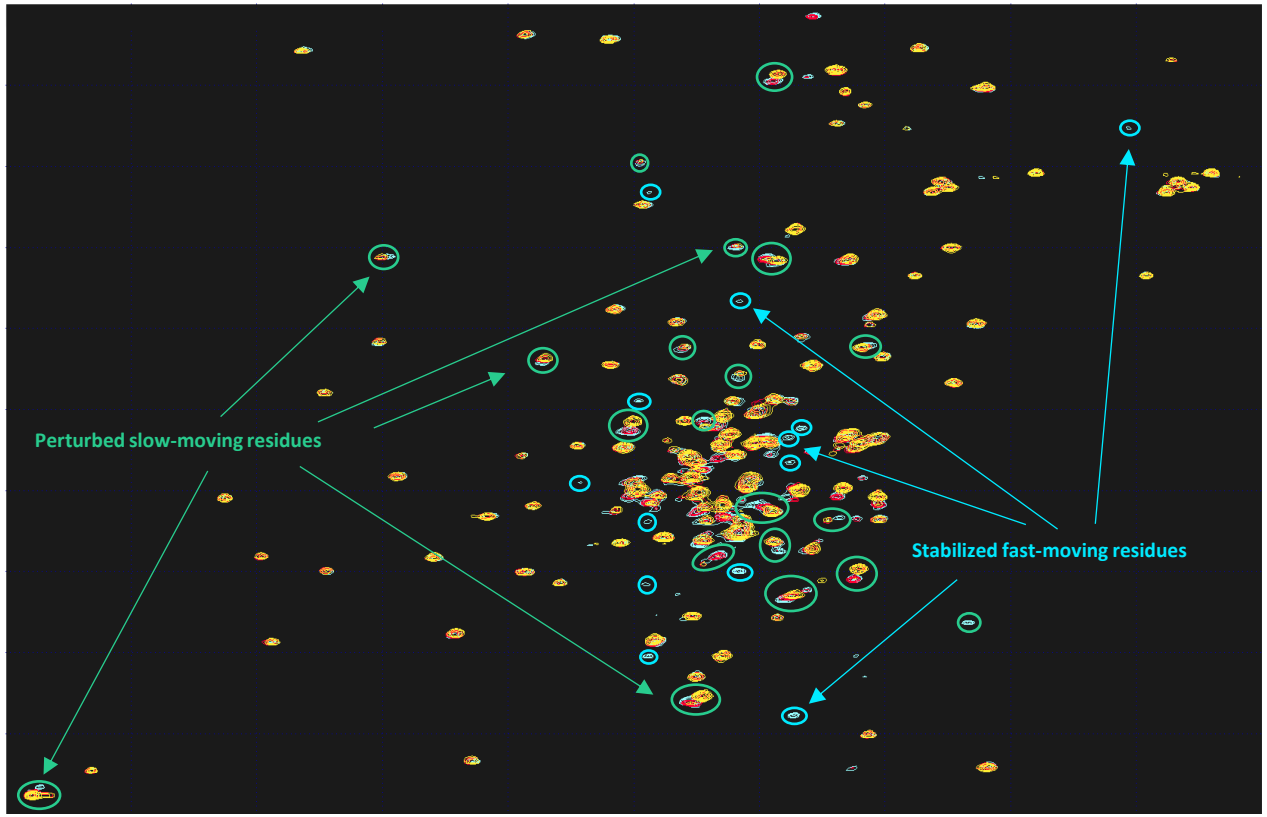
Protein interactions

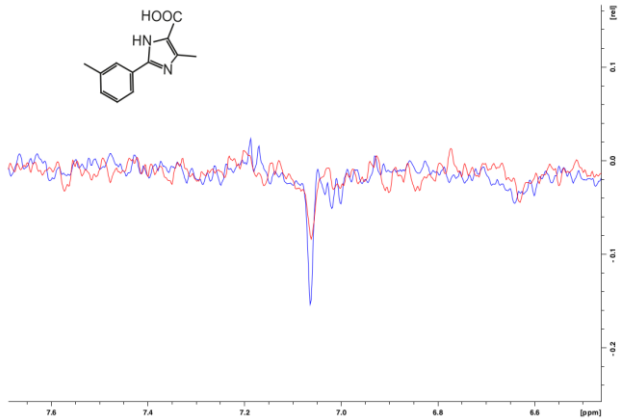


We Scrutinize Atomic Interactions with NMR

- We measure both sides:
  - 2D NMR (protein) → dozens of data points/day
  - ultra-fast 1D NMR (ligand) → hundreds of data points/day

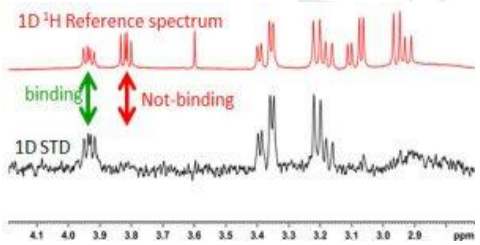
- Our NMR-AI platform fuses these data to discover new hits, grow/link fragments, and iterate design



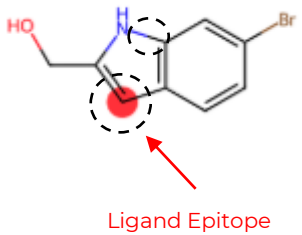


deepHitExplorer

Input → Neural Network → Virtual Screening → Multi-objective Genetic Algorithm → deepHitExplorer Viewer

