Classification of cancer pathology reports with Deep Learning methods

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Overview

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 - Cancer registries
 - ICD-O
- 2 Machine Learning
 - Representations
 - Classic models
 - RNN
 - Attention Models
- 3 Scientific questions
- Materials and Methods
 - Datasets
 - Models
- **5** Experiments
 - Bag-of-words VS word vectors, SVM VS deep learning
 - Preliminary attention VS max
 - Attention VS max, hierarchical VS plain
- 6 Conclusions



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

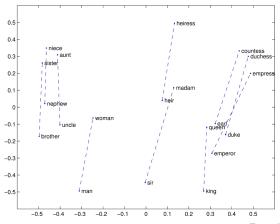


Term-Frequency Inverse-Document-Frequency (TF-IDF)

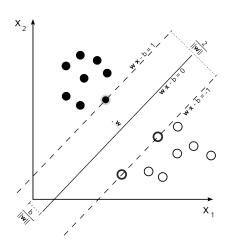
$$w_{i,j} = tf_{i,j} \times \log\left(\frac{N}{df_i}\right)$$

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)

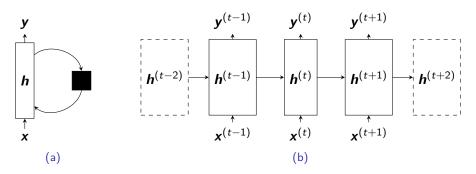


Figure: RNN, folded (a) and unfolded (b) models.

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

Long Short-Term Memory (LSTM)

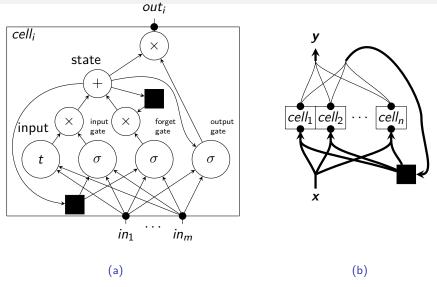


Figure: memory cell (a), and general scheme (b). The black box is a delay

Gated Recurrent Unit (GRU)

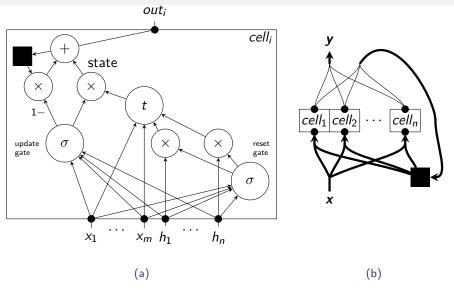
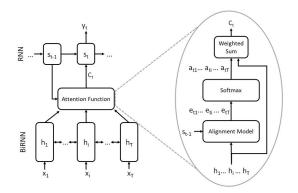


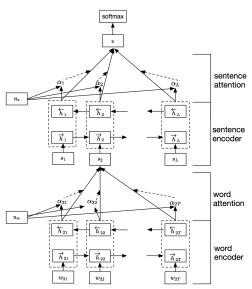
Figure: memory cell (a), and general scheme (b). The black box is a delay

Attention models

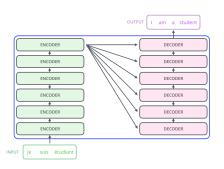
- ✓ Developed for seq-to-seq task
- ✓ State of the art in machine translation



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 (forthcoming), 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.

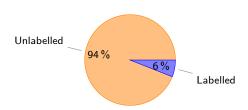
Journal of the American Medical Informatics Association, 25(3):321-330, Mar. 2018

- 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



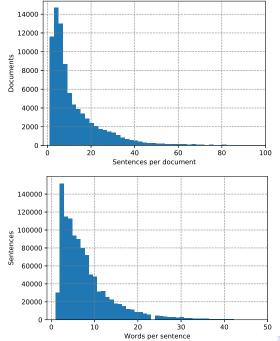
- ✓ 1592385 anatomopathological exam results
 - From Tuscany cancer registry
 - ► In period 2004-2013
- ✓ 94 524 (6%) labeled

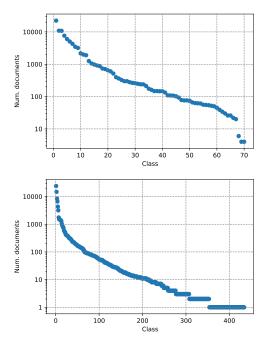
Structure

- ✓ 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

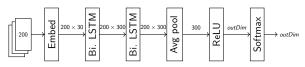


Figure: Scheme for **B-LSTM** model.

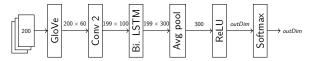


Figure: Scheme for *G-CRNN* model.

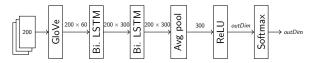


Figure: Scheme for *G-LSTM* model.

