Lecture 6: Electronic Health Records (Part 2)

Serena Yeung

BIODS 220: AI in Healthcare

Announcements

Upcoming deadlines:

- A1 due Tue 10/18
- Project proposal due Fri 10/21
 - Remember that you must train a deep learning model somewhere in your project!
- Project partner finding session during review section this Friday, 1:30pm, Alway M106

Agenda for today

- Finishing up from last time: RNN (LSTM) models for EHR prediction tasks
- More on EHR data
- More on feature representations
- A first look at model interpretability: soft attention

Last time: overview of electronic health records

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Patient chart in digital form, containing medical and treatment history

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Figure credit: Rajkomar et al. 2018

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A real example of EHR data: MIMIC-III dataset



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Examples of prediction tasks



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Remember: "vanilla" neural networks for predictions from clinical variables

Let us consider the task of regression: predicting a single real-valued output from input data

Model input: data vector $x = [x_1, x_2, ..., x_N]$

Model output: prediction (single number) \hat{y}

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Example: predicting hospital length-of-stay from clinical variables in the electronic health record

x = [age, weight, ..., temperature, oxygen saturation] $\hat{y} = length-of-stay (days)$

Recurrent Neural Network

We can process a sequence of vectors **x** by applying a **recurrence formula** at every time step:



Slide credit: CS231n

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V

Long Short Term Memory (LSTM) Recurrent Networks

Unrolled Vanilla RNN

Unrolled LSTM



Figure credit: https://colah.github.io/posts/2015-08-Understanding-LSTMs/

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Harutyunyan et al.

- Benchmarked LSTMs vs logistic regression on common prediction tasks using MIMIC-III data
- In-hospital mortality, decompensation, length-of-stay, phenotype classification
- Used a subset of 17 clinical variables from MIMIC-III

Variable	MIMIC-III table	Impute value	Modeled as
Capillary refill rate	chartevents	0.0	categorical
Diastolic blood pressure	chartevents	59.0	continuous
Fraction inspired oxygen	chartevents	0.21	continuous
Glascow coma scale eye opening	chartevents	4 spontaneously	categorical
Glascow coma scale motor response	chartevents	6 obeys commands	categorical
Glascow coma scale total	chartevents	15	categorical
Glascow coma scale verbal response	chartevents	5 oriented	categorical
Glucose	chartevents, labevents	128.0	continuous
Heart Rate	chartevents	86	continuous
Height	chartevents	170.0	continuous
Mean blood pressure	chartevents	77.0	continuous
Oxygen saturation	chartevents, labevents	98.0	continuous
Respiratory rate	chartevents	19	continuous
Systolic blood pressure	chartevents	118.0	continuous
Temperature	chartevents	36.6	continuous
Weight	chartevents	81.0	continuous
pH	chartevents, labevents	7.4	continuous

Harutyunyan et al. Multitask learning and benchmarking with clinical time series data. 2019.

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Harutyunyan et al.

- Logistic regression models

- Use hand-engineered feature vector to represent a time-series: min, max, mean, std dev, etc. of each feature in several subsequences (full series, first 10% of series, first 50%, last 10%, etc.)
- If feature does not occur in subsequence (missing data), impute with mean value from training set
- Categorical variables had meaningful numeric values -> no change
- Zero-mean unit-variance standardization of all features

Harutyunyan et al. Multitask learning and benchmarking with clinical time series data. 2019.

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Harutyunyan et al.



- LSTM models

- Bucket time series into regularly spaced intervals, take the value (or last value, if multiple) of each variable in the interval to create observation x_t
- Encode categorical variables using a one-hot vector (vector of 0s with a 1 in the observed position).
- If variable is missing in a time bucket, impute using most recent observed measurement if it exists, and mean value from training set otherwise
- Concat the values of each clinical variable with a binary mask indicating presence or not (i.e., missing and needed to impute) to form full observation feature vector x_t

Harutyunyan et al. Multitask learning and benchmarking with clinical time series data. 2019.

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Harutyunyan et al.: logistic regression vs LSTMs

Found better performance overall for LSTMs (S) vs logistic regression (LR). Also introduced more sophisticated variants and multi-task training (joint training of all tasks together).

