# Enabling cellular-resolution connectomics analysis of the primate cortex

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## Motivation and goals

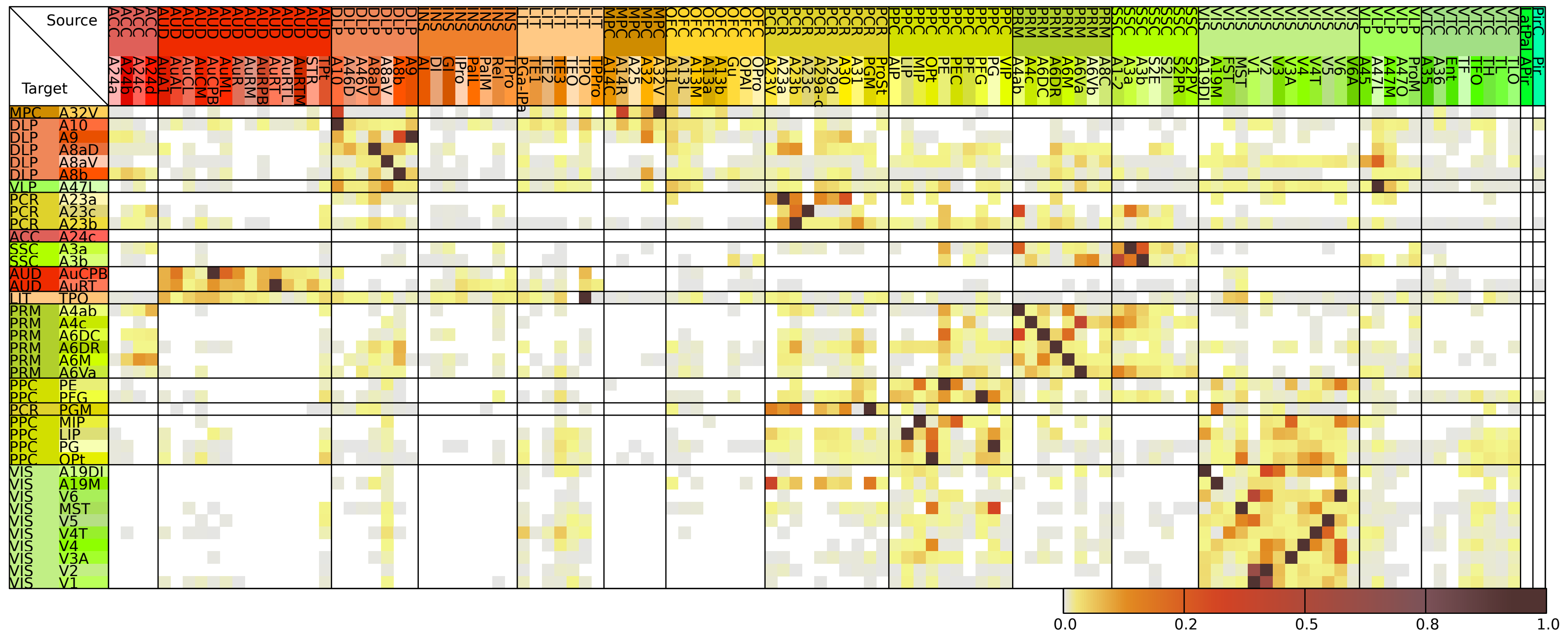
Processes such as perception, action and cognition are determined by the connectivity between different neuronal groups. Understanding the principles of this network is a core objective of present-day neuroscience.

This study aims at creating a publicly available, the world's most comprehensive repository of the afferent cortico-cortical connectivity of any primate species, enabling a new level of analysis and modelling. The connectome will be publicly available on-line making it possible to flexibly access all the data via a graphical front-end or via an application programming interface. It allows one to access unprocessed experimental data, mostly injections in dorsal prefrontal cortex, parietal and occipital lobes. Additionally, the locations of individual cells are expressed in atlas-based stereotaxic coordinates which allows one to perform either area-based or parcellation-free connectivity analyses.

The release of open access connectomes is known for triggering numerous follow-up modelling and theoretical studies. In a longer perspective, the unique nature of data in our project will help to understand how the highly complex network of neuronal connections enable brain functions in primates, and, in general, in mammals.

