# Classification of cancer pathology reports with Deep Learning methods

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#### Overview

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  - ICD-O
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  - Attention Models
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## Cancer



## Cancer registries

- ✓ Collect administrative and clinical data of a specific region
- ✓ Quantify the impact of the disease
- ✓ Provide analytic data to healthcare operators and decision makers
- Manual classification of reports



# International Classification of Diseases for Oncology (ICD-O-3)

### Topographical

```
C__ . _
```

- ✓ first two digits site
- ✓ third digit subsite
- E.g. C50.2 upper-inner quadrant (2) of breast (50)

### Morphological

\_\_\_/\_

- first four digits cell type
- ✓ fifth digit behaviour

E.g. 8140/3 is an adenocarcinoma (adeno 8140; carcinoma 3)

## Bag-of-words

## the dog is on the table

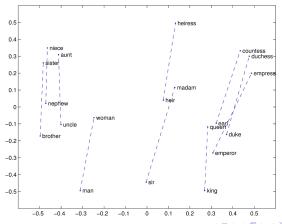


Term-Frequency Inverse-Document-Frequency (TF-IDF)

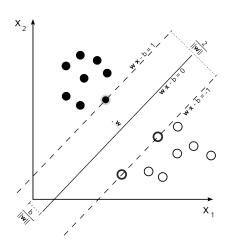
$$w_{i,j} = tf_{i,j} \times \log\left(\frac{N}{df_i}\right)$$

#### Word vectors

- Transforms words in vectors
- ✓ Unsupervised learning method
- ✓ Semantic relations encoded in vector space geometric relations



# Support Vector Machine (SVM)



## Recurrent Neural Network (RNN)

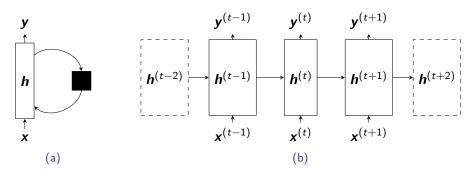


Figure: RNN, folded (a) and unfolded (b) models.

$$\mathbf{h}^{(t)} = f(\mathbf{h}^{(t-1)}, \mathbf{x}^{(t)}; \boldsymbol{\theta})$$

## Long Short-Term Memory (LSTM)

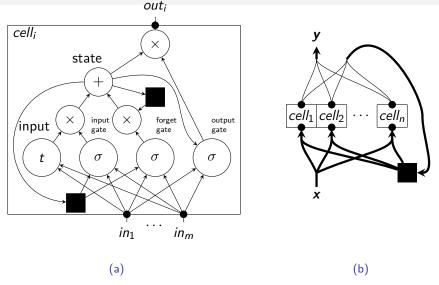


Figure: memory cell (a), and general scheme (b). The black box is a delay

# Gated Recurrent Unit (GRU)

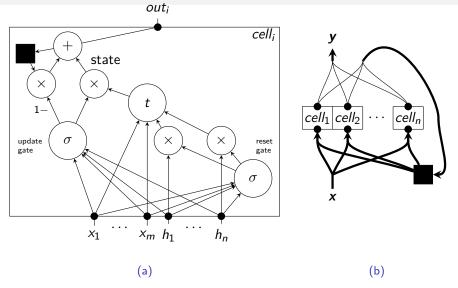
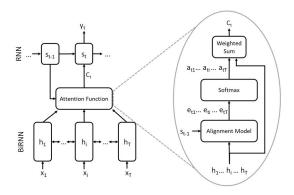


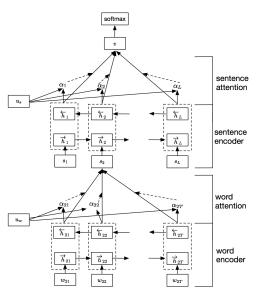
Figure: memory cell (a), and general scheme (b). The black box is a delay

#### Attention models

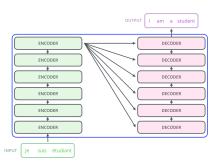
- ✓ Developed for seq-to-seq task
- ✓ State of the art in machine translation



# Hierarchical Attention Network (HAN)



# Bidirectional Encoder Representations from Transformers (BERT)



- ✓ State of the art in many NLP tasks
- Attention based
- ✓ Learn Context dependent word representations
- Pretrained on unlabeled data
- ✓ Fine tuned to specific task



# Existing works (linear classifiers)

V. Jouhet, G. Defossez, A. Burgun, P. Le Beux, P. Levillain, P. Ingrand, and V. Claveau.

Automated Classification of Free-text Pathology Reports for Registration of Incident Cases of Cancer:.

