Bronchopulmonary Dysplasia Prediction Using Support Vector Machine and LIBSVM

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Abstract—**The paper presents BPD (Bronchopulmonary Dysplasia) prediction for extremely premature infants after their first week of life. SVM (Support Vector Machine) algorithm implemented in LIBSVM[1] was used as classifier. Results are compared to others gathered in previous work [2] where LR (Logit Regression) and Matlab environment SVM implementation were used. Fourteen different risk factor parameters were considered and due to the high computational complexity only 3375 random combinations were analysed. Classifier based on eight feature model provides the highest accuracy which was 82.60%. The most promising 5-feature model which gathered 82.23% was reasonably immune to random data changes and consistent with LR results. The main conclusion is that unlike Matlab SVM[2] implementation, LIBSVM can be successfully used in considered problem, but it is less stable than LR. In addition, the article discusses influence of the model parameters selection on prediction quality.**

I. INTRODUCTION

BRONCHOPULMONARY dysplasia (BPD) is a chronic pulmonary morbidity which affects premature infants [3], [4]. It is most common among children who received prolonged mechanical ventilation to treat respiratory distress syndrome [5], [6] and those with low birth weight. Almost a third of infants with birth weight lower than 1000g [7] are affected. Due to the fact that the disease is poorly understood, many projects are focused on identifying its factors of risk. Since it can not be diagnosed until a 28th day of life [8], it is very important to predict such a result after the end of the first week, which would enable an early prevention of the disease[9]. Therefore, an intensive work has been done to define a classifier, based on static parameters (gathered after birth) and dynamic ones (collected during the first week of life), which would be able to predict the diagnosis. Although several prediction models of BPD [10], [11], [12], [13], [14], [15], [16], [17], [18], [19] used in research have been reported, none of them could be used in common clinical practice due to the variety of reasons and none use SVM.

II. RELATED WORKS

As mentioned before, there are numerous works related to BPD, its risk factors and prediction [20], [21], [22], [23]. The most popular one is the analysis of static data whose main features are gestational age and birth weight. The other factors considered are admission of surfactant, presence of patent ductus arteriosis (PDA), or respiratory support. In addition, dynamical data (which is much harder to obtain) is analysed in more sophisticated models. Most of such parameters are: arterial blood gas variables like fraction of inspired oxygen (FiO_2) or alveolar-arterial ratio (AA) [24] (which is respiratory distress degree measure); blood gas levels like oxygen saturation of arterial hemoglobin (SpO_2) and its standard deviation, mean value etc. [25] or even time series analysis [26]; heart beat and its derivatives.

$$AA = \frac{pO_2}{p_{ATM} \cdot FiO_2 - pCO_2},\qquad(1)$$

where pO_2— oxygen partial pressure, p_{ATM}—atmospheric pressure, pCO_2—carbon dioxide partial pressure, FiO_2—fraction of inspired oxygen.

Some of the papers introduced race and ethnicity or sex as factors which seem to be promising but require a very big set of data. It should be indicated that the vast majority of studies uses logit regression (LR) in prediction. Best LR models gain about 73% to 82% of accuracy. Many of authors mention use of support vector machine(SVM)[27] in future works, however it is difficult to find them. In our previous work[2] we compared SVM with LR classifiers. Unfortunately, due to internal Matlab SVM library usage results were highly unsatisfactory. The highest accuracy gained was only 79.39%. Moreover, the bigger features set was used the worse results we got. In general, only three and four feature models were able to gain accuracy higher than 70%. That is why we decided to use LIBSVM implementation instead, which gave us a very wide scope of parameters tuning. Although additional parameters highly increased computational complexity of optimal model search, even limited random parameters space exploration gave us quite good results, comparable to LR.