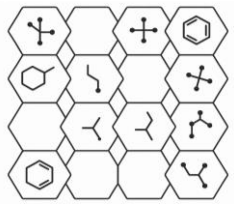


Ligand-observed NMR spectrum

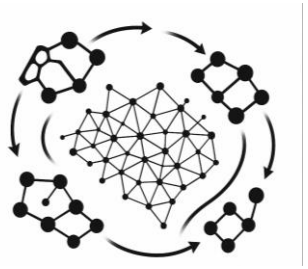


AI tool integrated with NMR data for enhanced molecule scoring

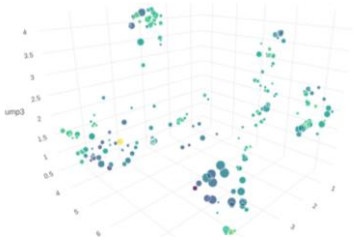
Molecule libraries



Compounds undergoing epitope prediction and scoring



Diverse molecules search based on chemical structure, predicted score and solubility



Interactive exploration of the diverse chemical space

deepHitExplorer Viewer

Fix selection and let the program suggest other chemically diverse, top-scored, soluble molecules

Filtering based on the molecule properties

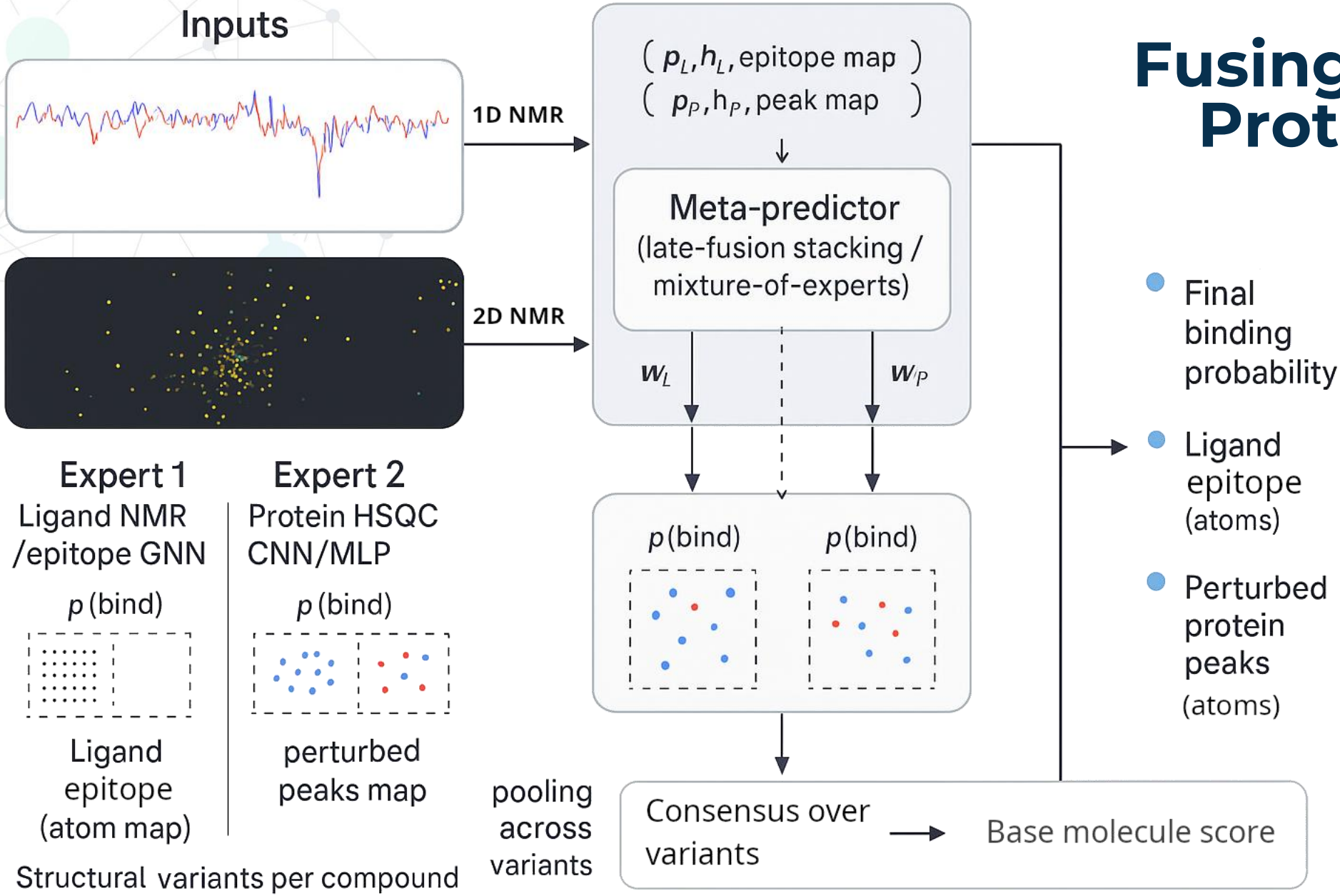
Pick and download your selection

Dive in the 3D scatter plot selecting the desired molecules for experimental testing

Visualize the predicted ligand epitope and molecular properties

Compare the picked molecules

Fusing Ligand & Protein NMR



Work in progress...

