NEUROANATOMY, NEUROLOGY AND BAYESIAN NETWORKS

Concha Bielza

Computational Intelligence Group
Artificial Intelligence Department
Technical University of Madrid, Spain

8th European Conference on Data Mining (DM2014)
8th International Conference on Intelligent Systems and Agents (ISA2014)
Lisbon, July 15, 2014
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
At the end of 2008, Universidad Politécnica de Madrid (UPM) and Instituto Cajal (IC) from the Spanish Research Council, until 2018

- **UPM**: data analysis, optimization, image analysis and visualization
- **IC**: morphology and function of neuronal cells
The BRAIN initiative

President Obama is calling on the science community to join him in pursuing a grand challenge.

BRAIN INITIATIVE

BRAIN RESEARCH THROUGH ADVANCING INNOVATIVE NEUROTECHNOLOGIES
The human brain

Brain lobes and layers

- **Weight**: 1.3kg, **width**: 140mm, **length**: 167mm, **height**: 93mm
The human brain

Brain at microscopic level

- Composed of neurons, blood vessels, glial cells
- Neuron is the basic structural and functional unit of the nervous system –neuron doctrine– (S. Ramón y Cajal, late 19th century)
- Just 4 microns thick → could fit 30,000 neurons on the head of a pin
- ~86,000 million neurons (more than known stars in the universe)
The neuron

3 parts of a neuron: dendrites, soma and axon

- Axons fill most of the space in the brain → >150,000 km in the human brain!!
- Each neuron connected to 1,000 neighboring neurons
- 10,000 synaptic connections each
Observing the neurons

**Optical (or light) microscope. Stain the tissue**

- Magnify image up to 2000 times
- Golgi’s method (1873)

**Modern electron microscope**

- Magnify image up to 2 million times
- 3D from multiple 2D images
“Visualizing” mental activities from brain images

Electrical activity directly or indirectly

Electroencephalography (EEG)

Positron Emission Tomography (PET)

Magnetic Res. Imaging (MRI)

Functional NIR Spectroscopy (fNIRS)

Single Photon Emission Computed Tomography (SPECT)

Functional MRI (fMRI)
Bayesian networks

- Graphical models used for knowledge representation and probabilistic reasoning under uncertainty.

A Bayesian network consists of **two components**

1. **Graphical structure** $\mathcal{G}$ is a directed acyclic graph (DAG)
   - **Vertices** $\rightarrow$ variables
   - **Directed edges** $\rightarrow$ conditional dependences

2. **Set of parameters** specifies the set of conditional probability distributions

Joint probability distribution: $P(x_1, \ldots, x_n) = \prod_{i=1}^{n} P(x_i \mid \text{pa}(x_i))$
Bayesian networks

<table>
<thead>
<tr>
<th>X₁</th>
<th>P(X₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.45</td>
</tr>
<tr>
<td>1</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Bayesian network learning

- Structure learning
- Parameter learning

Probabilistic inference

- Compute the conditional probability \( P(\text{Query} \mid \text{Evidence}) \)
Example of inference with network Asia

No evidence
Example of inference with network *Asia*

Test: “Smoker = yes”
Example of inference with network *Asia*

Evidence: “Asia = yes, Smoker = yes”
Example of inference with network *Asia*

Evidence: “Asia = yes, Smoker = yes, Dyspnea = yes”
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Classifying and naming neurons

Do we have an accepted catalog of neuron types and names?
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Classifying and naming neurons

An accepted catalog of neuron types and names, a debate for over a hundred years since S. Ramón y Cajal

Amount of data has grown rapidly; better staining methods ⇒ harder classification

Need of a consistent terminology for an effective communication and data sharing [Petilla Terminology, Ascoli et al. (2008)]

- Agreement: pyramidal neuron, non-pyramidal, interneuron, chandelier (clear morphological attributes)
- Disagreement: double bouquet, basket, Martinotti...
- Virtually every neuroanatomist has his own classification scheme and neuron terms
A ‘gardener’ classification of neurons

A ‘gardener’ approach (not a botanist), coarser and practical

Towards a consensus in naming GABAergic cortical interneurons

- 10-30% of the total neuron population and main component of inhibitory cortical circuits
- Located in all cortical layers and with a great variety of morphological, biochemical, and physiological characteristics

Goal: a community-based strategy for defining a morphological taxonomy, establishing a list of terms to be used by all researchers to distinguish neuronal morphologies

Collecting the data: 320 interneurons, 42 experts
Collecting the data: 320 interneurons, 42 experts
## Data

<table>
<thead>
<tr>
<th>Neuron</th>
<th>$E_1$</th>
<th>...</th>
<th>$E_{42}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>...</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>...</td>
<td>0</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td></td>
<td>...</td>
</tr>
<tr>
<td>320</td>
<td>0</td>
<td>...</td>
<td>0</td>
</tr>
</tbody>
</table>
## Data

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Feature 1</th>
<th>Feature 5</th>
<th>Feature 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E_1 \ldots E_{42})</td>
<td>(E_1 \ldots E_{42})</td>
<td>(E_1 \ldots E_{42})</td>
</tr>
<tr>
<td>2</td>
<td>1 \ldots 0</td>
<td>5 \ldots 8</td>
<td>0 \ldots 1</td>
</tr>
<tr>
<td>...</td>
<td>0 \ldots 0</td>
<td>5 \ldots 10</td>
<td>1 \ldots 1</td>
</tr>
<tr>
<td>320</td>
<td>0 \ldots 0</td>
<td>1 \ldots 4</td>
<td>1 \ldots 0</td>
</tr>
</tbody>
</table>
Inter-expert agreement
Inter-expert agreement

Martinotti (41)