III. GENERAL IDEAS OF USED METHODS

A. Logistic regression

Probability of the dependent variable equalling a BPD positive diagnosis ($y_k = 1$), on condition that explanatory variables (features of specific case k) equals $X_k = (x_{1,k}, x_{2,k}, .., x_{n,k})$, we define as:

$$p_k = P(y_k = 1|X_k) = \frac{e^{a_0 + \sum\limits_{i=1}^{n} a_i x_i}}{1 + e^{a_0 + \sum\limits_{i=1}^{n} a_i x_i}},\qquad(2)$$
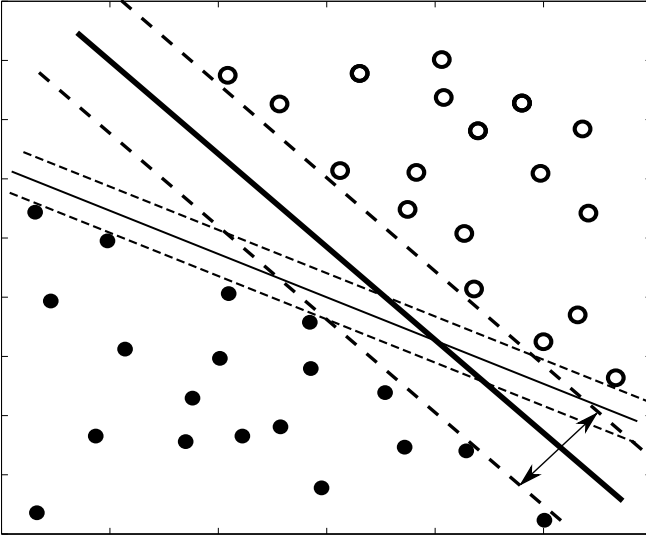
Fig. 1. Maximizing margin in SVM method.

where $x_{i,k}$—explanatory variables (feature values for case k), a_i—regression coefficients, n—number of features.

In contrast to linear regression, where we assume normal distribution of the independent variables and because explanatory variables variance are not equal, we can not use the method of least squares to obtain regression coefficients. Thus they are usually calculated using maximum likelihood estimation, maximizing likelihood function (L) or minimizing its negative logarithm using learning data:

$$L = \prod_{y_k=1} p_k \prod_{y_k=0} (1 - p_k), \qquad (3)$$

$$ln(L) = \sum_{k=1}^{m} [y_k \cdot ln(p_k) + (1 - y_k) \cdot ln(1 - p_k)], \qquad (4)$$

where k—observation number (learning case), y_k —diagnosis for case k, m—number of observations.

Having a_i regression coefficients, we can easily predict BPD positive diagnosis probability of case X using Eq. 2.

B. Support vector machine

We define the learning data D divided in two classes y as:

$$D = \{(X_k, y_k) | X_k \in R^n, y_k \in \{1, -1\}\}_{k=1}^{m} \qquad (5)$$

We are looking for hyperplane

$$W \bullet X + b = 0 \qquad (6)$$

which separates classes and provides maximum margin as on Fig. 1, which is the same as the problem of minimizing L :

$$L(W) = \frac{||W||^2}{2} + c \cdot \sum_{k=1}^{m} \varepsilon_k, \qquad (7)$$

with conditions:

$$y_k(W \cdot \phi(X_k) + b) \geq 1 - \varepsilon_k \qquad (8)$$

where $\varepsilon \geq 0$—slack variable, $c > 0$—penalty parameter for each point wrongly classified, ϕ—kernel function.

Thanks to the kernel functions for non linear separable problems, we can transform original data from n dimensional space to p dimensional ($p > n$, as on Fig. 2), in which there is much higher likelihood that they will be linear separable.

IV. DATA AND METHODS

Data was collected thanks to the Neonatal Intensive Care Unit of The Department of Pediatrics at Jagiellonian University Medical College using our own software. It includes 109 patients born prematurely with birth weight less than or equal to 1500g admitted, no later than on the second day of life. For 46 of them BPD have been diagnosed after fourth week of life.