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)
- $\checkmark \phi = \sum_t a_t(\boldsymbol{u}; \theta^a) u_t, \ a_t(\boldsymbol{u}; \theta^a) = \frac{e^{\langle c, c_t \rangle}}{\sum_i e^{\langle c, c_i \rangle}}, \ c_t = C(\boldsymbol{u}; \theta^a)$
- $\checkmark \phi_j = \max_t u_{j,t}$

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

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

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

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

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

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

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

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

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

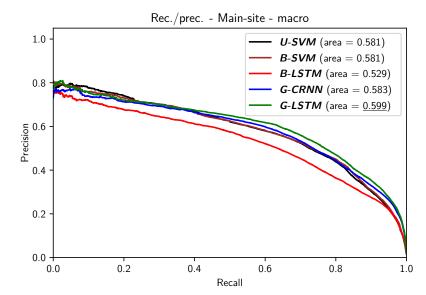
$$f(\mathbf{x}) = g(\bar{\phi}; \theta^c)$$

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, subsite, type, behavior)

Table: Results for Main-site task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		89.8 ± 2.0	89.8 ± 2.0	88.6 ± 2.0	90.0 ± 1.6	90.5 ± 1.6
kappa		88.5 ± 2.2	88.6 ± 2.3	87.2 ± 2.3	88.9 ± 1.8	89.3 ± 1.8
MAP	s	93.0 ± 1.5	93.0 ± 1.5	92.2 ± 1.5	93.5 ± 1.2	93.8 ± 1.1
MAP	С	61.6 ± 3.9	61.3 ± 4.0	55.7 ± 3.7	62.7 ± 3.5	64.1 ± 4.1
pre.	ma.	65.5 ± 4.8	64.7 ± 3.2	55.0 ± 2.8	61.5 ± 3.4	61.8 ± 3.7
pie.	we.	88.7 ± 2.0	88.8 ± 2.0	87.8 ± 1.8	89.2 ± 1.6	89.5 ± 1.7
rec.	ma.	55.7 ± 4.1	54.7 ± 3.8	51.6 ± 3.2	56.5 ± 3.0	58.1 ± 3.5
Tec.	we.	89.8 ± 2.0	89.8 ± 2.0	88.6 ± 2.0	90.0 ± 1.6	90.5 ± 1.6
f1s.	ma.	58.4 ± 4.1	57.5 ± 3.6	52.1 ± 3.1	57.0 ± 2.7	58.2 ± 3.3
	we.	88.9 ± 2.0	89.0 ± 2.1	88.0 ± 2.0	89.3 ± 1.6	89.7 ± 1.7

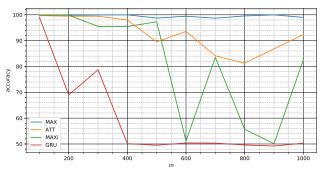


Preliminary attention VS max

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 1312 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

93564247033855469232955357804713663888869 606401549555976584

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

	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	18 (COLON) 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

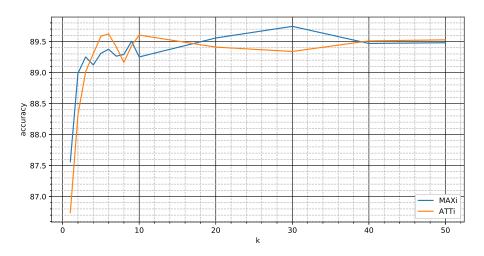


Figure: Training of a plain GRU model on a dataset created using G-MAXi and G-ATTi to keep the first k words

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)

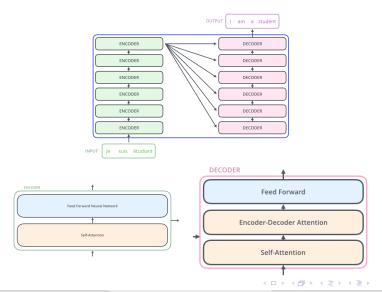


Table: Results for Full-site task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		68.4 ± 2.3	68.7 ± 2.0	67.4 ± 1.7	70.1 ± 2.1	<u>70.9</u> ± 2.0
kappa		66.5 ± 2.4	66.8 ± 2.1	65.6 ± 1.7	68.4 ± 2.2	69.3 ± 2.1
MAP	s	78.4 ± 1.9	78.4 ± 1.7	78.5 ± 1.3	80.6 ± 1.4	81.3 ± 1.4
MAP	С	43.1 ± 2.2	43.4 ± 2.2	36.8 ± 2.3	42.9 ± 2.6	<u>45.0</u> ± 2.0
pre.	ma.	41.4 ± 1.6	41.6 ± 1.5	33.0 ± 2.8	38.7 ± 3.1	39.8 ± 2.3
pre.	we.	66.3 ± 1.9	67.1 ± 1.7	66.1 ± 1.3	68.8 ± 1.9	69.5 ± 1.5
rec.	ma.	35.7 ± 1.9	35.1 ± 2.1	32.0 ± 2.5	36.6 ± 3.0	38.0 ± 2.2
Tec.	we.	68.4 ± 2.3	68.7 ± 2.0	67.4 ± 1.7	70.1 ± 2.1	70.9 ± 2.0
f1s.	ma.	36.6 ± 1.5	36.4 ± 1.7	31.2 ± 2.3	35.9 ± 2.9	37.3 ± 2.1
	we.	66.2 ± 2.1	66.8 ± 1.8	66.0 ± 1.3	68.5 ± 2.0	69.5 ± 1.8

