Alzheimer's Analysis and Detection with Copula Generated Random Graphs

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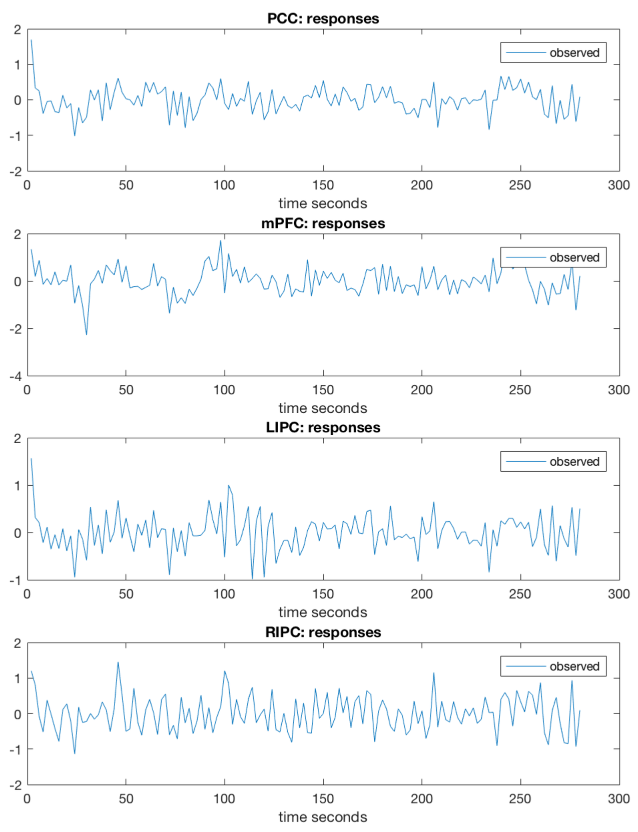
Abstract

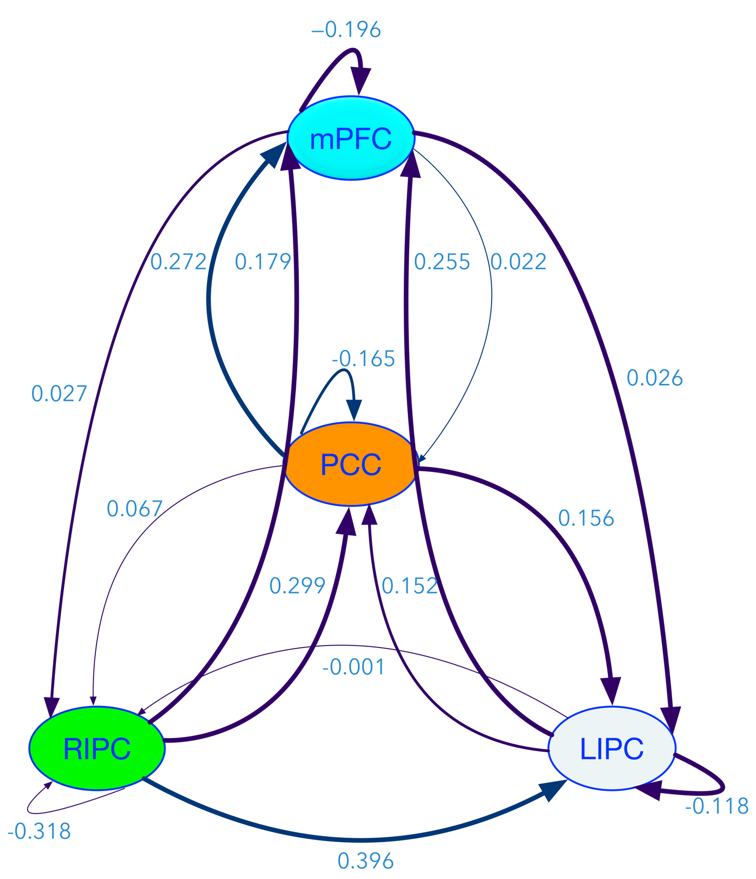
We model four nodes in the default mode network (DMN) as a Copula Generated Random Graph (developed in [1]). The copula's dependence parameter can model negative and positive patterns of reciprocity in brain networks. This estimated structure becomes data used to detect the presence of Alzheimer's. We demonstrate the efficacy of this procedure with the data examined in [4]. Then we compare the entropies of the fitted densities across disease groups.

From fMRI Data to a Regulation Network

- Resting state fMRI measurements were taken at four nodes in the brain.



- Transform the time series data to an effective connectivity network via the Dynamic Causal Model in [3].