To build a suitable model 14 different features mentioned in literature were considered:

- Binary such as:
  - presence of patent ductus arteriosus (PDA) [28] ,
  - use of a respirator ($RESPIMV$) during the first week of life,
  - administration of surfactant ($SURFACT$) [29] in the same period.
- Real-Valued (values range in parentheses) such as:
  - birth weight ($BWEIGHT$) (550-1500g),
  - gestational age ($GAGE$) (22-34 weeks),
  - alveolar-arterial ratio (AA) (0.05-1) measured during patient admission,
  - a percentage of the time during first week for which the oxygen saturation of hemoglobin was less than 85% ($LOW85$) (0.03%-12.45%) or higher than 94% ($HIGH94$) (14.56%-99.02%),
  - average number of heartbeats per minute ($BPMMEAN$)[5](124.69-161.42 bpm),
  - mean and standard deviation of oxygen saturation ($SPO2MEAN$, $SPO2DEV$) (accordingly 89.89%-98.99% and 1.19-7.98) and their trends (first day to first week ratio: $BPMMEAN\_TR$, $SPO2MEAN\_TR$, $SPO2DEV\_TR$) (accordingly 0.8-1.18 , 0.96-1.07 and 0.51-2.36).

Accuracy (ACC) defined as below was considered as preliminary result measure. The sensitivity(TPR) and specificity(SPC) were also obtained:

$$ACC = \frac{TP + TN}{TP + TN + FP + FN}, \qquad (9)$$

$$TPR = \frac{TP}{TP + FN}, \qquad (10)$$

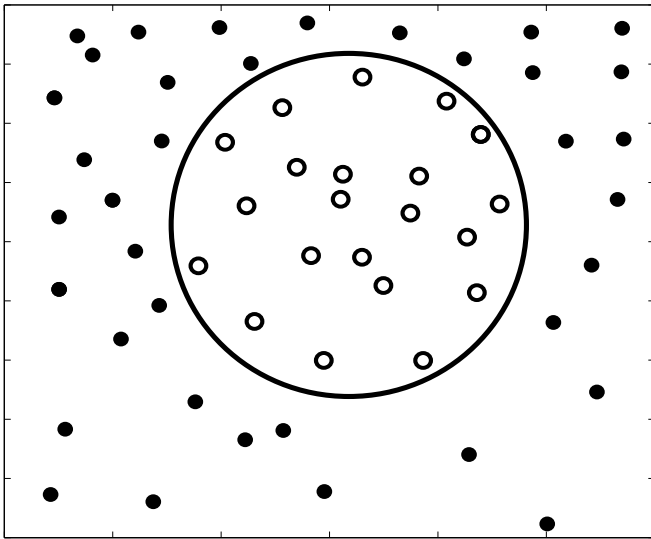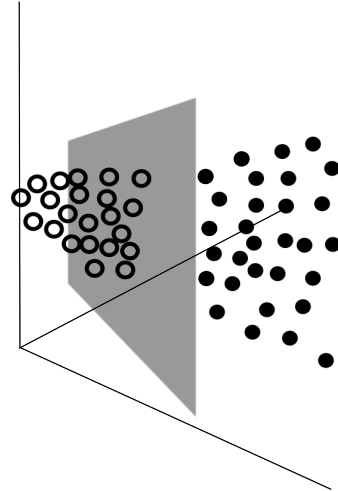$$SPC = \frac{TN}{TN + FP}, \qquad (11)$$

(a) data in R^2 space   (b) data transformed to R^3 space

Fig. 2. Making data linear separable with dimensional transformation.

where TP—True Positives, FP—False Positives, FN—False Negatives, TN—True Negatives.

As mentioned before in SVM computation version 3.17 of LIBSVM library was used. Based on a few arbitrary chosen and tested models it has been found that for specified problem C-SVC method is more effective than nu-SVC (range of parameter c (Eq. 7) is from zero to infinity, rather than as in nu always between [0,1]). It has also been discovered that sigmoid kernel function gives better results and is much faster in finding the separating hyperplane than radial basis (RBF) one.

$$K(X_i, X_j) \equiv \phi(X_i)^T \phi(X_j), \qquad (12)$$

$$RBF : K(X_i, X_j) = e^{-\gamma||X_i - X_j||^2}, \gamma > 0, \qquad (13)$$

$$Sigmoid : K(X_i, X_j) = tanh(\gamma X_i^T X_j + r), \qquad (14)$$

where γ, r—kernel parameters.