Phenotyping

1	Model	AUC-ROC
N	SAPS	0.720 (0.720, 0.720)
Ë	APS-III	0.750 (0.750, 0.750)
rta	OASIS	0.760 (0.760, 0.761)
Me	SAPS-II	0.777 (0.776, 0.777)
	LR	0.848 (0.828, 0.868)
bit	S	0.855 (0.835, 0.873)
SO	S + DS	0.856 (0.836, 0.875)
년	С	0.862 (0.844, 0.881)
표	C + DS	0.854 (0.834, 0.873)
	MS	0.861 (0.842, 0.878)
1	MC	0.870 (0.852, 0.887)

Macro AUC-ROC
0.739 (0.734, 0.743)
0.770 (0.766, 0.775)
0.774 (0.769, 0.778)
0.776 (0.772, 0.781)
0.773 (0.769, 0.777)
0.768 (0.763, 0.772)
0.774 (0.770, 0.778)

LR – logistic regression	C – channel-wise LSTM	MS – multitask standard LSTM
S – standard LSTM	DS – deep supervision	MC – multitask channel-wise LSTM

Figure credit: Harutyunyan et al. Multitask learning and benchmarking with clinical time series data. 2019.

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MS – multitask standard LSTM

MC – multitask channel-wise LSTM

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Found better performance for phenotyping acute vs chronic conditions -- makes sense!

Figure credit: Harutyunyan et al. Multitask learning and benchmarking with clinical time series data. 2019.

C – channel-wise LSTM

DS - deep supervision

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LR – logistic regression

S - standard LSTM

Recall: Harutyunyan et al. imputed missing data

- Logistic regression models

- Use hand-engineered feature vector to represent a time-series: min, max, mean, std dev, etc. of each feature in several subsequences (full series, first 10% of series, first 50%, last 10%, etc.)
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More on missing data

A common problem with clinical variable data

- Missing completely at random (MCAR)
 - Missingness does not depend on the missing variable or on other variables
 - Ex: A portion of patient pain surveys (producing variable of patient pain level) are randomly lost or unreadable
- Missing at random (MAR)
 - Missingness does not depend on the missing variable but may depend on other variables
 - Ex: Male patients are less likely to complete patient pain surveys
- Missing not at random (MNAR)
 - Missingness can depend on the missing variable itself
 - Ex: Patients with higher pain levels are less likely to complete patient pain surveys

More on missing data

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MNAR highest degree of bias / most challenging to accurately impute. Analysis of how well imputation methods work for MCAR / MAR / MNAR cases beyond the scope of this course -> just know that these are missingness characteristics that can make accurate imputation more or less challenging.

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- Simplest approaches:
 - Delete records with missing data
 - Fixed imputation of missing values with mean, median, previous value, interpolation, etc.

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- More sophisticated approaches:
 - K-nearest neighbors (impute based on feature value of k closest neighbors determined through non-missing values)
 - Predicting missing values (single imputation): Train regression or classification models to predict missing values based on other variables

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- Even more sophisticated approaches:
 - Predicting missing values (multiple imputation): Perform single imputation multiple times based on different random initializations, then aggregate for final imputation + uncertainty measurement

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- An ongoing active area of research:
 - Methods incorporating deep learning generative models, etc.

A	В	С
0.93	1.40	1.53
0.24	0.46	0.76
	0.80	
0.95	1.24	1.46
0.23	0.57	
0.90		1.28
0.15	0.42	
0.47	0.54	0.63
	1.14	
0.89	1.23	1.45

Red = missing values across features A,B,C

¹van Burren, 2011. Figure credit: https://cran.r-project.org/web/packages/miceRanger/vignettes/miceAlgorithm.html

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Fill in missing entries with initial values (random, means, randomly drawn from distribution, etc.)

¹van Burren, 2011. Figure credit: https://cran.r-project.org/web/packages/miceRanger/vignettes/miceAlgorithm.html

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Update missing values for feature A using regression model trained on all values (including red) of other features

¹van Burren, 2011. Figure credit: https://cran.r-project.org/web/packages/miceRanger/vignettes/miceAlgorithm.html

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Update missing values for feature B using regression model trained on all values (including red and updated/yellow) of other features

¹van Burren, 2011. Figure credit: https://cran.r-project.org/web/packages/miceRanger/vignettes/miceAlgorithm.html

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Continue this update process for feature C, and then circle back to feature A and repeat process in cycles until imputed values for all features have converged

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Continue this update process for feature C, and then circle back to feature A and repeat process in cycles until imputed values for all features have converged Full MICE Algorithm (multiple imputation) repeats this for N random initializations of the dataset and then aggregates for final imputation + uncertainty measure. We will not cover different initialization methods and implications.