Large basket (15), Common type (12), Common basket (12), Arcade (3)

C. Bielza
Neuroanatomy, Neurology and Bayesian Networks
Supervised classification of each feature

2,886 morphological predictors, 240 neurons

<table>
<thead>
<tr>
<th>Feature 1: Intralaminar vs. Translaminar</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>57.68</td>
<td>58.51</td>
<td>77.59</td>
<td>82.16*</td>
<td>72.2</td>
<td>73.44</td>
<td>82.57*</td>
<td>85.48*</td>
<td>82.16*</td>
<td>75.93</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>64.73</td>
<td>54.36</td>
<td>79.67</td>
<td>82.99*</td>
<td>69.71</td>
<td>75.93</td>
<td>83.82*</td>
<td>85.48*</td>
<td>84.23*</td>
<td>79.67</td>
</tr>
<tr>
<td>CfsSubset</td>
<td>75.93</td>
<td>75.1</td>
<td>81.33</td>
<td>84.23*</td>
<td>73.86</td>
<td>80.08</td>
<td>84.65*</td>
<td>80.08</td>
<td>82.16*</td>
<td>80.08</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature 2: Intracolumnar vs. Transcolumnar</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>59.75*</td>
<td>62.66*</td>
<td>52.28</td>
<td>75.52*</td>
<td>57.68*</td>
<td>65.56*</td>
<td>74.27*</td>
<td>68.46*</td>
<td>66.39*</td>
<td>58.09*</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>66.39*</td>
<td>63.07*</td>
<td>53.11</td>
<td>76.35*</td>
<td>64.32*</td>
<td>65.98*</td>
<td>75.52*</td>
<td>68.88*</td>
<td>70.12*</td>
<td>65.98*</td>
</tr>
<tr>
<td>CfsSubset</td>
<td>72.61*</td>
<td>65.56*</td>
<td>76.76*</td>
<td>81.33*</td>
<td>73.86*</td>
<td>73.03*</td>
<td>74.69*</td>
<td>70.54*</td>
<td>76.35*</td>
<td>69.29*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature 3: Centered vs. Displaced</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>62.24</td>
<td>53.94</td>
<td>54.77</td>
<td>68.88*</td>
<td>64.73*</td>
<td>68.05*</td>
<td>66.8*</td>
<td>67.63*</td>
<td>68.46*</td>
<td>62.24</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>64.73*</td>
<td>73.03*</td>
<td>65.98*</td>
<td>70.54*</td>
<td>65.56*</td>
<td>71.37*</td>
<td>70.54*</td>
<td>66.39*</td>
<td>72.2*</td>
<td>68.46*</td>
</tr>
<tr>
<td>CfsSubset</td>
<td>68.88*</td>
<td>73.86*</td>
<td>70.54*</td>
<td>73.03*</td>
<td>65.15*</td>
<td>68.05*</td>
<td>63.9*</td>
<td>71.78*</td>
<td>68.46*</td>
<td>65.15*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature 4: Ascending vs. Descending vs. Both</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>34.44</td>
<td>27.8</td>
<td>44.4*</td>
<td>49.38*</td>
<td>41.91</td>
<td>38.59</td>
<td>33.61 *</td>
<td>54.36*</td>
<td>40.25</td>
<td>37.76</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>43.57*</td>
<td>33.2</td>
<td>43.98*</td>
<td>49.79*</td>
<td>41.91</td>
<td>42.32</td>
<td>43.57*</td>
<td>46.89*</td>
<td>45.64*</td>
<td>42.74</td>
</tr>
<tr>
<td>CfsSubset</td>
<td>47.3*</td>
<td>51.87*</td>
<td>47.3*</td>
<td>58.51*</td>
<td>47.3*</td>
<td>52.28*</td>
<td>48.13*</td>
<td>42.32</td>
<td>60.17*</td>
<td>47.3*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature 5: Interneuron type (10 classes)</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>56.02</td>
<td>19.09</td>
<td>45.23*</td>
<td>58.51*</td>
<td>50.62*</td>
<td>53.94*</td>
<td>50.62*</td>
<td>47.72*</td>
<td>52.28*</td>
<td>40.25*</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>60.17*</td>
<td>26.14</td>
<td>58.92*</td>
<td>62.24*</td>
<td>49.79*</td>
<td>51.87*</td>
<td>48.55*</td>
<td>43.15*</td>
<td>58.09*</td>
<td>43.98*</td>
</tr>
<tr>
<td>CfsSubset</td>
<td>61*</td>
<td>43.57*</td>
<td>61.41*</td>
<td>60.58*</td>
<td>58.09*</td>
<td>56.85*</td>
<td>53.94*</td>
<td>49.38*</td>
<td>56.85*</td>
<td>51.45*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature 6: Characterized vs. Uncharacterized</th>
<th>NB</th>
<th>NBdisc</th>
<th>RBFN</th>
<th>SMO</th>
<th>IB1</th>
<th>IB3</th>
<th>J Rip</th>
<th>J48</th>
<th>RForest</th>
<th>RTree</th>
</tr>
</thead>
<tbody>
<tr>
<td>NoFSS</td>
<td>77.18</td>
<td>88.38</td>
<td>95.85</td>
<td>97.93*</td>
<td>97.51</td>
<td>97.51</td>
<td>97.93*</td>
<td>97.51</td>
<td>96.27</td>
<td>95.85</td>
</tr>
<tr>
<td>Gain Ratio</td>
<td>98.34*</td>
<td>73.86</td>
<td>97.51</td>
<td>96.68</td>
<td>97.1</td>
<td>97.51</td>
<td>97.93*</td>
<td>97.51</td>
<td>98.34*</td>
<td></td>
</tr>
<tr>
<td>CfsSubset</td>
<td>97.51</td>
<td>89.63</td>
<td>96.27</td>
<td>97.1</td>
<td>95.44</td>
<td>95.02</td>
<td>97.93*</td>
<td>96.27</td>
<td>97.51</td>
<td>99.17*</td>
</tr>
</tbody>
</table>
A Bayesian network learned for each expert
A Bayesian network learned for each expert
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Inducing a consensus Bayesian multinet from a set of expert opinions

