Characterizing neural dependencies with copula models

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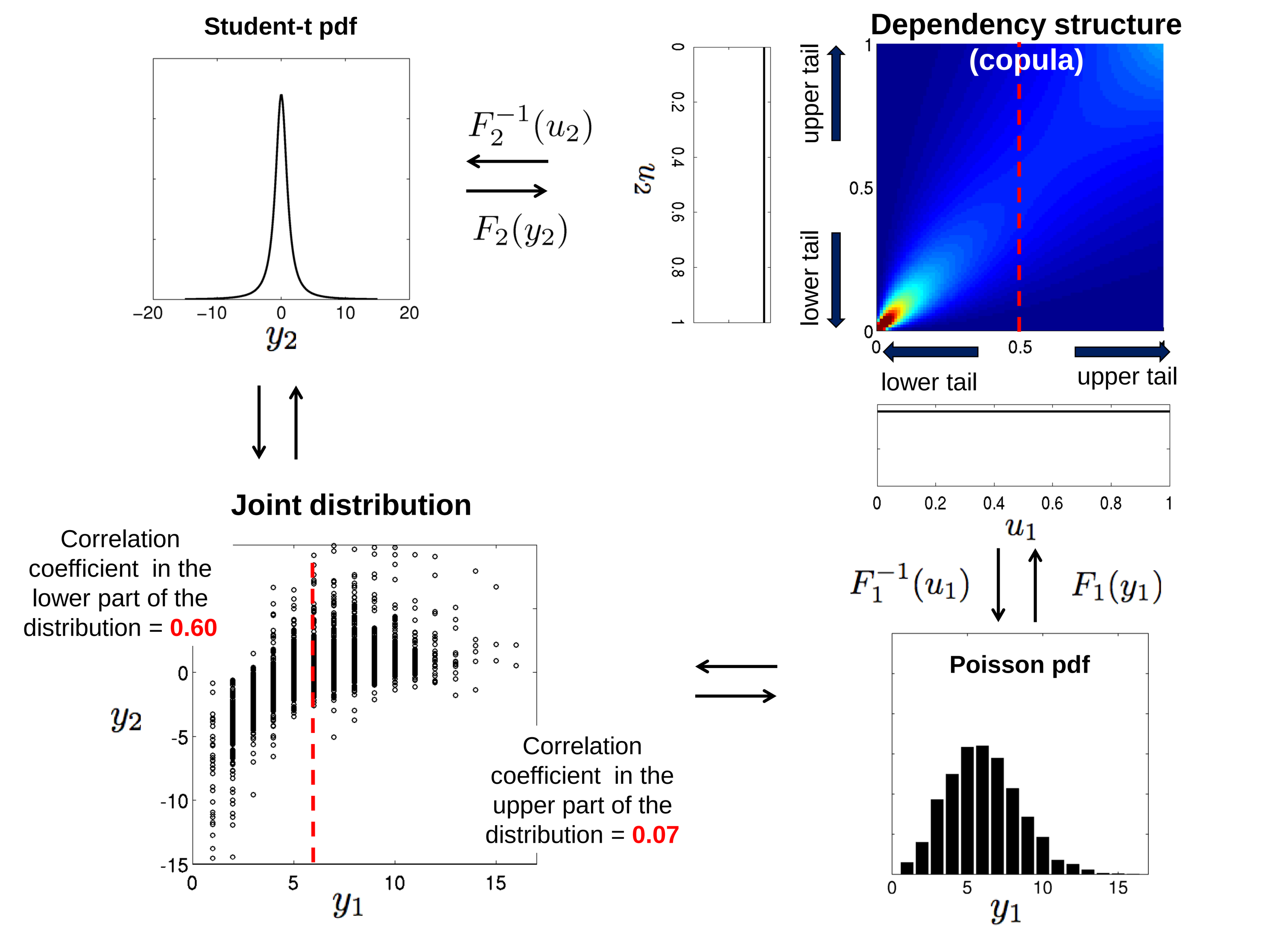
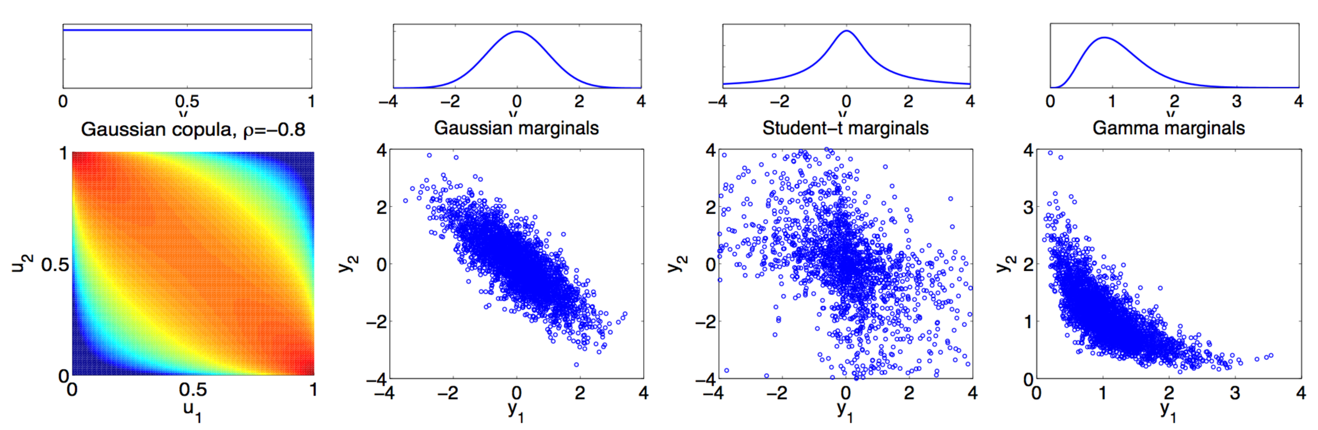
Introduction