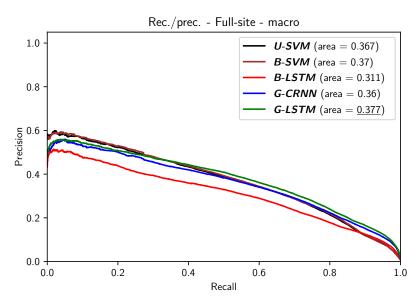


Table: Results for Type task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		81.9 ± 1.9	82.9 ± 2.0	82.8 ± 1.4	84.6 ± 1.4	84.9 ± 1.5
kappa		79.5 ± 2.2	80.7 ± 2.3	80.6 ± 1.6	82.7 ± 1.6	83.0 ± 1.7
MAP	s	87.8 ± 1.3	88.6 ± 1.4	88.7 ± 1.0	90.3 ± 0.9	90.6 ± 1.0
MAP	С	62.4 ± 1.6	64.4 ± 1.8	55.1 ± 3.1	64.2 ± 1.9	65.9 ± 1.9
pre.	ma.	56.1 ± 2.4	58.3 ± 1.9	47.0 ± 3.3	56.5 ± 1.8	57.0 ± 2.6
pie.	we.	80.3 ± 1.8	81.8 ± 1.9	82.0 ± 1.3	84.1 ± 1.3	84.3 ± 1.5
rec.	ma.	51.1 ± 2.6	52.2 ± 2.2	47.0 ± 2.6	56.8 ± 2.2	58.6 ± 2.0
Tec.	we.	81.9 ± 1.9	82.9 ± 2.0	82.8 ± 1.4	84.6 ± 1.4	84.9 ± 1.5
f1s.	ma.	51.4 ± 2.5	52.9 ± 1.9	45.0 ± 2.9	54.6 ± 1.9	55.5 ± 2.3
	we.	80.4 ± 2.0	81.7 ± 2.0	81.9 ± 1.3	83.8 ± 1.4	84.0 ± 1.5

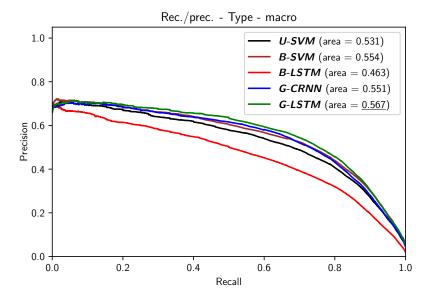
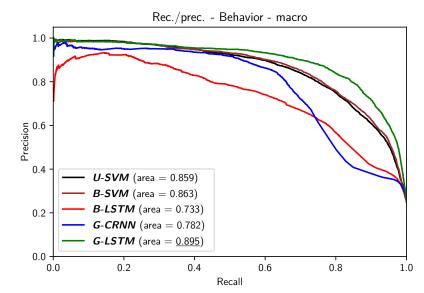


Table: Results for Behavior task.

		U-SVM	B-SVM	B-LSTM	G-CRNN	G-LSTM
accuracy		95.9 ± 1.0	96.0 ± 1.1	94.1 ± 3.0	94.4 ± 4.2	96.5 ± 0.8
kappa		82.3 ± 4.6	82.8 ± 5.0	70.4 ± 25.5	67.6 ± 35.9	<u>85.6</u> ± 3.4
MAPs		97.7 ± 0.6	97.8 ± 0.6	96.6 ± 1.8	96.8 ± 2.5	98.1 ± 0.5
MAP	С	85.4 ± 5.9	85.9 ± 5.7	71.4 ± 18.4	75.5 ± 26.4	89.5 ± 4.2
pro	ma.	87.0 ± 5.0	87.9 ± 4.8	69.9 ± 19.9	72.7 ± 27.1	85.5 ± 4.0
pre.	we.	95.8 ± 1.1	95.9 ± 1.2	92.6 ± 6.4	92.1 ± 9.0	96.6 ± 0.8
rec.	ma.	78.6 ± 7.3	78.6 ± 7.4	67.6 ± 17.4	72.1 ± 25.4	85.9 ± 4.9
Tec.	we.	95.9 ± 1.0	96.0 ± 1.1	94.1 ± 3.0	94.4 ± 4.2	96.5 ± 0.8
f1s.	ma.	81.7 ± 6.3	82.0 ± 6.3	68.0 ± 18.5	72.1 ± 26.0	85.5 ± 4.2
	we.	95.8 ± 1.1	95.9 ± 1.2	93.2 ± 4.8	93.1 ± 6.7	96.5 ± 0.8



Bibliography I

- 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.
- [2] 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.
- [3] 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 (forthcoming), 2013.
- [4] 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.