Clustering of BNs encoding similar expert opinions

1. Compute the JPD encoded by each BN
2. Cluster the JPDs
3. Find a representative Bayesian network for each cluster
   3.1. Build a weighted sample from each JPD in the cluster
   3.2. Learn a BN from the samples of the JPDs in the cluster
RESULT: A representative Bayesian network for each cluster
Clustering of BNs encoding similar expert opinions

1. Compute the JPD encoded by each BN
2. Cluster the JPDs
3. Find a representative Bayesian network for each cluster
   3.1. Build a weighted sample from each JPD in the cluster
   3.2. Learn a BN from the samples of the JPDs in the cluster

RESULT: A representative Bayesian network for each cluster

Steps 1 and 2
- Dataset with 42 JPDs × 121 values
- K-means algorithm ($K = 6$)
- Jensen-Shannon divergence as dissimilarity measure for JPDs

$$d_{JS}(p_1, p_2) = 0.5 \left( KL(p_1 \| m) + KL(p_2 \| m) \right)$$

where $m = 0.5(p_1 + p_2)$
- Compute the cluster center $\bar{p}_k$ from a set $\{p_1, \ldots, p_{N_k}\}$ in cluster $k$ using
  
  LOGARITHMIC COMBINATION POOL:

  $$\bar{p}_{jLogOp} = \frac{\prod_{i=1}^{N_k} p_{ij}^{\omega_i}}{\sum_{v=1}^{121} \prod_{i=1}^{N_k} p_{iv}^{\omega_i}}$$

  with $\omega_i = 1/N_k$
Clustering of BNs encoding similar expert opinions

1. Compute the JPD encoded by each BN

2. Cluster the JPDs

3. Find a representative Bayesian network for each cluster
   3.1. Build a weighted sample from each JPD in the cluster
   3.2. Learn a BN from the samples of the JPDs in the cluster

RESULT: A representative Bayesian network for each cluster

Step 3
- For each cluster, sample from its JPDs. Draw $\mu_i \times M$ observations from each $p_i$ in cluster $k$, where

$$\mu_i = \frac{1 - d_{JS}(p_i, \bar{p}_k)}{\sum_{j=1}^{N_k} (1 - d_{JS}(p_j, \bar{p}_k))}$$

(degree of membership for $p_i$ to cluster $k$)
- Learn a (representative) BN from the sample of size $M$
Cluster labeling (with marginals)

<table>
<thead>
<tr>
<th>Cluster</th>
<th># experts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Cluster 3
Fine-grained classification scheme, trying to distinguish between the different neuronal types

Cluster 4
Coarse classification scheme. High P to Common type

Cluster 5
Detailed classification scheme, distinguishing between Common type, Common basket and Large basket. Found the nomenclature incomplete (high P to Other)
Cluster labeling (with marginals)

<table>
<thead>
<tr>
<th>Cluster</th>
<th># experts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Cluster 3

Fine-grained classification scheme, trying to distinguish between the different neuronal types
Cluster labeling (with marginals)

<table>
<thead>
<tr>
<th>Cluster</th>
<th># experts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Cluster 4

Coarse classification scheme. High P to *Common type*
Cluster labeling (with marginals)

<table>
<thead>
<tr>
<th>Cluster</th>
<th># experts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Cluster 5

Detailed classification scheme, distinguishing between *Common type*, *Common basket* and *Large basket*. Found the nomenclature incomplete (high P to *Other*)
Final consensus Bayesian multinet representing all the experts

Finite mixture of Bayesian networks: \( P(X = x) = \sum_{k=1}^{K} \pi_k P_k(X = x | C = k) \)
with \( \pi_k = \frac{N_k}{42} \), \( P_k \)=representative BN

CONSENSUS BAYESIAN MULTINET

CLUSTER

1 2 K

BN CLUSTER 1
X3 X1 X6
X5
X4 X2

BN CLUSTER 2
X3 X1
X4
X5 X2 X6

BN CLUSTER K
X1
X3 X5 X4
X2 X6

C. Bielza
Neuroanatomy, Neurology and Bayesian Networks
Final consensus Bayesian multinet representing all the experts

Finite mixture of Bayesian networks: \( P(\mathbf{X} = \mathbf{x}) = \sum_{k=1}^{K} \pi_k P_k(\mathbf{X} = \mathbf{x} | C = k) \)

with \( \pi_k = \frac{N_k}{42} \), \( P_k \) = representative BN

Set evidence in \( X_6 \) to infer agreed definitions for neuron types:

- **Martinotti**: Translaminar (≈ .93), Displaced (≈ .88), Ascending (≈ .64)
- **Common type**: Translaminar (≈ .71)

Etc.
Outline

1 Introduction

2 Neuroanatomy: neurons and dendritic trees
   - 'Gardener' classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3 Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4 Conclusions
Computer simulation of dendritic morphology

Why so different dendritic tree shapes?
Dendritic morphology

- Tree shapes → *interconnectivity* and *functional roles* of neurons
- Their *normal function, in neurological diseases*, under the effects of some *drugs*

Typically grouped based on prominent *geometrical features*. Difficult to find 2 neurons with the same morphology → but *branching patterns*