Protein NMR

Spectral
Resolution: 2D < 3D < 4D < 5D
Sensitivity: 2D > 3D > 4D > 5D
Total time: 2D < 3D < 4D < 5D
Complexity: 2D < 3D < 4D < 5D

COMPETITORS

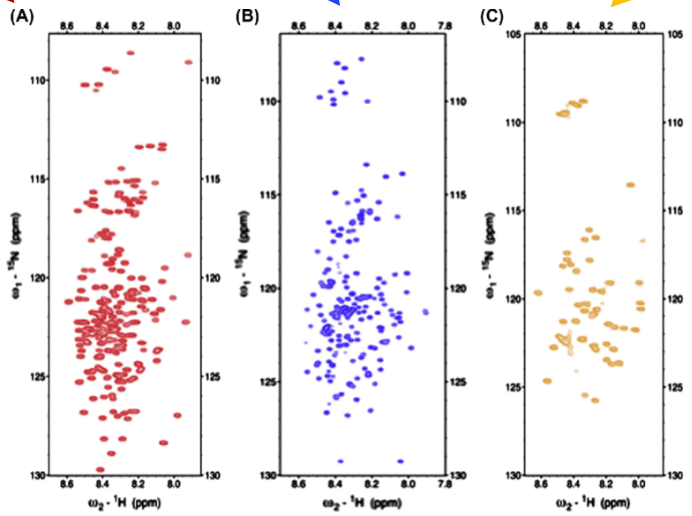
AIffinity MOLECULAR DESIGN

NMR | **NMR** | **X-ray Cryo-EM NMR AlphaFold**

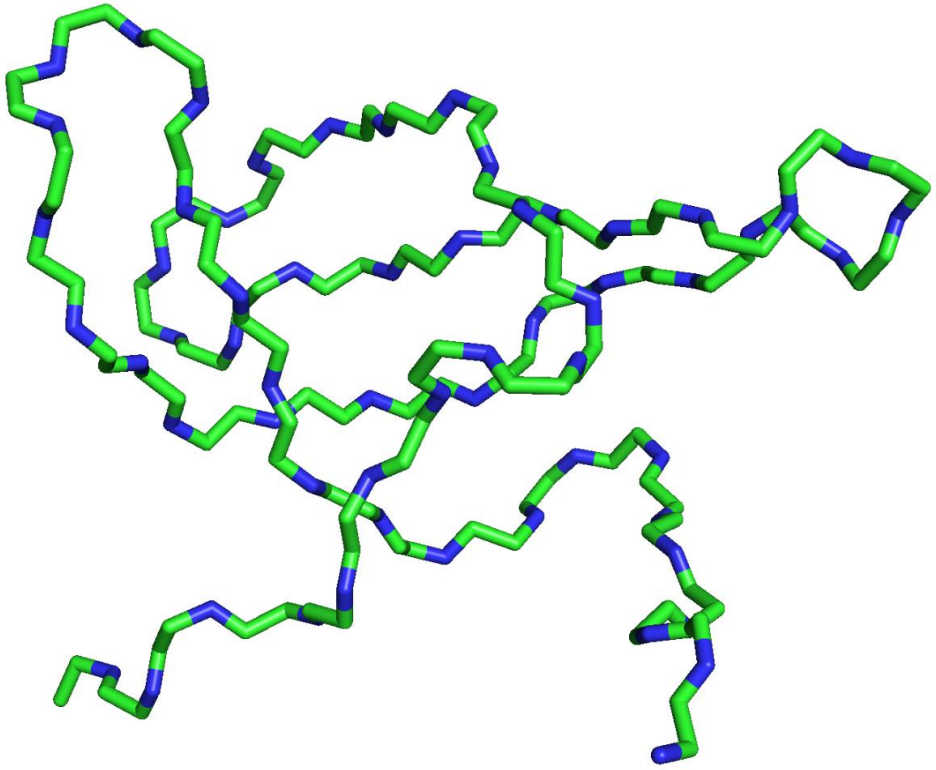
Our competitive advantages:

- Large proteins (>20 kDa)
- Intrinsically Disordered Proteins

2D NMR spectrum

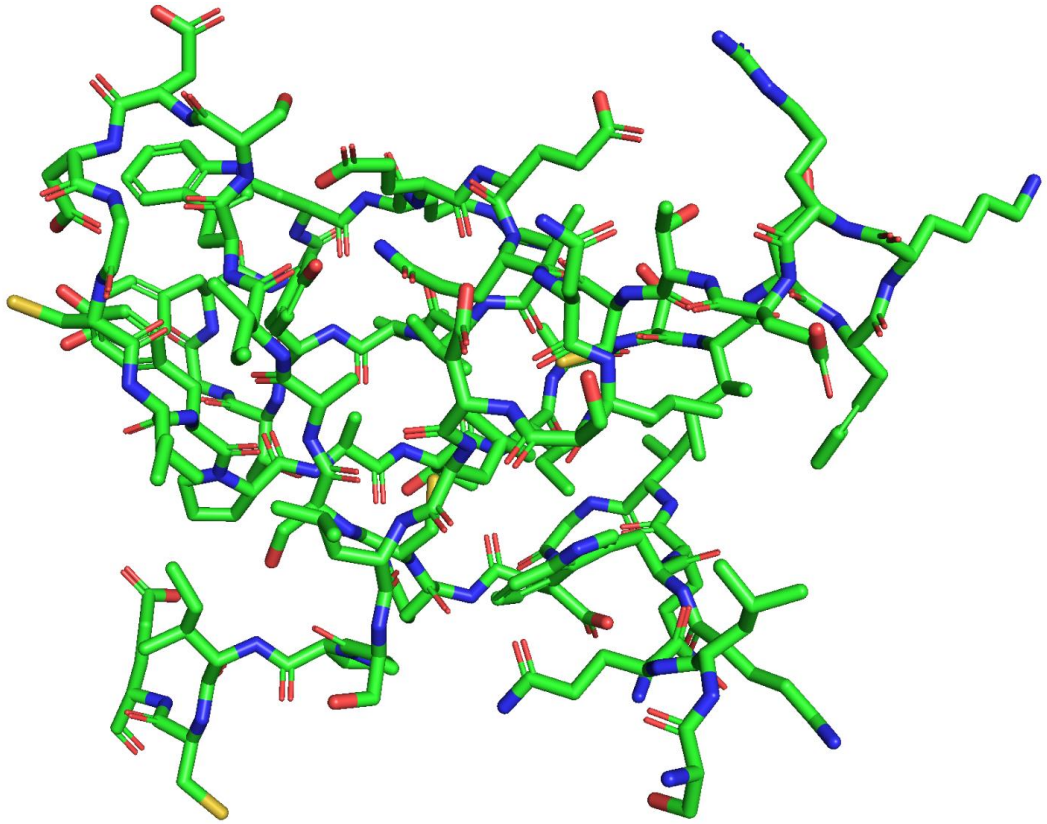


Interaction mapping by NMR – Backbone assignment



Protein backbone resonance assignment

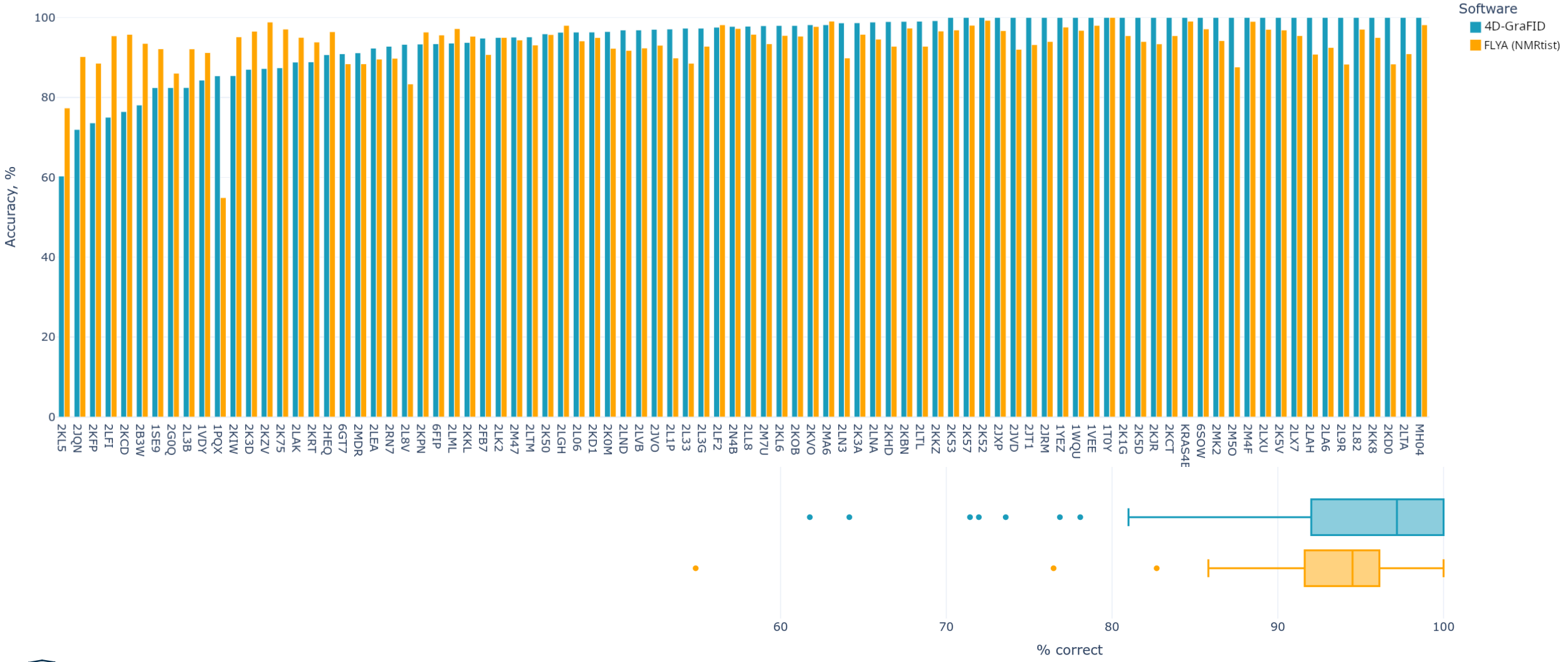
5 x 3D NMR spectra



Backbone & sidechain resonance assignment + 3D structure

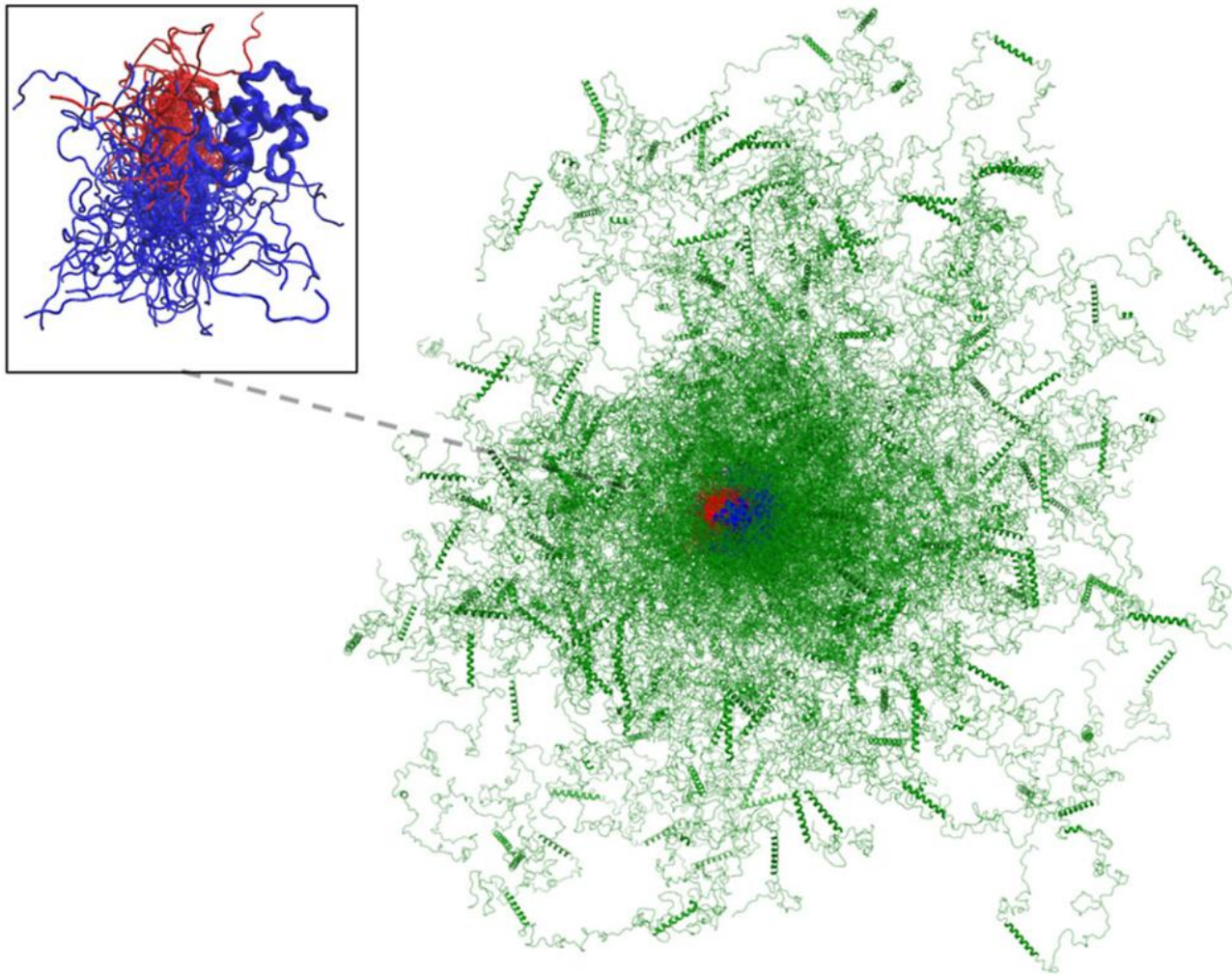
5 x 3D NMR spectra + 2 x 4D spectra

4D-GraFID: Superior Backbone Assignment



Androgen Receptor (AR-V7)

- IDPs (>30% of human proteome) lack defined 3D structure
