Natural Language Processing for e-Health

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LIMSI, CNRS, Université Paris-Saclay

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Plan

- 1 Introduction: LIMSI, NLP for e-Health
- 2 Information Normalization: Coding Death Certificates for Health Statistics
- Information Extraction from Social Networks for Pharmacovigilance
- 4 Human-Machine Dialogue to Train Medical Students



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LIMSI: An Interdisciplinary Laboratory for Mechanics and Information Sciences

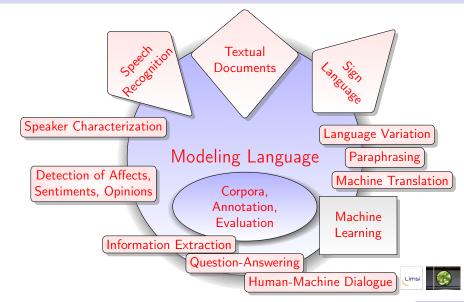
An Intramural CNRS Research Unit on the Université Paris-Saclay Campus

LIMSI's new building (currently moving in)



Human Language Processing at LIMSI

About 80 people including 30 permanent researchers



Natural Language Processing of Biomedical Text

Biomedical texts convey information and knowledge

 Natural Language Processing of these texts unlocks that information and knowledge for further computer processing



General Bibliography

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Ongoing e-Health NLP Research at LIMSI (1/3)

Information extraction from clinical text

- ANR Cabernet Building French resources for information extraction from medical text Campillos et al., 2017
- ANSM Vigi4med, PHARES Information extraction, linking to specialized entities from lay language Morlane-Hondère et al., 2016
- CépiDc collaboration ICD-10 coding with a large number of classes Lavergne et al., 2016
- De-identification MEDINA software Grouin & Névéol, 2014
- DigiCosme PhD, with CEA Temporal information extraction and event coreference Tourille et al., 2017

Information extraction from the scientific literature

- Paris-Saclay IDI PhD, with INRA Hybrid embedding of words and concepts Ferré et al., 2017
- H2020 ITN MiRoR Joint PhDs with Amsterdam U Spin detection; Text classification for systematic reviews Koroleva & Paroubek, 2017; Norman et al., 2018
- ANR MIAM Food and drug interaction Hamon et al., 2017



Ongoing e-Health NLP Research at LIMSI (2/3)

Question-answering and dialogue

- French-German ANR-DFG GoAsq (with LRI & TU Dresden) Hybrid question-answering with text and ontologies Kamath et al., 2018
- FUI Patient Genesys, SATT PVdial Human-machine dialogue with a very large concept and vocabulary space Campillos et al., 2016
- HEGP/Necker PhD QA from clinical datawarehouse A. Neuraz, A. Burgun, S. Rosset

*Activities listed in red are further presented in the present talk.



Ongoing e-Health NLP Research at LIMSI (3/3)

Text simplification

 ANR CLEAR — Lay vocabulary and expert vocabulary Grabar & Hamon, 2016

Multilingual access

- Cochrane collaboration, with LIMSI/TLP Machine translation of scientific abstracts, with a need for precision live et al., 2016
- Joint PhD with Sfax Term detection, transfert to Arabic Neifar et al., 2016
- AP-HP/Inserm PhD Multilingual terminology for interoperability Paris et al., 2018



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Coding Death Certificates for Health Statistics

Text classification: From the text of a certificate to one or mode labels (codes)

Needed in about every country for public health statistics

	 PART I. Enter the diseases, injuries, or complications that caused the death. Do not enter the mode of dying, such as cardiac or respiratory arrest, shock, or heart failure. List only one cause on each line. IMMEDIATE CAUSE (Final 				
	disease or condition	Rupture of myocardium	Mins.		
SEE INSTRUCTIONS ON OTHER SIDE	'	DUE TO (OR AS A CONSEQUENCE OF): Acute myocardial infarction	i 6 days		
	Sequentially list conditions, if any, leading to immediate	DUE TO (OR AS A CONSEQUENCE OF):	1		
	CAUSE (Disease or injury C.	Chronic ischemic heart disease	5 years		
	that initiated events resulting in death) LAST	DUE TO (OR AS A CONSEQUENCE OF):			
			i		
CAUSE OF DEATH		PERFORMED? AN (Yes or no.) CO	PERFORMED? AVAILABLE PRIOR TO		
		Yes	Yes		
	29. MANNER OF DEATH	30s. DATE OF INJURY 30b. TIME OF 30c. INJURY AT WORK? 30d. DESCRIBE HOW INJURY OCCURRED (Yes or no)	VORK? 30d. DESCRIBE HOW INJURY OCCURRED		
	XX Naturel Pending	м м			
	Suicide Could not be Homicide Determined	30e. PLACE OF INJURY—At home, farm, street, factory, office 30f. LOCATION (Street and Number or Rural Route Numb building, etc. (Specify)	er, City or Town, State)		

