Comp790-166: Computational Biology

Lecture 24

April 23, 2023

Today

- Technical Writing in Computational Biology
- Summary of themes we have discussed wrt graph-based techniques.

Technical Writing Motivation

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- Notation, figure presentation, publicly available code goes a long way.
- **Communication is Your Job!**
  - Good writing through simple language and organization
  - Well-documented publicly available code

Question

What part of technical writing do you find the most challenging?

Abstract: A Self Contained Story

- An elevator pitch of the main points

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- Sentence breakdown
  - 1 sentence background
  - 1 sentence about what is still missing
  - 1 sentence about what you did
  - 1 sentence about what results suggest
  - 1 inspirational sentence about how this advances the field.

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  - Always highlight the work of others in a positive way
- A paragraph where you compare and contrast previous solutions. You can still discuss limitations by spinning them in relation to all of the positive things that the other authors have done.
- Paragraph giving an overview of your contributions. Someone might only read this section of your paper. You need to sell your contribution in a human-readable way.

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- Indices should always map the same thing throughout the paper (for example i referring to cells and j referring to a feature of a cell)

Example Defining Notation

We start with some notation. We assume that we have an undirected graph $G = (V, E)$, where there are $n = |V|$ nodes with features on each node represented by a matrix $X \in \mathbb{R}^{n \times p}$. Let A be the adjacency matrix of the graph, D be the diagonal degree matrix, and S be the normalized adjacency matrix $D^{-1/2}AD^{-1/2}$. For the prediction problem, the node set V is split into a disjoint set of unlabeled nodes U and labeled nodes L, which are subsets of the indices $\{1, \ldots, n\}$. We will further split the labeled nodes into a training set L_t and validation set L_v. We represent the labels by a one-hot-encoding matrix $Y \in \mathbb{R}^{n \times c}$, where c is the number of classes (i.e., $Y_{ij} = 1$ if $i \in L$ is known to be in class j, and 0 otherwise, where the ith row of Y is all zero if $i \in U$), Our problem is transductive node classification: assign each node $j \in U$ a label in $\{1, \ldots, c\}$, given G, X, and Y.

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

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For example: 'For each cell, $\mathbf{x}_i \in \mathbb{R}^d$, we wish to learn its label, y_i through the use of the graph, $\mathcal{G}$.

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- For example, defining a graph? It doesn't hurt to remind them that nodes are cells and edges represent sufficient similarity between cells.
- Connect problem formulation to 'Figure 1'. In defining the overview of your problem, reference sub-panels of figure 1 of interest.

Example of a Comprehensive Figure 1

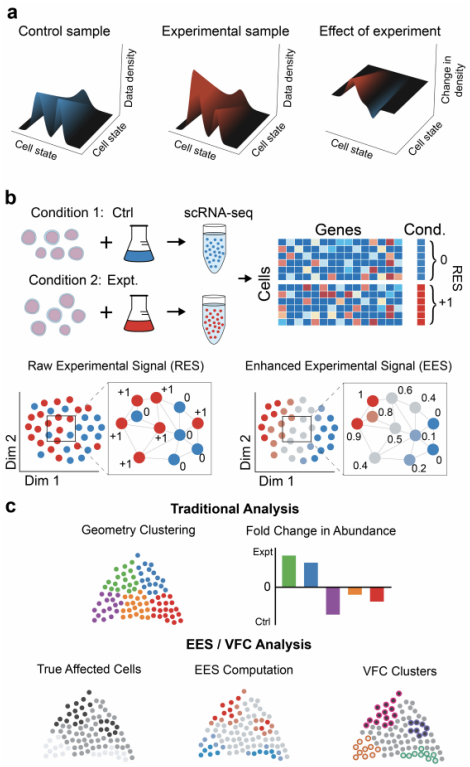

Figure: from Burkhardt *et al.* Nature Biotech. 2021.

Schematic Illustrations

If you draw cells, or patients, make sure these are carried through the entire figure.

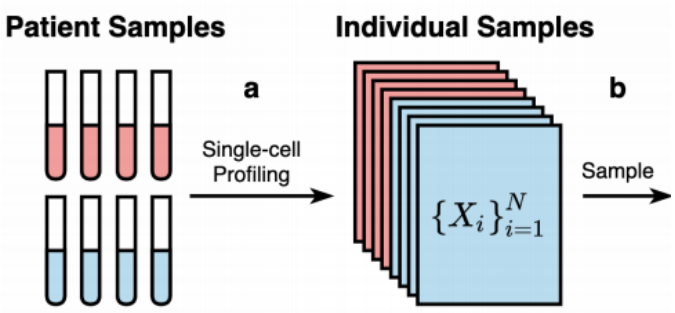

Figure: from Haidong Yi. `https://www.biorxiv.org/content/biorxiv/early/2021/04/14/2021.04.13.439702.full.pdf`

Pseudo-Code

Writing good pseudo code is extremely helpful. It can often by more helpful than the entire methods section.

