nature portfolio

| Corresponding author(s): | Schierle Schierle |
|----------------------------|-------------------|
| Last updated by author(s): | Apr 10, 2023 |

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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

| ⋖. | tっ | 1 | ıct | 100 |
|-----|----|---|-----|-----|
| .) | ıa | | וכו | ics |

| 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 (n) 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 Only common tests should be described solely by name; describe more complex techniques in the Methods section. |
| X | 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 P values as exact values whenever suitable.</i> |
| \boxtimes | For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| \boxtimes | For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| \boxtimes | 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 <u>statistics for biologists</u> contains articles on many of the points above. |

Software and code

Policy information about <u>availability of computer code</u>

Data collection

Bioscope Resolve system (Bruker, AXS GmBH)
FLUOstar Omega plate reader (BMG LABTECH GmbH, Ortenberg, Germany)

Data analysis Grasp version 8.20b (Charles Dewhurst, ILL) SASView (http://www.sasview.org)

Origin Pro

Nanoscope Analysis 9.1 (Brucker, AXS GmBH) MATLAB (MathWorks, Natick, MA, USA)

Fiji-ImageJ plugin, ThunderSTORM (https://imagej.net/software/fiji/)

GraphPad Prism 8 (Boston, USA)

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

Raw data are available at the University of Cambridge Repository https://doi.org/10.17863/CAM.87759. SANS data acquired at the Institut Laue-Langevin, Grenoble, France are available at http://doi.ill.fr/10.5291/ILL-DATA.8-03-999.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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

Field-specific reporting

| Please select the or | ne 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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size A minimum of three sample replicates and three experimental replicates were performed for ThT-based aggregation assays. Three experimental replicates and a total of 23 cells were analysed for dSTORM experiments.

Three experimental replicates and three fields of view were imaged for STED experiments.

One sample and one replicate were used for SANS experiments.

Two experiments and two fields of view were taken for SRS/CARS experiments.

Data exclusions No data was excluded

Replication See sample size for replication information

Randomization No randomization

Blinding No blinding

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 Involved in the study Involved in the study Antibodies ChIP-seq Eukaryotic cell lines Flow cytometry Palaeontology and archaeology MRI-based neuroimaging Animals and other organisms Clinical data Dual use research of concern Eukaryotic cell lines Policy information about <u>cell lines and Sex and Gender in Research</u> Cell line source(s) Induced pluripotent stem cells (kindly donated by Dr Edward Avezov of UK Dementia of Research Institute) were differentiated into cortical i3Neurons and cultured following the protocol by Fernandopulle, et al. Authentication No authentication Mycoplasma contamination Cells were tested for mycoplasma and none detected. Commonly misidentified lines (See ICLAC register) Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Animals and other research organisms

| Laboratory animals | Sprague-Dawley rats were bred and supplied by Charles River UK Ltd. | |
|-------------------------|---|--|
| | | |
| Wild animals | (N/A | |
| | | |
| Reporting on sex | Female | |
| | | |
| Field-collected samples | N/A | |
| | | |
| Ethics oversight | Sprague-Dawley rats were bred and supplied by Charles River UK Ltd., Scientific, Breeding and Supplying Establishment, registered under Animals (Scientific Procedures) Act 1986, and AAALAC International accredited. All animal work conformed to guidelines of animal husbandry as provided by the UK Home Office. Animals were sacrificed under schedule 1; procedures that do not require specific Home Office approval. Animal work was approved by the NACWO and University of Cambridge Ethics Board. | |

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