Methods of Information in Medicine, 51(3):242-251, July 2011

- ✓ SVM and Naive Bayes classifiers
- ✓ 5121 French pathology reports, 26 topographic classes and 18 morphological classes
- ✓ accuracy of 72.6% on topography and 86.4% on morphology

R. Kavuluru, I. Hands, E. B. Durbin, and L. Witt. Automatic extraction of ICD-O-3 primary sites from cancer pathology reports.

In Clinical Research Informatics AMIA symposium, 2013

- ✓ SVM, Naive Bayes, and logistic regression
- ✓ 56 426 English reports, 14, 42, and 57 topography classes
- ✓ Micro-averaged F1 measure of 90%

# Existing works (Deep Learning)

J. X. Qiu, H.-J. Yoon, P. A. Fearn, and G. D. Tourassi. Deep Learning for Automated Extraction of Primary Sites From Cancer Pathology Reports.

IEEE Journal of Biomedical and Health Informatics, 22(1):244-251, Jan. 2018

- ✓ CNN, word vectors pretrained on PubMed
- 942 breast and lung cancer English reports, 12 topography classes
- Micro-averaged F1 score of 72.2% on minimally populated, and 81.1% on well populated classes
- S. Gao, M. T. Young, J. X. Qiu, H.-J. Yoon, J. B. Christian, P. A. Fearn, G. D. Tourassi, and A. Ramanthan. Hierarchical attention networks for information extraction from cancer pathology reports.

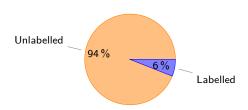
Journal of the American Medical Informatics Association, 25(3):321-330, Mar. 2018

- RNN with hierarchical attention
- ✓ Same dataset
- ✓ Micro-averaged F1 score of 80%

## Scientific questions

- Q1 Implement large scale study on machine learning applied to pathology reports, existing works are on
  - ✓ small datasets or
  - ✓ few classes
- Q2 Apply novel deep learning techniques, like attention models and BERT
- Q3 Compare classical bag-of-words techniques with newer deep learning techniques in this domain
- Q4 Compare novel attention-based and hierarchical techniques with simpler models
- Q5 Investigate the contribution and applicability of unsupervised learning techniques on uncommon text corpora
- Q6 Investigate the possibility to give interpretation to deep learning models

#### **Dataset**



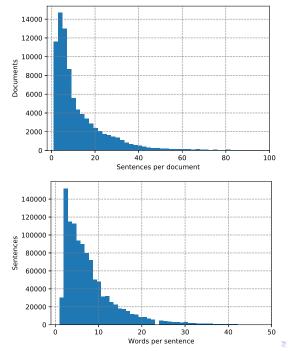
- ✓ 1592 385 anatomopathological exam results
  - From Tuscany cancer registry
  - ▶ In period 2004-2013
- ✓ 94 524 (6%) labeled

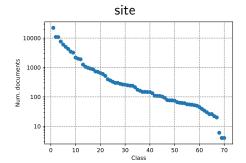
#### Structure

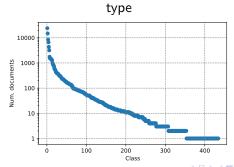
- ✓ 3 text fields: macroscopy, diagnosis, anamnesis
- ✓ field length from 0 to 1368 (quartiles 34, 62, 134)

## Preparation

- ✓ Data comes in two tables to merge:
  - 1. neoplasm table, containing administrative and clinical variables
  - 2. histology table, containing the text fields
  - there are neoplasms without histology associated
    - ★ (register have access to more data)
  - there are histologies without neoplasm associated
    - ★ (not tumor biopsies)
- ✓ The 3 text fields are merged