- The distributions of activity of individual neurons in cortex and many other areas of the brain are discrete and non-negative
- Neurons display strong dependencies due to common input and network connectivity
- We introduce copula models as a principled, parametric method to combine the neural activity distributions into a joint distribution with desired dependencies

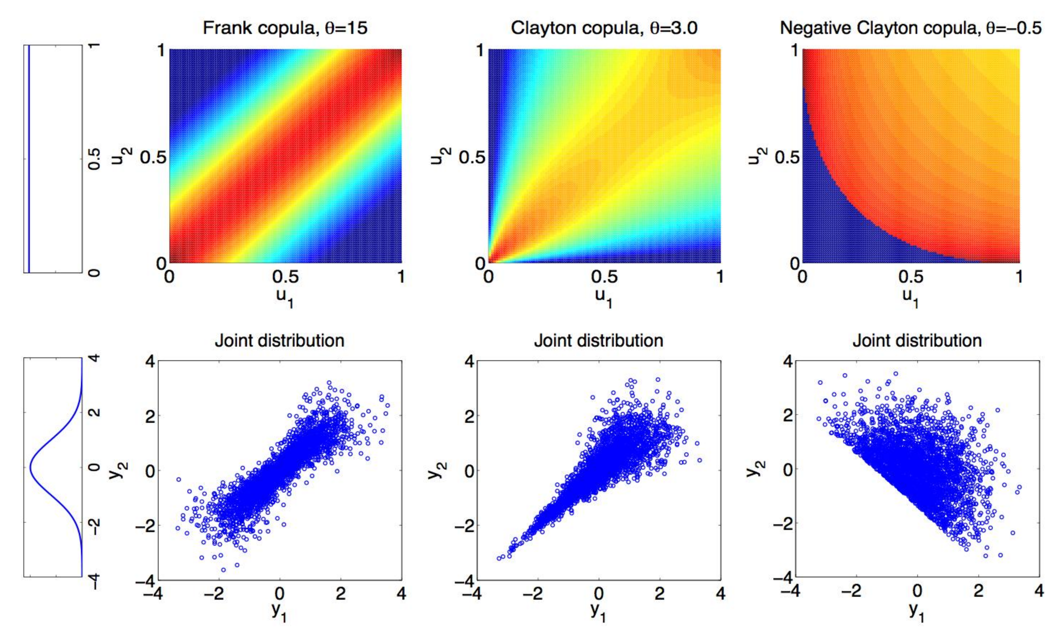
Key idea: Every distribution can be transformed into a uniform distribution between 0 and 1 using its cdf