As suggested in library documentation, data have been normalized to [-1,1] range and optimization of parameters γ ($\gamma = 2^{-15}, 2^{-14}, \ldots, 2^3$) and c ($c = 2^{-5}, 2^{-4}, \ldots, 2^{15}$) was performed for each model (Fig. 3). Unlike suggested, in presented results we did not use $grid.py$ script which provides cross-validation and parameters optimization. This method gives very promising results for considered problem, achieving easily up to 83-86% of ACC, but models found with this method turned out to be very unstable. Any random change of data (removing or adding samples) significantly decreased its accuracy.

It is very important to find a model the most possibly independent on specific learning data. Therefore, we decided to use a method similar to Jacknife [30]: for each pair c and γ parameters calculations were repeated 30 times, each time randomly excluding 30 samples of data and using cross-validation procedure (each patient was treated as a test sample while all other data was learning set) on the rest of it. This way deviation and mean value of accuracy, sensitivity and specificity were obtained, which gives an estimate on the model 'sensitivity' to data structure (it might be important when calculating on such a little data set as 109 patients). It should be mentioned that each time we refer in this paper to ACC, TPR or SPC values we mean average computed as above. The test was repeated once again for the best results, excluding the data of only 10 random patients - it shows wether extension of learning data increases or decreases accuracy and overfitting occurs. Due to the high computational complexity of proposed optimisation procedure only 3375 random models containing 2 to 14 parameters were analyzed - it took more than a week for modern 8-core Intel Core i7 based PC. Nevertheless, such little number of experiments gave satisfactory results.

To compare with LR algorithm we used data from previous article[2], where we reviewed all of the 2^{14} possible combinations of models with exactly same Jacknife and cross-validation procedure.

V. RESULTS

The most essential results are presented in Table II . To compare, in each presented model mean value of ACC, TPR and SPC were obtained with different Jacknife parameters, using both methods: LR and sigmoid SVM with LIBSVM. Where applicable we added RBF Matlab SVM implementation results (as M. SVM) from [2].

According to the assumptions in previous section the highest mean value of accuracy among SVM results gained eight-parameter model with 82.60%. Unfortunately standard deviation of ACC was 5.15, which in contrast to others was

TABLE I
SVM MODELS WITH BOTH TPR AND SPC HIGHER THAN 80%

Params count	BWEIGHT	GAGE	RESPIMV	AA	PDA	SURFACT	SPO2MEAN	SPO2DEV	LOW85	HIGH94	BPMMEAN	BPMMEAN_TR	SPO2DEV_TR	SPO2MEAN_TR	Items excluded with Jacknife	ACC	TPR	SPC	Method	ACC dev
																mean value				
8		•	•	•	•	•		•	•	•					10	82.60%	80.10%	84.37%	LIBSVM	5.15
															30	79.57%	75.84%	82.17%	LIBSVM	4.95
															10	77.49%	78.62%	76.43%	LR	1.51
															30	76.42%	76.72%	76.09%	LR	2.75
5		•	•		•						•	•			10	82.18%	83.68%	83.68%	LIBSVM	2.95
															10	81.62%	87.21%	77.47%	LR	1.51
															30	80.73%	85.99%	76.56%	LR	2.27
															30	79.79%	78.02%	81.03%	LIBSVM	3.42
11	•	•		•	•		•	•	•		•	•	•	•	10	81.41%	80.65%	82.01%	LIBSVM	3.33
															30	80.81%	75.82%	84.28%	LIBSVM	3.78
															10	79.83%	83.83%	76.90%	LR	2.22
															30	78.29%	80.05%	76.87%	LR	3.02
11		•	•	•	•	•	•	•	•	•		•	•		10	80.50%	80.17%	80.68%	LIBSVM	2.73
															30	77.26%	77.54%	76.91%	LIBSVM	3.07
															10	76.99%	80.30%	74.53%	LR	1.21
															30	76.00%	79.87%	72.71%	LR	3.00
9		•	•	•	•	•		•				•	•	•	10	80.38%	80.46%	80.31%	LIBSVM	2.65
															10	78.12%	82.49%	75.02%	LR	1.26
															30	77.58%	77.15%	77.67%	LIBSVM	4.29
															30	76.83%	83.04%	71.87%	LR	2.93

very high (STD values are presented in Table III). The TPR value was 80.10% and SPC 84.37%, which is a very good result in comparison with the fact that only five of examined SVM models achieved both parameters higher than 80% (see Table I).

