**Supplementary Text: A multi-scale cortical wiring space links cellular architecture and functional dynamics in the human brain**

Data represented in the Figures are contained in the S1\_Data.excel (also available at <https://github.com/MICA-MNI/micaopen/tree/master/structural_manifold>). When organised by nodes, the order corresponds to the use annotation files housed in the parcellation directory of the GitHub and may be called in MATLAB using *annot2classes.m*. (available in <https://github.com/MICA-MNI/micaopen>)

* Figure 1B: separate sheets hold the matrices (“HCPstyle\_GDmatrix”, “HCPstyle\_MPCmatrix”, “HCPstyle\_CSmatrix”, “HCPstyle\_affinitymatrix”) and variance explained by each eigenvector (“HCPstyle\_lambdas”).
* Figure 1C: In the sheet “HCPstyle\_nodewise”, the eigenvectors of the primary cohort are the columns “E1” and “E2” and the colour coding is provided as RGB scaled between [0:1] in “manifold\_colours\_R”, “manifold\_colours\_G”, “manifold\_colours\_B”.
* Figure 1D: wiring distance is provided as separate sheet (“HCPstyle\_WDmatrix”) and the mean wiring distance is the “mean\_wiring\_distance” column in “HCPstyle\_nodewise” sheet.
* Figure 2B: cytoarchitectural similarity is provided as separate sheet (“HCPstyle\_BBmatrix”)
* Figure 2C: externopyramidisation is the “externopyramidisation” column in “HCPstyle\_nodewise” sheet.
* Figure 3A: average expression of each cell type is provided in the “average\_expression” columns of “HCPstyle\_cellwise” sheet with the following order of regions: {'MFC', 'OFC', 'DFC', 'VFC', 'M1C', 'S1C', 'IPC', 'A1C', 'STC', 'ITC', 'V1C'}
* Figure 3B: the noncardinal axes are provided as “noncardinal\_axes” columns in the “HCPstyle\_nodewise” sheet. The r values of each cell type with the axes is presented in the “corr\_with\_noncardinal” columns, where the order aligns with the order in “noncardinal\_axes” columns in the “HCPstyle\_nodewise” sheet.
* Figure 4A-C: functional community assignment is the “yeo\_assignment” column in “HCPstyle\_nodewise” sheet and wiring distance is provided as separate sheet (“HCPstyle\_WDmatrix”).
* Figure 4D: functional connectivity matrix is provided as separate sheet (“HCPstyle\_FCmatrix”).
* Figure 4E-F: mean squared error for the predictive model is provided in the “mse\_combinations” columns in “HCPstyle\_nodewise” sheet, where order corresponds to the rows of Figure 4F.
* Figure 5B: R2 is provided for each node and frequency window in the “R2\_iEEG\_across\_Hz” columns in “HCPstyle\_nodewise” sheet.
* Figure 5C: cluster assignment for each node is the “clusters” column in “HCPstyle\_nodewise” sheet.
* Figure 5D: In the sheet “HCPstyle\_clusterwise”, we provide the coefficients of the principle component analysis in the “coeff” column and the characteristic phase slope index spectra in the “psi\_mean” columns, where the order corresponds to the frequency window. The mean and standard deviation of B weightings for the lasso model are provided in “B\_mean\_across\_lambda” and “B\_std\_across\_lambda”, where the order of columns relates to the lambda value.
* Figure 6: Thresholded phase slope index matrices are the “psi\_\*Hz\_across\_clusters” columns in the “HCPstyle\_clusterwise”, where rows and columns represent clusters. Hierarchical level assignments are the “hierarchical\_level\_\*Hz” columns in “HCPstyle\_clusterwise”.
* Supp Fig 1B: separate sheets hold the matrices (“FSstyle\_GDmatrix”, “FSstyle\_MPCmatrix”, “FSstyle\_CSmatrix”, “FSstyle\_affinitymatrix”) and variance explained by each eigenvector (“FSstyle\_lambdas”).
* Supp Fig 1C: In the sheet “FSstyle\_nodewise”, the eigenvectors of the primary cohort are the columns “E1” and “E2” and the colour coding is provided as RGB scaled between [0:1] in “manifold\_colours\_R”, “manifold\_colours\_G”, “manifold\_colours\_B”.
* Supp Fig 1D: wiring distance is provided as separate sheet (“FSstyle\_WDmatrix”) and the mean wiring distance is the “mean\_wiring\_distance” column in “FSstyle\_nodewise” sheet.
* Supp Fig 3A: the eigenvectors of the replication cohort are the columns “E1\_replication” and “E2\_replication” in the “FSstyle\_nodewise” and “HCPstyle\_nodewise” sheets.