- Ligand binding reweights the ensemble unpredictably → **structure-based** approaches are **unreliable**
- What matters: **atom-level contact maps** (protein atoms ↔ ligand atoms)
- Our drug design tech in based on **atomic interactions** captured by **NMR** both from the **ligand's** and the **protein's perspective → ideal for IDPs**



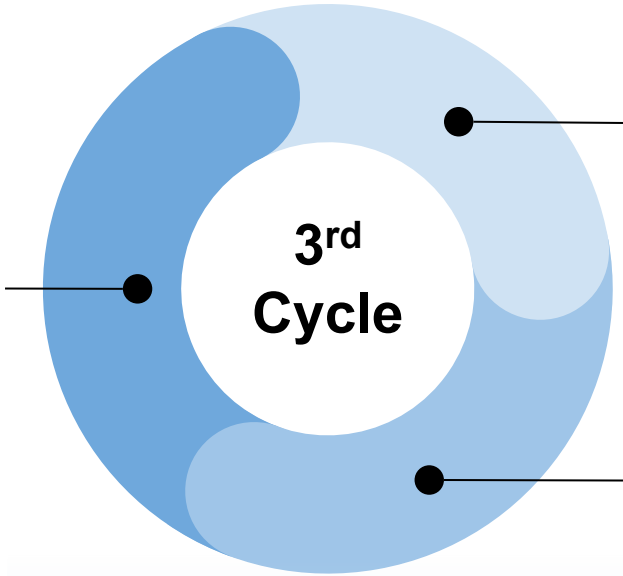
conformational ensemble from *Metadynamic Metainference*
J. Chem. Theory Comput. 2025, 21, 9, 4898–4909

4D-GraFID: protein structure from fewer spectra

Chemical shift assignment (**4D-GraFID**)

