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Reporting Summary

Nature Research 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 Research policies, see our Editorial Policies and the Editorial Policy Checklist.

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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.			
\boxtimes	A description of all covariates tested			
\boxtimes	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 statistics for biologists contains articles on many of the points above.

Software and code

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

Data collection

F-actin dataset

STED images of the F-Actin nanostructures were acquired on a 4 color Abberior Expert-Line STED microscope (Abberior Instruments GmbH, Germany), equiped with a 100x 1.4 NA oil objective and using pulsed (40 MHz) excitation (640 nm) and depletion (775 nm) lasers. Fluorescence was detected with an Avalanche Photodiode (APD) and a ET685/70 (Chroma, USA) fluorescence filter. Pixel size was set to 20

Electron microscopy dataset

Serial sections were imaged in a SEM (Zeiss Gemini 540) with the help of the ATLAS acquisition software. Images were acquired at a resolution of 5 nm/pixel, using acceleration voltage of 1.4kV and current of 1.2nA.

All other datasets are were available online.

Data analysis

Data analysis was done in Python 3.7 using the following open-source librairies: PyTorch (1.5), Numpy (1.18), Scipy (1.3), Scikit-Image (0.17), Scikit-Learn (0.21), and Matplotlib (3.1).

Data visualization was done using Fiji (ImageJ, 1.53c).

All code is made available on Github using an open-source license.

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 Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The F-actin dataset and EM dataset are made publicly available at the following address: https://s3.valeria.science/flclab-micranet/index.html. Other datasets MNIST, Cell Tracking Challenge, and P.vivax are available online. Open source code for the MICRA-Net approach is available online: https://github.com/FLClab/MICRA-Net

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 <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	For the two in-house datasets, all available images were used in the study. The public datasets (P.vivax and Cell Tracking Challenge) provided the split of training and testing datasets, we therefore took those as is. We used a 80%/20% to split the provided training set into training and validation respectively. For in-house datasets, we used a 70%/20%/10% for the F-actin dataset (training/valdiation/testing) and 60%/20%/20% for the electron microscopy dataset. This ensured a proper number of images within all sets.			
Data exclusions	We did not exclude any annotated images. The subset of manually annotated testing images on the Cell Tracking Challenge dataset was randomly sampled from the original testing set.			
Replication	Where applicable, we repeated the training of the network 5 times using different random seeds to validate the reproducibility of convergence.			
Randomization	We randomly allocated the samples through all stages of experiments.			

Reporting for specific materials, systems and methods

User-studies were blind: random names were assigned to the images prior to the annotation task.

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	n/a Involved in the study
Antibodies	ChIP-seq
Eukaryotic cell lines	Flow cytometry
Palaeontology and archaeology	MRI-based neuroimaging
Animals and other organisms	·
Human research participants	
Clinical data	
Dual use research of concern	

Antibodies

Blinding

Antibodies used

F-actin dataset

F-actin was stained with phalloidin-STAR635 (Abberior, cat. 2-0205-002-5, 1:50 dilution). Dendrites were identified using a staining against the microtubule-associated-protein-2 with Rabbit-anti-MAP2 PAB (Milipore Sigma, cat. AB5622, 1:1000) and GAR-STAR488 SAB (Abberior, cat. 2-0012-006-5, 1:250).

Electron microscopy dataset

The presence of APEX2 was revealed in axons arising from DRN-infected neurons using 3,3'diaminobenzidine (DAB; catalog no. D5637; Sigma-Aldrich) as the chromogen.

Validation

F-actin dataset

Lavoie-Cardinal, F., Bilodeau, A., Lemieux, M. et al. Sci Rep 10, 11960 (2020).

Electron microscopy dataset

Lam, S., Martell, J., Kamer, K. et al. Nat Methods 12, 51–54 (2015).

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

F-Actin:

Neuronal cultures were prepared from neonatal Sprague Dawley rats.

Electron microscopy

This study was carried out on 3-month-old mice, weighing 25-35g. Animals were housed under a 12h light-dark cycle with water and food ad libitum. Transgenic e-Pet Cre mice expressing Cre recombinase under the control of Fev promoter, known to be specific for

serotonin (5-HT) neurons were used.

Wild animals

The study did not involve wild animal.

Field-collected samples

The study did not require field-collected samples.

Ethics oversight

All manipulations were in accordance to the procedures approved by the animal care committee of Université Laval.

Electron microscopy:

All procedures were approved by the animal care committee of Université Laval, in accordance with the Canadian Council on Animal Care's Guide to the Care and Use of Experimental Animals (Ed2), and with the ARRIVE guidelines. Maximum efforts were made to minimize the number of animals used.

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