#### Models

```
U-SVM SVM trained on TF-IDF representations using unigrams
 B-SVM SVM trained on TF-IDF using unigrams and bigrams
 B-XGB XGBoost trained on TF-IDF using unigrams and bigrams
B-LSTM LSTM trained on TF-IDF using bigrams
G-CRNN mixed convolutional and LSTM trained on GloVe
G-LSTM LSTM trained on GloVe
 G-GRU GRU trained on GloVe
 G-ATT GRU with attention trained on GloVe
G-ATTh hierarchical GRU with attention trained on GloVe
  BERT pretrained on unlabeled data and fine tuned with labeled data
 G-MAX GRU with max pooling trained on GloVe
G-MAXh hierarchical GRU with max pooling trained on GloVe
G-MAXi GRU with max pooling, in interpretable setting, trained on GloVe
 G-ATTi GRU with attention, in interpretable setting, trained on GloVe
```

#### B-LSTM, G-CRNN, G-LSTM

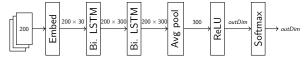


Figure: Scheme for *B-LSTM* model.

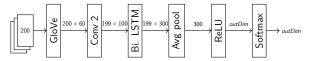


Figure: Scheme for *G-CRNN* model.

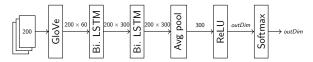


Figure: Scheme for *G-LSTM* model.

## G-GRU, G-ATT, G-MAX

#### Plain model

$$e_{t} = E(x_{t}; \theta^{e})$$

$$h_{t}^{f} = F(e_{t}, h_{t-1}^{f}; \theta^{f})$$

$$h_{t}^{r} = R(e_{t}, h_{t+1}^{r}; \theta^{r})$$

$$u_{t} = G(h_{t}; \theta^{h})$$

$$\phi = A(\mathbf{u}; \theta^{a})$$

$$f(\mathbf{x}) = g(\phi; \theta^{c})$$

- $\checkmark \phi = (h_T^f, h_1^r)$  (in this case G is the identity function)
- $\checkmark \phi = \sum_t a_t(\mathbf{u}; \theta^a) u_t$ ,  $a_t(\mathbf{u}; \theta^a) = \frac{e^{\langle c, c_t \rangle}}{\sum_{\cdot} e^{\langle c, c_t \rangle}}$ ,  $c_t = C(\mathbf{u}; \theta^a)$
- $\checkmark \phi_i = \max_t u_{i,t}$

## G-ATTi, G-MAXi

### Interpretable model

$$e_t = E(x_t; \theta^e)$$

$$h_t^f = F(e_t, h_{t-1}^f; \theta^f)$$

$$h_t^r = R(e_t, h_{t+1}^r; \theta^r)$$

$$u_t = G(h_t; \theta^h)$$

$$f(\mathbf{x}) = A(\mathbf{u}; \theta^a)$$

$$m{arphi}$$
  $\phi = \sum_t a_t(m{u}; \theta^a) u_t$ ,  $a_t(m{u}; \theta^a) = \frac{e^{\langle c, c_t \rangle}}{\sum_i e^{\langle c, c_i \rangle}}$ ,  $c_t = C(m{u}; \theta^a)$ 

 $\checkmark \phi_j = \max_t u_{j,t}$ 

## G-ATTh, G-MAXh

#### Hierarchical model

$$e_{s,t} = E(x_{s,t}; \theta^e)$$

$$h_{s,t}^f = F(e_{s,t}, h_{s,t-1}^f; \theta^f)$$

$$h_{s,t}^r = R(e_{s,t}, h_{s,t+1}^r; \theta^r)$$

$$u_{s,t} = G(h_{s,t}; \theta^h)$$

$$\phi_s = A(\mathbf{u}_s; \theta^a)$$

$$\bar{h}_s^f = \bar{F}(\phi_s, \bar{h}_{s-1}^f; \bar{\theta}^f)$$

$$\bar{h}_s^r = \bar{R}(\phi_s, \bar{h}_{s+1}^r; \bar{\theta}^r)$$

$$\bar{\phi} = \bar{A}(\bar{\mathbf{h}}; \bar{\theta}^a)$$

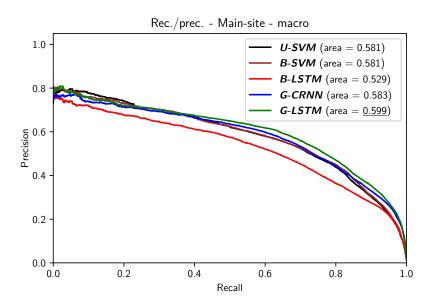
$$f(\mathbf{x}) = g(\bar{\phi}; \theta^c)$$