¹van Burren, 2011. Figure credit: https://cran.r-project.org/web/packages/miceRanger/vignettes/miceAlgorithm.html

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Sources of EHR data

- Open-source EHR datasets (MIMIC-III/IV, MIMIC-CXR, ...)
- Restricted EHR data from individual institutions
 - Major vendors: EPIC, Cerner, etc.
- Also: insurance claims data
 - Fills in blanks of patient health outside the hospital!
 - Visits with other care providers outside the hospital EHR system
 - Pharmacy visits

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Challenge: many of these data sources are in their own formats. How do we use multiple data sources?

OMOP Common Data Model

- Observational Medical Outcomes Partnership (OMOP)
- Created from public-private partnership involving FDA, pharmaceutical companies, and healthcare providers
- Standardized format and vocabulary
- Allows conversion of patient data from different sources into a common structure for analysis
- Intended to support data analysis



Figure credit: https://www.ohdsi.org/wp-content/uploads/2014/07/Why-CDM.png

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OMOP Common Data Model



Figure credit: https://ohdsi.github.io/TheBookOfOhdsi/images/CommonDataModel/cdmDiagram.png

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STARR: Stanford Hospital Data in OMOP

Stanford MEDICINE	Observational Medical Outcomes Partnership STAnford Research data Repository			≡
SUMMARY	ACCESS	LEARN	NERO	Q

Stanford Electronic Health Records in OMOP

STARR-OMOP is Stanford Electronic Health Record data from its two Hospitals in a Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). Use OMOP for observational science, population health science, collaborative network studies and reproducible data science.

Standardized Data

- Standardized vocabulary
- Transparent data transformations
- High mapping rate

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FHIR

- Fast healthcare interoperability resources (FHIR)
- Web-based standards / framework for secure exchange of electronic healthcare information across disparate sources
- Based on "resource" elements that contain information to be exchanged, as a JSON or XML object



Figure credit: https://www.hl7.org/fhir/DSTU1/shot.png

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FHIR



Figure credit: Choi et al. OHDSI on FHIR Platform Development with OMOP CDM mapping to FHIR Resources. 2016.

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FHIR



Figure credit: Choi et al. OHDSI on FHIR Platform Development with OMOP CDM mapping to FHIR Resources. 2016.

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JAMA, 2016.

platform for electronic health records.

Aside: improving EHR technology and utility major current issue in healthcare

- Have already seen one challenge: interoperability
 - EHR systems were built and adopted very quickly -- not enough time to design for interoperability
- Are EHRs being used meaningfully?
 - Clinicians spending huge amount of time on documentation and interfacing with EHR system -> burnout and reduced patient interaction
 - Lots of pain points. What are the benefits?
- Ongoing efforts to reduce pain points
 - Improving user experience and AI-assisted documentation (dictation, autocomplete, etc.)
- Ongoing efforts to improve value
 - Data analytics, clinical decision support

Rajkomar et al. 2018

- Clinical predictions from patients' entire raw EHR records, in FHIR format
- De-identified EHR data from two US academic centers with 216,221 adult patients
- Prediction tasks: in-hospital mortality, 30-day unplanned readmission, prolonged length of stay, patients' final discharge diagnoses
- 46,864,534,945 total data points across data (every event, every word in note, etc.)



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Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Data representation

FHIR Resource	Feature Type and Token ID	Embedding			
<pre>medication_order { contained { medication { code { text { value: "Zosyn" }</pre>	1-< 17>	-0.30 +0.4	1		
<pre>system { value: kxNorm } Concatenate and tox code { value: "1659133" } } ingredient { item_codeable_concept { text { value: "Piperacillin" }</pre>	* 2-< 35>	-0.49 +0.7	2 +0.23	•	• •
<pre>coding { system { value: "Hospital A. Ingredient Code" } code { value: "203134" } } }</pre>	4-<702>	-0.33 +0.3	9]	
<pre>ingredient { item_codeable_concept { text { value: "Tazobactam" } coding {</pre>	- 3-< 19>	-0.31 +0.4	1		
<pre>code { value: "221167" } } } } } } effective_period { start { value_us: 882518400000000 } } } + Converted /// // /// //</pre>	+ 4-<913>	-0.70 +0.8	8 -0.13	•	