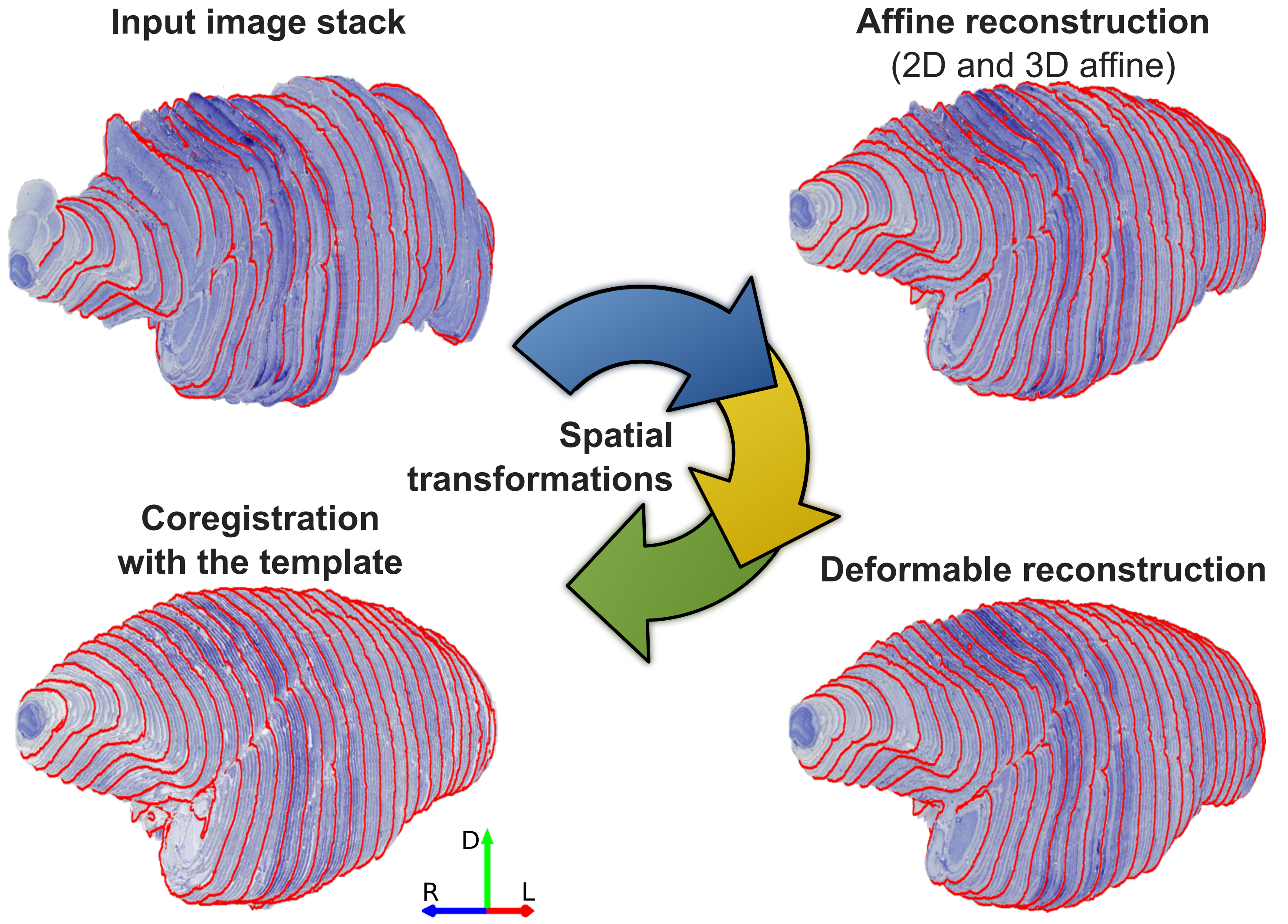
Several animal models are used to investigate this relationship between structure and function, among them marmosets, small monkeys (300-400 g) whose brain retains all defining features of the primate brain.

Marmosets show accelerated development in comparison with most other primates (e.g. Macaques), but retain all unique features of the primate brain. This includes well developed frontal and temporal lobes, a sophisticated visual cortex, multiple cortical areas involved in planning of movements, and systems involved in the interpretation of vocal communication.



(**top**): Weighted connectivity matrix. Each column represents 1 of the 114 source areas; each row represents 1 of the 39 injected target areas. The color shows the strength of the projection as indicated by the color bar with white corresponding to absent connections.