#### Answered questions

- Q1 Implement large scale study on deep learning applied to pathology reports
- Q3 Compare classical bag-of-words techniques with newer deep learning techniques in this domain
- Q5 Investigate the contribution and applicability of unsupervised learning techniques on uncommon text corpora
  - ✓ 10-fold cross validation
  - ✓ All tasks (main site, site+subsite, type, behavior)

Figure: Results for Main-site task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		$89.8 \pm 2.0$	$89.8 \pm 2.0$	$88.6 \pm 2.0$	$90.0 \pm 1.6$	$90.5 \pm 1.6$
kappa		$88.5 \pm 2.2$	$88.6 \pm 2.3$	$87.2 \pm 2.3$	$88.9 \pm 1.8$	$89.3 \pm 1.8$
MAP	s	$93.0\pm1.5$	$93.0\pm1.5$	$92.2\pm1.5$	$93.5\pm1.2$	$93.8 \pm 1.1$
MAP	С	$61.6\pm3.9$	$61.3 \pm 4.0$	$55.7 \pm 3.7$	$62.7 \pm 3.5$	$64.1 \pm 4.1$
pre.	ma.	$65.5 \pm 4.8$	$64.7 \pm 3.2$	$55.0 \pm 2.8$	$61.5 \pm 3.4$	$61.8 \pm 3.7$
pie.	we.	$88.7 \pm 2.0$	$88.8 \pm 2.0$	$87.8 \pm 1.8$	$89.2 \pm 1.6$	$89.5 \pm 1.7$
rec.	ma.	$55.7 \pm 4.1$	$54.7 \pm 3.8$	$51.6 \pm 3.2$	$56.5 \pm 3.0$	$58.1 \pm 3.5$
Tec.	we.	$89.8 \pm 2.0$	$89.8 \pm 2.0$	$88.6 \pm 2.0$	$90.0\pm1.6$	$90.5 \pm 1.6$
f1s.	ma.	$58.4 \pm 4.1$	$57.5\pm3.6$	$52.1 \pm 3.1$	$57.0 \pm 2.7$	$58.2 \pm 3.3$
115.	we.	$88.9 \pm 2.0$	$89.0 \pm 2.1$	$88.0 \pm 2.0$	$89.3 \pm 1.6$	$89.7 \pm 1.7$

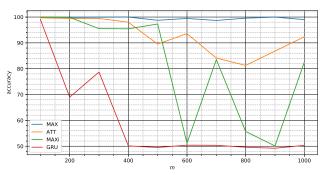


## Preliminary attention VS max

#### Answered questions

- Q4 Compare novel attention model with simpler max pooling
- Q6 Investigate the possibility to give interpretation to deep learning models
- ✓ Artificial dataset
- ✓ Same-size models

## Preliminary attention VS max



0 9 2 1 8 4 2 8 9 1 4 6 8 8 6 6 8 7 3 0 2 5 9 7 9 5 8 2 4 9 5 5 6 5 1 7 6 3 2 2 2 131 2 5 0 8 9 5 4 0 3 2 3 0 6 0 0 8 6 7 9 1 6 4 0 5 7 0 6 4 6 0 6 1 5 4 3 2 5 2 6 7 4 2 5 2 5 8 9 9 5 7 6 5 4 2 7 9

5 3 6 9 0 9 1 8 0 1 5 4 5 0 4 7 1 6 2 3 2 9 2 6 8 8 2 6 1 1 2 3 6 3 6 4 4 6 6 8 9 9 3 5 6 4 2 4 7 0 3 3 8 5 5 4 6 9 2 3 2 9 5 5 3 5 7 8 0 4 7 1 3 6 6 3 8 8 8 8 6 9 6 0 6 4015 4 9 5 5 5 9 7 6 5 8 4

## Attention VS max, hierarchical VS plain

#### Answered questions

- Q1 Implement large scale study on deep learning applied to pathology reports
- Q2 Apply novel deep learning techniques, like attention models and BERT
- Q3 Compare classical bag-of-words techniques with newer deep learning techniques in this domain
- Q4 Compare novel attention-based and hierarchical techniques with simpler models
- Q6 Investigate the possibility to give interpretation to deep learning models
- ✓ Temporal setting
- On main site and type tasks
- ✓ Different difficulty classes

