Comp790-166: Computational Biology

Lecture 16

March 8, 2023

Today

- Graph Neural Networks vs Label Propagation vs LP + Correct and Smooth
- Examples of circumstances where spatial context is and is not helpful revealed through work with GNNs

Announcements

- Extra office hours Thursday 9am to 9:45
- Please sign up for your project here, `https://docs.google.com/document/d/1x9mIJCZAkeogAhmGlpqJkXwuoAKlB_0gewV1LpXZDoU/edit?usp=sharing`
- Homework hopefully returned in the next few days. Thanks for your patience!

Good Morning Question

- What kind of model did LEPAH use?
- After defining the Ω in LEAPH, what was the optimization problem formulated to accommodate spatial information?

Ω Clean-Up

$$\min_{\Omega} - \sum_{i=1}^{N} \sum_{j=1}^{M} \Omega_{ij} \log_2 \left(\Omega_{ij} \right) + \lambda \sum_{(m,n)} w_{mn} ||\Omega_m - \Omega_n||_2$$

- w_{jk} is a weight, calculate as the reciprocal of distance between cells j and k in the image
- The first term is basically an entropy term of ownership confidence
- The second term is promoting spatial coherence.
- λ controls the tradeoff between spatial coherence and membership confidence.

GNN vs Simple Things

- You all love GNNs
- Recently there has been some work to study why GNNs are outperforming simpler methods and how to incorporate this intuition back to simpler methods

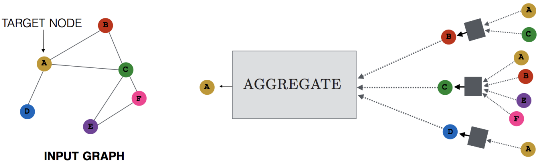


Figure: from https://www.cs.mcgill.ca/~wlh/grl_book/files/GRL_Book-Chapter_5-GNNs.pdf. Messages are aggregated from the neighborhood of some target node.

Neural Message Passing

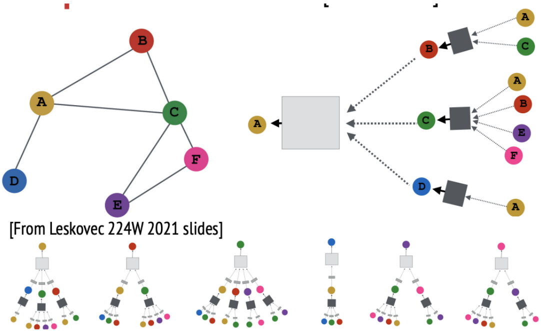
- **Input:** $\mathcal{G} = (\mathcal{V}, \mathcal{E})$ and a set of node features, $\mathbf{X} \in \mathbb{R}^{d \times |\mathcal{V}|}$
- **Output:** Node embeddings, $\mathbf{z}_u, \forall u \in \mathcal{V}$
- **Each Message-Passing Iteration:** A hidden embedding $\mathbf{h}_u^{(k)}$ is updated according to information aggregated from node u's neighborhood, $\mathcal{N}(u)$.

Update Rule

$$\begin{aligned}\mathbf{h}_u^{(k+1)} &= \text{UPDATE}^{(k)}\left(\mathbf{h}_u^{(k)}, \text{AGGREGATE}^{(k)}\left(\left\{\mathbf{h}_v^{(k)}, \forall v \in \mathcal{N}(u)\right\}\right)\right) \\ &= \text{UPDATE}^{(k)}\left(\mathbf{h}_u^{(k)}, \mathbf{m}_{\mathcal{N}(u)}^{(k)}\right)\end{aligned}$$

- $\mathbf{m}_{\mathcal{N}_{(u)}}^{(k)}$ is the *message* that is aggregated from u's graph neighborhood, $\mathcal{N}(u)$
- At each iteration, the AGGREGATE function takes as input the set of embeddings of the nodes in u's graph neighborhood, $\mathcal{N}(u)$ and applies it to a previous embedding $\mathbf{h}_u^{(k-1)}$ to generate the updated embedding $\mathbf{h}_u^{(k)}$

Illustrated..