⇒ Anatomical characterization is *statistical* in nature
Our proposal: advantages

...with Bayesian networks

- (In)dependences between morphological properties automatically found from real data \((vs. \text{ prior conditional relationships ad hoc})\)
- Model the joint probability distribution of all variables \((vs. \leq \text{ trivariate and standard distributions})\)
- Reliable evaluation: statistical tests to compare original vs. simulated distributions, both uni and multivariate \((vs. \text{ on new 1D pars and visual inspection})\)

Data: pyramidal neurons

- 3D reconstructions of 90 pyramidal neurons from the mouse neocortex, traced with *Neurolucida* package
- Layer III of different cortical regions: M2, S2, V2L/TeA ⇒ 3 databases
- Each basal arbor with 6 (average) main trunks—dendritic trees—, each made up of several dendrites

<table>
<thead>
<tr>
<th>Cortex region</th>
<th>Database</th>
<th># dendr. trees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td>M2</td>
<td>104</td>
</tr>
<tr>
<td>Somatosensory</td>
<td>S2</td>
<td>103</td>
</tr>
<tr>
<td>Lateral visual and association temporal</td>
<td>V2L/TeA</td>
<td>156</td>
</tr>
</tbody>
</table>

Publicly available at [http://neuromorpho.org](http://neuromorpho.org) as part of DeFelipe’s archive (same lab)
Morphological parameters

- For each pair of sibling segments (line between two branch points), measure 41 variables.
- Widely used and also new, to capture context influence and neuritic competition.
- **Evidence** variables: measure the part of the tree **previous to a pair of sibling segments** (subtree and subdendrite involved). Measured during the simulation, used as information to sample construction variables.
- **Construction** variables: define the morphology of a segment (segment length, orientation, bifurcation). Sample from them to incrementally construct trees.
### List of variables

<table>
<thead>
<tr>
<th>No.</th>
<th>Type</th>
<th>Variable</th>
<th>No.</th>
<th>Type</th>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E</td>
<td>subtree degree (no. endings)</td>
<td>22</td>
<td>E</td>
<td>neighbor distance</td>
</tr>
<tr>
<td>2</td>
<td>E</td>
<td>subtree no. bifurcations (no. nodes)</td>
<td>23</td>
<td>E</td>
<td>neighbor inclination</td>
</tr>
<tr>
<td>3</td>
<td>E</td>
<td>subtree total length</td>
<td>24</td>
<td>E</td>
<td>neighbor azimuth</td>
</tr>
<tr>
<td>4</td>
<td>E</td>
<td>subtree width</td>
<td>25</td>
<td>E</td>
<td>neighbor extension</td>
</tr>
<tr>
<td>5</td>
<td>E</td>
<td>subtree height</td>
<td>26</td>
<td>E</td>
<td>neighbor angle</td>
</tr>
<tr>
<td>6</td>
<td>E</td>
<td>subtree depth</td>
<td>27</td>
<td>E</td>
<td>parent segment length</td>
</tr>
<tr>
<td>7</td>
<td>E</td>
<td>subtree box volume</td>
<td>28</td>
<td>E</td>
<td>parent segment inclination</td>
</tr>
<tr>
<td>8</td>
<td>E</td>
<td>subtree max distance between nodes</td>
<td>29</td>
<td>E</td>
<td>parent segment azimuth</td>
</tr>
<tr>
<td>9</td>
<td>E</td>
<td>subtree max distance to soma</td>
<td>30</td>
<td>E</td>
<td>root segment length</td>
</tr>
<tr>
<td>10</td>
<td>E</td>
<td>subtree max length</td>
<td>31</td>
<td>E</td>
<td>root segment inclination</td>
</tr>
<tr>
<td>11</td>
<td>E</td>
<td>subtree min length</td>
<td>32</td>
<td>E</td>
<td>root segment azimuth</td>
</tr>
<tr>
<td>12</td>
<td>E</td>
<td>subtree max order</td>
<td>33</td>
<td>E</td>
<td>segment centrifugal order</td>
</tr>
<tr>
<td>13</td>
<td>E</td>
<td>subtree min order</td>
<td>34</td>
<td>C</td>
<td>left segment length</td>
</tr>
<tr>
<td>14</td>
<td>E</td>
<td>subdendrite length</td>
<td>35</td>
<td>C</td>
<td>left segment inclination</td>
</tr>
<tr>
<td>15</td>
<td>E</td>
<td>subdendrite width</td>
<td>36</td>
<td>C</td>
<td>left segment azimuth</td>
</tr>
<tr>
<td>16</td>
<td>E</td>
<td>subdendrite height</td>
<td>37</td>
<td>C</td>
<td>left segment bifurcates</td>
</tr>
<tr>
<td>17</td>
<td>E</td>
<td>subdendrite depth</td>
<td>38</td>
<td>C</td>
<td>right segment length</td>
</tr>
<tr>
<td>18</td>
<td>E</td>
<td>subdendrite box volume</td>
<td>39</td>
<td>C</td>
<td>right segment inclination</td>
</tr>
<tr>
<td>19</td>
<td>E</td>
<td>subdendrite distance to soma</td>
<td>40</td>
<td>C</td>
<td>right segment azimuth</td>
</tr>
<tr>
<td>20</td>
<td>E</td>
<td>subdendrite inclination</td>
<td>41</td>
<td>C</td>
<td>right segment bifurcates</td>
</tr>
<tr>
<td>21</td>
<td>E</td>
<td>subdendrite azimuth</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Variables **discretized** (2-3 values) trying to preserve empirical distributions
Overview of the learning