Next we present generally the best ACC model which was six-parameter LR which gained 82.79% with TPR=84.20%, SPC=81.73% and standard deviation of ACC as low as 1.11. Both above models give quite good results, but only using specific algorithm (LR or SVM).

In contrast to the above fact, we present next two best five- and six-parameter models which give accuracy higher than 81% for both methods. Particularly noteworthy model is the five-parameter one - it gives respectively 82.23% for SVM and 82.59% for LR of ACC which was the best of examined five-parameter models for both methods. Although the TPR result for SVM was only 77.13%, this model seems to be a very reasonsonable choice with SPC=85.87% for SVM and TPR=84.65%, SPC=81.07% for LR. Even in that case, where standard deviation of ACC for SVM was 3.04, it was about twice higher than 1.49 for LR. An interesting similar 5-parameter model with little lower accuracy is presented in Table I.

Afterwards we made a review of the best accuracy results for each method and each model size:

- 4-parameter models - for LR we succeeded to obtain 82.01% of ACC and only 80.85% for SVM. However, this second model (bolded in Table III) draws attention

due to its simplicity, low ACC standard deviation (about 1.4) and ACC higher than 80% for both methods.

- 3-parameter models - 81.29% for LR and 80.57% for SVM are good results just as standard deviation of ACC lower than 1.5, though none of models exceeds the psychological barrier of 80% of ACC for both methods at a time.

- 2-parameter models - SVM results are unsatisfactory due to 76.01% of highest ACC and its standard deviation as high as 5.81. However, LR was able to gain 80.30% of ACC, which is quite interesting.
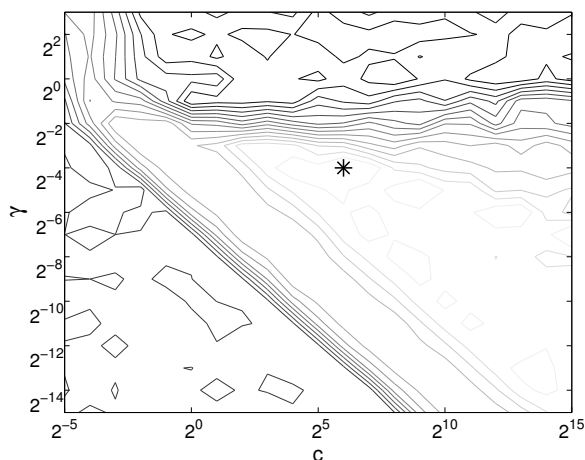
Lastly, it must be noted that full 14-parameter SVM model gained 76.86% and LR 77.55% of ACC. As a graphic example two-parameter model result was presented on Fig. 4.
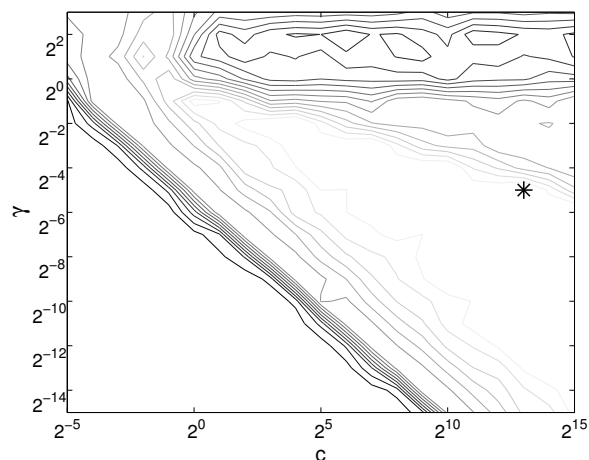
VI. DISCUSSION