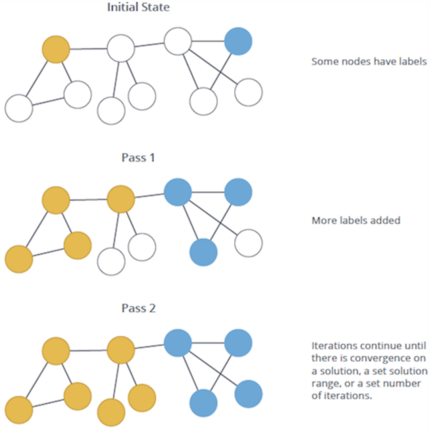


[From Leskovec 224W 2021 slides]

Figure: from `https://www.cs.cornell.edu/~arb/slides/2021-03-12-northeastern.pdf`

What is Label Propagation?

Some of your nodes are labeled, others are unlabeled, and you predict labels of unlabeled nodes based on the structure of the graph.



Initial State

Some nodes have labels

Pass 1

More labels added

Pass 2

Iterations continue until there is convergence on a solution, a set solution range, or a set number of iterations.

Label Propagation Algorithm

Label Propagation Formulation

Consider l labeled and u unlabeled nodes, where each node belongs to one of C classes. First define an $(l+u) \times (l+u)$ probabilistic transition matrix, T as,

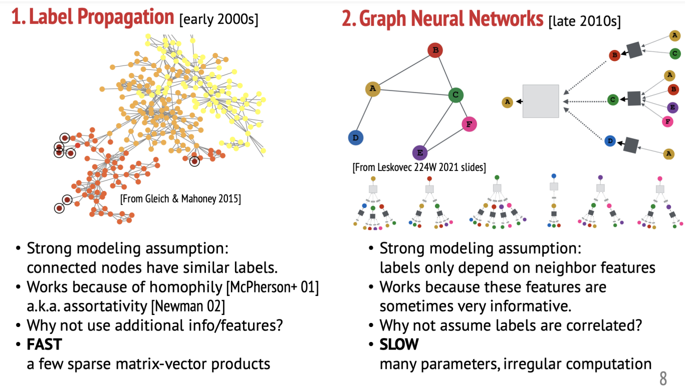
$$T_{ij} = P(j \to i) = \frac{w_{ij}}{\sum_{k=1}^{l+u} w_{kj}}$$

.

Here, W is encoding our weighted adjacency matrix.
Also define a $(l+u) \times C$ label matrix, Y, where the ith row gives the probability toward each of the C clusters.

- $Y \leftarrow TY$. Update until convergence
- Row-normalize Y.
- Clamp the labeled data, or put all of the probability mass on the correct cluster index.

The Debate



1. Label Propagation [early 2000s]

[From Gleich & Mahoney 2015]

- Strong modeling assumption: connected nodes have similar labels.
- Works because of homophily [McPherson+ 01] a.k.a. assortativity [Newman 02]
- Why not use additional info/features?
- **FAST** a few sparse matrix-vector products

2. Graph Neural Networks [late 2010s]

[From Leskovec 224W 2021 slides]

- Strong modeling assumption: labels only depend on neighbor features
- Works because these features are sometimes very informative.
- Why not assume labels are correlated?
- **SLOW** many parameters, irregular computation

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Figure: from https://www.cs.cornell.edu/~arb/slides/2021-03-12-northeastern.pdf. Tumor labels cannot be inferred based on cell-type frequencies, but instead should glean insights from the overall tissue architecture.