- Learn and use a BN for **each part** of the dendritic tree, to allow specific relationships at each part

\[
P(X_1, \ldots, X_{41}) = \prod_{i=1}^{n=41} P(X_i|\Pi_i) \quad \Pi_i = \text{parents of } X_i \text{ in the graph}
\]

- Learn the **structure** via BIC score and K2 heuristic search
  - MWST algorithm for having an **ordering** between nodes (weight=BIC)
  - Force evidence variables **before** construction variables
  - Fix an upper bound on the **max number of parents** for any node (=3)

- Learn the **parameters** (probabilities) via MLE

\[
P(X_i = x_i|\Pi_i = \pi_i) = \frac{\text{freq}(X_i = x_i, \Pi_i = \pi_i)}{\text{freq}(\Pi_i = \pi_i)}
\]
Bayesian networks learned

For M2 database

- A, B, C, D → root segments, order 1, order 2, > 2 order, resp. Shaded = construction variables

- Found relationships conform to biological knowledge, e.g.
  - Segment length (34, 38) and bifurcation (37, 41) occurrence → more bifurcations close to the soma and shorter segments, whereas segments that do not branch spread away from the soma
Bayesian networks learned

For M2 database

- A, B, C, D → root segments, order 1, order 2, > 2 order, resp. Shaded = construction variables

- Found relationships conform to biological knowledge, e.g.
  - Subdendrite width (15) and segment bifurcation (37) [wider → doesn't bifurcate] → constrain tree size.
  - Smaller inclination angles (35) for taller subdendrites (16), etc.

C. Bielza
Simulation of virtual dendritic trees

Procedure (breadth-first way)

1. Generate a root segment
2. Measure evidence variables from the dendritic tree built so far
3. Sample construction variable values from the Bayesian network
4. If a segment bifurcates, consider that the dendrite is still incomplete and go to 2. Else, the dendrite has ended
Model validation

Compare real/simulated prob. distributions

- Simulate the same number of dendritic trees than in the original database
- Univariate statistical tests (compare marginal distributions): KS, Wilcoxon rank-sum, KL (with bioDist R package to estimate KL for continuous variables, and bootstrap to estimate percentile 95)
- Repeat 100 times to consider statistical variability and perform a sign test for each test to check if the number of rejections was significant in the 100 repetitions

Some rejections in evidence variables in higher orders (high variability)
No rejections for construction vars
Model validation

Compare real/simulated prob. distributions

- **Multivariate** statistical test (compare the joint distribution), used for the first time in this context
- ...Use **multivariate KL estimator** based on k-NN density estimation [Wang et al., 2006]

\[
\hat{KL}(p||q) = \frac{n}{N_p} \sum_{i=1}^{N_p} \log \frac{\nu_{D_q}(i)}{\rho_{D_p}(i)} + \log \frac{N_q}{N_p - 1}
\]

Datasets $D_p, D_q$ with $n$-dim samples of sizes $N_p, N_q$.

$\rho_{D_p}(i)$=distance from $x_i \in D_p$ to its NN in $D_p$, $\nu_{D_q}(i)$=distance to its NN in $D_q$

 Worse for higher orders (high variability) –perhaps due to the previous variables
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

Prevalence of dementia cases in the UK

- Male: 2.17%
- Female: 1.10%

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
# Dementia: Prevalence, cost and investment in research

<table>
<thead>
<tr>
<th>Dementia cases in the UK</th>
<th>Diagnosed/undiagnosed dementia cases in the UK</th>
<th>Economic costs of dementia</th>
<th>How the cost of dementia is met</th>
<th>Cost of one dementia patient</th>
<th>Investment in research</th>
</tr>
</thead>
</table>

## Prevalence of dementia cases in the UK

<table>
<thead>
<tr>
<th>Age</th>
<th>30-59</th>
<th>60-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75-79</th>
<th>80-84</th>
<th>85-89</th>
<th>90-94</th>
<th>95-99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.04%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.67%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

Prevalence of dementia cases in the UK

- Male: 12.12%
- Female: 13.50%

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

Prevalence of dementia cases in the UK

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Dementia: Prevalence, cost and investment in research

<table>
<thead>
<tr>
<th>Dementia cases in the UK</th>
<th>Diagnosed/undiagnosed dementia cases in the UK</th>
<th>Economic costs of dementia</th>
<th>How the cost of dementia is met</th>
<th>Cost of one dementia patient</th>
<th>Investment in research</th>
</tr>
</thead>
</table>

**Annual cost (£) of one dementia patient**

![Bar chart showing the annual cost of one dementia patient compared to other conditions](http://www.alzheimersresearchuk.org/dementia-statistics/)
Dementia: Prevalence, cost and investment in research

http://www.alzheimersresearchuk.org/dementia-statistics/
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Knowledge discovery in Alzheimer’s disease

Can we discover knowledge in AD from microarray data with a few brains?
Alzheimer’s disease

- Primarily affects the elderly and manifests through memory disorders, cognitive decline and loss of autonomy

In 2014, 44 million cases worldwide (7.2 in Europe). By 2050, rates could exceed 135 million

Every 4 seconds, a new case of dementia occurs somewhere

Sixth-leading cause of death in USA

Alois Alzheimer (1864-1915)
Knowledge discovery in Alzheimer’s disease

Alzheimer’s disease and DNA microarrays

- Idea in [Small et al., 2005]: microarray data **selectively** from the brain site most **vulnerable** to AD to maximize expression differences between AD and controls: **entorhinal cortex (EC)**

- **6 AD brains + 6 control brains** ⇒ **12 tissue samples and 7,610 variables**

Knowledge discovery in Alzheimer’s disease

⇒ Re-analyze the data differently to gain robustness (small sample size!)
⇒ Find out explicit new (or validate old) biological relationships and genes not previously reported