123.3 Rupture of cardiac wall without haemopericardium as current complication following acute myocardial infarction

(急性心筋梗塞合併症心膜血腫伴心(壁)破裂)

I21.9 Acute myocardial infarction, unspecified (急性心筋梗塞,詳細不明)





NLP Challenge: Variation and Ambiguity

Study of pneumonectomie in death certificates

= removing lung

pneumonectomie pneumectomie poumon unique lobectomie pulmonaire résection pulmonaire pneumonectomisé PNEUMECTOMISEE

cancer du poumon traité chimio et lobectomie carcinome bronchique lobaire supérieur gauche lobectomisé adénocarcinome bronchique (récidive métastatique controlatérale) avec lobectomie primitive

~

__ ICD **Z**90.2:

Acquired absence of lung [part of]

PNEUMECTONIE DROITE

BPCO SEVERE /
LOBECTOMIE MOYENNE
ET SUPERIEURE DROITE
POUR ADENOCARCINOME
lobectomie supérieure gauche



NLP Challenge: Variation

Terms for myocardial infarction in the UMLS Metathesaurus

Terme	Libellé (Variante)	Terme	Libellé (Variante)
L0027051	Myocardial Infarction (PF)	L0308108	Myocardial Infarct (PF)
L0027051	MYOCARDIAL INFARCTION (VC)	L0308108	MYOCARDIAL INFARCT (VC)
L0027051	Myocardial infarction (VC)	L0308108	Myocardial infarct (VC)
L0027051	myocardial infarction (VC)	L0308108	Myocardial Infarcts (VP)
L0027051	Myocardial Infarctions (VP)	L0308108	Infarct, Myocardial (VW)
L0027051	Infarctions (Myocardial) (VWP)	L0308108	Infarcts, Myocardial (VWP)
L0027051	Infarctions, Myocardial (VWP)	L0308108	INFARCT MYOCARDIAL (VCW)
L0027051	Infarction, myocardial (VCW)	L0308108	Infarct myocardial (VCW)
L0027051	Infarction;myocardial (VCW)	L0873038	Myocardial necrosis (PF)
L0027051	Infarction, Myocardial (VW)	L1007490	Attack coronary (PF)
L0027051	Myocardial infarction, NOS (VO)	L1007490	ATTACK CORONARY (VC)
L0284112	Heart attack, NOS (PF)	L1022045	Myocardial infarction syndrome (P
L0284112	HEART ATTACK (VO)	L1024662	Necrosis myocardium (PF)
L0284112	Heart Attacks (VO)	L1024662	NECROSIS MYOCARDIUM (VC)
L0284112	Heart attack (VO)	L1024664	Myocardial necrosis syndrome (PF
L0284112	heart attack (VO)	L1088741	CT - Coronary thrombosis (PF)
L0284112	ATTACK HEART (NOS) (VCW)	L0586860	MI - Myocardial infarction (PF)
L0284112	Attack heart (NOS) (VCW)	L0026809	mi <1> (PF)
L0306107	Infarction of heart, NOS (PF)	L0026809	MI (vo)
L0306107	HEART INFARCTION (VO)	L0026809	mi (VO)
L0306107	Infarction, heart (VO)	L1217656	AMI <3> (PF)
L0306107	Infarction;heart (VO)	L1217656	AMI (VO)
L0379717	Cardiac infarction, NOS (PF)	L1374411	Cardiopathy necrotic (PF)
			14 / 39

NLP Challenge: Contextual Coding

• The same input may express two different overall phenomena

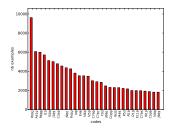
Certificate (FR)	choc hémorragique	R571
Certificate (FR)	hémorragie digestive	K922
Certificate (FR)	Cirrhose hépatique alcoolique	K703
English gloss	hemorrhagic shock	R571
English gloss	gastrointestinal bleeding	K922
English gloss	alcoholic liver cirrhosis	K703
Certificate (FR)	choc hémorragique	T794
Certificate (FR)	polytraumatisme	T07
Certificate (FR)	accident de la voie publique	V892
English gloss	hemorrhagic shock	T794
English gloss	polytrauma	T07
English gloss	traffic accident	V892

- R571 Hypovolaemic shock < R57 Shock, not elsewhere classified
- T79.4 Traumatic shock < T79 Certain early complications of trauma, not elsewhere classified



NLP Challenges

- Large number of classes + Zipf's law
 - >3,000 disease codes in dataset



ightarrow use both supervised learning (frequent) and dictionary (rare)