## Attention VS max, hierarchical VS plain

	Topography			Morphology				
	Acc.	Top 3	Top 5	MacroF1	Acc.	Top 3	Top 5	Macro F1
U-SVM	89.7	95.9	96.8	60.0	82.4	94.0	95.6	53.7
B-XGB	89.1	95.8	97.2	58.0	84.1	94.4	96.5	59.6
G-GRU	89.9	96.5	97.7	58.3	83.3	94.6	96.6	55.2
BERT	89.9	96.3	97.8	56.6	84.3	93.2	94.9	51.1
G-MAXi	88.0	95.4	96.2	46.1	73.4	91.0	93.6	31.3
G-MAXh	89.9	96.2	97.8	58.8	83.7	94.4	96.4	54.5
G-ATTh	89.9	96.3	97.7	58.0	83.7	94.4	96.2	57.5
G-MAX	90.3	96.6	98.1	61.9	84.6	95.0	96.9	59.2
G-ATT	90.1	96.2	97.6	60.0	84.8	94.9	96.9	61.3

		Topography		Morphology			
	easy	avg.	hard	easy	avg.	hard	
	(1000 < s)	$(100 < s \le 1000)$	$(s \le 100)$	(1000 < s)	$(100 < s \le 1000)$	$(s \le 100)$	
	(4 cls)	(18 cls)	(39 cls)	(5 cls)	(18 cls)	(111 cls)	
U-SVM	95.7	86.9	50.9	90.5	68.6	48.4	
B-XGB	95.6	86.4	48.2	92.0	72.4	54.8	
G-GRU	96.1	72.2	48.0	91.4	71.6	49.7	
BERT	95.7	73.2	44.9	92.9	74.4	43.9	
G-MAXi	95.0	66.6	31.4	87.1	41.9	25.1	
G-MAXh	95.8	72.4	48.8	92.7	71.8	48.8	
G-ATTh	96.0	73.1	47.1	91.9	72.3	52.6	
G-MAX	96.0	73.3	53.1	92.7	72.3	53.8	
G-ATT	96.0	73.1	50.3	92.8	72.3	56.7	

## Interpretability

T	D =1====+ 6	y polonost b
Уi	Relevant $\mathbf{h}_{i,j}$	$x_{i,j}$ , relevant $h_{i,j}$ DISOMOGENICITA ' DIFFUSE . PSA NON PERVENUTO . ADENOCARCINOMA
61	61 (PROSTATE GLAND)	PROSTATICO A GRADO DI DIFFERENZIAZIONE MEDIO - BASSO ( GLEASON 3 + 4 ) NEI PRELIEVI DI CUI AI NN . 2 E 3 . AGOBIOPSIA DELLA PROSTATA : 1 ) 1 PRELIEVO LL DX . 2 ) 2 PRELIEVI ML DX . 3 ) 2 PRELIEVI M DX . 4 ) 1 PRELIEVO M SX . 5 ) 2 PRELIEVI ML SX . 6 ) 1 PRELIEVO LL SX . 7 ) 1 PRELIEVO TRANSIZIONALE SX . 8 ) 1 PRELIEVO TRANSIZIONALE DX .
20	20 (RECTUM) 21 (ANUS AND ANAL CANAL)	ISOLATI FRAMMENTI RIFERIBILI AD ADENOMA TUBULARE INTESTINALE DI ALTO GRADO . FRAMMENTI ( NR . 2 ) DI POLIPO PEDUNCOLATO A 20 CM DALL ' ORIFIZIO ANALE . ( ESEGUITA COLORAZIONE EMATOSSILINA - EOSINA ) .
34	34 (BRONCHUS AND LUNG) 56 (OVARY) 67 (BLADDER) 80 (UNKNOWN PRIMARY SITE)	VERSAMENTO PLEURICO SX DI N . D . D . E ADDENSAMENTI POLMONARI DI N . D . D . , NODULI PARETE ADDOMINALE . INFILTRAZIONE CANCERIGNA DEGLI STROMI CONNETTIVO - ADIPOSI . IMMUNOISTOCHIMICA : CK7 + , CK20 - , TTF - 1 - , PROTEINA S - 100 LESIONE DI CM 2 , 0 X 1 , 3 X 0 , 7 . 1 - 2 ) SEZIONI SERIATE .