Tradeoffs

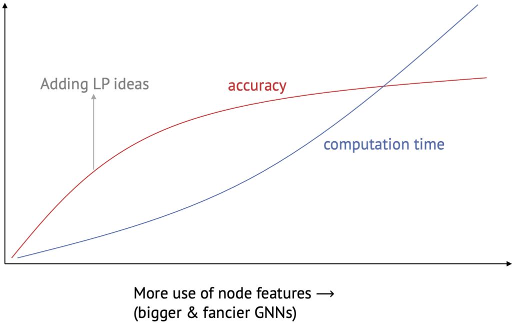


Figure: from `https://www.cs.cornell.edu/~arb/slides/2021-03-12-northeastern.pdf`

Correct and Smooth Approach

- The goal is to compare how a couple of simple methods/intuition can be strung together can be used to classify nodes
- The main idea is to start with a cheap base prediction based on node features (e.g. attributes or coordinates of a spectral embedding), and clean up graph structure through label propagation (**correct and smooth**).

Three Step Process

1. A base prediction made with node features that ignores the graph structure (e.g. with a linear model)
2. A correction step which propagated uncertainties from the training data across the graph to correct the base prediction
3. A smoothing of the predictions over the graph.

Overview of Correct and Smooth Approach

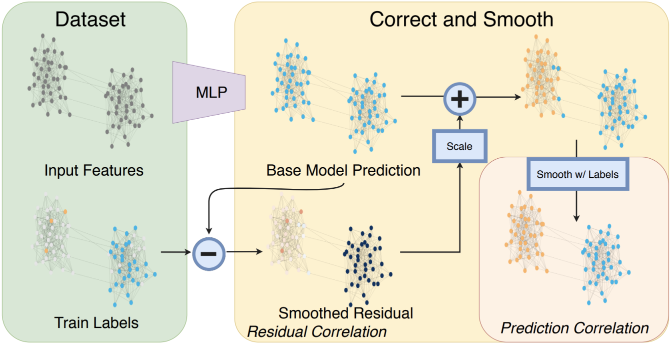


Figure: from Huang *et al.* ICLR. 2021

Notation Preliminaries

- Let there be n nodes.
- Assume we have a feature vector for each node, such that node features are encodes in an $n \times p$ matrix, X.
- Similarly, let A be the adjacency matrix of the graph
- Split nodes into labeled (L) and unlabeled (U) sets
- Define an $n \times c$ matrix, Y with a binary indicator for whether node i is in class c.

Simple Base Predictor

Given the matrix of **features** for each node, X and labels, Y, train a simple model to minimize,

$$\sum_{i \in L_t} \ell\left(f\left(x_i\right), y_i\right)$$

- ℓ is some loss
- Here L_t denotes the set of labeled training nodes
- Specify a matrix, Z containing these base predictions.

Error Correlation - Label Spreading Technique

- The intuition is that errors are expected to be correlated across edges in the graph. Hence, spread uncertainty across the edges.

Define and error matrix, $E \in \mathbb{R}^{n \times c}$ as,

$$E_{L_t,:} = Y_{L_t,:} - Z_{L_t,:}, \quad E_{L_v,:} = 0, \quad E_{U,:} = 0$$

This means that the only non-zero entries are those that correspond to labeled training nodes! These entries represent **residuals**.

Smooth the Error Using a Label Spreading Technique

The errors are smoothed as follow with a label spreading technique,

$$\hat{E} = \underset{W \in \mathbb{R}^{n \times c}}{\arg\min}\ \text{trace}\left(W^T (I - S) W\right) + \mu \|W - E\|_F^2$$

- S is the normalized adjacency matrix, $D^{-1/2} A D^{-1/2}$
- The first term encourages smoothness of the error over the graph
- The second term keeps W close to the initial estimate of error, E.

Our Friend Smoothness and Quadratic Form

We keep seeing the quadratic form come up if we are talking about smoothness. Reminder that,

$$\text{trace}(W^T(I-S)W) = \sum_j w_j^T(I-S)w_j$$

.

