

Intraoperative Decision Making with Rough Set Rules for STN DBS in Parkinson Disease

Konrad Ciecierski¹, Zbigniew W. Raś^{1,2}, and Andrzej W. Przybyszewski^{3,4}

¹ Warsaw Univ. of Technology, Institute of Comp. Science, 00-655 Warsaw, Poland

² Univ. of North Carolina, Dept. of Comp. Science, Charlotte, NC 28223, USA

³ UMass Medical School, Dept. of Neurology, Worcester, MA 01655, USA

⁴ Polish-Japanese Institute of Information Technology, 02-008 Warsaw, Poland

K.Ciecierski@ii.pw.edu.pl, ras@uncc.edu,

Andrzej.Przybyszewski@umassmed.edu

Abstract. In neurosurgical treatment of the Parkinson Disease (*PD*) the target is a small (9 x 7 x 4 mm) deep within brain placed structure called *SubthalamicNucleus (STN)*. The goal of the Deep Brain Stimulation (*DBS*) surgery is the permanent precise placement of the stimulating electrode within target nucleus. As this structure poorly discriminates in CT¹ or MRI² it is usually stereotactically located using microelectrode recording. Several microelectrodes are parallelly inserted into the brain and in measured steps they are advanced towards expected location of the nucleus. At each step, from 20 mm above the target, the neuronal activity is recorded. Because *STN* has a distinct physiology, the signals recorded within it also present specific features. By extracting certain features from recordings provided by the microelectrodes, it is possible to construct a classifier that provides useful discrimination. This discrimination divides the recordings into two classes, i.e. those registered within the *STN* and those registered outside of it. Using the decision tree based classifiers, the best results have been obtained using the Random Forest method. In this paper we compared the results obtained from the Random Forest to those provided by the classification based upon rules extracted by the rough set approach.

Keywords: Parkinson's disease, DBS, STN, Decision Tree, Random Forest, Rough Set, Classification Rule, RSES.

1 Introduction

Recordings obtained by means of microrecording during *PD DBS* surgeries can be discriminated into those obtained from the *STN* and from structures adjacent to it. It is possible due to specific physiology of the *STN*. This physiology manifests in the activity that differs from that observed in neuronal structures

¹ Computer Tomography.

² Magnetic Resonance Imaging.

being both dorsal³ and ventral⁴ to this structure [1][2]. Authors in [3][4][5] provided computational basis for calculation of attributes that when calculated for neurophysiological recordings can be successfully used for their discrimination. Those attributes have been used for construction of various decision tree based classifiers. The clinical database presently contains 16377 recordings obtained during 153 surgeries. In the case of both Random Forest and C4.5 the obtained sensitivity is above 0.9 and specificity above 0.98. Such results clearly fulfill the requirements for medical appliance [6] and allowed us to develop a recommender system that is currently in clinical use during neurosurgeries at Warsaw Institute of Psychiatry and Neurology. The goal of this paper is to compare results obtained from Random Forest to those generated by the classification based upon rules extracted by the rough set approach.

2 Methods

Parkinson Disease (PD) is a chronic and progressive movement disorder. The risk factor of the disease increases with the age. As the average human life span elongates also the number of people affected with PD steadily increases. According to the present medical knowledge, the *PD* disease is caused by low levels of the neurotransmitter: dopamine. Dopamine is produced by specific cells in deep placed brain region called *Substantia Nigra pars compacta* (SNc). The main cause of PD is cell-death of those cells. As the main cause of death of those cells is not clear, different treatments focus on symptom's improvements. The main treatment for the disease is the pharmacological one. Unfortunately, as more *SNc* cells are dying, the level of the dopamine is fast changing. PD patients have to take medications more often which may result in strong symptoms fluctuations (ON / OFF states). In such cases, patients may be qualified for the surgical treatment of the PD.