Gaussian dependency structure, different marginals



Gaussian marginals, different dependency structures



Definition: A *copula* C is a multivariate distribution over the unit cube with uniform marginals.

Sklar's theorem (1959): *Given $y_1, \ldots, y_n$ random variables with continuous distribution functions $F_1,\ldots,F_n$ and joint distribution F, there exists a unique copula C such that for all x:*

$$C(u_1, ..., u_n) = F(F_1^{-1}(u_1), ..., F_m^{-1}(u_n))$$

Conversely, given any distribution functions $F_1,\ldots,F_m$ and copula C,

$$F(y_1, \ldots, y_n) = C(F_1(y_1), \ldots, F_n(y_n))$$

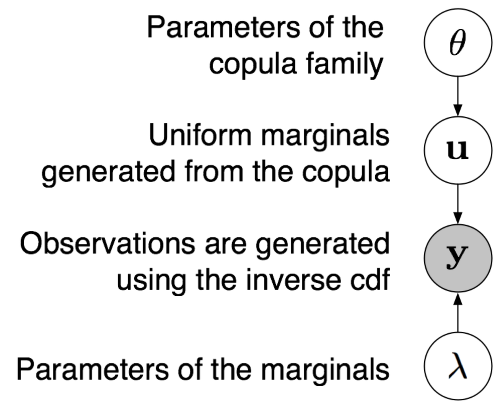
is a n-variate distribution function with marginal distribution functions $F_1, \ldots, F_m$.

- Principled way to quantify dependencies that go beyond correlation coefficients
- Independent of nonlinear transformation of variables (Nelsen, 1999)
- Estimating mutual information between stimulus and response Jenison & Reale, 2004).

Modeling neural dependencies

- We propose to **fit parametric families of copula models to joint neural activity** by Maximum Likelihood estimation
- The selection of an appropriate parametric family for the copula distribution can be addressed by **cross-validation**

Dealing with discrete marginals: Learning a copula model with discrete marginals requires care, because the cdf maps data to a finite set of points in the copula space (Genest & Naslehova, 2007). Our strategy is to derive a generative model on the data and **integrate** over the uniform marginals:



$$p(\mathbf{u}|\theta) = c_\theta(u_1, \ldots, u_n)$$

$$p(y_i|\mathbf{u}, \lambda) = \begin{cases} 1, & y_i = F_i^{-1}(u_i; \lambda_i) \\ 0, & \text{otherwise} \end{cases}$$

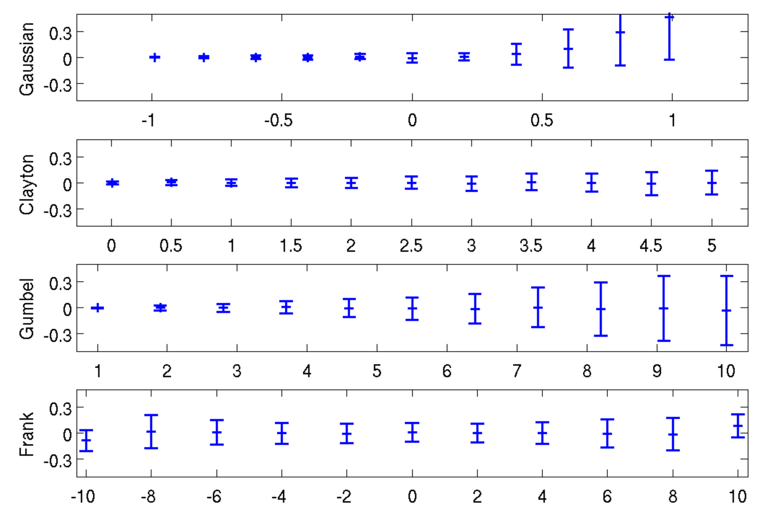
Likelihood function:

$$p(\mathbf{y}|\theta) = \int p(\mathbf{y}|\mathbf{u}, \theta) p(\mathbf{u}|\theta)\, \mathrm{d}\mathbf{u} = \int_{F_1(y_1-1)}^{F_1(y_1)} \cdots \int_{F_n(y_n-1)}^{F_n(y_n)} c_\theta(u_1, \ldots, u_n)\, \mathrm{d}\mathbf{u}$$

For example, in the bivariate case:

$$p(\mathbf{y}|\theta) = C_\theta(F_1(y_1), F_2(y_2)) + C_\theta(F_1(y_1-1), F_2(y_2-1)) - C_\theta(F_1(y_1-1), F_2(y_2)) - C_\theta(F_1(y_1), F_2(y_2-1))$$

Estimation is unbiased for a wide range of parameters:



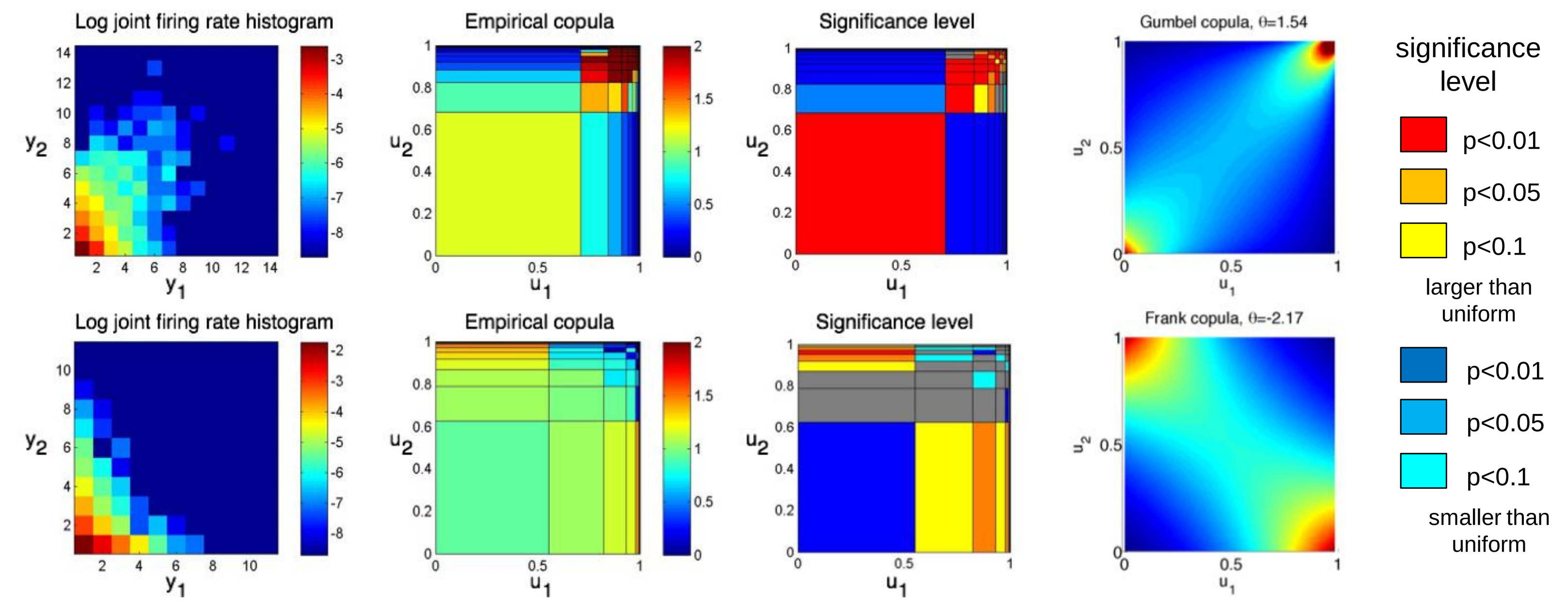
3500 data points (1000 for Gaussian) were generated from the model with Poisson marginals with parameters λ_1=2, λ_2=3; the estimation is repeated 200 times (100 for Gaussian) to compute mean and standard deviation of the ML estimate.