Reliable-$k$DB classifier with robust gene interactions

- Learn a Bayesian network classifier. We use $k$DB structures with at most $k$ parents (excluding the class)

- Induce many $k$DB by a resampling method (bootstrap) with an inner FSS
- Output a network with those arcs above a reliability threshold $t$: arcs occurring $\geq t$ times are retained
- Approach is a consensus feature selection on the final gene interaction network

Reliable-\(k\)DB classifier – An example

\[ G_t \]
Reliable-$k$DB classifier – An example

$G_t$
Reliable-$k$DB classifier – An example

$G_t$
Reliable-\(k\)DB classifier – An example

\(G_t\)
Reliable-$k$DB classifier – An example

$G_t$
Reliable-$k$DB classifier – An example

$G_t$
Reliable-$k$DB classifier – An example

$G_t$

$X_9$ \(\xrightarrow{431} X_5\)
$X_10$ \(\xrightarrow{467} X_5\)
$X_11$ \(\xrightarrow{515} X_5\)
$X_8$ \(\xrightarrow{455} X_5\)
$X_1$ \(\xrightarrow{520} X_5\)
$X_2$ \(\xrightarrow{490} X_5\)
$X_5$ \(\xrightarrow{790} X_1\)
$X_3$ \(\xrightarrow{760} X_5\)
$X_4$ \(\xrightarrow{556} X_5\)
$X_6$ \(\xrightarrow{650} X_5\)
$X_7$ \(\xrightarrow{400} X_5\)
$X_{13}$ \(\xrightarrow{400} X_5\)

$t$
800
798
790
: 
700
600
500
400 <
: 
100
: 
1

C. Bielza

Neuroanatomy, Neurology and Bayesian Networks
Reliable-$k$DB classifier – An example

$G_t$

C. Bielza

Neuroanatomy, Neurology and Bayesian Networks
Reliable-$k$-DB classifier – An example
Knowledge discovery in Alzheimer’s disease

AD vs. Controls (12 samples) with $k = 4$, $B = 10000$, $t = 1000$

Muscular atrophies
X-linked mental retardation
Huntington
Bipolar disorder

Parkinson

C. Bielza
Neuroanatomy, Neurology and Bayesian Networks
Outline

1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Is it possible to map from PD patient’s perception PDQ-39 to the general health scale EQ-5D?
PDQ-39 and EQ-5D: quality of life instruments to measure the degree of disability in PD

39-item Parkinson’s Disease Questionnaire: a specific instrument

PDQ-39 captures patient’s perception of his illness covering 8 dimensions:

1. Mobility
2. Activities of daily living
3. Emotional well-being
4. Stigma
5. Social support
6. Cognitions
7. Communication
8. Bodily discomfort

PDQ-39 QUESTIONNAIRE

Please complete the following

Please tick one box for each question

Due to having Parkinson’s disease, how often during the last month have you...

1. Had difficulty doing the leisure activities which you would like to do?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all

2. Had difficulty looking after your home, e.g. DIY, homework, cooking?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all

3. Had difficulty carrying bags of shopping?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all

4. Had problems walking half a mile?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all

5. Had problems walking 100 yards?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all

6. Had problems getting around the house as easily as you would like?
   - Never
   - Occasionally
   - Sometimes
   - Often
   - Always or cannot do at all
European Quality of Life - 5 Dimensions: a generic instrument

EQ-5D is a generic measure of health for clinical and economic appraisal

- **Mobility**
  - I have no problems in walking about
  - I have some problems in walking about
  - I am confined to bed

- **Self-care**
  - I have no problems with self-care
  - I have some problems washing and dressing myself
  - I am unable to wash and dress myself

- **Usual activities** (eg. work, study, housework, family or leisure activities)
  - I have no problems with performing my usual activities
  - I have some problems with performing my usual activities
  - I am unable to perform my usual activities

- **Pain/discomfort**
  - I have no pain or discomfort
  - I have moderate pain or discomfort
  - I have extreme pain or discomfort

- **Anxiety/depression**
  - I am not anxious or depressed
  - I am moderately anxious or depressed
  - I am extremely anxious or depressed
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Mapping PDQ-39 to EQ-5D

\[
h : (PDQ_1, \ldots, PDQ_{39}) \rightarrow (EQ_1, \ldots, EQ_5)
\]

Borchani, Bielza, Martínez-Martín, Larrañaga (2012). Multidimensional Bayesian network classifiers applied to predict the European quality of life-5 dimensions (EQ-5D) from the 39-item Parkinson’s disease questionnaire (PDQ-39), Journal of Biomedical Informatics, 45, 1175-1184
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Multi-dimensional Bayesian network classifier (MBC)

- The set of variables $\mathcal{V}$ is partitioned into:
  - $\mathcal{V}_c = \{C_1, \ldots, C_d\}$ of class variables and
  - $\mathcal{V}_x = \{X_1, \ldots, X_m\}$ of feature variables

Most probable explanation (MPE)

$$(c_1^*, \ldots, c_d^*) = \max_{c_1, \ldots, c_d} p(C_1 = c_1, \ldots, C_d = c_d | X_1 = x_1, \ldots, X_m = x_m)$$

Four MBC learning algorithms

1. **Markov blanket – Multi-dimensional Bayesian classifier**
   \((\text{MB-MBC})\) [Borchani et al., 2011]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. **Markov blanket - Multi-dimensional Bayesian classifier (MB-MBC)** [Borchani et al., 2011]

C. Bielza
Neuroanatomy, Neurology and Bayesian Networks
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. Markov blanket - Multi-dimensional Bayesian classifier (MB-MBC) [Borchani et al., 2011]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. **Markov blanket - Multi-dimensional Bayesian classifier** (MB-MBC) [Borchani et al., 2011]