## Reconstruction and mapping workflow[2]



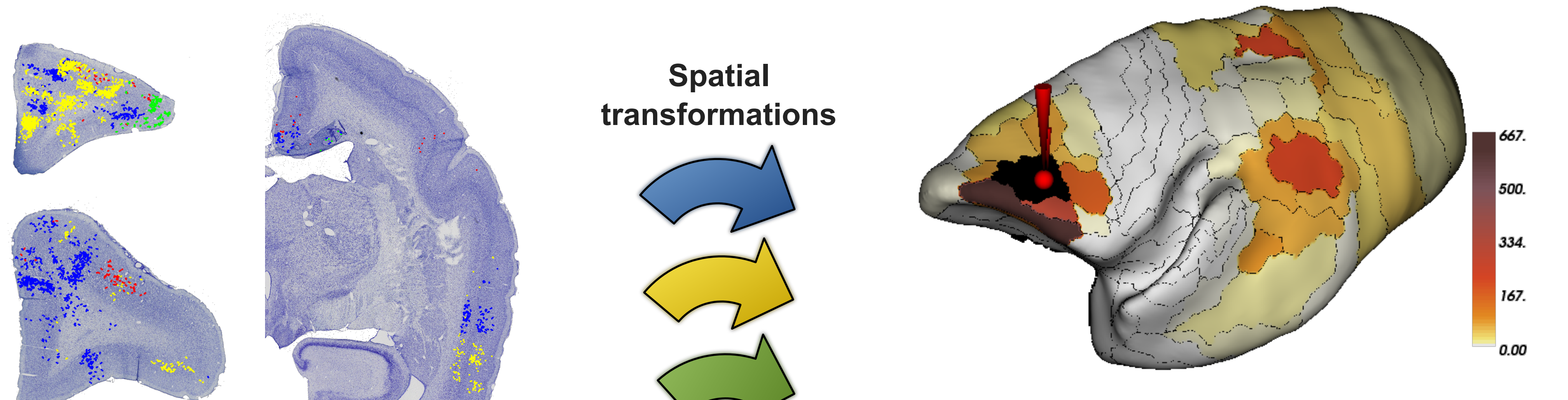
**Input image stack:**
- lacks spatial consistency (sections are not aligned to one another)

**Affine reconstruction:**
- takes the anatomical shape of the reference brain
- consecutive sections are only roughly aligned
- sharp transitions between sections due to local distortions

**Deformable warping step:**
- removes section specific distortions,
- allows for more reliable subsequent mapping to the atlas

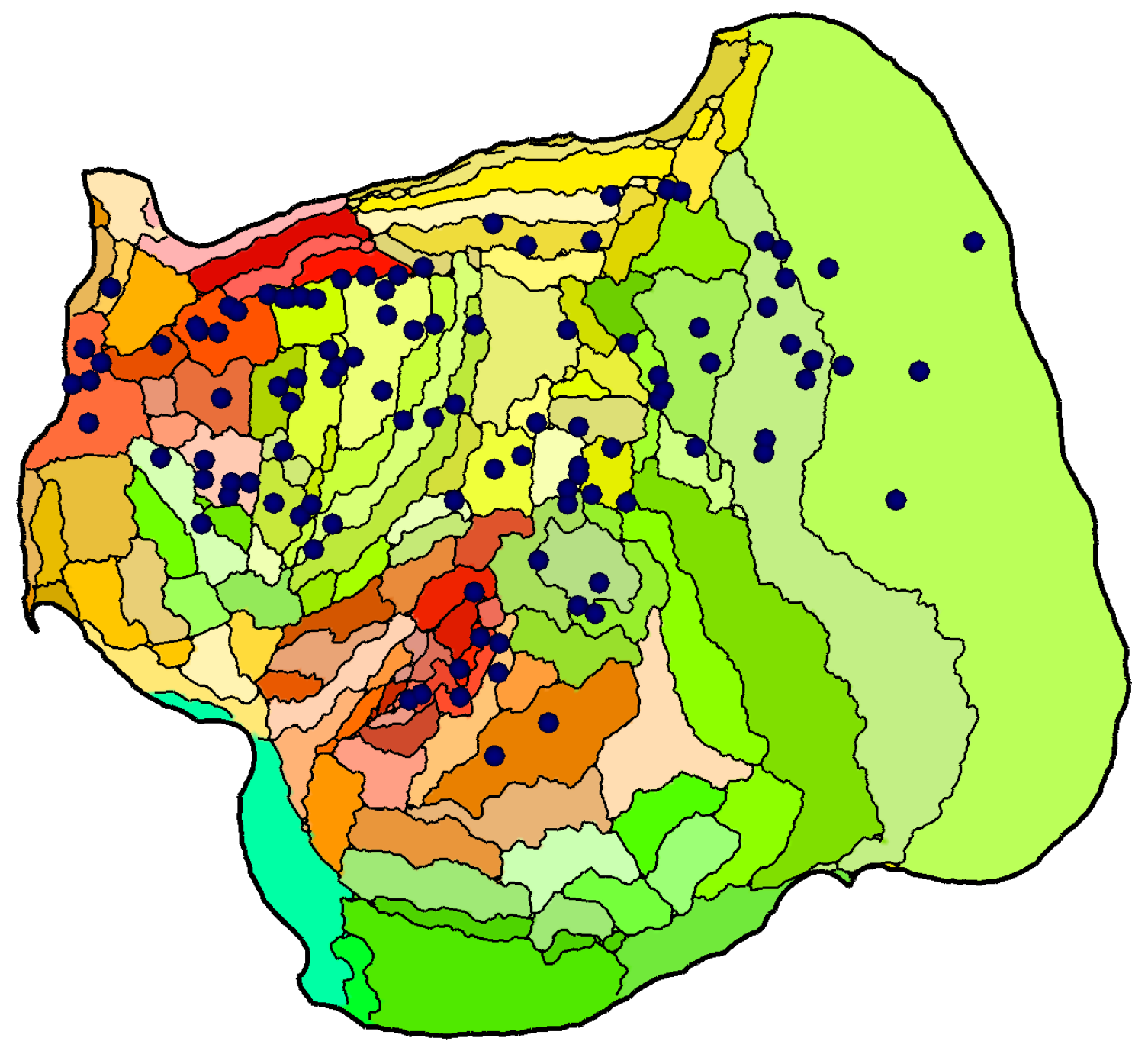
**Coregistration with the template**(1)
- accounts for global distortions (depressions or lesions)