Analysis of neural dependency

Neural data

We analyzed pairwise dependencies in neural data recorded from 10x10 array implanted in the pre-motor cortex (PMd) area of a macaque monkey (center-out reaching task, including data between trials) (Serruya *et al.*, 2002, Suner *et al.*, 2005). We collected spike responses in 100ms bins. Training set: 4000 bins; test set: 2000 bins.

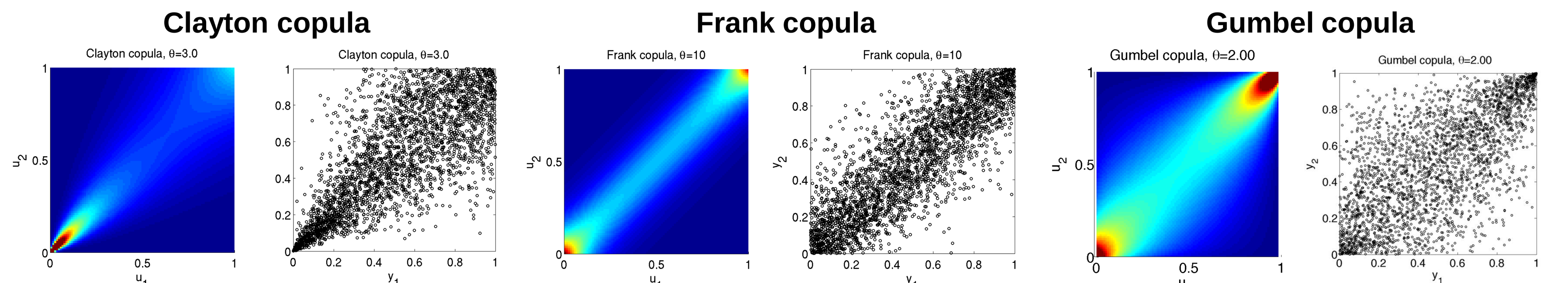
Out of a total of 194 neurons we select a subset of 33 neurons that fired a minimum of 2500 spikes over the whole data set.



For every pair of neurons in this subset (528 pairs), we fit the parameters of several copula families to the joint firing rate using the **empirical cdf**. The models are scored according to the improvement in bits/sec over a model that assumes independence.

$$KL(p^*||p_{indep}) - KL(p^*||p_\theta) = -H(p^*) - \int \mathrm{d}p^* \log p_{indep} + H(p^*) + \int \mathrm{d}p^* \log p_\theta \approx -\sum_{y\sim p^*} \log p_{indep}(y) + \sum_{y\sim p^*} \log p_\theta(y)\,.$$