The first conclusion is that SVM classification algorithm can be almost as accurate as LR and if its parameters are properly chosen it gives rewarding results, even for a complicated multi-parameter model of BPD. The best choice for such a prediction is to use the LIBSVM instead of Matlab's implementation, which gives less control on computation process. Most likely that was the reason why the bigger parameter set we used the worse results we got using Matlab[2]. Although we did not test all possible 2^{14} combinations of parameters (only 3375 random models), nonetheless looking on Table III it can be concluded that standard deviation of accuracy for SVM is much higher than for logit regression. Using bigger learning set (only 10 samples excluded) for best results it reaches even

TABLE II
MODELS AND METHODS ACCURACY COMPARISON

Params count	BWEIGHT	GAGE	RESPIMV	AA	PDA	SURFACT	SPO2MEAN	SPO2DEV	LOW85	HIGH94	BPMMEAN	BPMMEAN_TR	SPO2DEV_TR	SPO2MEAN_TR	Items excluded with Jacknife	ACC (mean value)	TPR (mean value)	SPC (mean value)	Method	Model comment
8		•	•	•	•	•		•	•	•					10	**82.60%**	**80.10%**	84.37%	**LIBSVM**	best LIBSVM
															30	79.57%	75.84%	82.17%	LIBSVM	
															10	77.49%	78.62%	76.43%	LR	
															30	76.42%	76.72%	76.09%	LR	
6		•		•	•	•					•	•			10	**82.79%**	**84.20%**	**81.73%**	**LR**	best LR
															30	80.85%	82.72%	79.36%	LR	
															30	78.49%	72.35%	82.78%	LIBSVM	
															10	78.22%	73.38%	81.77%	LIBSVM	
															10	70.01%	64.56%	74.01%	M.SVM	
															30	69,00%	61.91%	74.00%	M.SVM	
6	•	•			•	•		•			•				10	82.67%	87.50%	79.09%	LR	6-feature both methods ACC > 81%
															30	81.12%	85.78%	77.62%	LR	
															10	81.50%	77.98%	84.04%	LIBSVM	
															30	78.22%	72.38%	82.30%	LIBSVM	
															10	70.48%	65.77%	73.83%	M.SVM	
															30	69.90%	64.58%	73.69%	M.SVM	
5		•		•		•					•	•			10	**82.59%**	**84.65%**	**81.07%**	**LR**	5-feature best LR &SVM
															10	**82.23%**	**77.13%**	**85.87%**	**LIBSVM**	
															30	81.46%	81.53%	81.30%	LR	
															30	80.46%	74.31%	84.82%	LIBSVM	
															10	72.10%	64.12%	77,88%	M.SVM	
															30	71.40%	63.94%	76.69%	M.SVM	
4		•		•		•					•				10	82.01%	84.38%	80.34%	LR	4-feature best LR
															30	80.64%	80.08%	81.02%	LR	
															10	78.78%	72.96%	83.07%	LIBSVM	
															30	77.89%	72.25%	81.97%	LIBSVM	
															10	75.38%	71.32%	78.31%	M.SVM	
															30	74.68%	69.58%	78.16%	M.SVM	
4		•				•					•	•			10	80.85%	71.95%	87.32%	LIBSVM	4-feature best LIBSVM
															30	80.35%	71.11%	86.96%	LIBSVM	
															10	80.19%	73.27%	85.07%	LR	
															30	79.90%	74.31%	83.94%	LR	
3		•				•			•						10	81.29%	88.70%	75.90%	LR	3-feature best LR, best M.SVM
															30	81.05%	88.52%	75.34%	LR	
															10	80.15%	78.73%	81.17%	M.SVM	
															10	79.83%	78.51%	80.77%	LIBSVM	
															30	79.19%	79.84%	78.71%	M.SVM	
															30	79.02%	77.73%	79.68%	LIBSVM	
3		•				•		•							10	80.57%	78.83%	81.82%	LIBSVM	3-feature best LIBSVM
															10	79.66%	78.94%	80.19%	M.SVM	
															30	79.47%	79.70%	79.25%	LIBSVM	
															30	79.43%	79.08%	79.54%	M.SVM	
															10	79.40%	87.20%	73.57%	LR	
															30	79.32%	86.36%	73.98%	LR	
2		•				•									30	81.06%	84.39%	78.62%	LR	2-feature best LR
															10	80.30%	83.48%	78.01%	LR	
															10	73.57%	57.54%	85.22%	LIBSVM	
															30	73.22%	55.87%	85.28%	LIBSVM	
															30	71.38%	52.67%	84.98%	M.SVM	
															10	71.02%	51.68%	84.90%	M.SVM	
2		•						•							30	77.35%	72.50%	80.41%	LR	2-feature best LIBSVM
															10	76.85%	69.73%	81.95%	LR	
															10	76.01%	56.68%	90.09%	LIBSVM	
															30	73.04%	58.38%	83.77%	LIBSVM	