First Normalize Text as Much as Possible

First transform input string to reduce variation

- Downcase characters
 - AVC hémorragique → avc hémorragique
- * Split line into 'words' (tokens) (avc, hémorragique)
- Remove 'stop words' (of the and...)
- Remove diacritics
 - hémorragique → hemorragique
 - Behçet sévère → Behcet severe
- Fix some spelling errors based on training corpus and dictionaries
 - syndrome:4526 ← sydrome:15
 - hemorragique:2573 ← hemorragqiue:3
- Stem each token
 - hemorragie, digestive → hemorrag, digest
 - avc, hemorragique → avc, hemorrag



Then Extract Text Features for Supervised Classifier

Features computed from the normalized text of a death certificate

avc hemorrag

Encoding a sequence of words as a set of...

- Word N-grams
 - u: unigrams: 'avc', 'hemorrag'
 - b: bigrams: 'avc hemorrag'

longer n-grams are more precise

- Character N-grams
 - bigrams: _a, av, vc, c_, _h, he, em, mo, or, rr, ra, ag, g_
 - trigrams: _av, avc, vc_, _he, hem, emo, ... rra, rag, ag_

character n-grams are more robust



Dictionary Text Features

Take advantage of a priori knowledge

[colon perforation leading to stercoral peritonitis] colon perfor lead stercor peritoniti

Use dictionary to generate features for classifier

- Dictionary entries (pre-processed with same normalization)
 - colon perfor/K631 (colonic perforation/K631)
 - peritoniti/K659 (peritonitis/K659)
- Dictionary lookup
 - → Features: p:colon perfor, c:K631, p:peritoniti, c:K659



Also Extract Features from Metadata

Features obtained from metadata provided with a death certificate

- Year of coding (e.g., 2011)
- Age of the deceased (e.g., 85)

Encoding a point in an ordered set as a set of intervals

- y: Coding year: coding rules change over the years
 - 2×9 features instantiated for $y \in [2006...2014]$
 - $2011 \rightarrow >2006, >2007, \ldots >2010, \leq 2011, \ldots \leq 2014$
- a: Patient's age
 - 2×11 features instantiated for $a \in [0 \dots 100]$
 - $85 \to >0$, >5, >10, >15, >20, ... >80, ≤ 85 , ≤ 90 , ≤ 95 , ≤ 100



Outcomes

Top results on CLEF eHealth 2017 data

- US death certificates
 - P=90, R=81, F=85
- French death certificates
 - P=89, R=77, F=83
- French death certificates, line-aligned
 - P=87, R=87, F=87

Collaboration with users for take-up

- CepiDc: Epidemiology center on medical causes of death (WHO coding center)
 - Insert into coding workflow
- Santé Publique France: National public health agency
 - Detect "syndromic groups" for yearly outbreak surveillance and public health monitoring



Coding Causes of Death

Acknowledgements

- Classification: with Thomas Lavergne (LIMSI, Univ. Paris-Sud)
- CLEF eHealth 2016-2018 Shared Tasks with
 - Cyril Grouin, Thomas Lavergne, Aurélie Névéol (LIMSI)
 - Aude Robert, Grégoire Rey (INSERM, French CépiDc data)
 - Robert Anderson (US CDC data)
 - Francesco Grippo and Chiara Orsi (Italian data)
 - László Pelikán (Hungarian data)

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Social Networks

New sources of information on health



View More Posts Ignore

Maybe there's already a discussion out there for this, but I thought I would start a new one to see if we could compile some specifics. I just started cabergoline (3 doses down already) and wanted to hear about experiences people have had on it. I know I was terrified (partly because I know too much already & partly from what I've read online) and really wanted to know what to expect. What sort of side effects have you had? How long before they go away? Do certain things never go away? What do you do or take to combat those side effects?

So far I've done pretty well. First dose gave me horrible headache & brain fog for a day. After that I've really just had mild dizzy spells, headaches off and on (never had a headache from tumor) & insomnia, I'll fall asleep fine, then toss & turn a few hours later & wake up several hours before I usually do. Then I'm wide awake (at 4am). Then of course I'm tired all day. Not much nausea but I find that I don't want to eat much & get full right away, Almost that "take it or leave it" kind of attitude. I love that part! Definitely would love to lose 10lbs!

I don't want to take anything for the insomnia because I don't want to mess with too many brain chemicals all at once. I'm hoping it will eventually go away. Nothing really seems to help the headaches either but I'm thinking that will go away too?