2. **Class-Bridge - Multi-dimensional Bayesian classifier** (CB-MBC) [Borchani et al., 2010]
Four MBC learning algorithms

1. **Markov blanket – Multi-dimensional Bayesian classifier** (MB-MBC) [Borchani et al., 2011]

2. **Class-Bridge – Multi-dimensional Bayesian classifier** (CB-MBC) [Borchani et al., 2010]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. **Markov blanket – Multi-dimensional Bayesian classifier** (MB-MBC) [Borchani et al., 2011]

2. **Class-Bridge – Multi-dimensional Bayesian classifier** (CB-MBC) [Borchani et al., 2010]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. Markov blanket – Multi-dimensional Bayesian classifier (MB-MBC) [Borchani et al., 2011]

2. Class-Bridge – Multi-dimensional Bayesian classifier (CB-MBC) [Borchani et al., 2010]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. **Markov blanket – Multi-dimensional Bayesian classifier (MB-MBC)** [Borchani et al., 2011]

2. **Class-Bridge – Multi-dimensional Bayesian classifier (CB-MBC)** [Borchani et al., 2010]

---

C. Bielza
Neuroanatomy, Neurology and Bayesian Networks
Four MBC learning algorithms

1. **Markov blanket - Multi-dimensional Bayesian classifier** (MB-MBC) [Borchani et al., 2011]

2. **Class-Bridge - Multi-dimensional Bayesian classifier** (CB-MBC) [Borchani et al., 2010]

3. **Independent Markov blanket classifiers with HITON algorithm** (Indep-MB-HITON) [Aliferis et al., 2010]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. Markov blanket – Multi-dimensional Bayesian classifier (MB-MBC) [Borchani et al., 2011]

2. Class-Bridge – Multi-dimensional Bayesian classifier (CB-MBC) [Borchani et al., 2010]

3. Independent Markov blanket classifiers with HITON algorithm (Indep-MB-HITON) [Aliferis et al., 2010]

4. Independent Markov blanket classifiers with PC algorithm (Indep-MB-PC) [Le and Doctor, 2011]
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

Four MBC learning algorithms

1. **Markov blanket – Multi-dimensional Bayesian classifier (MB-MBC)** [Borchani et al., 2011]

2. **Class-Bridge – Multi-dimensional Bayesian classifier (CB-MBC)** [Borchani et al., 2010]

3. **Independent Markov blanket classifiers with HITON algorithm (Indep-MB-HITON)** [Aliferis et al., 2010]

4. **Independent Markov blanket classifiers with PC algorithm (Indep-MB-PC)** [Le and Doctor, 2011]

Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson

488 Parkinson’s patients. Estimated measures over 5-fold cross-validation

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean accuracy</th>
<th>Global accuracy</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB-MBC</td>
<td>0.7119 ± 0.0338</td>
<td>0.2030 ± 0.0718</td>
<td>0.0650 ± 0.0156</td>
</tr>
<tr>
<td>CB-MBC</td>
<td>0.6807 ± 0.0285</td>
<td>0.1865 ± 0.0429</td>
<td>0.0905 ± 0.0167</td>
</tr>
<tr>
<td>Indep-MB-HITON</td>
<td>0.7009 ± 0.0427</td>
<td>0.2051 ± 0.0835</td>
<td>0.0699 ± 0.0188</td>
</tr>
<tr>
<td>Indep-MB-PC</td>
<td>0.6587 ± 0.0636</td>
<td>0.1867 ± 0.0937</td>
<td>0.0909 ± 0.0909</td>
</tr>
<tr>
<td>MNL</td>
<td>0.6926 ± 0.0430</td>
<td>0.1802 ± 0.0713</td>
<td>0.0759 ± 0.0152</td>
</tr>
<tr>
<td>OLS</td>
<td>0.4201 ± 0.0252</td>
<td>0.0123 ± 0.0046</td>
<td>0.1832 ± 0.0373</td>
</tr>
<tr>
<td>CLAD</td>
<td>0.4254 ± 0.0488</td>
<td>0.0143 ± 0.0171</td>
<td>0.1962 ± 0.0360</td>
</tr>
</tbody>
</table>

\(d = 5, N = 488\)

- **Mean accuracy** over the \(d\) class variables: 
  \[
  Acc_m = \frac{1}{d} \sum_{i=1}^{d} \frac{1}{N} \sum_{l=1}^{N} \delta(\hat{c}_{li}, c_{li})
  \]

- **Global accuracy** over the \(d\)-dimensional class variable: 
  \[
  Acc_g = \frac{1}{N} \sum_{l=1}^{N} \delta(\hat{c}_l, c_l)
  \]

- **MSE** between the true and predicted EQ-5D utility scores
Multi-dimensional classification for EQ-5D health states from PDQ-39 in Parkinson
1. Introduction

2. Neuroanatomy: neurons and dendritic trees
   - ‘Gardener’ classification of neurons
   - Bayesian networks to model consensus among experts
   - Computer simulation of dendritic morphology

3. Neurology: Parkinson and Alzheimer
   - Dementia: Prevalence, cost and investment in research
   - Knowledge discovery in Alzheimer’s disease
   - Multi-dimensional classification for EQ-5D from PDQ-39 in Parkinson’s disease

4. Conclusions
Neuroscience and Bayesian networks

Challenging machine learning problems in modeling the brain

- **Joint Probability Distribution**: Bayesian networks (classifying neuron types, dendritic morphology)
- **Consensus of Probabilistic Models**: Bayesian networks and multinets (a neuroscientist $\equiv$ a model)
- **Bootstrap for Reliable Models**: $k$-DB Bayesian classifiers (knowledge discovery in Alzheimer’s disease)
- **Multi-dimensional Classification**: multi-dimensional Bayesian classifiers (from PDQ-39 to EQ-5D in Parkinson’s disease)
Ongoing work