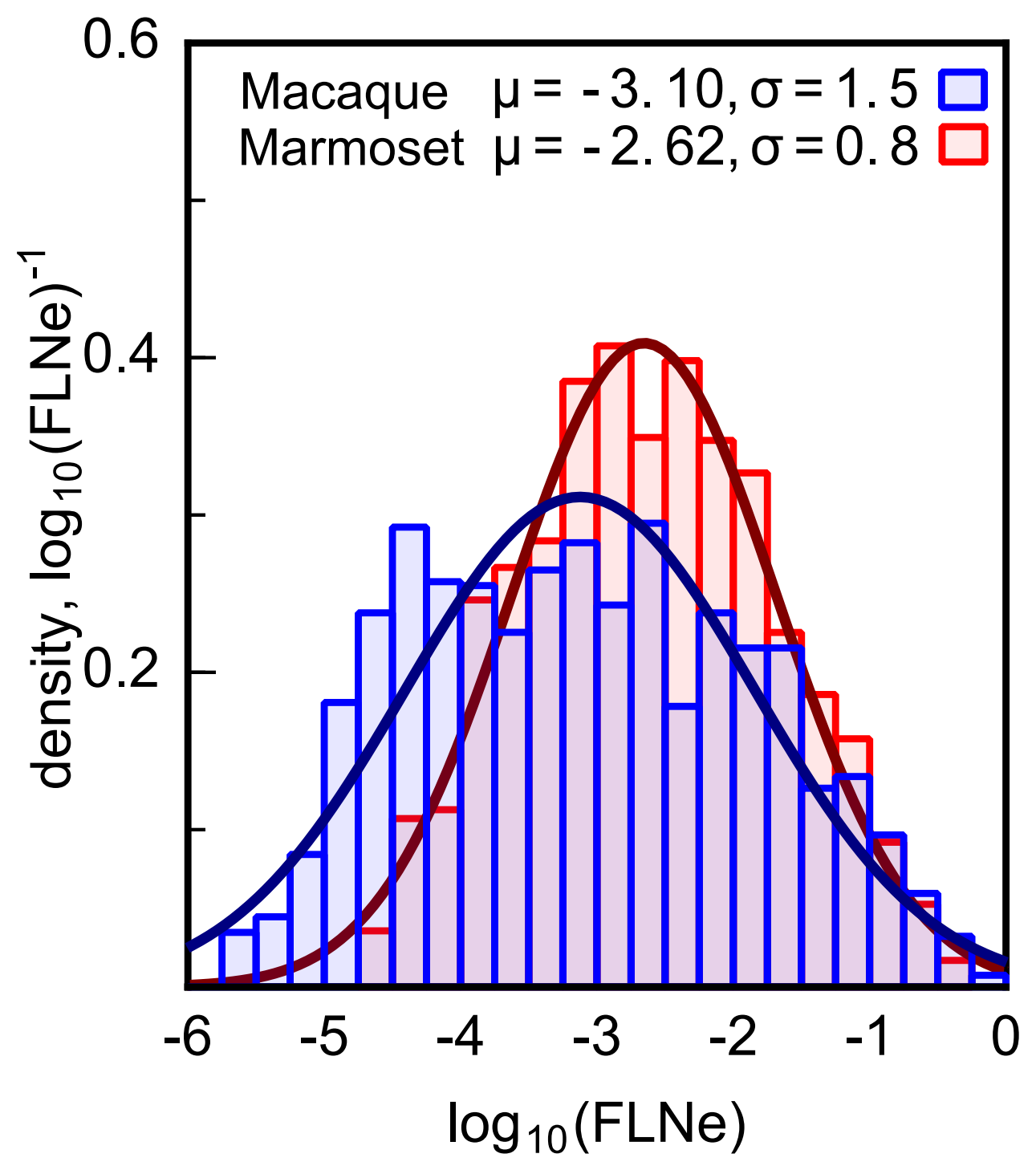
The reconstruction process yields a set of transformations that are applied to the actual cells locations. In the final step, individual cells are assigned to a particular brain structure based on the atlas parcellation.