Posted on 02/21/11, 07:46 am





Hug pharm... Send to a Friend Share This

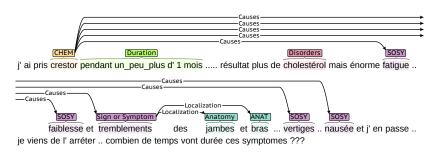




Watch this

Objectives and Methods

Spotting adverse drug event signals: pharmacovigilance, needed for drug safety



NLP challenges: non-standard vocabulary, variability, ambiguity Methods: supervised information extraction; collect non-standard variants



Robust Construction of Semantic Classes

Collecting standard and non-standard term variants

- Large terminology resources: e.g., drug names
 - UMLS semantic class
- Bootstrapping: e.g., drug-taking verbs
 - I take aspirin every day
 - → prendre, prescrire, être sous, donner, avoir...
 - \rightarrow Drug names absent from our lists
 - e.g., food complements, Canadian drug names
 - → Intentional variants
 - Lévothyrox \rightarrow lévo
 - Duphaston → dudu
 - ullet pilule du lendemain o pdl
 - → Spelling errors
- Unsupervised distributed representations, word clusters
 - → gynécologue, gynécolgue, gynécoloque, gynéco, gynécho, génico, gyné, gygy, etc.



Outcome: Baclofen study (Lillo-Le Louet et al., ISOP 2017)

Baclofen safety and its use in social media: a preliminary pharmacovigilance study

- 61,256,905 posts processed
- 18,570 posts mentioning baclofen and a clinical finding retrieved from NLP output database
 - ullet Exclude alcohol dependence ightarrow 2621 posts
- Reviewed by two evaluators from pharmacovigilance center
 - 782 (29.2%) mentioned potential adverse drug reactions
- Compared to cases in French National Database
 - 717 ADR cases with baclofen
- Main findings
 - Information about baclofen dosage more frequent in posts (27.7% vs 9.2%)
 - 75% of the patients had a daily dosage over 90 mg, higher than the maximum recommended daily dosage
 - Demographic information (gender, age) scarce in posts



Pharmacovigilance from Social Media

Acknowledgements

Cyril Grouin, François Morlane-Hondère (LIMSI) Funding: ANSM: National Agency for Drug Safety

Vigi4med (2014-2017)

- PI: Dr Cédric Bousquet
 - St-Étienne Medical School
 - LIMICS, Inserm, Paris
- 2 pharmacovigilance centers
- Detect adverse drug reactions
- Proof of concept, batch processing

PHARES (2017–2019)

- PI: Dr Marie-Christine Jaulent
 - LIMICS, Inserm, Paris
- 1 pharmacovigilance center
- Strengthen causal link detection
- Explore drug misuse
- On-line processing

LIMSI: NLP



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A Virtual Patient to Train Medical Students



A Virtual Patient to Train Medical Students

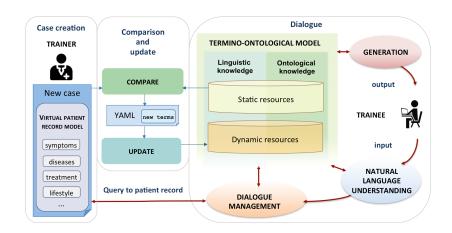


- D: What brings you here?
- P: I am seeing you about persistent backache
- D: When did it start? P: I don't remember
- D: Where is the pain exactly?
- P: I have pain in the lower back, the pain is located in the lower back and sometimes down the legs D: Can you sleep well?
- P: The pain often makes it difficult to fall asleep
- D: Do you suffer from any disease?
- P: Chronic stomac ulcers
- D: Do you follow any treatment for that?
- P: Omeprazole for the chronic stomach ulcers. Maybe there is more information in my file

NLP challenges

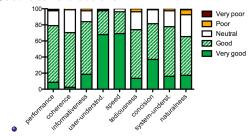
- Match user vocabulary to patient case vocabulary
- Large concept and vocabulary space
- Need for precision
- Includes question-answering
- Dialogue management, instantaneous answer

System Architecture



Outcomes

- Functional system
 - Good user evaluations



- Robust across medical specialties
- Robust on unseen patient cases
- Ready for transfer to company



A Virtual Patient to Train Medical Students

Acknowledgements

- Sophie Rosset, Éric Bilinski
- Leonardo Campillos Llanos, Catherine Thomas, Dhouha Bouamor
- LIMSI, CNRS
- FUI / BPI ; SATT Paris-Saclay
- Interaction Healthcare / SimForHealth, CHU d'Angers, Voxygen, Vidal

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Conclusion

- Multiple applications of NLP to biomedical text processing
- Key role of entity normalization / entity linking
- Relative importance of human and data-driven knowledge
- Remaining challenges
 - Variability of data and generalizability
 - Need for annotations for supervised learning
 - Access to clinical text to train systems



Thank You!

Welcome to MEDINFO 2019 International Conference on Medical Informatics Lyon, France, August 2019



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