- $W \in \mathbb{R}^{n \times c}$

Solution

Given

$$\hat{E} = \underset{W \in \mathbb{R}^{n \times c}}{\arg\min} \operatorname{trace}\left(W^T(I - S)W\right) + \mu \|W - E\|_F^2$$

it was previously shown that the solution can be obtained through the following iteration,

$$E^{(t+1)} = (1 - \alpha)E + \alpha S E^{(t)}$$

The quickly converges to $\hat{E}$ and therefore gives corrected predictions as,

$$Z^r = Z + \hat{E}$$

Smoothing Final Predictions with Prediction Correlation

- The next assumption to be used for correction is that adjacent nodes in the graph are likely to have similar labels (e.g. homophily)
- Another round of label propagation will be used to encourage smoothness over distribution of labels.

Starting with the best guess of the labels, H, with $H_{L_t,:} = Y_{L_t,:}$ and $H_{L_v \cup U,:} = Z^{(r)}_{L_v \cup U,:}$, propagate labels as,

$$H^{(t+1)} = (1 - \alpha)H + \alpha S H^{(t)}$$

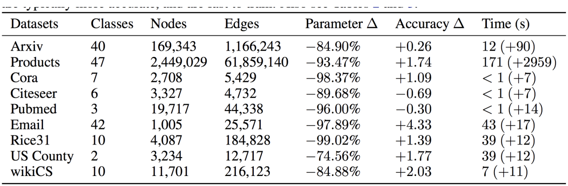
Final Prediction

The following has now been applied

- Base prediction
- Residual correction
- Label smoothing

After convergence of $H^{(t+1)} = (1-\alpha)H + \alpha S H^{(t)}$, get a final prediction, $\hat{Y} \in \mathbb{R}^{n \times c}$, and assign node to the class with the max predicted probability.

Results



Datasets	Classes	Nodes	Edges	Parameter Δ	Accuracy Δ	Time (s)
Arxiv	40	169,343	1,166,243	−84.90%	+0.26	12 (+90)
Products	47	2,449,029	61,859,140	−93.47%	+1.74	171 (+2959)
Cora	7	2,708	5,429	−98.37%	+1.09	< 1 (+7)
Citeseer	6	3,327	4,732	−89.68%	−0.69	< 1 (+7)
Pubmed	3	19,717	44,338	−96.00%	−0.30	< 1 (+14)
Email	42	1,005	25,571	−97.89%	+4.33	43 (+17)
Rice31	10	4,087	184,828	−99.02%	+1.39	39 (+12)
US County	2	3,234	12,717	−74.56%	+1.77	39 (+12)
wikiCS	10	11,701	216,123	−84.88%	+2.03	7 (+11)

Figure: from Table 1. Performance is reported wrt SOTA GNN.

Accuracy vs Number of Parameters

Higher accuracy with less parameters on one of the datasets (and training is also significantly faster)

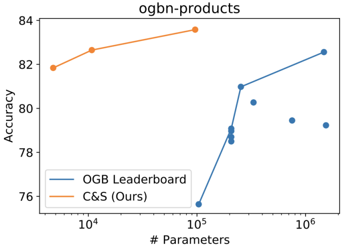
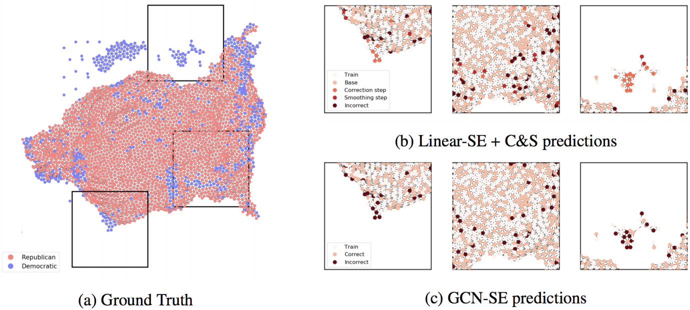


Figure: from Fig. 2

Visualizing which correction step fixed error



(a) Ground Truth

(b) Linear-SE + C&S predictions

(c) GCN-SE predictions

Figure: from Fig. 3. Colors in the correct and smooth panel show at which step labels became correct.