## Interpretability

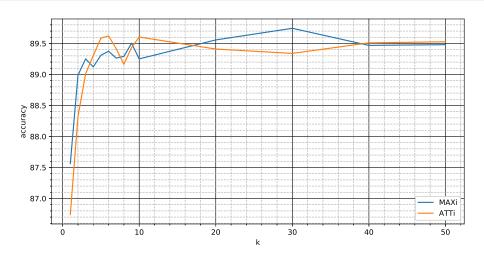


Figure: Training of a plain GRU model on a dataset created using G-MAXi and G-ATTi to keep the first k words

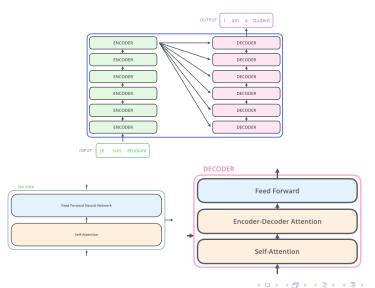
#### Conclusions

- ✓ We effectively implemented a large scale study on classical machine learning and novel deep learning methods applied to pathology reports
- ✓ In this context, bag-of-words techniques are not considerably worst than deep learning
- ✓ Hierarchical model are not beneficial
- Attention models are almost equivalent to a simpler element-wise max pooling model
- ✓ Word vectors can be effectively employed
- ✓ We can implement interpretable models without catastrophic loss

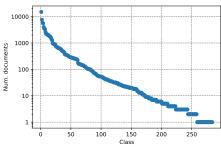


Questions? Thank you!

# Bidirectional Encoder Representations from Transformers (BERT)



#### site+subsite



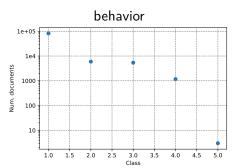


Figure: Results for Full-site task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		$68.4 \pm 2.3$	$68.7 \pm 2.0$	$67.4 \pm 1.7$	$70.1\pm2.1$	<u>70.9</u> ± 2.0
kappa		$66.5 \pm 2.4$	$66.8 \pm 2.1$	$65.6\pm1.7$	$68.4 \pm 2.2$	$69.3 \pm 2.1$
MAP	s	$78.4 \pm 1.9$	$78.4 \pm 1.7$	$78.5 \pm 1.3$	$80.6 \pm 1.4$	$81.3 \pm 1.4$
MAP	С	$43.1\pm2.2$	$43.4 \pm 2.2$	$36.8 \pm 2.3$	$42.9\pm2.6$	$45.0 \pm 2.0$
pre.	ma.	$41.4\pm1.6$	$41.6 \pm 1.5$	$33.0 \pm 2.8$	$38.7 \pm 3.1$	$39.8 \pm 2.3$
pie.	we.	$66.3 \pm 1.9$	$67.1 \pm 1.7$	$66.1 \pm 1.3$	$68.8 \pm 1.9$	$69.5 \pm 1.5$
rec.	ma.	$35.7\pm1.9$	$35.1\pm2.1$	$32.0 \pm 2.5$	$36.6 \pm 3.0$	$38.0 \pm 2.2$
Tec.	we.	$68.4 \pm 2.3$	$68.7 \pm 2.0$	$67.4 \pm 1.7$	$70.1\pm2.1$	<u>70.9</u> ± 2.0
f1s.	ma.	$36.6\pm1.5$	$36.4 \pm 1.7$	$31.2\pm2.3$	$35.9 \pm 2.9$	$37.3 \pm 2.1$
115.	we.	$66.2 \pm 2.1$	$66.8 \pm 1.8$	$66.0 \pm 1.3$	$68.5 \pm 2.0$	$69.5 \pm 1.8$