Quantification of the results: Approx. ~0.85 correlation in comparison with the results obtained by expert.

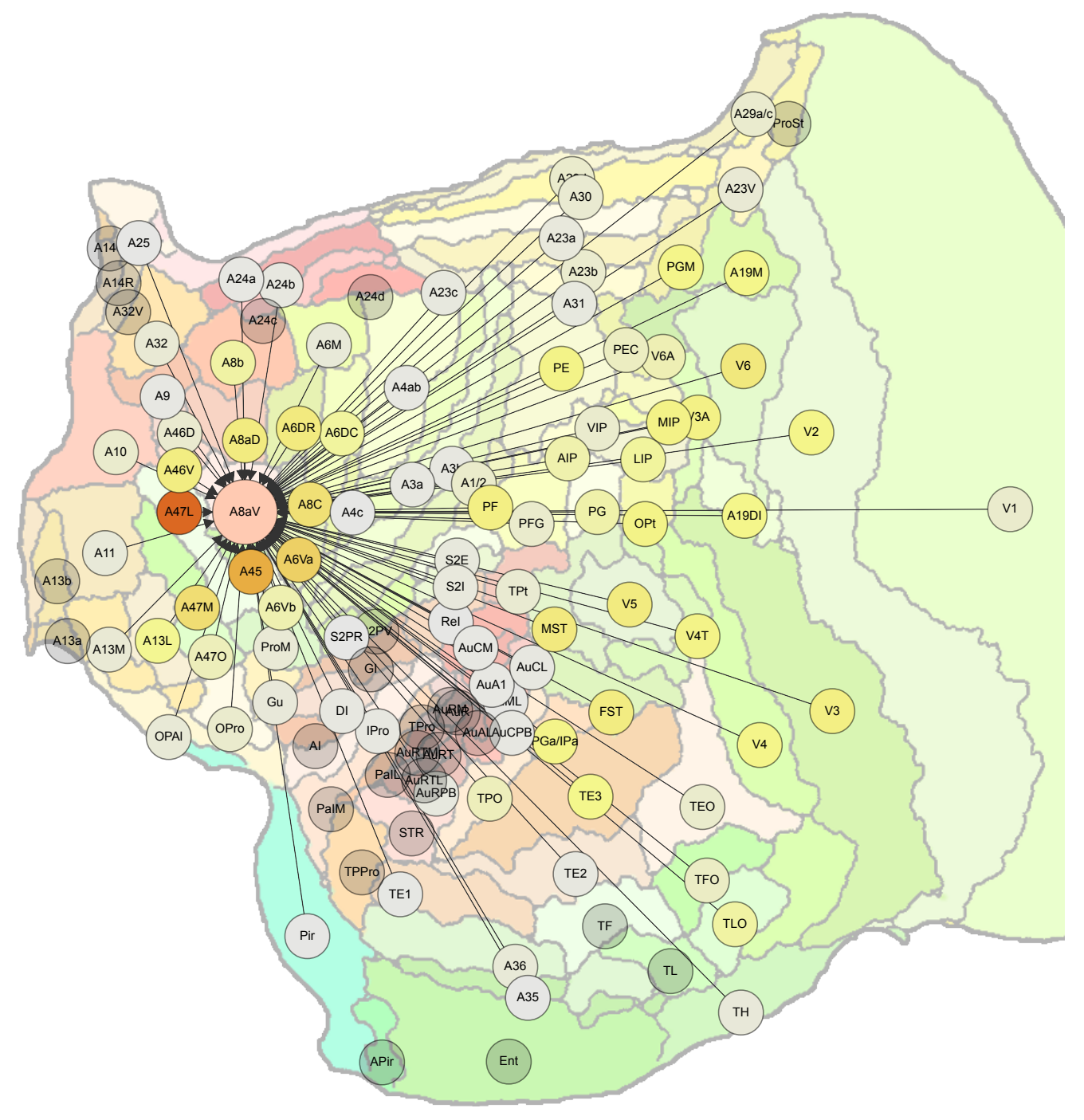
## Area-based connectivity analyses

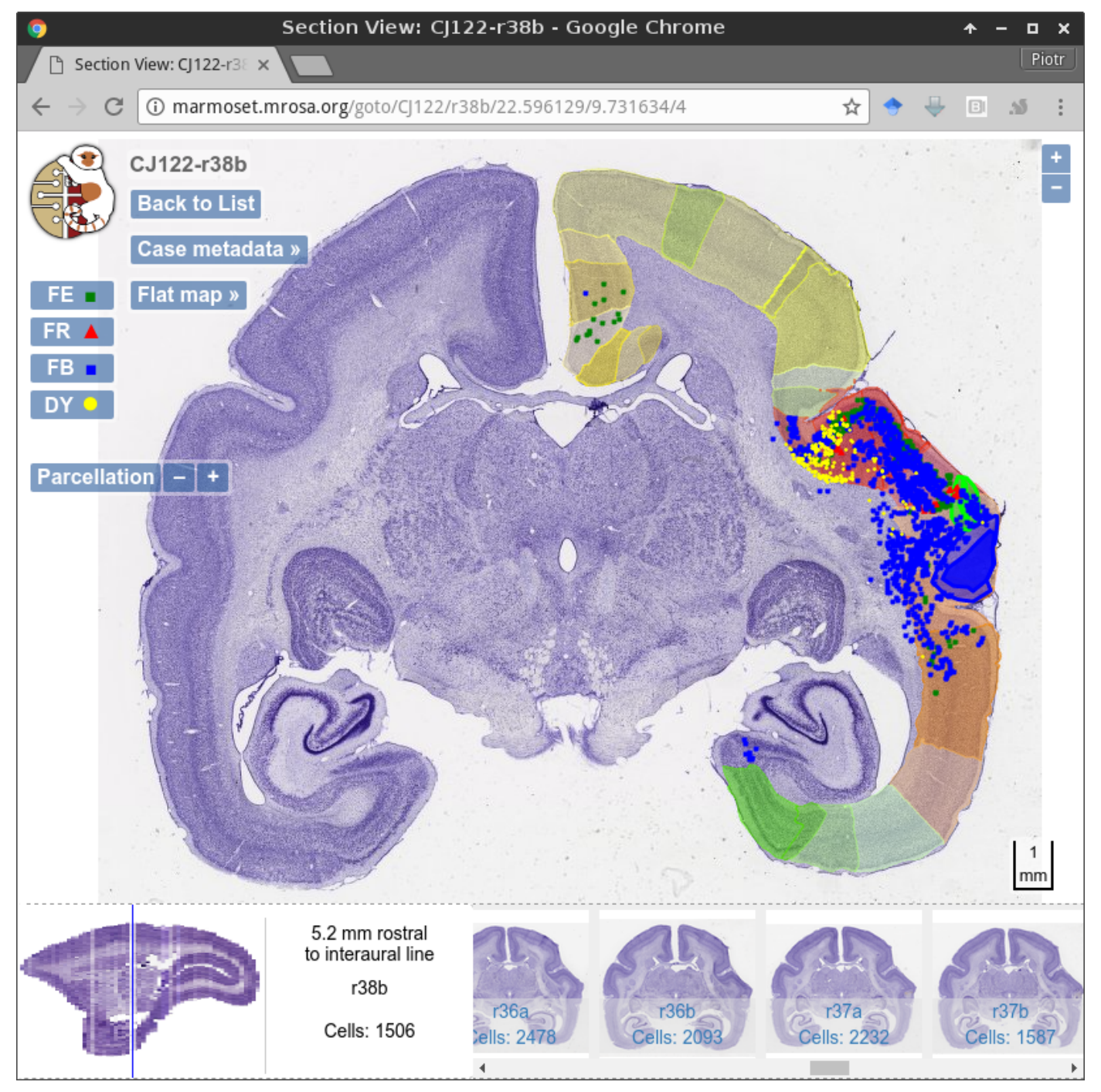




(**right**): Lognormal distribution of FLNe values for marmoset and macaque (data from (3)), the values span five orders of magnitude. The solid lines correspond to Gaussian fits for marmoset (dark red) and macaque (dark blue) data. Both, the fitted means and standard deviations are expressed in units of $\log_{10}$(FLNe).

