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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 Authors & Referees 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 (*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<br>*Only common tests should be described solely by name; describe more complex techniques in the Methods section.* |
| ☒ | ☐ | 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. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted<br>*Give P values as exact values whenever suitable.* |
| ☒ | ☐ | 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 *d*, Pearson's *r*), 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 | CryoEM data collected using Thermo Scientific EPU v2.7 |
| Data analysis | CryoEM data processed using following packages: RELION-3.1, cryoSPARC v2.14, CTFfind4 v.4.1.10, MotionCor2 v.1.2.6, crYOLO v1.4, Coot v.0.9, PHENIX v.1.17 |

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/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 data availability statement. 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

Maps and models have been deposited in the Electron Microscopy Data Bank, http://www.ebi.ac.uk/pdbe/emdb/ (Accession Nos. EMD-11647, EMD-11648). Models have been deposited in the Protein Data Bank, https://www.ebi.ac.uk/pdbe/ (PDB ID codes 7A5S, 7A5R).

# 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 study design

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

| | |
|---|---|
| Sample size | All cryoEM datasets consist of several thousand images. The number of images were sufficient to achieve the reported resolution, according to the most commonly reported resolution measure in cryoEM described in Rosenthal and Henderson 2003 as cited in the manuscript. |
| Data exclusions | cryoEM single particles were included and excluded using standard image processing classification techniques and criteria were not pre-established before data analysis. Details of numbers of selected images for different steps in the calculations are shown in Supplementary Figure 4. |
| Replication | Biophysical measurements were repeated at least 3 times with similar results and with no unsuccessful replications. |
| Randomization | Not applicable to this study, as samples were not assigned to experimental groups and data were collected and processed according to standard techniques for cryoEM. |
| Blinding | Not applicable to this study, as there was no experimental group allocation in data collection and analysis. |

# 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

| n/a | Involved in the study |
|---|---|
| ☐ | ☒ Antibodies |
| ☐ | ☒ Eukaryotic cell lines |
| ☒ | ☐ Palaeontology |
| ☒ | ☐ Animals and other organisms |
| ☐ | ☒ Human research participants |
| ☒ | ☐ Clinical data |

## Methods

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

## Antibodies

| | |
|---|---|
| Antibodies used | Anti-SARS-CoV Non-structural Protein 8 antibody<br>(Antibodies Online; catalogue number ABIN233792)<br>polyclonal<br>Lot no. 17040<br>Dilution used: 1:1000<br><br>Goat Anti-Rabbit IgG (H+L)-HRP Conjugate (Biorad; #1706515)<br>polyclonal<br>Lot no. 64082491<br>Dilution used: 1:1000 |
| Validation | The antibodies were purchased from commercial companies, who provide documentation of validation with each batch. |

## Eukaryotic cell lines

Policy information about cell lines

| | |
|---|---|
| Cell line source(s) | Details of cell line:<br>Vero E6 cells (kindly provided by NIBSC, UK)<br><br>Details of virus strain:<br>SARS CoV-2 (hCoV-19/England/02/2020, EPI_ISL_407073, kindly provided by Public Health England) |
| Authentication | The cell line was provided by the National Institute for Biological Standards and Control (NIBSC) and sourced from the European Collection of Authenticated Cell Cultures and has not been authenticated further |
| Mycoplasma contamination | The cell line tested negative for mycoplasma contamination |

| | |
|---|---|
| Commonly misidentified lines (See ICLAC register) | The cell line is not commonly misidentified |

## Human research participants

Policy information about studies involving human research participants

| | |
|---|---|
| Population characteristics | A single human serum sample was included in the neutralisation assay as an assay control. The sample was donated by a volunteer who remains anonymous to the authors. The characteristic of the volunteer requested was that the individual had a PCR confirmed infection with SARS-CoV-2 and had fully recovered. |
| Recruitment | Staff members at a collaborating institute, St George's, University of London, were invited to give blood samples for the purposes of this research. Full details of the research to be performed were given and volunteers provided written informed consent. Anonymised samples were provided to us at The Francis Crick Institute. |
| Ethics oversight | St Georges, University of London provided ethical consent for volunteers (from among staff members) to provide serum samples for the purposes of this research. |

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