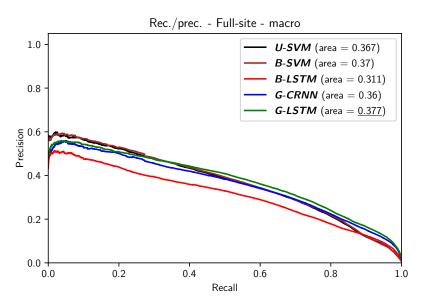


Figure: Results for Type task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		$81.9 \pm 1.9$	$82.9 \pm 2.0$	$82.8 \pm 1.4$	$84.6 \pm 1.4$	$84.9 \pm 1.5$
kappa		$79.5 \pm 2.2$	$80.7\pm2.3$	$80.6\pm1.6$	$82.7\pm1.6$	$83.0 \pm 1.7$
MAP	s	$87.8 \pm 1.3$	$88.6 \pm 1.4$	$88.7 \pm 1.0$	$90.3 \pm 0.9$	$90.6 \pm 1.0$
MAP	С	$62.4\pm1.6$	$64.4\pm1.8$	$55.1 \pm 3.1$	$64.2\pm1.9$	$\underline{65.9} \pm 1.9$
pre.	ma.	$56.1 \pm 2.4$	$58.3 \pm 1.9$	$47.0 \pm 3.3$	$56.5\pm1.8$	$57.0 \pm 2.6$
pie.	we.	$80.3 \pm 1.8$	$81.8\pm1.9$	$82.0 \pm 1.3$	$84.1 \pm 1.3$	$84.3 \pm 1.5$
rec.	ma.	$51.1 \pm 2.6$	$52.2 \pm 2.2$	$47.0 \pm 2.6$	$56.8 \pm 2.2$	$58.6 \pm 2.0$
Tec.	we.	$81.9 \pm 1.9$	$82.9 \pm 2.0$	$82.8 \pm 1.4$	$84.6 \pm 1.4$	$84.9 \pm 1.5$
f1s.	ma.	$51.4\pm2.5$	$52.9\pm1.9$	$45.0\pm2.9$	$54.6\pm1.9$	$55.5 \pm 2.3$
115.	we.	$80.4 \pm 2.0$	$81.7 \pm 2.0$	$81.9 \pm 1.3$	$83.8 \pm 1.4$	$84.0 \pm 1.5$

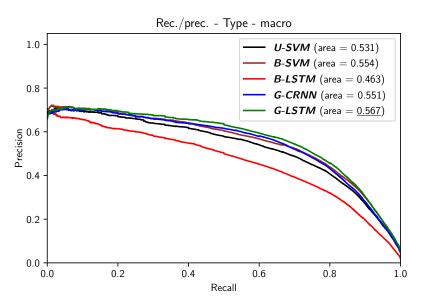
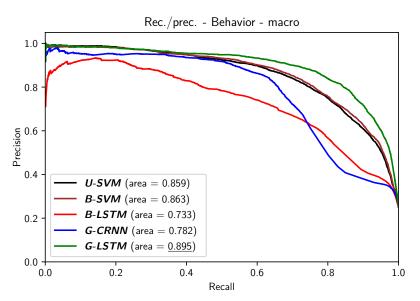


Figure: Results for Behavior task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		$95.9 \pm 1.0$	$96.0 \pm 1.1$	$94.1 \pm 3.0$	$94.4 \pm 4.2$	$96.5 \pm 0.8$
kappa		$82.3 \pm 4.6$	$82.8 \pm 5.0$	$70.4 \pm 25.5$	$67.6 \pm 35.9$	85.6 ± 3.4
MAPs		$97.7 \pm 0.6$	$97.8 \pm 0.6$	$96.6\pm1.8$	$96.8 \pm 2.5$	$98.1 \pm 0.5$
MAP	С	$85.4 \pm 5.9$	$85.9 \pm 5.7$	$71.4\pm18.4$	$75.5 \pm 26.4$	$89.5 \pm 4.2$
pre.	ma.	$87.0 \pm 5.0$	$87.9 \pm 4.8$	$69.9 \pm 19.9$	$72.7 \pm 27.1$	$85.5 \pm 4.0$
pre.	we.	$95.8 \pm 1.1$	$95.9 \pm 1.2$	$92.6 \pm 6.4$	$92.1 \pm 9.0$	$96.6 \pm 0.8$
rec.	ma.	$78.6 \pm 7.3$	$78.6 \pm 7.4$	$67.6 \pm 17.4$	$72.1 \pm 25.4$	$85.9 \pm 4.9$
Tec.	we.	$95.9 \pm 1.0$	$96.0 \pm 1.1$	$94.1 \pm 3.0$	$94.4 \pm 4.2$	$96.5 \pm 0.8$
f1s.	ma.	$81.7 \pm 6.3$	$82.0 \pm 6.3$	$68.0 \pm 18.5$	$72.1 \pm 26.0$	$85.5 \pm 4.2$
115.	we.	$95.8 \pm 1.1$	$95.9 \pm 1.2$	$93.2 \pm 4.8$	$93.1 \pm 6.7$	$96.5 \pm 0.8$



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