Summary

- Simple LP, diffusion, and GNN are fundamentally related
- Augmenting graph information with attributes, spectral features, etc. can be helpful for classifying nodes
- A base prediction is corrected according to smoothing over residual errors and encouraging closely connected nodes to have similar labels.

Recent Example Using GNNs to Study Spatial Context

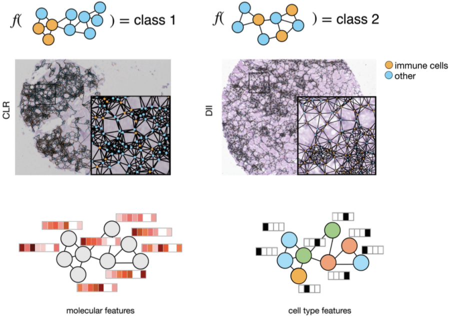


Figure: from https://www.biorxiv.org/content/10.1101/2022.12.08.519537v1.full.pdf. Two colorectal tumor cases Crohn's-like reaction (CLR) and diffuse inflammatory infiltration (DII) cannot be distinguished based on the spatial distribution of immune cells, but instead needs the tissue architecture.

Ultimate Task - Sample-Level Encodings

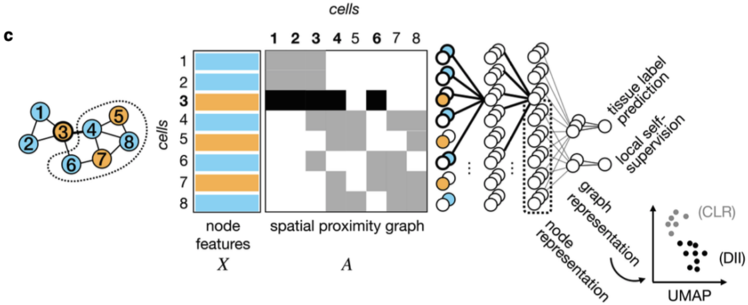


Figure: from Fischer *et al.* 2023. The learned encodings for cell's within a sample can ultimately be averaged to create a pooled feature vector that can separate tumor types.

Step 1 : Spatial Proximity Graph

Define an adjacency matrix, **A** such that with $a_{ij} = 1$ if,

$$||z_i - z_j||_2 < r$$

- z_i is the 2-D location for pixel i
- r is some user-defined radius

Graph Convolutional Network (GCN)

The node embedding layers for the GCN are defined as,

$$\mathbf{H}^{l+1} = \sigma(\mathbf{A}^{*}\mathbf{H}^{l}\mathbf{W}^{l})$$

- $\mathbf{A}^{*} = \mathbf{D}^{-1/2}\mathbf{A}\mathbf{D}^{-1/2}$
- $\mathbf{A}$ is the raw adjacency matrix and $\mathbf{D}$ is the diagonal degree matrix.
- $\mathbf{H}^{l}$ is the input matrix of nodes × input features
- $\mathbf{W}^{l}$ is a weight matrix of input features × output features

Results- Breast Cancer vs Colorectal Cancer

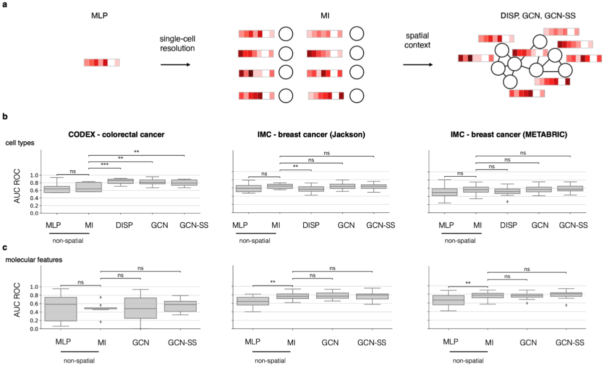


Figure: from Fischer *et al.* 2023. Results compared to just using original features for prediction. Spatial context helps things in the colorectal cancer dataset, but not so much in the breast cancer dataset.