Prediction of the next medication order to assist prescription verification by pharmacists in a health care center

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Université de Montréal

Unité de Recherche en Pratique Pharmaceutique (URPP)

Maxime Thibault, B.Pharm, M.Sc; Maxime Bergeron Pharm.D; Denis Lebel, B.Pharm, M.Sc, FCSHP

Contact: maxime.thibault.2@umontreal.ca

Background

- In North American health care centers, pharmacists review medication orders to ensure:
  - The absence of drug related problems
  - Adequate medication usage
  - Correct order entry
- Drug order verification is a repetitive cognitive process that is prone to distractions[1-2] or lapses in attention. Machine learning could help detect problems and focus pharmacist attention.
- Detection of atypical orders would involve predicting drug orders and warning when actual orders deviate from those expected.
- Previous studies used conventional statistics or natural language processing alone and were either limited to selected drugs or limited in time[3-5]. One study used sequential pattern mining and obtained 70.2% top 20 accuracy for prediction of the next prescribed medication[6].
- The objective of this project was to determine the feasibility of predicting the next prescribed drug during hospitalization using machine learning. We also aimed to compare the predictions with pharmacist rating of orders.

Methods

Setting and data

- 500-bed mother-child, tertiary care university hospital center.
- Access to the institutional pharmacy database was authorized.

Training and testing set

- All inpatient orders and some (e.g. special access) outpatient orders
- Training set: all orders from 2013 to 2017 inclusively
- Test set: all orders from January to July 2018 inclusively
- Extracted data:
  - Anonymized patient encounter identifier
  - Drug identification and classification (AHFS)
  - Order start and end times (precise to the minute)

Preprocessing

- Label: each individual order (drug identification)
- Features associated with each label:
  - Sequence of drug orders preceding the target
  - Active drugs and drug classes at the time the label was ordered
  - Department on which the order was placed

Representations

- Sequence of orders before target: **word2vec embeddings**
- Active medications, active classes and departments: bag of words encoded as **multi-hot vector** (binary count vectorization)

Training word2vec embeddings

- Word2vec embeddings were initially trained alone to find the best training hyperparameters for this representation.
- Given that vectors between word2vec embeddings for a semantic relationship are similar (e.g. vectors from man to woman and from king to queen are similar), we built a list of analogies such as:

  "Acetaminophen oral tablet is to acetaminophen oral suspension as furosemide oral tablet is to…"

- Grid search was used to optimize the accuracy of these analogies.

Training the neural network

- 5-fold cross-validation and a time-series split was used for all tests.
- Multiple network configurations and hyperparameters were tested.
- Final model was tested against the 2018 test set.

Prediction validation using a survey

- Orders representing 20 clinical situations (e.g. routine order, possible but rare combination, simulated prescribing error) were adapted from real patient profiles. Predictions for these situations were obtained from a model prototype deployed on the institutional intranet.
- Pharmacists were asked to rate how atypical they considered each order on a 4-point scale. The ranks of the model predictions were binned into 4 groups. Predictions were compared with pharmacist ratings.

Results

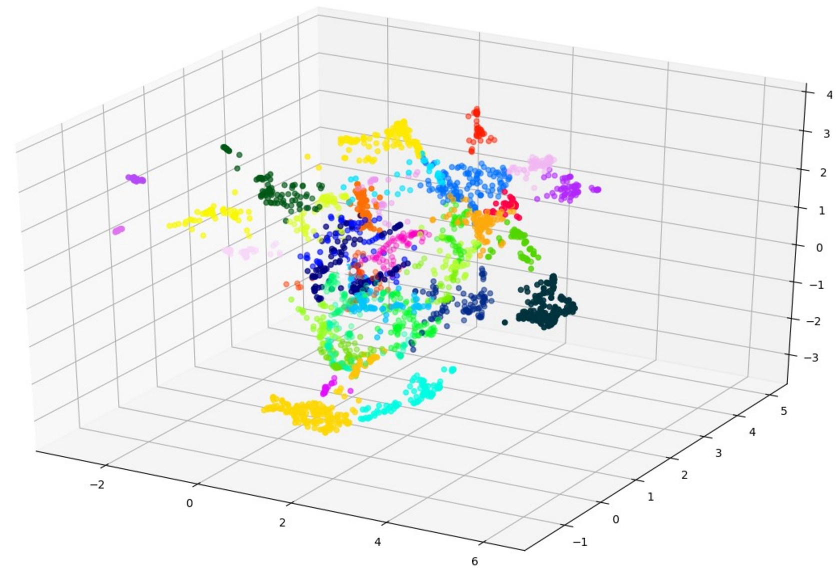
	Training set	Test set
Patient encounters	96,590 patient encounters	9,978 patient encounters
Orders	1,022,272 orders	95,310 orders
Orders per encounter	11.3 ± 22.7 orders per encounter	10.2 ± 15.3 orders per encounter
Drugs	3145 drugs	1843 drugs

Word2vec embeddings

The best training hyperparamterers yielded an analogy accuracy of **77.1% (118/153)**.