### http://marmoset.braincircuits.org/





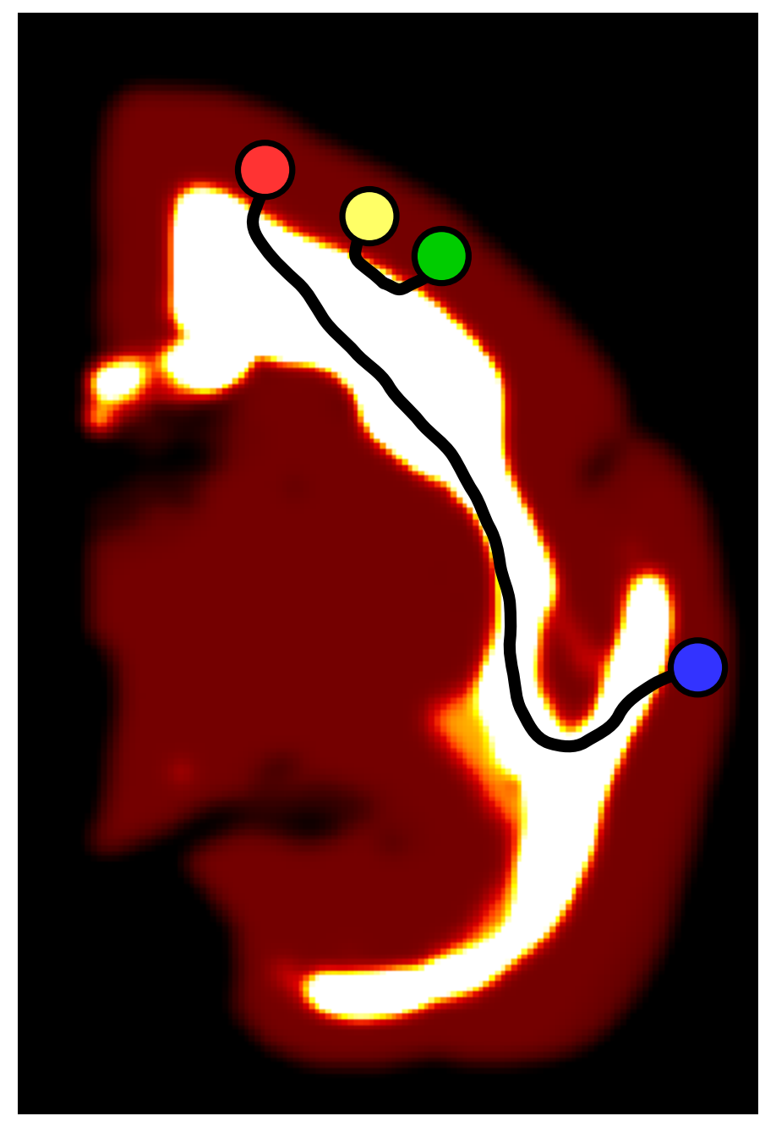
5.2 mm rostral to interaural line
r38b
Cells: 1506

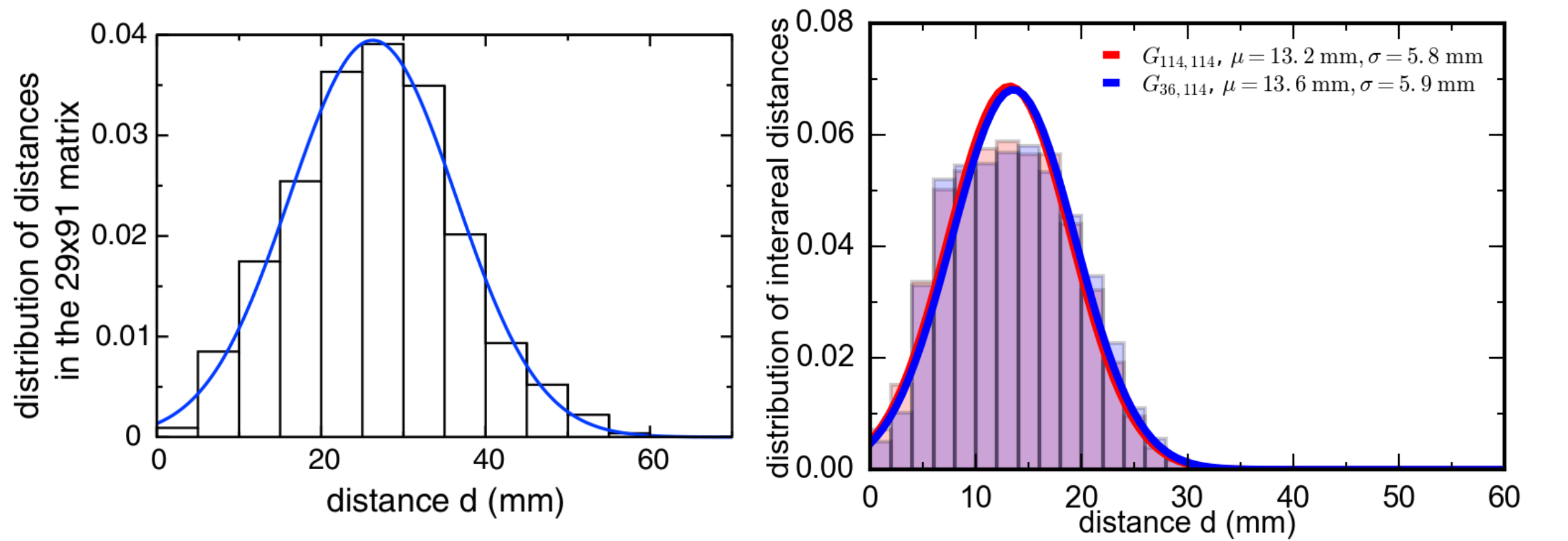
r36a Cells: 2478
r36b Cells: 2093
r37a Cells: 2232
r37b Cells: 1587

## Exponential distance rule?

Model for estimation of interareal distances:
- Calculate barycenters of individual areas.
- Assume that traversing through the white matter is fast (cheap) while passing through the gray matter is slow (expensive).
- Find the shortest (geodesic) path between any two chosen points.
- The term *speed* refers to a parameter of the fast marching method (FMM) and is not used in a biological context here.