- Background information on the patients was also collected, $\mathbf{x}_s$.
- Patients belong to one of three groups: Alzheimer's (AD), Mild Cognitive Impairment (MCI) or Normal.
- Construct a probability distribution for the collection of regulation networks.
- Sample from the posterior distribution of the associated model parameters.

Copula Generated Random Graphs

1. Denote the observed network for unit s by $A^{(s)}$.
2. The value of the edge from node i to node j, $A_{ij}^{(s)}$, has marginal distribution

$$\mathcal{N}\left(\delta_i^{g_s} + \gamma_j^{g_s} + \beta^\top \mathbf{x}_s, (\sigma^{g_s})^2\right),$$

   - δ_i refers to the **sender** effect of node i.
   - γ_j represents the **receiver** effect of node j.
   - β captures the effect of $\mathbf{x}_s$ on the edge value.
   - g_s is the disease group for unit s.

3. Bind the marginal distributions within each dyad with the Frank copula.

$$-\frac{1}{\rho^{g_s}}\log\left[1+\frac{\left(e^{-\rho^{g_s}F(A_{ij}^{(s)})}-1\right)\left(e^{-\rho^{g_s}F(A_{ji}^{(s)})}-1\right)}{e^{-\rho^{g_s}}-1}\right]$$

   - ρ^{g_s} is the reciprocity parameter for g_s.
   - $F(\cdot)$ is the cumulative distribution function.

4. The joint probability density for edge values within the same dyad is

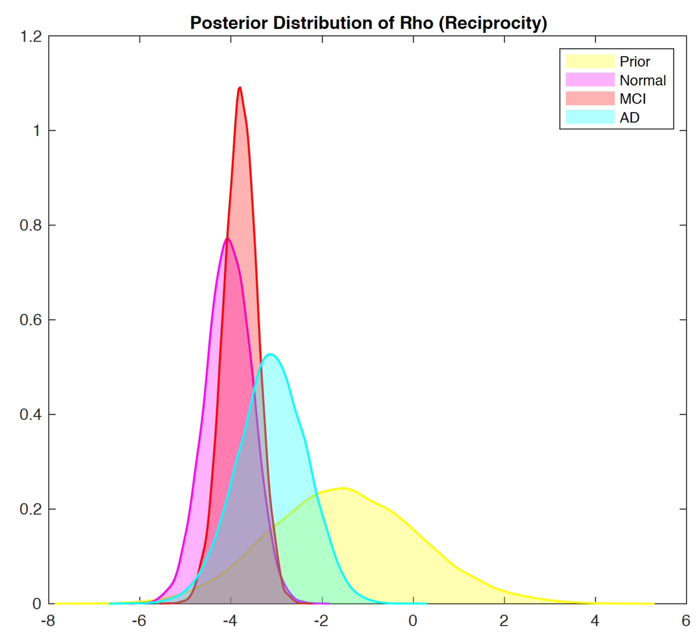
$$\frac{\partial}{\partial F(A_{ij}^{(s)})}\frac{\partial}{\partial F(A_{ji}^{(s)})}C_\rho\left(F(A_{ij}^{(s)}),F(A_{ji}^{(s)})\right)f\left(A_{ij}^{(s)}\right)f\left(A_{ji}^{(s)}\right).$$

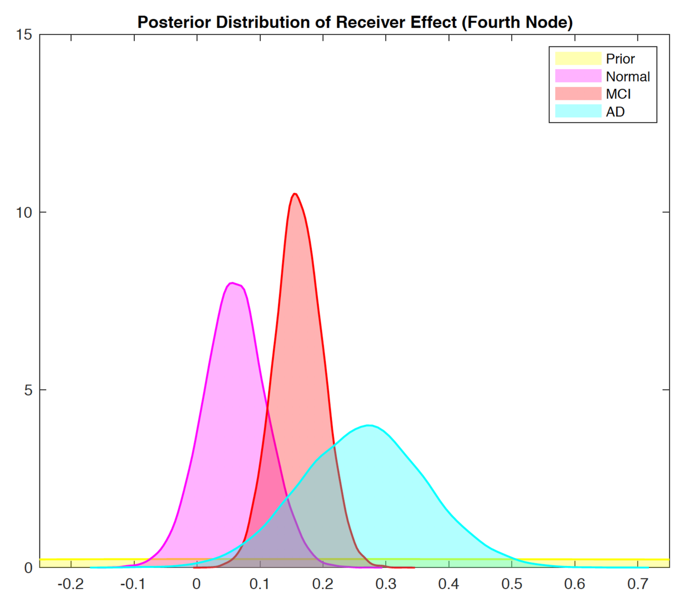
5. Then the likelihood function for the observed data $\left\{A^{(s)}\right\}$ is

$$L\left(\rho,\delta,\gamma,\sigma^2|\left\{A^{(s)}\right\}\right)=\prod_{s=1}^{S}\prod_{i=1}^{n}\prod_{j<i}p\left(A_{ij}^{(s)},A_{ji}^{(s)}|\theta^{(g_s)}\right).$$

Hierarchical Bayesian Inference

- Parameters share a common prior.
- For example, $\pi(\rho^{g_s}) = \mathcal{N}(\rho_0, \sigma_\rho^2)$.