(a) eight-parameter model

(b) five-parameter model

Fig. 3. Parameter γ and c optimization for eight-parameter and five-parameter models bolded in Table II.

TABLE III
STANDARD DEVIATION OF MODELS ACCURACY

| Parameters count | Method | Jacknife excluded count | | | |
| | | 10 | | 30 | |
		ACC	ACC STD	ACC	ACC STD
8	LIBSVM	82.60%	5.15	79.57%	4.95
	LR	77.49%	1.51	76.42%	2.75
6	LR	82.79%	1.11	80.85%	2.52
	LIBSVM	78.22%	1.96	78.49%	2.74
6	LR	82.67%	1.19	81.12%	2.56
	LIBSVM	81.50%	4.89	78.22%	5.06
5	LR	82.59%	1.49	81.46%	2.51
	LIBSVM	82.23%	3.04	80.46%	2.44
4	LR	82.01%	1.73	80.64%	2.60
	LIBSVM	78.78%	2.68	77.89%	4.36
4	LIBSVM	**80.85%**	**1.39**	80.35%	2.28
	LR	**80.19%**	**1.43**	79.90%	2.89
3	LR	81.29%	1.74	81.05%	2.36
	LIBSVM	79.83%	1.73	79.02%	3.34
3	LIBSVM	80.57%	1.48	79.47%	3.06
	LR	79.40%	1.28	79.32%	2.30
2	LR	80.30%	1.62	81.06%	2.38
	LIBSVM	73.57%	2.40	73.22%	3.01
2	LR	76.85%	1.14	77.35%	2.41
	LIBSVM	76.01%	5.81	73.04%	2.70

5.81 while for LR it is rarely as high as 1.74. In other words, SVM fits to data very well and even minor random changes of data causes instability of results accuracy. For this reason, when we execute our test procedure for certain model few times, we get results which differ even 2%. According to our observations such an effect occurs mostly for a very high or very low parameter models. For logit regression effect has not been noticed, which may be encouraging to select that algorithm.

We also observed that for almost all cases the more data we exclude from the test results the worse accuracy and deviation we achieve (results with Jacknife exclusion of 10 samples are generally better), which is promising - it shows that overfitting does not occur and classifier is well generalizing to cases not known during learning. The exception from that rule are very high-deviation and some simple two-parameter models mentioned before. In such cases, there is a concern that because of its oversimplification or excessive complication hard learning takes place. For this reason, it seems more secure to use logit regression or four- to six-parameter model.

Analyzing sensitivity and specificity of the best results from Table II we have the following observations:

- for SVM differences between TPR or SPC and ACC are from 1.32% to 6.47%, while for LR 1.06% to 7.8% which is quite similar,
- the exceptions are 2-parameter SVM models, for which this differences were up to 19.33%,
- as mentioned before only five of all the examined SVM models achieved both parameters higher than 80%, which is not a problem for many LR models - all five are presented in Table I.