* Supp Fig 4C-E: the inter-individual variation, average prediction across individuals and standard deviation across individuals are the columns “interindividual\_variation”, “mean\_individual\_mse” and “std\_individual\_mse” in the “FSstyle\_nodewise” and “HCPstyle\_nodewise” sheets. The functional community and level of laminar differentiation assignments are “yeo\_assignment” and “mesulam \_assignment” in the “FSstyle\_nodewise” and “HCPstyle\_nodewise” sheets
* Supp Fig 5B: cytoarchitectural similarity is provided as separate sheet (“FSstyle\_BBmatrix”)
* Supp Fig 5C: externopyramidisation is the “externopyramidisation” column in “FSstyle\_nodewise” sheet.
* Supp Fig 6A: average expression of each cell type is provided in the “average\_expression” columns of “FSstyle\_cellwise” sheet with the following order of regions: {'MFC', 'OFC', 'DFC', 'VFC', 'M1C', 'S1C', 'IPC', 'A1C', 'STC', 'ITC', 'V1C'}
* Supp Fig 6B: the noncardinal axes are provided as “noncardinal\_axes” columns in the “FSstyle\_nodewise” sheet. The r values of each cell type with the axes is presented in the “corr\_with\_noncardinal” columns, where the order aligns with the order in “noncardinal\_axes” columns in the “FSstyle\_nodewise” sheet.
* Supp Fig 4C-E: In the “FSstyle\_nodewise” and “HCPstyle\_nodewise” sheets, the group average cortical morphology measures are coded as “thickness” and “curvature”, the “parc\_centroid” is ordered [x,y,z], and unimodal gradients are the “E1\_GDonly”, ”E1\_MPConly”, “E1\_TSonly”, ”E2\_GDonly”, “E2\_MPConly, “E2\_TSonly” columns
* Supp Fig 8A-C: functional community assignment is the “yeo\_assignment” column in “FSstyle\_nodewise” sheet and wiring distance is provided as separate sheet (“FSstyle\_WDmatrix”).
* Supp Fig 8D: functional connectivity matrix is provided as separate sheet (“FSstyle\_FCmatrix”).
* Supp Fig 8E-F: mean squared error for the predictive model is provided in the “mse\_combinations” columns in “FSstyle\_nodewise” sheet, where order corresponds to the rows of Figure 4F.
* Supp Fig 9B: the hyperparameters are provided for each node as “learning\_rate” and “number\_of\_estimators” columns in the “HCPstyle\_nodewise” sheet.
* Supp Fig 10: the eigenvectors of the patient cohort are the columns “E1\_patients” and “E2\_ patients” in the “HCPstyle\_nodewise” sheet.
* Supp Fig 11B: R2 is provided for each node and frequency window in the “R2\_iEEG\_across\_Hz” columns in “FSstyle\_nodewise” sheet.
* Supp Fig 11C: cluster assignment for each node is the “clusters” column in “FSstyle\_nodewise” sheet.
* Supp Fig 11D: In the sheet “FSstyle\_clusterwise”, we provide the coefficients of the principle component analysis in the “coeff” column and the characteristic phase slope index spectra in the “psi\_mean” columns, where the order corresponds to the frequency window. The mean and standard deviation of B weightings for the lasso model are provided in “B\_mean\_across\_lambda” and “B\_std\_across\_lambda”, where the order of columns relates to the lambda value.
* Supp Fig 12A: the number of edges represented between each cluster is provided in “electrodes\_used\_across\_cluster\_pairs” columns of the “HCPstyle\_clusterwise” sheet, where rows and columns are clusters.
* Supp Fig 12C: the weighting of the pca coefficients are provided in the “pca\_coeff\_across\_loo” columns of the the “HCPstyle\_clusterwise” sheet, where columns are leave-one-out-iterations.
* Supp Fig 12D: the mean and standard deviation of psi estimates resulting from the leave-one-out-procedure are provide weighting of the pca coefficients are provided in the “mean\_psi\_loo\_\*Hz\_across\_clusters” and “std\_psi\_loo\_\*Hz\_across\_clusters” columns of the “HCPstyle\_clusterwise” sheet, where rows and columns are clusters.
* Supp Fig 13: Thresholded phase slope index matrices are the “psi\_\*Hz\_across\_clusters” columns in the “FSstyle\_clusterwise”, where rows and columns represent clusters. Hierarchical level assignments are the “hierarchical\_level\_\*Hz” columns in “FSstyle\_clusterwise”.