2.1 STN DBS Surgery in PD

STN DBS surgery stands for Deep Brain Stimulation of the **S**ub**T**halamic **N**ucleus. Goal of the surgery is the placement of the permanent stimulating electrode into the *STN*. This nucleus is a small – deep in brain placed – structure that unfortunately does not show well neither in CT⁵ nor MRI⁶ scans. Above techniques allow only for approximate localization of the *STN*. Stimulating electrode, when properly placed disrupts overactive neural circuits that are responsible for the forming of the rigidity which is typical for the advanced stage of the PD disease. Incorrect placement of the stimulating electrode might evoke various serious adverse side effects such as severe emotional imbalance [7].

³ Anatomically located above.

⁴ Anatomically located beneath.

⁵ Computer Tomography.

⁶ Magnetic Resonance Imaging.

During the process of selection of the part of the *STN* into which the permanent electrode will be implanted a series of test stimulations are performed. During those stimulations the improvement of the patient condition is assessed. Care is also taken to exclude any areas which when stimulated produce side effects. As these procedures require interaction between patient and neurologist, the general anesthesia cannot be used during the neurosurgical phase of the *STN* DBS surgery. Patient must be conscious and is only locally anesthetized.

Having only an approximate location of the *STN*, during DBS surgery a precise localization of the *STN* is achieved by means of stereotactic navigation and intra-operative mapping based on microrecording. During the surgery, by means of probing microelectrodes, brain activity in areas near the expected *STN* location is recorded. Typically neurosurgeons use 3 to 5 parallel microelectrodes. Electrodes are advanced to a position that is about 10 mm above expected *STN* location. Later electrodes are advanced for about 15 mm with 1 mm steps. At each step a 10 s long recording of brain tissue activity is obtained. All recordings analyzed in this paper were sampled with 24 KHz.

Computer classification of recordings performed during surgery at operation theatre gives neurosurgeons valuable information about which of the electrodes and at which depths passed through the *STN*. In this way a precise dorsal and ventral boundaries of the *STN* are obtained and finally the stimulating electrode can safely be implanted.

Main advantages given by the recommender (decision support) system during *STN* DBS surgery are:

- From classification of the recordings it is possible to obtain information, which of the electrodes passed through the *STN*. It is also possible to obtain depth at which given electrode entered and exited this structure. When taking into account that information from all electrodes, the rough dorsal and ventral boundaries of the *STN* can be estimated.
- Besides the results of classification, values of the attributes give additional information that can be used to estimate the brain activity at any electrode inspected depth. Usually the best treatment results are obtained when the stimulating electrode is placed in one of the most active areas [7].
- One of the risks of the *STN* DBS surgery involves incorrect placement of the stimulating electrode. As part of the *STN* is involved in the control of emotions (limbic part), and in the vicinity of the *STN* – among others – are structures involved in emotions, eye movement and sight (OP - optic tract), wrong placement of the stimulating electrode might lead to life threatening situations. Additional computer based verification of the *STN* boundaries reduces risk of improper placement of the stimulating electrode.
- Any surgery is in some measure stressful for the patient. Recommender system allows faster selection of right areas for test stimulations. This shortens the time of the surgery when patient has to be awake.

2.2 Attributes Description

Attributes extracted from *DBS* recordings can be divided into two groups:

Spike based attributes are calculated basing on the occurrence of the neuronal action potentials i.e. spikes. The neural tissue is electrically active and its information processing involves generation and transmission of electrical impulses. Those impulses – spikes – are generated in neurones mainly by the sodium (calcium) membrane channels activations. Microelectrode registers the spiking activity from neurons that are within the $50 \mu m$ radius around its recording lead. As shape of spikes generated by a single cell is characteristic, derived from its morphology [1] and mostly unchanging, it is possible to calculate those attributes for all cells within $50 \mu m$ radius or for any of them separately.

Background based attributes are calculated basing upon the signal's background noise. Cells that are farther than $50 \mu m$ away from electrode's lead are too far away for their spikes to be clearly registered. Their summary electrical activity creates the background noise ever present in signals obtained from microrecording. This background activity is a rough measure of amount and activity of neuron cells in the broader vicinity of the electrode.

