Development and Evaluation of AI-based Parkinson’s Disease Related Motor Symptom Detection Algorithms

Ahlrichs, Claas

Department of Computer Science
University of Bremen

July 6, 2015
Motivation

Introduction

Parkinson’s Disease (PD) is generally attributed to elderly people
- slowness, loss of (motor) function, etc.
- large number of motor and non motor symptoms
- reduced quality of life
- burden for in-/directly affected

1.2M \[^{15}\] - 2.0M \[^{18}\] PD patients within Europe
Motor Symptoms

Introduction

- **cardinal symptoms**
  - tremor at rest
  - rigidity
  - akinesia
  - postural instability

- **drug-induced symptoms**
  - dyskinesia
  - multitude of non motor symptoms
Motor States

Introduction

- **ON-state**
  - patient is on medication
  - motor symptoms are almost invisible
  - patients feel fairly fluid

- **OFF-state**
  - patient is off medication
  - patients experience symptoms such as tremor, freezing of gait, bradykinesia, etc.
- detailed records on symptoms and motor states are a necessity
- automatic monitoring of symptoms can replace subjective patient diaries with objective measurements and aid on motor state detection
Objectives

Introduction

1. (primary) development and improvement of algorithms for detecting PD related motor symptoms and
2. (secondary) to develop a framework for time series analysis
Part I: Framework
Frameworks for Time Series Analysis
Related Work

- Waikato Environment for Knowledge Analysis (WEKA): a machine learning (ML) / data mining (DM) workbench \[^{[27, 10, 16]}\]
- massive online analysis (MOA): a framework for clustering and classification of evolving data streams \[^{[8]}\]
- Unstructured Information Management Architecture (UIMA): aiding in the transformation of unstructured information to structured information \[^{[26]}\]
- streams: stream-based data processing \[^{[9]}\]
### Frameworks for Time Series Analysis

#### Related Work

<table>
<thead>
<tr>
<th>Feature</th>
<th>WEKA</th>
<th>MOA</th>
<th>UIMA</th>
<th>Streams</th>
</tr>
</thead>
<tbody>
<tr>
<td>stream-based</td>
<td>X</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>iterative</td>
<td>(X)</td>
<td>✓</td>
<td>(✓)</td>
<td>✓</td>
</tr>
<tr>
<td>scalability</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>flexibility</td>
<td>(✓)</td>
<td>X</td>
<td>(✓)</td>
<td>(✓)</td>
</tr>
<tr>
<td>reusability</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>extensibility</td>
<td>(✓)</td>
<td>(✓)</td>
<td>(✓)</td>
<td>(✓)</td>
</tr>
<tr>
<td>support for distribution</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

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requirements are broken down into manageable pieces

architecture developed by means of UML class diagrams

data processing environment

built around principles of modularity, reusability and extensibility
Extensibility and Applications
A Framework for Time Series Analysis

- extensibility
  - adding modules and links
  - wrapping and decorating modules
  - data sources and sinks
  - functions across the entire graph
  - alternative traversal methods

- applications and scenarios
  - recognizing PD motor symptoms
  - generating trading decisions
  - analysis of network traffic
  - quality control of OpenStreetMap-data
Part II: Algorithms
Machine Learning
Background on Parkinson’s Disease and Temporal Data Mining

- have a computer recognize (motor) symptoms when they appear
- typical classification task
- requires data and (human) annotations
- training vs. testing (generalization, abstraction)
- common classification algorithms
  - support vector machines (SVMs)
  - neural networks (NNs)
  - ...
Literature Review
Related Work

- literature review
  - characteristics PD
  - symptoms and side effects
- findings
  - limited size of data sets
  - only single symptom
  - various sensors
  - results vary
# Tremor at Rest

## Related Work

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Sensor(s)</th>
<th>Result(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salarian et al.[23]</td>
<td>G</td>
<td>Sen.: 76.6% Spe.: 98.0%</td>
</tr>
<tr>
<td>Salarian et al.[24]</td>
<td>G</td>
<td>Sen.: 99.5% Spe.: 94.2%</td>
</tr>
<tr>
<td>Zwartjes et al.[28]</td>
<td>4xA,4xG</td>
<td>Acc.: 84.7%</td>
</tr>
<tr>
<td>Rigas et al.[21]</td>
<td>6xA</td>
<td>Acc.: 87.0%</td>
</tr>
<tr>
<td>Cole et al.[12]</td>
<td>A, E</td>
<td>Sen.: 93.0% Spe.: 95.0%</td>
</tr>
<tr>
<td>Roy et al.[22]</td>
<td>4xA, 4xE</td>
<td>Sen.: 91.2% Spe.: 93.4%</td>
</tr>
<tr>
<td>Niazmand et al.[19]</td>
<td>8xA</td>
<td>Sen.: 80.0% Spe.: 98.5%</td>
</tr>
</tbody>
</table>