Bayesian classifiers for probabilistic class labels

Feature 1

Neuron
1
2
...
320

Feature 5

Feature 6

\[
\begin{array}{cccc}
E_1 & \cdots & E_{42} \\
1 & \cdots & 0 \\
0 & \cdots & 0 \\
\vdots & \ddots & \vdots \\
0 & \cdots & 0 \\
\end{array}
\]

\[
\begin{array}{cccc}
E_1 & \cdots & E_{42} \\
5 & \cdots & 8 \\
5 & \cdots & 10 \\
\vdots & \ddots & \vdots \\
1 & \cdots & 4 \\
1 & \cdots & 0 \\
\end{array}
\]

\[
\begin{array}{cccc}
E_1 & \cdots & E_{42} \\
0 & \cdots & 1 \\
1 & \cdots & 1 \\
\vdots & \ddots & \vdots \\
1 & \cdots & 0 \\
\end{array}
\]
Bayesian classifiers for probabilistic class labels
Ongoing work

Feature 1

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Feature 1</th>
<th>Feature 5</th>
<th>Feature 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E₁ ... E₄₂</td>
<td>E₁ ... E₄₂</td>
<td>E₁ ... E₄₂</td>
</tr>
<tr>
<td>2</td>
<td>1 ... 0</td>
<td>5 ... 8</td>
<td>0 ... 1</td>
</tr>
<tr>
<td>...</td>
<td>0 ... 0</td>
<td>5 ... 10</td>
<td>1 ... 1</td>
</tr>
<tr>
<td>320</td>
<td>0 ... 0</td>
<td>1 ... 4</td>
<td>1 ... 0</td>
</tr>
</tbody>
</table>
**Ongoing work**

### Semi-supervised classification/clustering

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Feature 1</th>
<th>Feature 5</th>
<th>Feature 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E_1 \ldots E_{42})</td>
<td>(E_1 \ldots E_{42})</td>
<td>(E_1 \ldots E_{42})</td>
</tr>
<tr>
<td>2</td>
<td>1 \ldots 0</td>
<td>5 \ldots 8</td>
<td>0 \ldots 1</td>
</tr>
<tr>
<td>...</td>
<td>0 \ldots 0</td>
<td>5 \ldots 10</td>
<td>1 \ldots 1</td>
</tr>
<tr>
<td>320</td>
<td></td>
<td>1 \ldots 4</td>
<td>1 \ldots 0</td>
</tr>
</tbody>
</table>

- 128 Axon, 86 Dendrite, 10 Soma
- \(\geq 26\) votes

<table>
<thead>
<tr>
<th>Neuron</th>
<th>(X_1)</th>
<th>(X_2)</th>
<th>(\ldots)</th>
<th>(X_{224})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.4</td>
<td>7.1</td>
<td>(2.1)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>5.4</td>
<td>(4.0)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>7.3</td>
<td>2.0</td>
<td>(1.1)</td>
<td></td>
</tr>
<tr>
<td>...</td>
<td>(\ldots)</td>
<td>(\ldots)</td>
<td>(\ldots)</td>
<td></td>
</tr>
<tr>
<td>240</td>
<td>3.7</td>
<td>2.8</td>
<td>(5.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martinotti (27)</td>
</tr>
<tr>
<td>?</td>
</tr>
<tr>
<td>?</td>
</tr>
<tr>
<td>...</td>
</tr>
<tr>
<td>Basket (32)</td>
</tr>
</tbody>
</table>

---

C. Bielza

Neuroanatomy, Neurology and Bayesian Networks
Ongoing work

Multi-dimensional classification (data streams?)
Ongoing work

Bayesian networks with angular variables: association, classification
Ongoing work

“Dynamic” Bayesian networks with continuous and angular variables: clustering
Ongoing work

Hierarchical integration

M1A-Bas: Angles
- conditional von Mises
- multivariate sine von Mises
- von Mises graphical model
- von Mises Bayesian network
- von Mises-Fisher Bayesian network

M1B-Bas: Dendritic tree
- MoPs/MoTBPs based Bayesian network with feasible learning and inference
- universal Bayesian network

M2-Bas: Basal arbor
- hierarchy of universal Bayesian networks

M2-Api: Apical arbor
- structural EM algorithm in universal Bayesian network

M3: Spines
- spatial point process:
  - BN-Gibbs with replicated patterns
  - spatial Bayesian network
  - MoPs/MoTBPs Bayesian network for probabilistic clustering and discovering associations

M4: Soma
- MoPs/MoTBPs Bayesian network for probabilistic clustering and discovering associations
- multi-objective optimization with EDAs
- multireponse Bayesian network regressors

M5: Pyramidal cell integration
- hierarchy of universal Bayesian networks
- most/least probable explanation in universal Bayesian networks
- optimal dendritic wiring design
- software tool
Ongoing work

Multi-output regression
Many thanks to colleagues

Technical University of Madrid
Armañanzas, Borchani, Larrañaga, López-Cruz

The Cajal Institute
Benavides-Piccione, DeFelipe
NEUROANATOMY, NEUROLOGY AND BAYESIAN NETWORKS

Concha Bielza

Computational Intelligence Group
Artificial Intelligence Department
Technical University of Madrid, Spain

8th European Conference on Data Mining (DM2014)
8th International Conference on Intelligent Systems and Agents (ISA2014)
Lisbon, July 15, 2014