There is one decision attribute that has value *STN* for recordings from the *STN* and value *MISS* for all other recordings. For each 10 s long recording there are five spike based attributes, four background attributes and four attributes being the five element wide moving average of background attributes.

AvgSpkRate is the average number of spikes detected per second

AvgSpkRateScMax maximal *AvgSpkRate* observed for single cell

BurstRatio percentage of intervals between spikes that are smaller than $33 ms$

BurstRatioScMax maximal *BurstRatio* observed for single cell

MPWR power of the derived meta signal, explained in detail in [5]

RMS Root Mean Square of the signal

PRC80 80^{th} percentile of amplitude's module

LFB power of the signal's background in range $0 - 500 Hz$

HFB power of the signal's background in range $500 - 3000 Hz$

MRMS five element wide moving average of RMS

MPRC80 five element wide moving average of PRC80

MLFB five element wide moving average of LFB

MHFB five element wide moving average of HFB

In Table 1 one can observe, that for all background attributes and for 3 out of 5 spike based attributes the Q3 for *MISS* class is below Q1 for *STN* class.

Out of 16377 recordings, 3736 (22.8 %) recordings have decision attribute *STN*. 12641 (77.2 %) have decision attribute *MISS*.

Table 1. Statistics for attributes

Attributes	Class	Q1	Q2	Q3	μ	σ
<i>AvgSpkRate</i>	<i>MISS</i>	0.000	0.000	7.400	5.555	9.859
	<i>STN</i>	10.700	18.900	29.225	21.509	15.181
<i>AvgSpkRateScMax</i>	<i>MISS</i>	0.000	0.000	4.700	3.578	6.334
	<i>STN</i>	6.500	11.300	18.000	13.261	9.597
<i>BurstRatio</i>	<i>MISS</i>	0.238	0.414	0.596	0.195	0.262
	<i>STN</i>	0.458	0.603	0.727	0.551	0.230
<i>BurstRatioScMax</i>	<i>MISS</i>	0.194	0.333	0.510	0.165	0.231
	<i>STN</i>	0.361	0.495	0.632	0.469	0.221
<i>MPWR</i>	<i>MISS</i>	0	0	858	448.025	546.937
	<i>STN</i>	1023	1315	1595	1275.836	485.373
<i>RMS</i>	<i>MISS</i>	0.939	1.006	1.153	1.064	0.230
	<i>STN</i>	1.757	2.069	2.493	2.190	0.598
<i>PRC80</i>	<i>MISS</i>	0.962	1.011	1.137	1.064	0.196
	<i>STN</i>	1.702	1.982	2.362	2.087	0.530
<i>LFB</i>	<i>MISS</i>	0.825	1.005	1.284	1.164	0.741
	<i>STN</i>	2.592	3.833	5.851	4.778	3.725
<i>HFB</i>	<i>MISS</i>	0.909	1.032	1.339	1.185	0.532
	<i>STN</i>	3.028	4.205	6.009	4.942	3.021
<i>MRMS</i>	<i>MISS</i>	0.998	1.020	1.195	1.111	0.212
	<i>STN</i>	1.653	1.929	2.254	1.997	0.466
<i>MPRC80</i>	<i>MISS</i>	0.999	1.022	1.183	1.106	0.190
	<i>STN</i>	1.614	1.852	2.145	1.916	0.427
<i>MLFB</i>	<i>MISS</i>	0.976	1.027	1.400	1.304	0.735
	<i>STN</i>	2.512	3.566	5.107	4.180	2.559
<i>MHFB</i>	<i>MISS</i>	0.997	1.056	1.496	1.336	0.623
	<i>STN</i>	2.903	3.861	5.184	4.341	2.267

2.3 Rough Set Approach

All above data can be stored as a decision table. Such table would have 16377 rows – objects. For each object there are defined 13 condition attributes i.e. *AvgSpkRate ... MHFB* and one decision attribute *Class*.

Together they form a decision system $S = (U, A)$ where U is the set of objects and A is the set of attributes. For any attribute $a \in A$ and object $u \in U$ the value of attribute a for object u is denoted as $a(u)$.

