Smooth network inference from neural tracing data

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Motivation
Broadly, understand interplay of brain structure and information representation

Improve the resolution of the connectivity weight matrix to voxel scale: underconstrained w/o regularization

Tracing experiments

Previous work: regional model
Oh et al., 2014, Nature 508(7495):207-214
Integrate source and target expression over regions to produce regional vectors of expression $\mathbf{x}^{(r)}$ and $\mathbf{y}^{(r)}$:

$\mathbf{x}^{(r)} = \sum_i x_i W_{ij} \mathbf{W}^{(r)}$  
$\mathbf{y}^{(r)} = \sum_j y_j W_{ij} \mathbf{W}^{(r)}$

Then fit the $(n_x \times n_y)$ weight matrix $W^{(r)}$ via least squares by solving

$$\min_W \left\| \mathbf{Y}^{(r)} - W^{(r)} \mathbf{X}^{(r)} \right\|_F^2$$

This is the same as choosing a voxel scale $W$ where $W_{ij}$ is constant for all voxels $i$ in region $A$ and $j$ in region $B$, for all regions $A$ and $B$.

Evidence for smoothness

Retinotopy (map representation of visual field) in primary visual cortex is maintained from V1 into deeper areas analogous to V2, etc.

Smoothness regularized model
Find the voxel-resolution connection matrix $W$ that balances goodness of fit and smoothness:

$$\min_{W} \left\| \mathbf{Y} - W \mathbf{X} \right\|_F^2 + \lambda \left\| \mathbf{W} L^T \mathbf{W} + \mathbf{L}^T \mathbf{W} \right\|_F^2$$

where

$\mathbf{Y} = [y_1, \ldots, y_{n_y}]$  
$\mathbf{X} = [x_1, \ldots, x_{n_x}]$

The choice of a Laplacian penalty in this regression is analogous to so-called “thin-plate splines” for curve fitting or interpolation

Method must be scalable to work with $O(10^5)$ voxels in dataset

Result: With $n_y$ small (relative to $n_x$, $n_y$) a low rank ($\approx 3 \times n_y$) solution $W = UV^T$ works well in our 1-dimensional test problem

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Challenges and future work

- Algorithmic bottleneck is Sylvester equation solve
- Regularization parameter & goodness of fit w/ cross-validation
- Does this work equally well in higher dimensions?
- How much injection coverage is needed?
- Hope to recover retinotopy correlation from connectivity
- Fit entire mouse visual system... fit entire mouse brain