Various clusters represented different concepts:

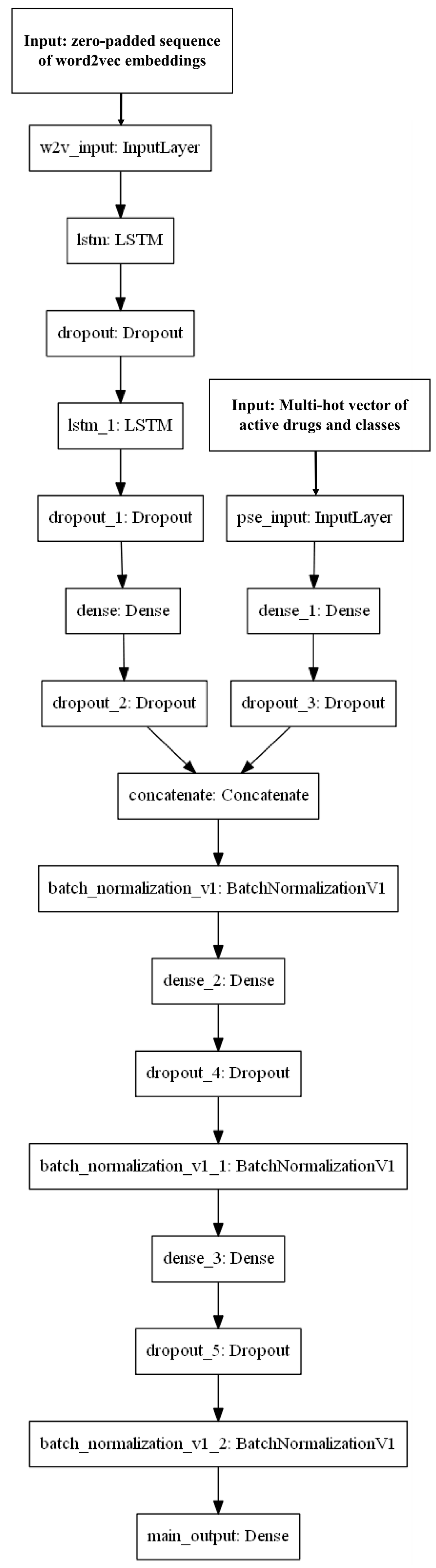
- Departments (neonatology, intensive care…)
- Specialties (psychiatry, dermatology…)
- Types of products (vaccines, wound care…)
- Clinical conditions (tuberculosis, hyperemesis…)



UMAP 3D projection of word2vec embeddings

Neural network

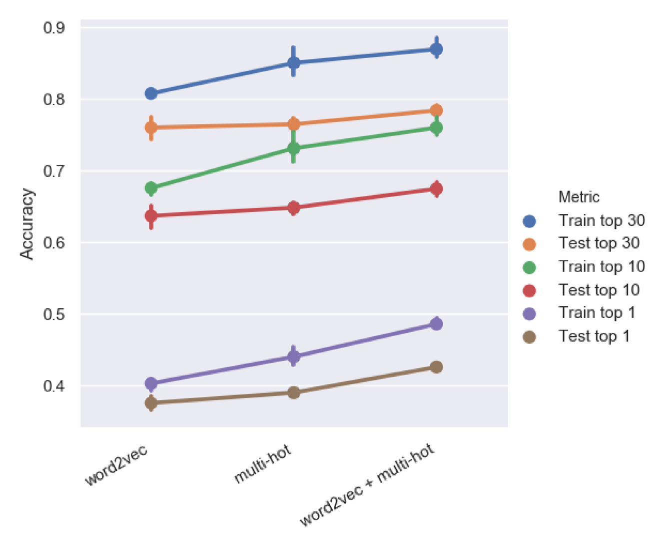
Final structure



Prediction accuracy

	Top 1	Top 10	Top 30
Baseline on training set (dummy classifier)	4.5%	23.6%	44.1%
Cross-validation accuracy (mean ± sd)	44.0 ± 0.4%	68.2 ± 1.3%	78.8 ± 1.3 %
Test set accuracy	**44.4%**	**69.9%**	**80.4%**

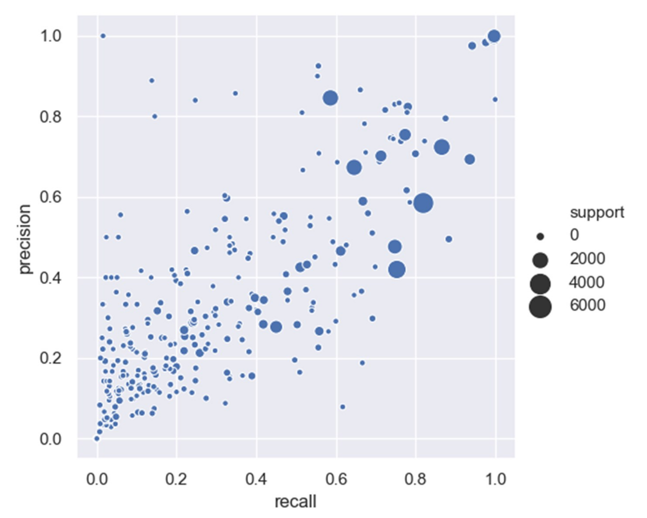
Validation of the two-input approach



Combining the sequence of word2vec embeddings with the multi-hot vector of active drugs and classes is better than either approach alone.

Classification metrics on test set (2018)

(drugs prescribed >1x/week)



Weighted averages

Precision: 0.415

Recall: 0.444

AUROC: 0.959

Comparison of predictions with pharmacist ratings

18/35 (51.4%) pharmacists answered

Experts don't agree ! Fleiss Kappa between pharmacists **0.283**

	Accuracy	Cohen Kappa	Precision (weighted avg)	Recall (weighted avg)
Overall (n=20)	0.550	0.338	0.617	0.550
Real orders (excl. errors, n=16)	0.594	0.334	0.679	0.594

Conclusions

- Our prototype showed interesting performance for the prediction of the next medication order.
- Comparison of predictions with pharmacist ratings proved difficult because pharmacists didn't rate the same orders uniformly.
- Future research will focus on validating the approach with data from another center and evaluating usefulness in clinical practice.

References

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