Introduction

Gamenet GAMENet: Graph Augmented MEmory networks for recommending medication combination by tackles the limitation of instance-based recommendations with patient history to give better recommendations. It uses previous work that uses memory banks augmented by DDI graphs and dynamic memory based on patient history.

It uses a novel deep learning approach by constructing 2 RNN hidden layers, one for diagnosis and one for procedure. It uses this constructed patient representation with a pre-generated memory bank from DDI graph and EHR graph. The papers claim that this approach outperforms all current baselines in effectiveness measures, and achieved 3.60% DDI rate reduction. (Shang, J. et al (2019))

Link to Code

Google collab notebook :

https://drive.google.com/file/d/1fRjaGcQB2TQV0DdfXIl4As3mRGJ7GqAv/view?usp=drive_link

Instructions to run

You will need to make a shortcut in your own drive and change the root_path on the top of the notebook.

Scope of reproducibility:

Hypothesis 1:

The papers claim that this approach outperforms all current baselines in effectiveness measures, and achieved 3.60% DDI rate reduction. We will reproduce the results with our model to verify this measure is achieved.

Hypothesis 2 :

Author : Without DDI knowledge, GAMENet (w/o DDI) is also better than other methods which shows the overall framework does work

We will evaluate if this holds true for the GAMENET model by comparing it with some pre established baselines created from other models.

Data

- The data raw data is the diagnoses, prescriptions, procedure data from MIMIC-3 . A freely-available database comprising deidentified health-related data associated with over forty thousand patients who stayed in critical care units of the Beth Israel Deaconess Medical Center between 2001 and 2012.(Johnson et al , 2016)
- The data also includes drug-drug interaction (TWOSIDEs dataset) .Drug side effects and drug-drug interactions were mined from publicly available dat. (Offside , n. d.)

Statistics on data

Name	Statistic
Number of patients considered	6350
Total Clinical events	15016
Total Diagnosis (	1958
Total Medications prescribed	145
Total Procedure	1426
Avg Diagnoses per patient	10.514717634523175

Avg medicines per patient	8.80420884389984
Avg procedures per patient	3.8445657964837507
Avg visits per patient	2.3647244094488187

Refining the dataset

Data Split

Training data = 8/10

Validation data = 2/10

Create patient visit feature DB

- we will remove duplicate entries from the 3 datasets
- the values will be sorted by subject_id
- there will be one row for each visit in the input dataset to the model
- we will group all the diagnoses, medication, and procedure codes into arrays for every visit. The medication array would be one of the expected outputs
- we will convert NDC to ATC
- we might do some limits on the number of procedures, medications, and diagnoses to keep in our testing due to processing constraints

Creating feature vocabularies and patient record

Each diagnosis code, Medication NDC code, and procedure code will be mapped to a unique feature value. These feature vocabularies will be used in our modeling

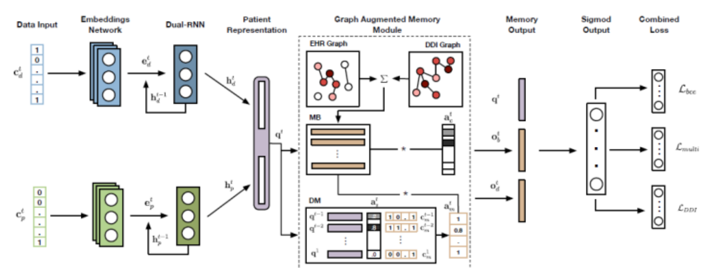
We will use the unique value to create another state of patient record which is numerical and therefore can be processed by the GAMENET model and any other model we may compare it against.

Creating adjacency matrix

The adjacency matrix of DDI and NDC codes is needed to create the "memory banks" by running them through GCNs. These will be convoluted with input patient presentations to give an output. This is only needed to validate the results proposed in the model.

Model

Our final model will follow the architecture outlined in the paper.



Data Input

There is 2 visit sequences that are ran through the model the include history of procedures and diagnoses by another patient . They are of size , (visit_dim, procedure_count) and (visit_dim,diagnoses_count). Visit size will include the 0^{th} visit to the current visit. We will also send the in the medication in the same format as it will be used for key value store.

For initial experiment we are using

Diagnosis count	1958
Medications prescribed count	145
Procedure count	1426

Embedding Network

Each vector(medication, diagnosis, procedure) will be reduced using an embedding which will output a size emb_dim which is set at 64 for now.

Dual RNN

GRU will be used for this step . We will have one GRU for diagnoses and one for procedures. The input dimension would be 64 as that is the output of embedding network. The output dimension will be doubled.

Patient Representation and query

We combine the GRU results by doing a concatenation to create a patient representation of procedure and diagnoses.

We run this through a linear layer with RelU to get a queries for the entire sequence.

The current query is the last element .

Memory Bank

This is created using the adjacency matrix created in the data pre-processing sections. We created 2 Graph convoluted networks, one for EHR adjacency matrix and one for DDI. We use the implementation provided in the paper to create these GCNs. It doesn't have input, just weights associated with the adjacency matrix that are adjusted during training

Key Value store

The keys are all the queries for the past visits. This is taken from the GRU results.

The values are the medication for the past visits.

Ob and od

Ob = memory_bank_contribution = softmax(query . memory_bank_transpose). Memory_bank

Od = key-store contribution = memory_bank . (key_value_store_values). Softmax(key store keys . query)

Sigmoid Output

We apply a sigmoid out to each of the outputs to scale them between 0 and 1. Anything above 0.5 is assumed 1 and anything below 0.5 is assumed 0.

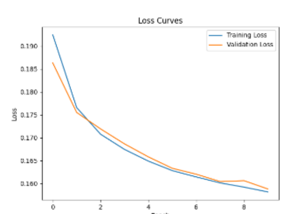
Combined Loss

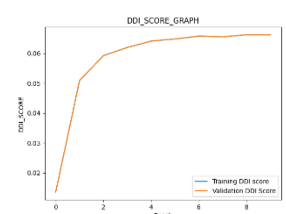
The target is the medication array for the visit for which we calculate the loss score. For initial iteration we are using binary cross entropy with logits as described in the paper. For final results we will be using will take different transformation of the output which will be combined to give a final result.

DDI Score

The features of medications sigmoid output will be fed into the ddi_score function to calculate drug-drug interaction scores. We will aim to minimize this function along with the loss of the predicted medications.

Results





Discussions

The GAMENet paper was reproducible, and we have shown the work above, however, the loss function that we have employed confirms the trainability of the Model, and we are converging. The paper has used a combined loss function, which penalizes the model for increasing DDI. This will be included in the next phase.

The code that came with the paper was well modularized, and defined, and made it easy to reproduce.

The Model definition, and the design was also a bit confusing. The NeuralNetwork that became the GAMENET augmented Seq2Seq model is implemented in one network, which makes the Network a bit complex.

In the next phase, we will:

- Update our loss function.
- Modularize the Neural Network, to facilitate easier implementation.
- Perform some model comparisons.

References

[1] Johnson, A., Pollard, T., & Mark, R. (2016, September 4). *Mimic-III clinical database*. MIMIC-III Clinical Database v1.4. https://physionet.org/content/mimiciii/1.4/

[2] Offsides and twosides (NSIDES v0.1) – tlab. (n.d.). http://tatonettilab.org/offsides/

[3] Shang, J., Xiao, C., Ma, T., Li, H., & Sun, J. (2019). GAMENet: Graph Augmented MEmory networks for recommending medication combination. *Proceedings of the . . . AAAI Conference on Artificial Intelligence*, *33*(01), 1126–1133. https://doi.org/10.1609/aaai.v33i01.33011126