Sidechain spectra:
4D HCNH NOESY
4D HCCH NOESY

Backbone spectra:
3D CBCA(CO)NH
3D HNCACB
3D HN(CO)CA
3D HNCA
3D HNCO

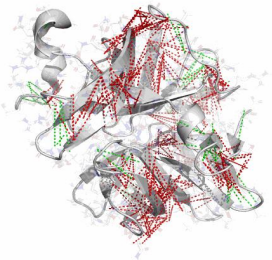


NMR restraint optimization

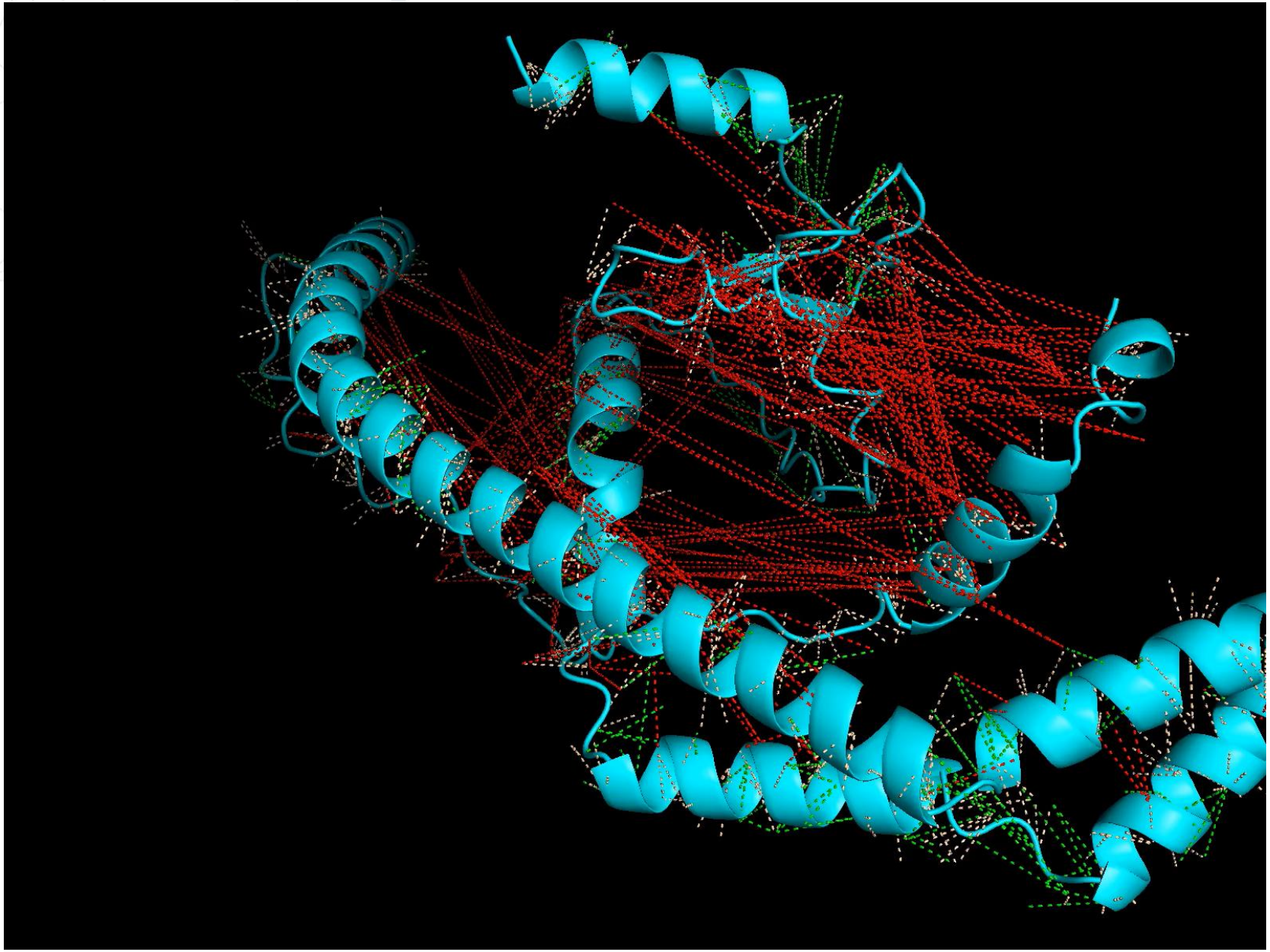
3D structure model generation

powered by OpenFold AlphaFold For

Final model



Medium-range and long-range NOE distance restraints



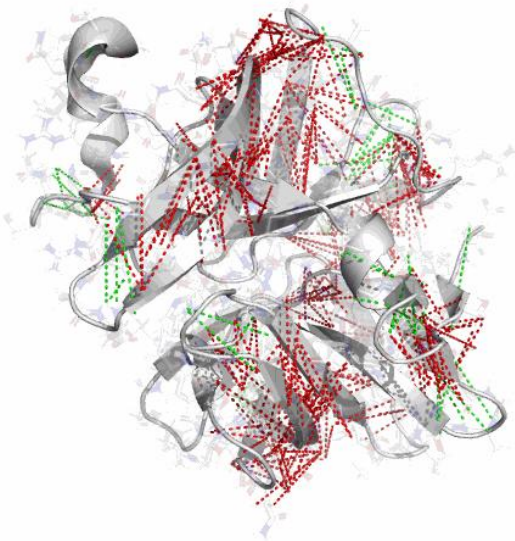
- **Modified OpenFold**
- **nEIt (248 amino acids)**
- **Only 4D HCNH NOESY spectrum**

1.8 mM, 20 mM sodium phosphate
(pH 6.5), 100 mM NaCl, 5% D2O, 37 °C.