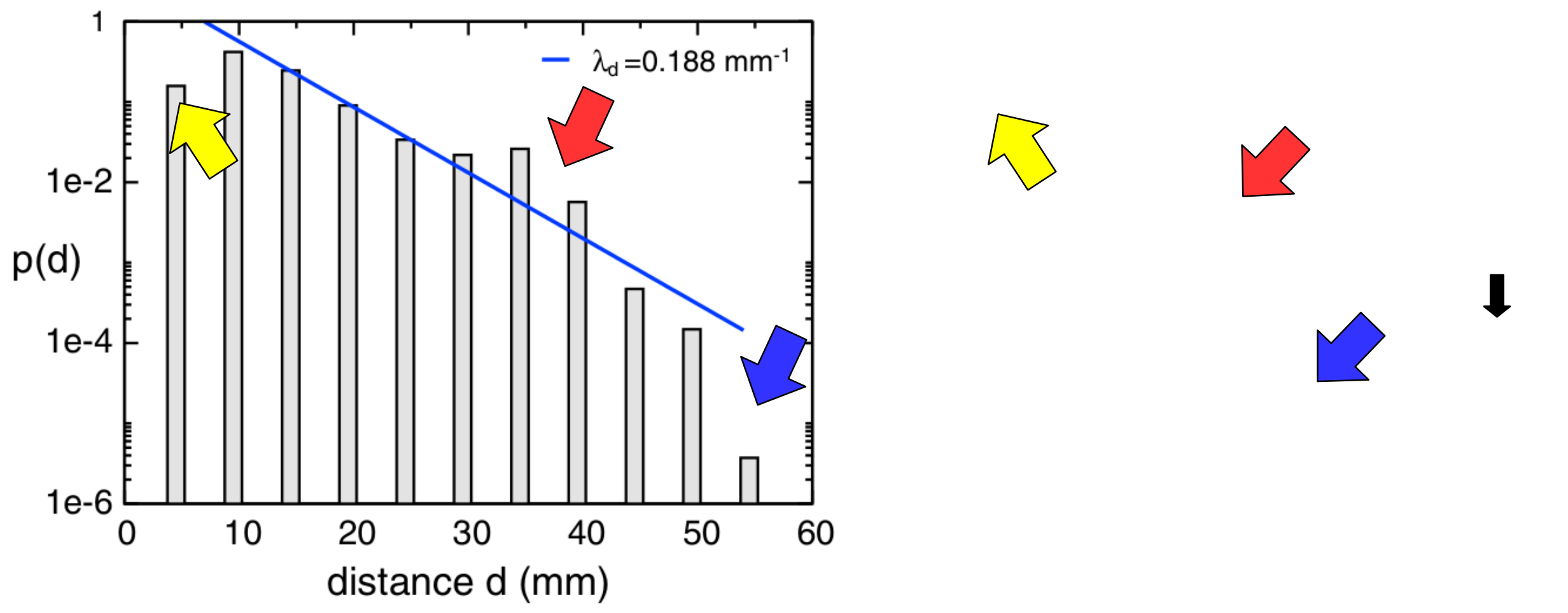
(**right**): Illustration of the principle of the method. Note: Only a 2D cross-section of the 3D volume is shown.





(**left**): Fig. 2C from (3): Distribution of interareal distances in $G_{29x91}$ matrix, a purely geometrical property, is best approximated by a Gaussian distribution ($\mu$ = 26.57 mm; $\sigma$ = 10.11 mm). (**right**): Distribution of interareal distances in marmoset cerebral cortex. Red $G_{114x114}$ matrix, blue: $G_{39x114}$ matrix.

Illustration of the exponential distance rule: $p(d) = c \exp(-\lambda_d d)$ in macaque and marmoset data:



**References**

(1) Paxinos, G., Watson, C., Petrides, M., Rosa, M., & Tokuno, H. (2011). The Marmoset Brain in Stereotaxic Coordinates (1st ed.). Academic Press | (2) Majka, P. et al. (2016). Towards a comprehensive atlas of cortical connections in a primate brain: Mapping tracer injection studies of the common marmoset into a reference digital template. Journal of Comparative Neurology, 524(11), 2161–81. 10.1002/cne.24023 | (3) Ercsey-Ravasz et al. (2013). A Predictive Network Model of Cerebral Cortical Connectivity Based on a Distance Rule. Neuron, 80(1), 184–197. 10.1016/j.neuron.2013.07.036.