

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐ For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give <i>P</i> values as exact values whenever suitable.</i>
☐	☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	We used either existing openly available datasets (see data availability section) or generated the data using the following codes: Available data: a) Cryo-EM map: EMD-13800 and PDB:7q4b b) Cryo-EM map: EMD-13809 and PDB:7q4m Code: a) PLUMED.2.6.0-dev package used to performs metadynamic electron microscopy metainference (MEMMI): git clone https://github.com/tlhr/plumed2.git b) gmmconvert utility package used to express the experimental voxel map data as a data GMM: https://gitlab.pasteur.fr/rpellari/recursive-gmconvert Generated data: Generated MEMMI ensembles for the Aβ42 type I filament and Aβ42 type II filament can be found in https://zenodo.org/records/10567141 (SIMULATIONS.zip)
Data analysis	python3.9, matplotlib-v3.5.2, Seaborn-v0.11.2, pandas-v1.4.4, numpy-v1.21.5, mdtraj-v1.9.7, MDAnalysis-v2.5.0, jupyter-notebook-v6.4.12, plumed-v2.6.0-dev, chimera-v1.2.5, HADDOCK 2.4 server

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Input files for reproducing the MEMMI simulations, the resulting ensembles, and the codes used for the analysis are available at <https://zenodo.org/records/10567141>.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

N/A

Reporting on race, ethnicity, or other socially relevant groupings

N/A

Population characteristics

N/A

Recruitment

N/A

Ethics oversight

N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

The sample size of our metadynamic electron microscopy metainference structural ensembles was chosen so that it represented a converged structural ensemble. In other words the equilibrium properties did not change when we further extended the sampling.

Data exclusions

No data were excluded

Replication

For restraining to the Cyro-EM maps using Metainference no replication was necessary as Metainference already deals with the multiple copies of the system. In particular each MEMMI simulation involved eight replicas which run parallel and the EM map restraints act on the average over the 8 replicas.

Randomization

The eight replicas in metadynamic electron microscopy metainference start from different initial configurations obtained from a short nvt equilibration. The velocities of these initial configurations are randomized.

Blinding

No intervention was performed by the investigators in the generation of the structural ensembles by MEMMI method. The method generated the ensembles and analysis was performed on it to retrieve biological relevant informations.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

Methods

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks

N/A

Novel plant genotypes

N/A

Authentication

N/A