A: acceleration, G: gyroscope, E: electromyograph (EMG)
recordings from 92 participants
36 females and 56 males
clinical diagnosis of PD
mean age: 68 years (±7.9 years)
  married or live with a partner: 74 participants
  single: 5 participants
  widowed: 8 participants
  separated / divorced: 5 participants
Data Acquisition: Sensors

- **wrist sensor:**
  - to detect tremor
  - capture data at 80 Hz
  - send data to the waist platform

- **waist sensor:**
  - to detect other gait related symptoms, like dyskinesia and bradykinesia
  - includes a microprocessor, data storage, ...
  - capture data at 200 Hz
Data Acquisition: Protocols

Database: Patients and Their Symptoms

- screening / base-lining
  - before any data acquisition
  - verify inclusion and exclusion criteria
- data acquisition
  - various scripted and unconstrained activities
  - two recording sessions: ON and OFF state
  - sessions were partly videotaped and directly annotated with tablet computer

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## Tremor at Rest (Wrist)

Database: Patients and Their Symptoms

<table>
<thead>
<tr>
<th>Label</th>
<th>ON-State</th>
<th>OFF-State</th>
<th>Intermediate</th>
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</thead>
<tbody>
<tr>
<td>Undefined</td>
<td>633.02</td>
<td>490.59</td>
<td>109.33</td>
</tr>
<tr>
<td>Without tremor</td>
<td>763.79</td>
<td>633.25</td>
<td>109.47</td>
</tr>
<tr>
<td><strong>Right hand/arm tremor</strong></td>
<td>45.11</td>
<td>105.85</td>
<td>0.00</td>
</tr>
<tr>
<td>Right foot/leg tremor</td>
<td>5.13</td>
<td>15.58</td>
<td>0.00</td>
</tr>
<tr>
<td>Trunk tremor</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Left hand/arm tremor</strong></td>
<td>43.56</td>
<td>77.00</td>
<td>9.65</td>
</tr>
<tr>
<td>Left foot/leg tremor</td>
<td>0.18</td>
<td>12.53</td>
<td>0.00</td>
</tr>
</tbody>
</table>
**Idea**

**Indication of Tremor at Rest**

- iterative approach, start simple
- tremor at rest is largely determined by a rhythmical shaking
- first approach: directly classify windows with a SVM
- two SVM kernels are evaluated: linear and radial basis function (RBF)
- two feature sets: reduced and full
Ideas for Further Iterations

Indication of Tremor at Rest

- minimization of resources for detecting tremor
  - time windows must be short (i.e. few seconds)
  - false positives (FPs) and false negatives (FNs)
- perform meta analysis
  - remove isolated segments
  - aggregate classification results
  - determine confidence value
refined methodology
- resampled to 40 Hz
- reduce data but retain characteristics of human movement
- divided into equally sized windows (3.2s) with 50% overlap
- SVM is trained from features
- aggregate classification results over time

refined model selection
- time frame: 10s, 15s, 20s, 25s, 30s, 45s, 60s
- \{upper, lower\} threshold: 0%, 5%, 10%, ... , 95%, 100%
## Results of Final Iteration

### Indication of Tremor at Rest

<table>
<thead>
<tr>
<th>Kernel Features</th>
<th>RBF red.</th>
<th>linear red.</th>
<th>RBF full</th>
<th>linear full</th>
</tr>
</thead>
<tbody>
<tr>
<td>time frame</td>
<td>60</td>
<td>45</td>
<td>60</td>
<td>30</td>
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<tr>
<td>lower threshold</td>
<td>0.650</td>
<td>0.150</td>
<td>0.500</td>
<td>0.500</td>
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<tr>
<td>upper threshold</td>
<td>1.000</td>
<td>0.950</td>
<td>1.000</td>
<td>0.800</td>
</tr>
<tr>
<td>Sensitivity (test)</td>
<td>0.910</td>
<td>0.884</td>
<td>0.964</td>
<td>0.884</td>
</tr>
<tr>
<td>Specificity (test)</td>
<td>0.979</td>
<td>0.993</td>
<td>0.989</td>
<td>0.972</td>
</tr>
<tr>
<td>Data Usage (test)</td>
<td>0.772</td>
<td>0.539</td>
<td>0.713</td>
<td>0.871</td>
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<tr>
<td>Geometric Mean (test)</td>
<td>0.944</td>
<td>0.937</td>
<td>0.976</td>
<td>0.927</td>
</tr>
<tr>
<td>Accuracy (test)</td>
<td>0.976</td>
<td>0.989</td>
<td>0.988</td>
<td>0.969</td>
</tr>
</tbody>
</table>
### Tremor at Rest