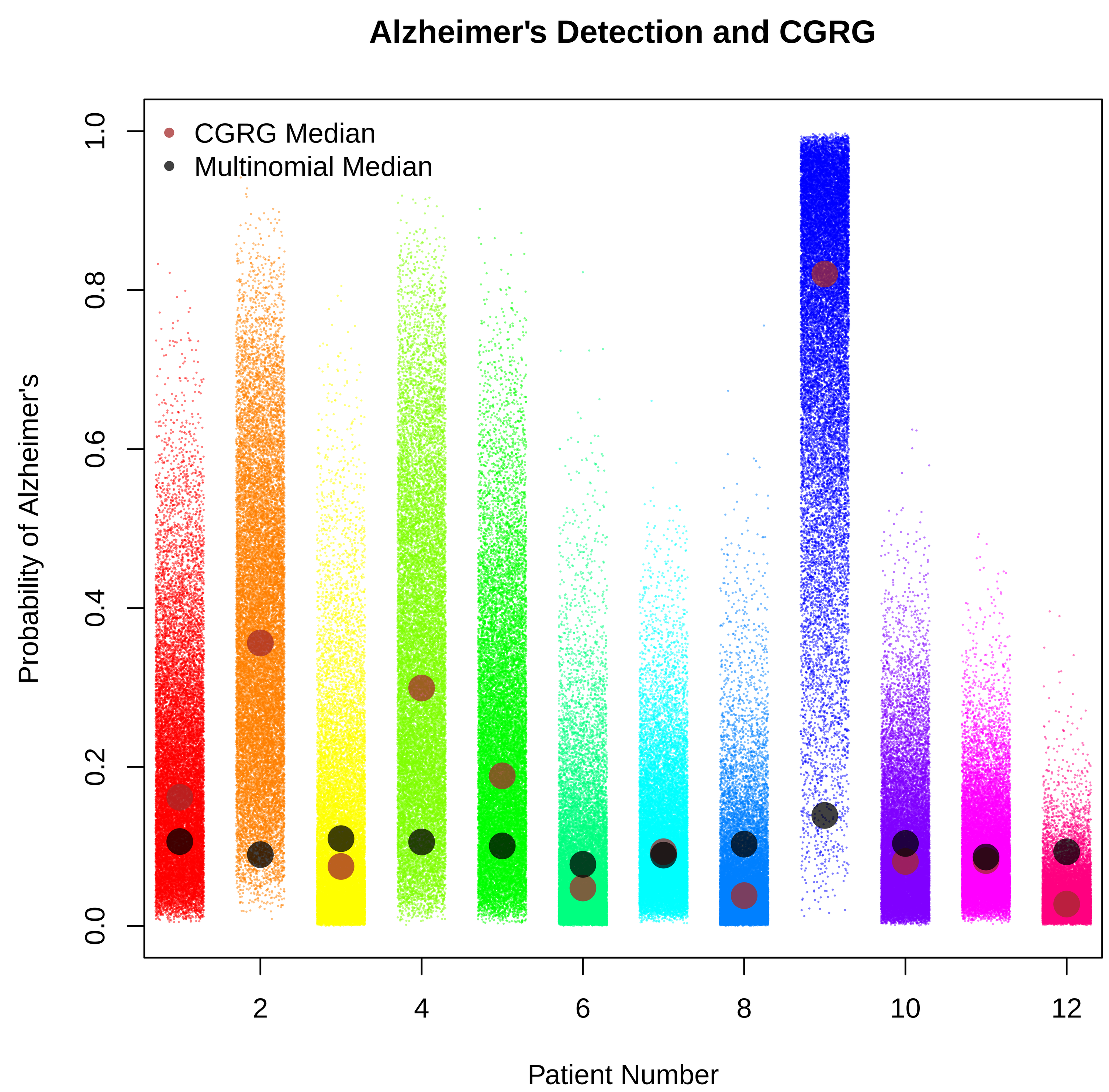


Figure 1: Posterior Distributions of the Probability of Alzheimer's Among Units in the AD Group.