Crucial to the rough set is the definition of the *indiscernibility relation*. Indiscernibility relation is defined for a subset of attributes $B \subseteq A$ and is denoted as I_B . Two elements are in relation I_B iff for any attribute from B , its value is equal for both of them [8][9].

$$x I_B y \iff \forall_{a \in B} a(x) = a(y) \tag{1}$$

This relation obviously is reflexive, symmetric and transitive. From this, relation I_B is an equivalence relation and partitions the set U into equivalence classes.

Now, we define $IND(B)$ as:

$$IND(B) = \{(x, y) \in U^2 : x I_B y\} \quad (2)$$

Having defined the IND one can provide the definition of the reduct of information system. $B \subset A$ is said to be a reduct of information system if $IND(B) = IND(A)$ and no proper subset of B has this property. $B \subset A$ is a decision reduct if $IND(B) = IND(d)$ where d is a decision attribute.

Those reducts can further be used for obtaining attribute dependencies [10] and finally, rules that lead from the values of the conditional attributes to value of the decision attribute [11].

In information system the set of attributes A consists of set of conditional attributes C and decision attribute d . If $C = \{c_1, \dots, c_m\}$ is the set of conditional attributes then decision rule can be formulated as

$$(c_{i_1} = v_1) \wedge \dots \wedge (c_{i_k} = v_k) \implies (d = v_d) \quad (3)$$

where

$$1 \leq i_1 < \dots < i_k \leq m$$

If any object has conditional attributes that satisfy the left hand site of a rule, its outcome gives value of the decision attribute of that object.

While rules basing on equality of attributes to certain values might have a very big confidence, they may have low support and as such are poorly suited for generalization and for further classification.

Much more general rules can be obtained when conditional attributes are not expected to be equal to certain values but to fall into certain ranges. This ranges are obtained by cutting the initial range of the attributes into intervals.

For example let's inspect the following rule

$$(PRC80 < 1.15279) \wedge (MRMS < 1.22111) \implies (CLASS = MISS)$$

which applies to 7854 recordings and states that they have not been recorded within the *STN*.

In contrast to decision tree classification, not every $u \in U$ must be matched by some rule. This leads to possible existence of objects for whom there are no fitting rules and which cannot be classified using given rule set. This feature is measured by the *coverage* of the rule set which gives the fraction of the tested objects that can be classified.

Classification Results

The following results were obtained using the Random Forest method and by means of classification based upon rules extracted by the rough set approach.

For Random Forest the Weka⁷ v. 3.7.9 implementation has been used. Rough Set based classification has been done using RSES⁸ v. 2.2.2 software [12]. All classifiers were run on unconstrained database containing described attributes for 16377 DBS recordings from 153 neurosurgeries.

Random Forest Classification Results

Random Forest Classification for All Objects with Division into 90% for Training and 10% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RF</i> classification	<i>STN</i>	353	20	373
	<i>MISS</i>	29	1236	1265
Total		382	1256	1638

$$sensitivity = \frac{353}{353+29} \approx 0.924 \qquad specificity = \frac{1236}{1236+20} \approx 0.984$$

$$accuracy = \frac{353+1236}{353+29+1236+20} \approx 0.970$$

For training of this classifier a random subset containing 90 % of objects have been chosen. Classifier has then been tested on remaining 10 % of objects. Both sensitivity and specificity are very good and above 0.9. The *Kappa* statistic was also very good: 0.916. Coverage for level 0.95 was 99.451 % of objects.

Random Forest Classification for All Objects with Division into 60% for Training and 40% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RF</i> classification	<i>STN</i>	1317	79	1396
	<i>MISS</i>	110	5045	5155
Total		1427	5124	6551

$$sensitivity = \frac{1317}{1317+110} \approx 0.923 \qquad specificity = \frac{5045}{5045+79} \approx 0.985$$

$$accuracy = \frac{1317+5045}{1317+110+5045+79} \approx 0.971$$

For training of this classifier a random subset containing 60 % of objects have been chosen. Classifier has then been tested on remaining 40 % of objects. Both sensitivity and specificity are very good and above 0.9. The *Kappa* statistic was also very good: 0.915. Coverage for level 0.95 was 99.435 % of objects.