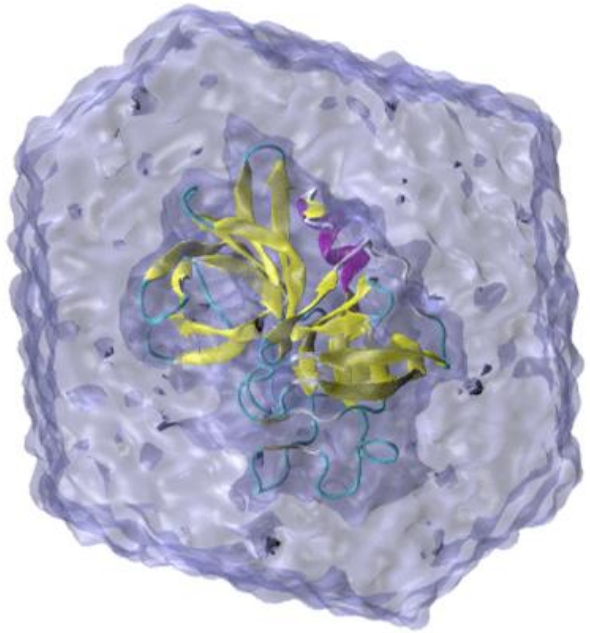
Video on YoutTube

4D-GraFID: protein structure from 2x 4D spectra

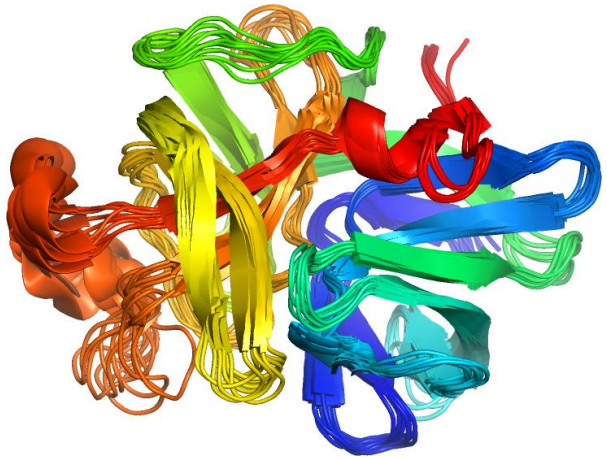
Final model



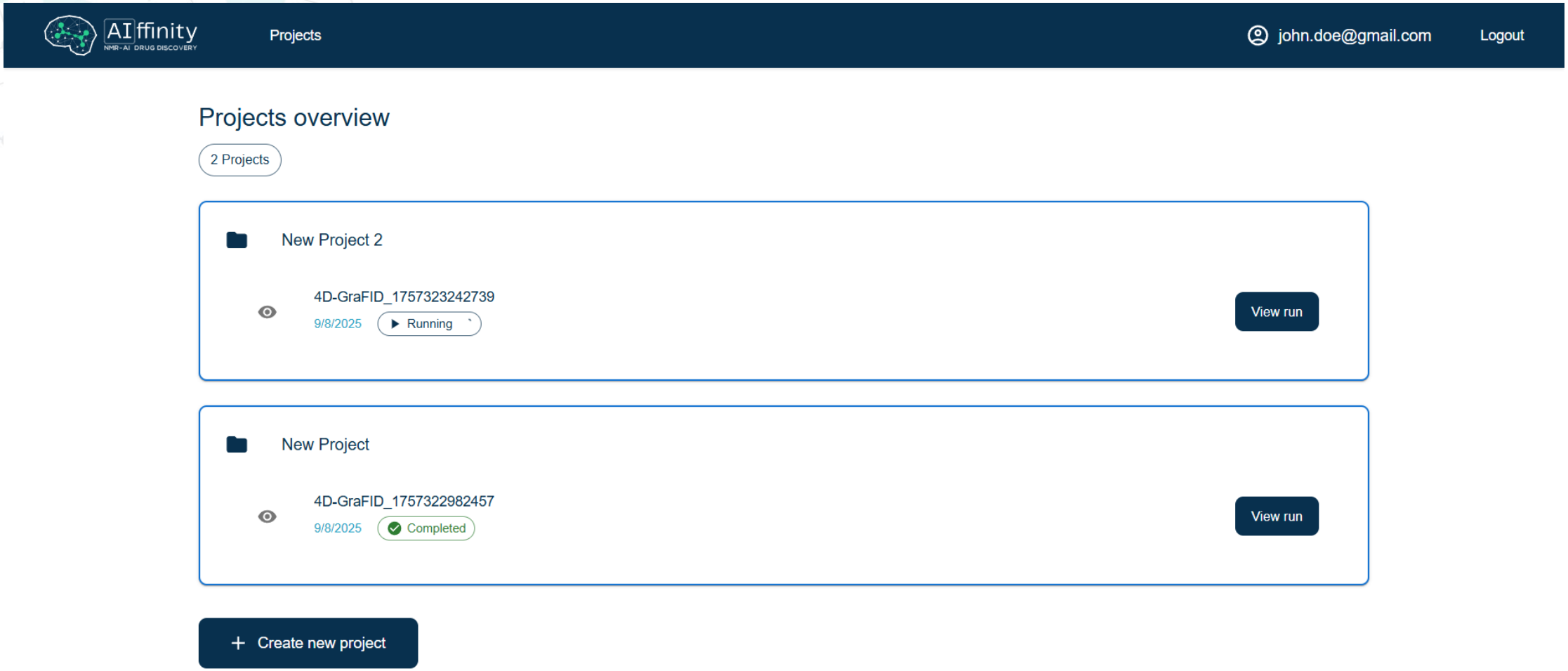
Explicit solvent equilibration



3D structure ensemble



SaaS platform available *online* or *on-premise*



Our Wet-Lab Facilities for Protein Production & Biochemical Assays

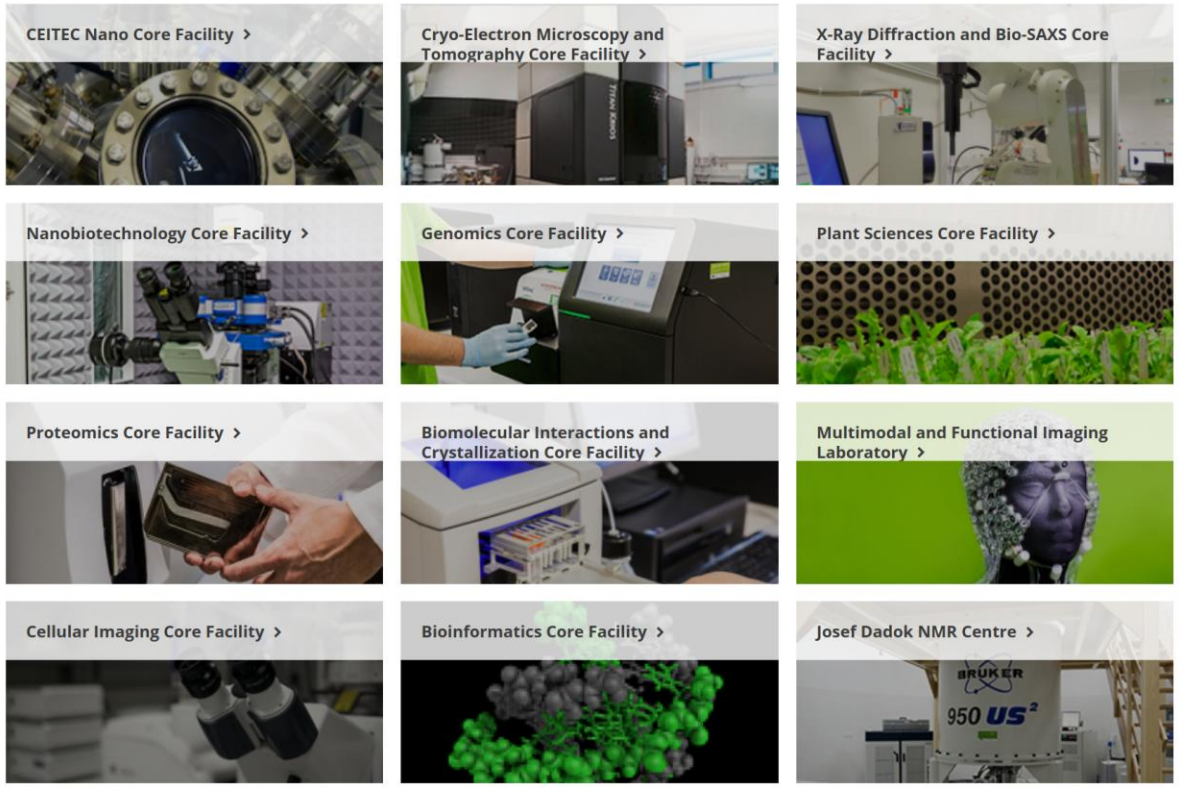
A) General bench & centrifuge

B) Class II biosafety cabinet

C) Plate reader & liquid handling

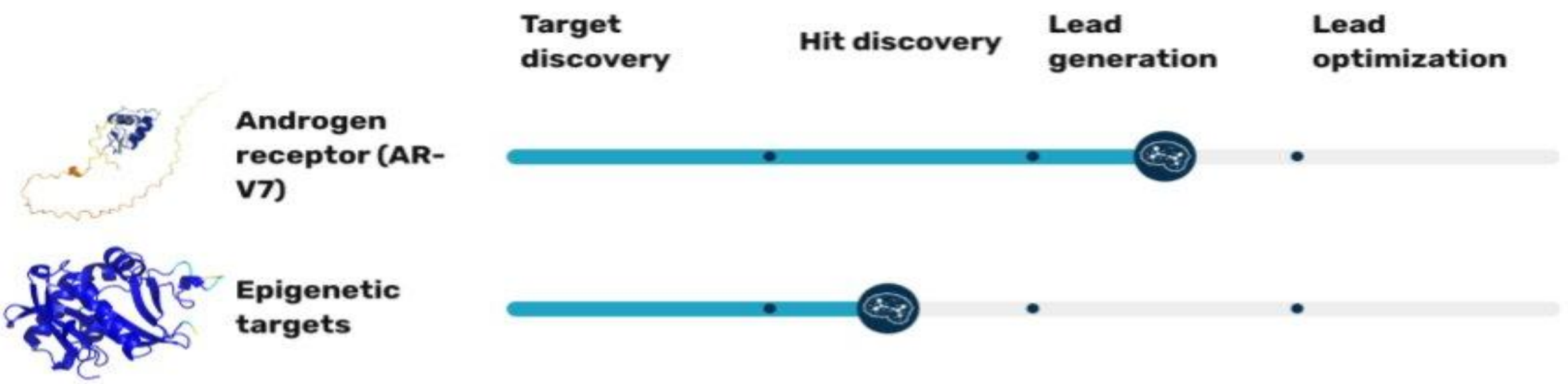
D) Automation & PCR)

Privileged access to full-fledged biophysical facilities



- **structure determination** (NMR, X-ray, SAXS)
- **compound screening** (MST, SPR)
- **binding validation & interactions mapping** (HDX-MS, CD, SEC, ITC)

Joint Drug Discovery powered by our NMR-AI tech



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Computational Biologist

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Research & Development
Computational Chemist

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Research & Development
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Research & Development
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SaaS Dev Team
Computational Biophysicist

Affiliated Contributors

Václav Hanzl, Ing., CSc.

Contributor
ML Expert

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MOLECULAR DESIGN

Open Positions:

Cheminformatics Developer

https://www.linkedin.com/jobs/view/4293495038/

PhD position in Cheminformatics-NMR

https://www.linkedin.com/jobs/view/4296103102/

"Focus and excel"

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Investors:

GARAGE ANGELS

VENTURE GROWTH INVESTMENTS

UNICO

1D NMR methods in Drug Design

- Photo-CIDNP, STD, WaterLOGSY
- Photo-CIDNP: more sensitive, faster (1,500 samples/day), benchtop NMR
- Protein 3D structure not necessary
- Give the atoms of the small molecule that interact with the protein (**ligand epitope**)
- We develop both **Generative AI** and **Virtual Screening solutions** incorporating ligand epitope information