Disease Detection

- Compute the probability that unit s belongs to group g as

$$p(g_s=g|A^s,\rho,\delta,\gamma,\mathbf{x}_s)=\frac{p(A^s|g_s=g,\rho^g,\delta^g,\gamma^g,\mathbf{x}_s)p(g_s=g|\theta,\mathbf{x}_s)}{\sum_{g=1}^{G}p(A^s|g_s=g,\rho^g,\delta^g,\gamma^g,\mathbf{x}_s)p(g_s=g|\theta,\mathbf{x}_s)}.$$

- Model the probability of group membership as the multinomial distribution

$$p(g_s=g|\theta,\mathbf{x}_s)=\frac{\exp\left\{\theta_g^\top\mathbf{x}_s\right\}}{\sum_{g=1}^{G}\exp\left\{\theta_g^\top\mathbf{x}_s\right\}}.$$

Entropy Computation

Sample networks and approximate the entropy via

$$-\int_A f(A)\ln(f(A))dA \approx -\frac{1}{R}\sum_{r=1}^{R}p\left(A^{(r)}\right)\ln p\left(A^{(r)}\right).$$

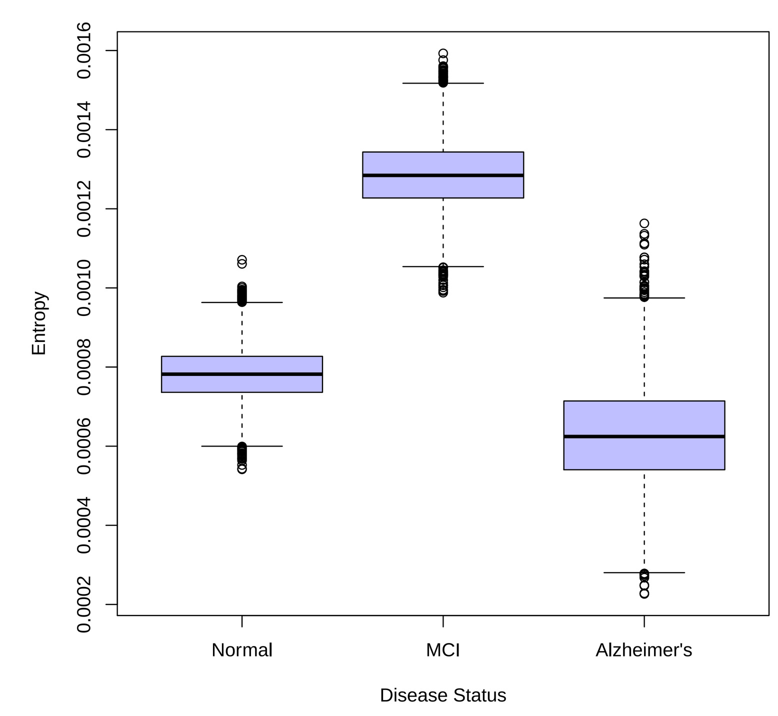


Figure 2: Entropy of Fitted Densities (3 Groups).

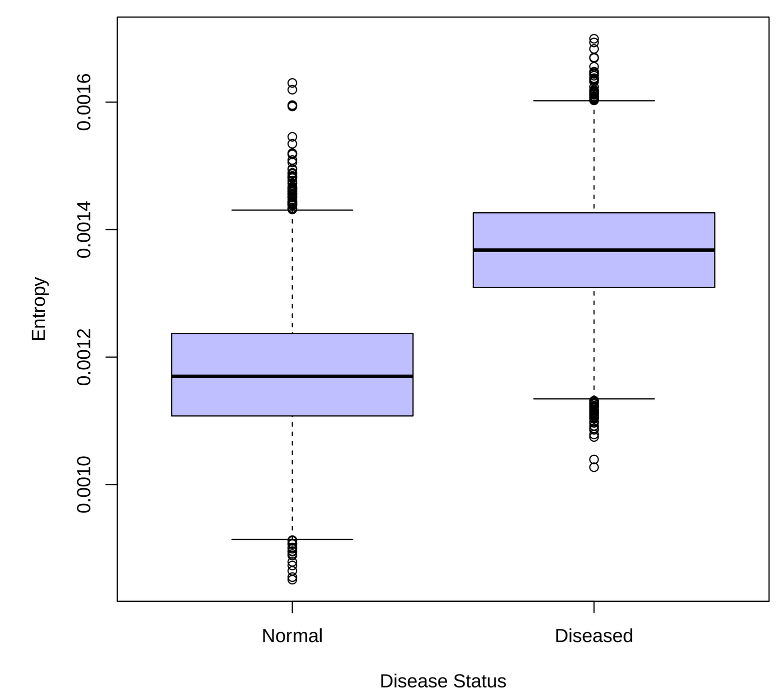


Figure 3: Entropy of Fitted Densities (2 Groups).

Discussion

- We estimate interpretable structural parameters.
- Patients with AD have less hierarchical DMNs.
- With more data, our method can improve disease detection.

References

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