⁷ www.cs.waikato.ac.nz/ml/weka

⁸ logic.mimuw.edu.pl/~rses/start.html

Random Forest Classification for All Objects With Ten Fold Cross-Validation

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RF</i> classification	<i>STN</i>	3473	169	3642
	<i>MISS</i>	263	12472	12735
Total		3736	12641	16377

$$sensitivity = \frac{3473}{3473+263} \approx 0.930 \quad specificity = \frac{12472}{12472+169} \approx 0.987$$

$$accuracy = \frac{3473+12472}{3473+263+12472+169} \approx 0.974$$

Both sensitivity and specificity are very good and above 0.9. Especially good is the specificity 0.987 which is very important in case of DBS[5]. The *Kappa* statistic was also very good: 0.924. Coverage for level 0.95 was 99.432 % of objects. This classifier is currently in clinical use during neurosurgeries.

RSES Rule Based Classification Results

RSES Rule Classification for All Objects with Division into 90% for Training and 10% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	153	133	286
	<i>MISS</i>	119	740	859
Total		272	873	1145

$$sensitivity = \frac{153}{153+119} \approx 0.562 \quad specificity = \frac{740}{740+133} \approx 0.848$$

$$accuracy = \frac{153+740}{153+119+740+133} \approx 0.780 \quad coverage = \frac{1145}{1638} \approx 0.699$$

In this case the specificity is acceptable but the sensitivity is very poor. Classifier failed to adequately detect objects from the *STN* class. It is also evident that resulting rules fail to classify over 30% of the objects.

RSES Rule Classification for All Objects with Division into 60% for Training and 40% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	607	504	1111
	<i>MISS</i>	516	2720	3236
Total		1123	3224	4347

$$sensitivity = \frac{607}{607+516} \approx 0.541 \quad specificity = \frac{2720}{2720+504} \approx 0.844$$

$$accuracy = \frac{607+2720}{607+516+2720+504} \approx 0.765 \quad coverage = \frac{4347}{6550} \approx 0.664$$

In this case the specificity is acceptable and the sensitivity is even worse than in previous case. Classifier failed to detect almost half of objects from the *STN* class. Resulting rules fail to classify over 33% of the objects.

RSES Rule Classification for All Objects with Ten Fold Cross-Validation

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	155.5	131.5	287
	<i>MISS</i>	127.9	709.8	837.7
Total		283.4	841.3	4347

$$sensitivity = \frac{155.5}{155.5+127.9} \approx 0.548$$

$$specificity = \frac{709.8}{709.8+131.5} \approx 0.844$$

$$accuracy = \frac{155.5+709.8}{155.5+127.9+709.8+131.5} \approx 0.769$$

$$coverage = \frac{1124.7}{1637} \approx 0.687$$

In this case the specificity is acceptable and the sensitivity is as poor as in two previous cases. Classifier failed to detect almost half of objects from the *STN* class. Resulting rules fail to classify over 33% of the objects.

Classifications based on rules extracted from raw attributes by the rough set approach give good specificity. Still the sensitivity is very poor and over 30 % of objects are not matched by any rule.

RSES Rule Based Classification Results for Discretized Attributes

In following classifications, the conditional attributes have all been discretized i.e. cut into adjacent intervals. Cuts were made automatically by the RSES package. Number of intervals produced per attribute ranged from two for *AvgSpkRate* up to eight for *MHFB*. Resulting cuts were not of uniform size.