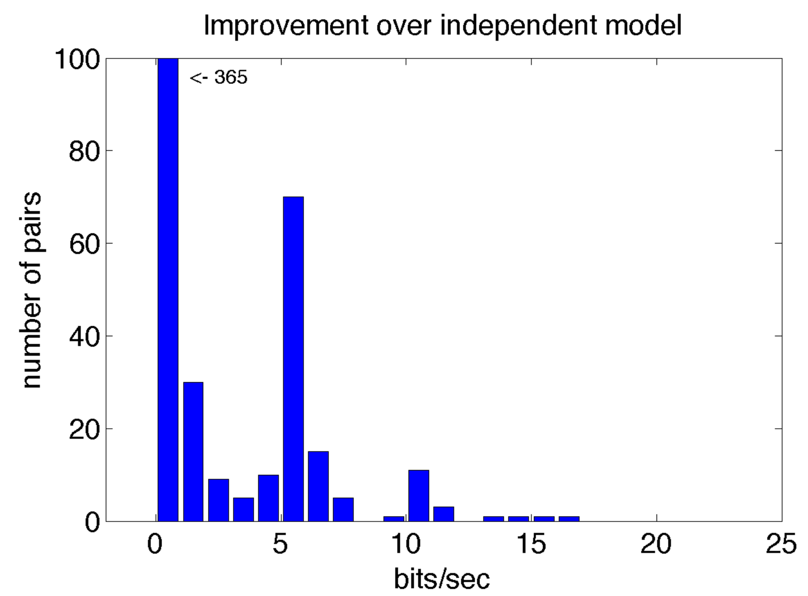
We considered a total of ten copula families (Gauss, Student-t, Clayton and associated copulas, Gumbel, Frank, and the two-parameter family BB1). Based on cross-validation and redundancies between the copulas, we selected three families that consistently fit the data better.

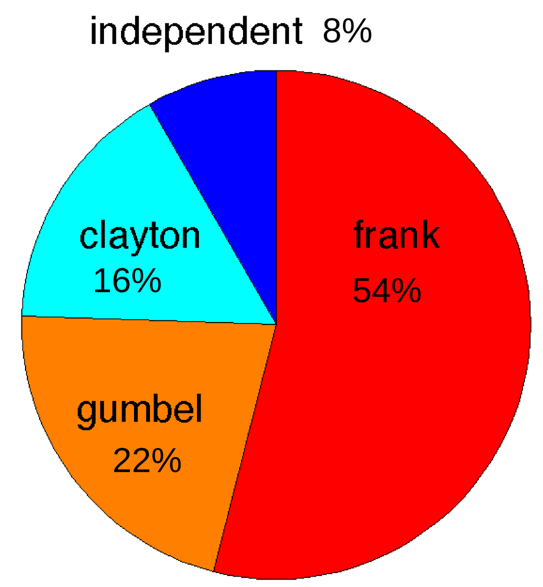


$$C_\theta^{Cl}(u_1, u_2) = (u_1^{-\theta} + u_2^{-\theta} - 1)^{-1/\theta}$$

$$C_\theta^{Fr}(u_1, u_2) = -\frac{1}{\theta} \ln\left(1 + \frac{(e^{-\theta u_1} - 1)(e^{-\theta u_2} - 1)}{e^{-\theta} - 1}\right)$$

$$C_\theta^{Gu}(u_1, u_2) = \exp\left(-(\tilde{u}_1^\theta + \tilde{u}_2^\theta)^{1/\theta}\right),\ \tilde{u}_j = -\log u_j$$



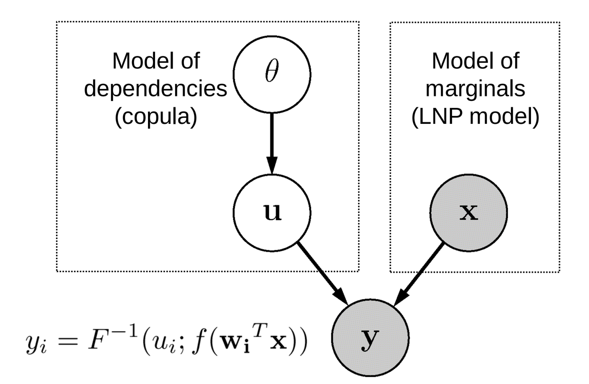


Out of 528 pairs, 484 showed improvement with respect to independent model (163 > 1bit/sec). More than one third of all pairs showed dependencies concentrated in the upper or lower tails of the distribution.

Future challenges

- taking into account multiple neurons: make the fitting procedure scale, introduce new multivariate copulas

- stimulus dependency: Preliminary results show that after fitting a Linear-Nonlinear-Poisson (LNP) model to the data, there are residual dependencies that can be captured by copula models.



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