Raw data as FHIR resources

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Data representation

Each element is mapped to a token ID (e.g. medication=zosyn), with a token "feature type"

FHIR Resource E	eature Type and Token ID	Embed	ding			
<pre>medication_order { contained { medication { code { text { value: "Zosyn" }</pre>	- 1-< 17>	-0.30	+0.41			
<pre>system { value: "RxNorm" } Concatenate and token code { value: "1659133" } } ingredient { item_codeable_concept { text { value: "Piperacillin" }</pre>	^{Nook-up} 2-< 35> 3-< 85>	-0.49	+0.72	+0.23	•	•••
<pre>coding { system { value: "Hospital A. Ingredient Code" } code { value: "203134" } } } ingredient { item_codeable_concept {</pre>	4-<702>	-0.33	+0.39	• • •		
<pre>text { value: "Tazobactam" } coding { system { value: "Hospital A. Ingredient Code" } code { value: "221167" } } } } }</pre>	4-<913>	-0.31	+0.41			
effective_period { start { value_us: 882518400000000 } } } + Converted to Idifferent for #	delta-time each model)	-0.70	+0.88	-0.13	•	• •

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Data representation

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FHIR Resource	Feature Type and Token ID	Embedding		
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<pre>coding { system { value: "Hospital A. Ingredient Code" } code { value: "203134" } } } ingredient { item_codeable_concept {</pre>	4-<702>	-0.33 +0.39		
<pre>text { value: "Tazobactam" } coding { system { value: "Hospital A. Ingredient Code" } code { value: "221167" } } }</pre>	4-<913>	-0.31 +0.41		
effective_period { start { value_us: 882518400000000 } } } + Converted to (different for	each model)	-0.70 +0.88	-0.13	

Every unique token is numerically represented by an "embedding vector" that will represent the token in the model. The embedding vector values are learned; similar tokens will probably have similar embedding vectors.

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Token embeddings

1xN token input (one-hot selection of token)

0.5	0.2	0.1
0.6	0.1	0.6
0.5	0.8	0.2
0.7	0.9	0.3
0.3	0.5	0.1

[0.5 0.8 0.2]

=

D-dim token embedding

N x D embedding matrix

. . .

0.8

0.7

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0.1

Token embeddings

1xN token input (one-hot selection of token)

0.5	0.2	0.1		
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0.5	0.8	0.2		
0.7	0.9	0.3		
0.3	0.5	0.1		
0.7	0.8	0.1		

[0.5 0.8 0.2]

=

D-dim token embedding

In general, learning embedding matrices are a useful way to map discrete data into a semantically meaningful, continuous space! Will see frequently in natural language processing.

N x D embedding matrix

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Embedding matrix has values that are randomly initialized at the beginning, then learned through training (backpropagation)!



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One vector representation for each token "feature type" (e.g. medication, procedure). Embeddings of multiple tokens corresponding to a same feature type are combined through averaging.

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A little bit of added complexity: each feature type has its own embedding dimension D. A hyperparameter!

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Also include an embedding representation of time delta from last RNN input.



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Refer to paper for other details, e.g. bucketing of continuous data types into discrete token IDs.

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Rajkomar et al.

Compared deep learning

subset of variables

approach with baselines (e.g.

vs hand-crafted features from

logistic regression), and using all

variables in data (flattened vector)