RSES Rule Classification with Attribute Cut Done for All Objects with Division into 90% for Training and 10% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	359	38	397
	<i>MISS</i>	24	1216	1240
Total		383	1254	1637

$$sensitivity = \frac{359}{359+24} \approx 0.937$$

$$specificity = \frac{1216}{1216+38} \approx 0.970$$

$$accuracy = \frac{359+1216}{359+24+1216+38} \approx 0.962$$

$$coverage = \frac{1637}{1637} = 1.000$$

In this case both specificity and sensitivity are very good and above 0.9. Classifier has also perfect coverage. In comparison to analogous Random Forest results RSES provided slightly better sensitivity and slightly worse specificity.

RSES Rule Classification with Attribute Cut Done for All Objects with Division into 60% for Training and 40% for Testing Purposes

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	1446	160	1606
	<i>MISS</i>	79	4865	4944
Total		1525	5025	6550

$$sensitivity = \frac{1446}{1446+79} \approx 0.948$$

$$specificity = \frac{4865}{4865+160} \approx 0.968$$

$$accuracy = \frac{1446+4865}{1446+79+4865+160} \approx 0.964$$

$$coverage = \frac{6550}{6550} = 1.000$$

In this case also both specificity and sensitivity are very good and above 0.9. Classifier has also perfect coverage. In comparison to analogous Random Forest results RSES provided better sensitivity and worse specificity.

RSES Rule Classification with Attribute Cut Done for All Objects with Ten Fold Cross-Validation

		Human classification		Total
		<i>STN</i>	<i>MISS</i>	
<i>RSES</i> classification	<i>STN</i>	355.7	35.7	391.4
	<i>MISS</i>	17.7	1227.9	1245.6
Total		373.4	1263.6	1637

$$sensitivity = \frac{355.7}{355.7+17.7} \approx 0.953$$

$$specificity = \frac{1227.9}{1227.9+35.7} \approx 0.972$$

$$accuracy = \frac{355.7+1227.9}{355.7+17.7+1227.9+35.7} \approx 0.967$$

$$coverage = \frac{1637}{1637} = 0.687$$

In this case specificity and sensitivity are very good and above 0.95. Classifier has perfect coverage. In comparison to analogous Random Forest results RSES provided better sensitivity and worse specificity. Still in case of both classifiers the sensitivity and specificity were above 0.93.

3 Summary

As shown in Table 2, in all tested cases the rough set rule based classification did not perform well when run on raw nondiscretized attributes. That was due to the continuous nature of all conditional attributes. Sets of rules produced by RSES for continuous attributes were huge and most of those rules matched only single objects. For example, rule generation for 90 % (14739 objects) subsample of objects with continuous attributes resulted in 154651 rules basing on equality of attributes. Not surprisingly such rule set had poor coverage during the test phase, more than 30 % of test object were not classified at all.

However when rules were produced basing on the discretized attributes, the obtained results were very good and in some aspects they outperformed those produced by the Random Forest. In all test scenarios (i.e. 90 % train & 10 % test; 60 % train & 40 % test; 10 fold cross-validation) while the RSES provided better sensitivity the Random Forest approach gave better specificity. On average the RSES sensitivity was better by 0.02 and Random Forest specificity was better by 0.015.

In conclusion it must be stated that both methods, i.e. Weka implementation of Random Forest and RSES implementation of rough set rule based classification for discretized attributes gave very good and comparable results. Also in both cases after the classifier / rule set has been constructed, the classification of new objects is very fast and certainly feasible for use at the operation theatre.

Table 2. Sensitivity, specificity and coverage

		<i>Sensitivity</i>	<i>Specificity</i>	<i>Coverage</i>
90% train; 10% test	<i>Weka RF</i>	0.924	0.984	1.000
	<i>RSES</i>	0.562	0.848	0.699
	<i>Cut RSES</i>	0.937	0.970	1.000
60% train; 40% test	<i>Weka RF</i>	0.923	0.985	1.000
	<i>RSES</i>	0.541	0.844	0.664
	<i>Cut RSES</i>	0.948	0.968	1.000
10 fold cross-validation	<i>Weka RF</i>	0.930	0.987	1.000
	<i>RSES</i>	0.548	0.844	0.687
	<i>Cut RSES</i>	0.953	0.972	1.000

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