**Benchmark of Symptom Detecting Algorithms**

<table>
<thead>
<tr>
<th>Variation / Author(s)</th>
<th>Acc.</th>
<th>Sens.</th>
<th>Spec.</th>
<th>D.U.</th>
<th>Subjects</th>
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<tbody>
<tr>
<td>Salarian et al. [23]</td>
<td>0.766</td>
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<td>Salarian et al. [24]</td>
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<tr>
<td>Cole et al. [12]</td>
<td>0.930</td>
<td>0.950</td>
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<td></td>
<td>12</td>
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<tr>
<td>Roy et al. [22]</td>
<td>0.912</td>
<td>0.934</td>
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<tr>
<td>Niazmand et al. [19]</td>
<td>0.800</td>
<td>0.985</td>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>RBF+red.</td>
<td>0.976</td>
<td>0.910</td>
<td>0.979</td>
<td>0.772</td>
<td>89</td>
</tr>
<tr>
<td>linear+red.</td>
<td>0.989</td>
<td>0.884</td>
<td>0.993</td>
<td>0.539</td>
<td>89</td>
</tr>
<tr>
<td>RBF+full</td>
<td>0.988</td>
<td>0.964</td>
<td>0.989</td>
<td>0.713</td>
<td>89</td>
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<tr>
<td>linear+full</td>
<td>0.969</td>
<td>0.884</td>
<td>0.972</td>
<td>0.871</td>
<td>89</td>
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## Benchmark of Symptom Detecting Algorithms

<table>
<thead>
<tr>
<th>Variation / Author(s)</th>
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<th>Sens.</th>
<th>Spec.</th>
<th>D.U.</th>
<th>Subjects</th>
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<tr>
<td>Djurić-Jovičić et al.[14]</td>
<td>0.840</td>
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<tr>
<td>Cole et al.[13]</td>
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<td>0.973</td>
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<td>Niazmand et al.[20]</td>
<td>0.883</td>
<td>0.853</td>
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<td>Bächlin et al.[11]</td>
<td>0.731</td>
<td>0.816</td>
<td></td>
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<tr>
<td>RBF+red.</td>
<td>0.985</td>
<td>0.900</td>
<td>1.000</td>
<td>0.823</td>
<td>20</td>
</tr>
<tr>
<td>linear+red.</td>
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<td>0.889</td>
<td>1.000</td>
<td>0.919</td>
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<tr>
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<td>0.900</td>
<td>1.000</td>
<td>0.949</td>
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<tr>
<td>linear+full</td>
<td>0.987</td>
<td>0.923</td>
<td>1.000</td>
<td>0.987</td>
<td>20</td>
</tr>
</tbody>
</table>
## Dyskinesia

### Benchmark of Symptom Detecting Algorithms

<table>
<thead>
<tr>
<th>Variation / Author(s)</th>
<th>Acc.</th>
<th>Sens.</th>
<th>Spec.</th>
<th>D.U.</th>
<th>Subjects</th>
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<tbody>
<tr>
<td>Keijsers et al.\textsuperscript{[17]}</td>
<td>0.968</td>
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<td>Tsipouras et al.\textsuperscript{[25]}</td>
<td>0.937</td>
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<tr>
<td>Cole et al.\textsuperscript{[12]}</td>
<td></td>
<td>0.910</td>
<td>0.930</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Roy et al.\textsuperscript{[22]}</td>
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<td>0.900</td>
<td>0.934</td>
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<td>0.889</td>
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</tr>
<tr>
<td>RBF+full</td>
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<td>0.815</td>
<td>0.965</td>
<td>0.272</td>
<td>90</td>
</tr>
<tr>
<td>linear+full</td>
<td>0.931</td>
<td>0.905</td>
<td>0.932</td>
<td>0.354</td>
<td>90</td>
</tr>
</tbody>
</table>
list of symptoms was narrowed down to commonly experienced motor symptoms

set of publications with respect to these symptoms was compiled
Conclusions

- proposals for improving state-of-the-art techniques were developed
- algorithms for detecting tremor at rest, freezing episodes and dyskinesia
- flexible, configurable and patient-independent methodology was developed around a SVM and a meta-analysis
methodology is compared to state-of-the-art techniques

methodology is shown to outperform related works in case of resting tremor and freezing of gait (FoG)

in case of dyskinesia, the results do not exceed those of state-of-the-art techniques but yield to similar results.
Contributions IV

Conclusions

- software-architecture for a general-purpose data processing environment
- focus on modularity, reusability and extensibility
- can handle arbitrary data and model non-linear processes
Conclusions

- 1 journal article \cite{2} and 2 journal articles have been submitted \cite{6, 7}
- 2 conference / workshop papers \cite{5, 3}
- 1 technical report \cite{4}
- 1 poster \cite{1}
Future Work

Conclusions

- methodology could be applied to detect other symptoms
- use wrist sensor only to detect symptoms
- have a single SVM for detecting all symptoms (rather than a single SVM for each symptom)
- implement and use algorithms like Hoeffding Trees, D-Stream or count-min to detect PD symptoms and side effects
Thanks!