We confirmed that one of the most important risk factors mentioned in literature [5], [6], [8], [9], [28], [29], [31] is the $GAGE$ which exists in almost all (all presented in Table I and II) of the models with acceptable accuracy. Most classifiers presented in the literature consist $BWEIGHT$ and $RESPIMV$ parameters. Unexpectedly, $RESPIMV$ parameter is indeed present in SVM models in Table I with very good (over 82% of ACC) results, but it is not in any LR model worth to present. However, $BWEIGHT$-containing one was indeed on the third place with 82.67% ACC, but it was the only one in the first twenty, which is a group with ACC higher than 82%. Among the most frequently mentioned parameters there is FiO_2 which depends on the AA (Eq. 1) feature used in our work that is indeed present in the best model, but also only in five others of the best twenty. On the other hand,

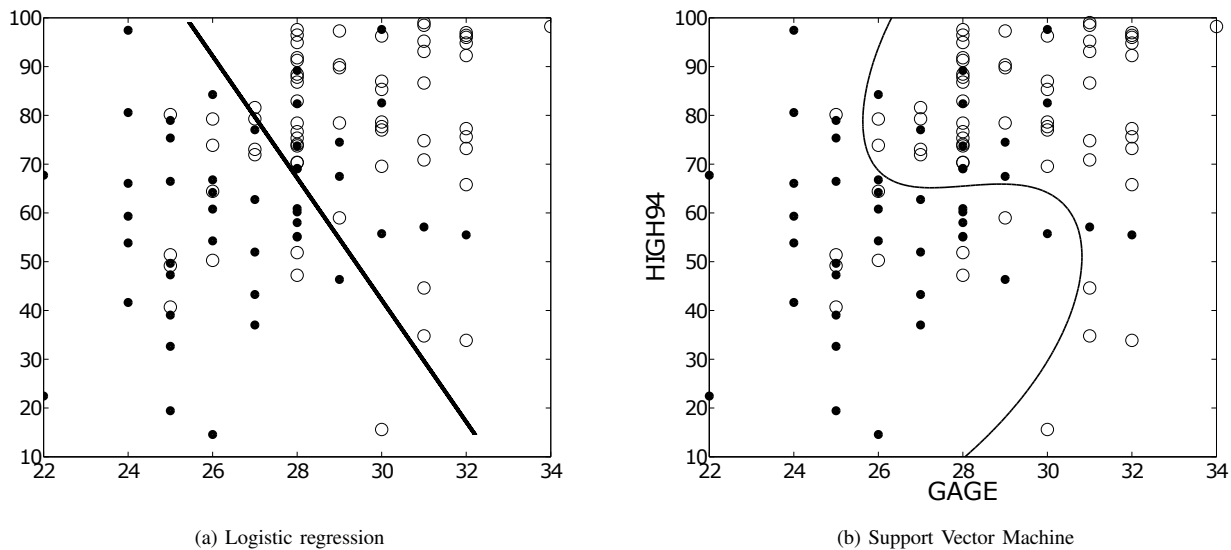(a) Logistic regression

(b) Support Vector Machine

Fig. 4. Prediction result sample for two-parameter ($GAGE$, $HIGH94$).

PDA feature appeared in 15 out of the best 20 models which is consistent with published results [8], [9], [25], [28]. The same situation occurs with $BPMMEAN$ parameter, which is the second most important factor after GAGE especially in LR models - it is in all of the first 20 models. The only one parameter related to SpO_2 which is in more than half of the best 20 classifiers is LOW85. The average importance features are $SURFACT$ and $HIGH94$ while $SPO2DEV$, $SPO2DEV\_TR$, $SPO2MEAN\_TR$ parameters seem to have even less effect on the occurrence of diseases.

As a final conclusion we confirmed [32] that prediction of BPD after 7th day of life is possible with the accuracy higher than 82%, not only with LR but also using Support Vector Machine algorithm. Results are slightly worse than in the Logit Regression method and more attention should be paid on model selection because many of them are sensitive to even small data changes. However, it can be very useful when we have limited set of parameters (above RESPIMV example), which are not so important in LR models as in SVM. Having wide scope of algorithms we can choose the one which is more suitable for our parameter set and thereby obtain better classification results. With that knowledge it is a good idea to construct expert system that would advise which algorithm and model to use having certain parameters measured.

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