**Table A**: Variance explained (R2) in externopyramidisation with alternative procedures and input measures

|  |  |  |
| --- | --- | --- |
|  | HCP-style | Freesurfer-style |
| GD only | 0.2931 | 0.50975 |
| MPC only | 0.2062 | 0.49381 |
| TS only | 0.2577 | 0.62106 |
| GD + MPC | 0.2579 | 0.64716 |
| GD + TS | 0.2832 | 0.52581 |
| MPC + TS | 0.2239 | 0.54945 |
| GD, MPC + TS | 0.2609 | 0.65076 |

**Table B: Statistical relationships between cell-type specific gene expression and wiring space.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Regional expression modelled by wiring space eigenvectors 1 & 21 | | | | Spearman correlation between co-expression and wiring distance | | | |
|  | HCP-style | | Freesurfer-style | | HCP-style | | Freesurfer-style | |
| Cell-type | r | p2 | r | p2 | r | p | r | p |
| Astrocyte | 0.86 | 0.033 | 0.91 | 0.002 | -0.44 | <0.001 | -0.74 | <0.001 |
| Endothelial cells | 0.81 | 0.018 | 0.81 | 0.282 | -0.34 | 0.012 | -0.55 | <0.001 |
| Microglia | 0.75 | 0.042 | 0.76 | 0.037 | -0.34 | 0.011 | -0.75 | <0.001 |
| Neurons - excitatory | 0 | 0.169 | 0 | 0.127 | -0.42 | 0.002 | -0.68 | <0.001 |
| Neurons -inhibitory | 0.48 | 0.060 | 0.46 | 0.040 | -0.42 | 0.002 | -0.68 | <0.001 |
| OPCs | 0.95 | 0.002 | 0.89 | 0.027 | -0.40 | 0.003 | -0.65 | <0.001 |
| Oligodendrocytes | 0 | 0.280 | 0 | 0.360 | -0.37 | 0.006 | -0.52 | <0.001 |
| Pericytes | 0.09 | 0.258 | 0.35 | 0.253 | -0.42 | 0.001 | -0.64 | <0.001 |

1 Expression ~ 1+ β1eigenvector1 + β2eigenvector2+ ε

2 Comparison to null model with 10000 permutations of spatial maps with matched spatial autocorrelation 121

**Table C: Model comparison for prediction of resting state functional connectivity**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | |  |  | | |  | | mean squared error (mse) | | | |
| features | | | fusion | embedding | | | learner | | HCP-style | | Freesurfer-style | |
| GD | MPC | TS | E1 | E2 | E3 | linear | ML | mean | std | mean | std |
| x |  |  |  |  |  |  | x |  | 0.911 | 0.109 | 0.856 | 0.167 |
|  | x |  |  |  |  |  | x |  | 0.907 | 0.114 | 0.858 | 0.164 |
|  |  | x |  |  |  |  | x |  | 0.920 | 0.046 | 0.900 | 0.050 |
| x | x | x | x |  |  |  | x |  | 1.425 | 0.286 | 1.348 | 0.494 |
| x |  |  | x | x | x |  | x |  | 0.808 | 0.150 | 3.154 | 4.017 |
|  | x |  | x | x | x |  | x |  | 1.282 | 0.344 | 6.303 | 11.129 |
|  |  | x | x | x | x |  | x |  | 0.872 | 0.087 | 1.283 | 0.704 |
| x | x |  | x | x | x |  | x |  | 2.521 | 1.842 | 0.681 | 0.214 |
| x |  | x | x | x | x |  | x |  | 0.879 | 0.161 | 0.995 | 0.418 |
|  | x | x | x | x | x |  | x |  | 0.834 | 0.136 | 5.567 | 9.878 |
| x | x | x | x | x | x |  | x |  | 0.751 | 0.179 | 0.676 | 0.216 |
| x | x | x | x | x | x | x | x |  | 0.721 | 0.173 | 0.722 | 0.241 |
| x |  |  | x | x | x |  |  | x | 0.647 | 0.145 | 1.272 | 0.433 |
|  | x |  | x | x | x |  |  | x | 1.341 | 0.332 | 1.024 | 0.357 |
|  |  | x | x | x | x |  |  | x | 0.844 | 0.094 | 1.306 | 0.326 |
| x | x |  | x | x | x |  |  | x | 1.596 | 0.427 | 0.494 | 0.188 |
| x |  | x | x | x | x |  |  | x | 0.781 | 0.142 | 0.715 | 0.210 |
|  | x | x | x | x | x |  |  | x | 0.786 | 0.142 | 1.076 | 0.393 |
| **x** | **x** | **x** | **x** | **x** | **x** |  |  | **x** | **0.492** | **0.159** | **0.484** | **0.192** |
| x | x | x | x | x | x | x |  | x | 0.514 | 0.145 | 0.436 | 0.217 |

*Note: bolded row is the primary structural manifold model.*