Hospital A Hospital B Inpatient Mortality, AUROC¹(95% CI) Deep learning 24 hours after admission 0.95(0.94-0.96)0.93(0.92-0.94)Full feature enhanced baseline at 24 hours after admission 0.93(0.92-0.95)0.91(0.89-0.92)Full feature simple baseline at 24 hours after admission 0.93(0.91-0.94)0.90(0.88-0.92)Baseline ($aEWS^2$) at 24 hours after admission 0.85(0.81-0.89)0.86(0.83-0.88)30-day Readmission, AUROC (95% CI) Deep learning at discharge 0.77(0.75-0.78)0.76(0.75-0.77)0.75(0.74-0.76)Full feature enhanced baseline at discharge 0.75(0.73-0.76)Full feature simple baseline at discharge 0.73(0.72-0.74)0.74(0.73-0.76)Baseline (mHOSPITAL³) at discharge 0.70(0.68-0.72)0.68(0.67-0.69)Length of Stay at least 7 days AUROC (95% CI) Deep learning 24 hours after admission 0.86(0.86-0.87)0.85(0.85-0.86)Full feature enhanced baseline at 24 hours after admission 0.85(0.84-0.85)0.83(0.83-0.84)Full feature simple baseline at 24 hours after admission 0.83(0.82-0.84)0.81(0.80-0.82)Baseline (mLiu⁴) at 24 hours after admission 0.76(0.75 - 0.77)0.74(0.73-0.75)

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¹ Area under the receiver operator curve

² Augmented early warning score

³ Modified HOSPITAL score

⁴ Modified Liu score

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Rajkomar et al.

Compared deep learning

after admission, discharge

subset of variables

Hospital A Hospital B Inpatient Mortality, AUROC¹(95% CI) Deep learning 24 hours after admission 0.95(0.94-0.96)0.93(0.92-0.94)Full feature enhanced baseline at 24 hours after admission 0.93(0.92-0.95)0.91(0.89-0.92)0.90(0.88-0.92)Full feature simple baseline at 24 hours after admission 0.93(0.91-0.94)approach with baselines (e.g. Baseline ($aEWS^2$) at 24 hours after admission 0.85(0.81-0.89)0.86(0.83-0.88)logistic regression), and using all 30-day Readmission, AUROC (95% CI) variables in data (flattened vector) Deep learning at discharge 0.77(0.75-0.78)0.76(0.75-0.77)vs hand-crafted features from Full feature enhanced baseline at discharge 0.75(0.73-0.76)0.75(0.74-0.76)Full feature simple baseline at discharge 0.73(0.72-0.74)0.74(0.73-0.76)Baseline (mHOSPITAL³) at discharge 0.68(0.67-0.69)0.70(0.68-0.72)Length of Stay at least 7 days AUROC (95% CI) Deep learning 24 hours after admission 0.86(0.86-0.87)0.85(0.85-0.86)Full feature enhanced baseline at 24 hours after admission 0.85(0.84-0.85)0.83(0.83-0.84)Evaluated model at different time Full feature simple baseline at 24 hours after admission 0.83(0.82-0.84)0.81(0.80-0.82)points, e.g., at admission, 24 hrs Baseline (mLiu⁴) at 24 hours after admission 0.76(0.75 - 0.77)0.74(0.73-0.75)¹ Area under the receiver operator curve ² Augmented early warning score

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Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

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Also trained a model with "soft attention" on a simpler task (in-hospital mortality, subset of data variables) to obtain interpretability

Rajkomar et al. Scalable and accurate deep learning with electronic health records. Npj Digital Medicine, 2018.

Lecture 6 - 61

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Soft attention

- Weight input variables by an "attention weights" vector p
- Learn to dynamically produce p for any given input, by making it a function of the input x and a fully connected layer f_A(with learnable parameters A)
 - By optimizing for prediction performance, network will learn to produce p that gives stronger weights to the most informative features in x!



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Soft attention

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Output y Rest of the neural network Input $x = [x_1, x_2, ..., x_D]$ Ζ Attention weights p $=[p_1, p_2, , p_D]$ Soft attention weighting Attention-weighted input $z = [z_1, z_2, , z_D]$ Х р Learnable fully connected layer f_{Δ} with weights A

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Soft attention

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Soft attention in RNNs

Note that f_A produces attention weights as a function of both current input x as well as previous hidden state h!



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Soft attention in RNNs

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Active areas of research

- Improving prediction models for clinically meaningful tasks



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Active areas of research

- Improving prediction models for clinically meaningful tasks
 - Another popular task: early warning for critical conditions such as sepsis



Active areas of research

- Improving prediction models for clinically meaningful tasks
 - Another popular task: early warning for critical conditions such as sepsis
 - Multimodal modeling: more effective joint reasoning over different modalities of data (e.g. text, lab results, images, etc.)

Summary

Today's topics

- More on EHR data, missing values, and data formats
- More on feature representations
- A first look at model interpretability: soft attention

Next lecture

- More on text data and representations