Bayesian Analysis of Connectivity in Macaque Cerebral Cortex using JAGS and Stan

A. Toumazi\textsuperscript{a,b,c}, M. Privat\textsuperscript{a,d}, H. Kennedy\textsuperscript{a,b,e} and K. Knoblauch\textsuperscript{a,b,f}

\textsuperscript{a} Inserm U846, Stem Cell and Brain Research Institute
18 avenue du Doyen Lépine, 69675 Bron cedex, France
\textsuperscript{b} Université Lyon 1, Lyon, France
\textsuperscript{c} artemis.toumazi@inserm.fr
\textsuperscript{d} martin.privat@ens-lyon.fr
\textsuperscript{e} henry.kennedy@inserm.fr
\textsuperscript{f} ken.knoblauch@inserm.fr

\textbf{Keywords:} JAGS, Stan, Bayesian, Statistics, Connectome, Prediction, Neuroscience.

There is currently great interest in understanding the network structure (or connectome) of the nonhuman primate (NHP) cortex as it will be much more informative about human cortical organization than other animal models. Our group has assembled a consistent data base of the weighted inputs to 29 areas (of the 91 in our cortical parcellation) distributed across the macaque cortex, using retrograde tract-tracing techniques \cite{3}. In retrograde tracing, an injected marker is transported along axons from the target site of injection to the cell bodies in a source area that project to the injection site. The number of marked neurons is exhaustively counted for each cortical source area projecting to the target. We analyze a measure of strength of projection for each source called the extrinsic \textit{Fraction of Labelled Neurons} (FLN\textsubscript{e}) defined as the proportion of marked neurons from a source with respect to all marked neurons in the cortex external to the target area. The data constitute a $29 \times 91$ weighted and directed graph, $G_{29 \times 91}$. We also study the $29 \times 29$ edge-complete subgraph of the connections only between the 29 injection sites, $G_{29 \times 29}$. Since the injection sites are distributed across the cortex, the $G_{29 \times 29}$ subgraph is expected to be representative of the full connectivity matrix of the brain, $G_{91 \times 91}$. We have characterized the variability of the data base \cite{2} and found a number of regularities in it that indicate fundamental principles of cortical organization. Connection strength decreases approximately exponentially with distance traversed by a projection \cite{1}. This \textit{Exponential Distance Rule} (EDR) predicts a surprising number of features of macaque cortical organization. We are exploring the use of Bayesian models that incorporate the observed characteristics of our data base in order to construct a probabilistic map of connectivity across the cortex covering unexplored areas and to evaluate where to place new injections to minimize uncertainty about the full connectivity matrix. We are currently building models using JAGS \cite{4} and Stan \cite{5} and running these from R with interfacing packages.

Because of overdispersion \cite{3}, the neuron counts were assumed to be distributed as a negative binomial. To model the FLN\textsubscript{e}, the log of the total counts for each injection was used as an offset. Since, Target areas vary in their number of Sources by almost a factor of 3, using the EDR to predict FLN\textsubscript{e} rather than treating each Source as an independent level of a factor, enormously reduces the number of parameters to estimate (see Figure\textsuperscript{1}). To account for variations in the EDR across Target areas, however, the space constant was treated as exchangeable with a hyperprior distribution. The current model provides a reasonable description of the FLN\textsubscript{e} profiles for 4 Target areas in which we have data for multiple repeat injections. We are seeking to extend the model to the full set of 29 injections and to use it to estimate characteristics of
the unobserved connectivity profiles of the Target areas that are as yet uninjected.

Figure 1: FLN$_e$ values for 5 repeat injections in primary visual cortex, area V1. The lines are the mean estimates for a Bayesian model fit with 95% prediction intervals, using JAGS. On the left, the Source areas are treated as levels of a factor. On the right, the distance of each projection to the target is used as a covariate, i.e., assuming the EDR.

References