Algorithm 2 xNetMF ($G_1, G_2, p, K, \gamma_s, \gamma_a$)

========== STEP 1. Node Identity Extraction ==========
for node u in $\mathcal{V}_1 \cup \mathcal{V}_2$ **do**
  for hop k up to K **do** ▷ counts of node degrees of k-hop neighbors of u
    $\mathbf{d}_u^k$ = CountDegreeDistributions($\mathcal{R}_u^k$) ▷ $1 \leq K \leq$ graph diameter
  end for
  $\mathbf{d}_u = \sum_{k=1}^{K} \delta^{k-1} \mathbf{d}_u^k$ ▷ discount factor $\delta \in (0, 1]$
end for
========== STEP 2. Efficient Similarity-based Representation ==========
========== STEP 2a. Reduced $n \times p$ Similarity Computation ==========
$\mathcal{L}$ = ChooseLandmarks(G_1, G_2,p) ▷ choose p nodes from G_1, G_2
for node u in $\mathcal{V}$ **do**
  for node v in $\mathcal{L}$ **do**
    $c_{uv} = e^{-\gamma_s \cdot ||\mathbf{d}_u - \mathbf{d}_v||_2^2 - \gamma_a \cdot \text{dist}(\mathbf{f}_u, \mathbf{f}_v)}$
  end for
end for ▷ Used in low-rank approx. of similarity graph (not constructed)
========== STEP 2b. From Similarity to Representation ==========
$\mathbf{W} = \mathbf{C}[\mathcal{L}, \mathcal{L}]$ ▷ Rows of $\mathbf{C}$ corresponding to landmark nodes
$[\mathbf{U}, \mathbf{\Sigma}, \mathbf{V}] = \text{SVD}(\mathbf{W}^\dagger)$
$\tilde{\mathbf{Y}} = \mathbf{C}\mathbf{U}\mathbf{\Sigma}^{-\frac{1}{2}}$ ▷ **Embedding**: *implicit* factorization of similarity graph
$\tilde{\mathbf{Y}} = Normalize(\tilde{\mathbf{Y}})$ ▷ **Postprocessing**: make embeddings have magnitude 1
$\tilde{\mathbf{Y}}_1, \tilde{\mathbf{Y}}_2$ = Split($\tilde{\mathbf{Y}}$) ▷ **Separate** representations for nodes in G_1, G_2
return $\tilde{\mathbf{Y}}_1, \tilde{\mathbf{Y}}_2$

Figure: from `https://arxiv.org/pdf/1802.06257.pdf`

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- Colors: choose them well. Try changing default colors and removing grids from plots, etc.

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- **Description of Experiments:** Experiments need to be clearly described, including small details like the number of times you repeated such experiment. Always reference the figure or table where the results appear wrt a given experiment.

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- **Inspirational Parting Thought:** What is the main reason people should care and why does your work advance the field?

Publishing in Comp Bio

- Conferences
  - ISMB
  - RECOMB
  - ACM BCB
- Journals
  - Bioinformatics
  - Cell Systems
  - Nature Journals (Nature Methods, Nature Biotech, Nature Communications)

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- More appealing to biology audience.
- Very expensive to publish

Providing Code

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- Repository should contain a pre-processed version of the data and instructions about how to run code on these data.

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- Writing a version of your paper with all of the technical details for ArXiv is very good practice.

A Word of Advice for Being a PhD Student in Comp Bio

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- Check where your potential collaborators put their comp bio people in the author list.

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- You need to translate your complex model to a series of steps that don't involve mathematical phrases that we all take for granted. For example, don't say phrases like 'L1 penalty'

Choosing What to Work On

Inspired by the talk of Quaid Morris
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- Choose hard problems rooted in biology that other people wouldn't have thought to ask because they don't read the biological literature.
- Watch the superstars who speak both languages. Watch how they publish and what they choose to work on.

Transitioning and Summarizing What we Have Covered

We have focused on representing data as graphs and using the graphs to help us to answer questions.

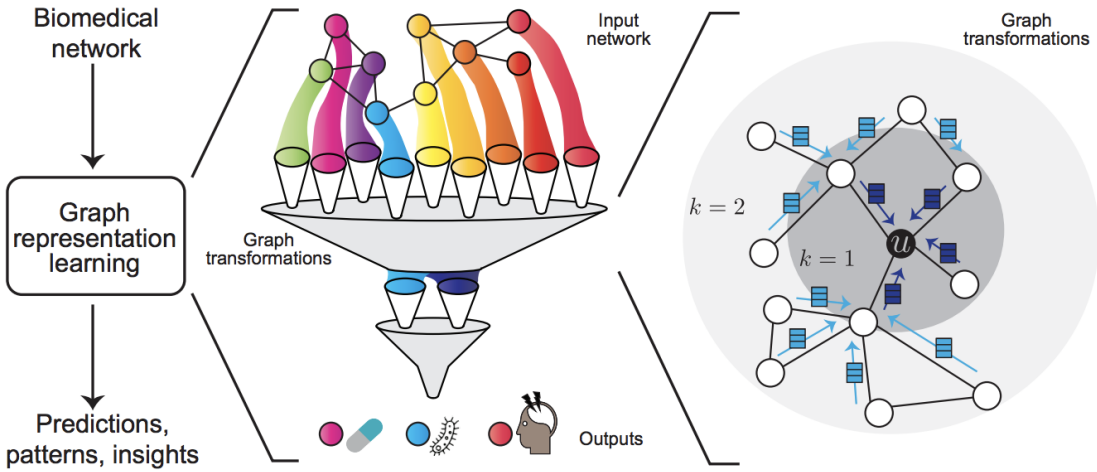
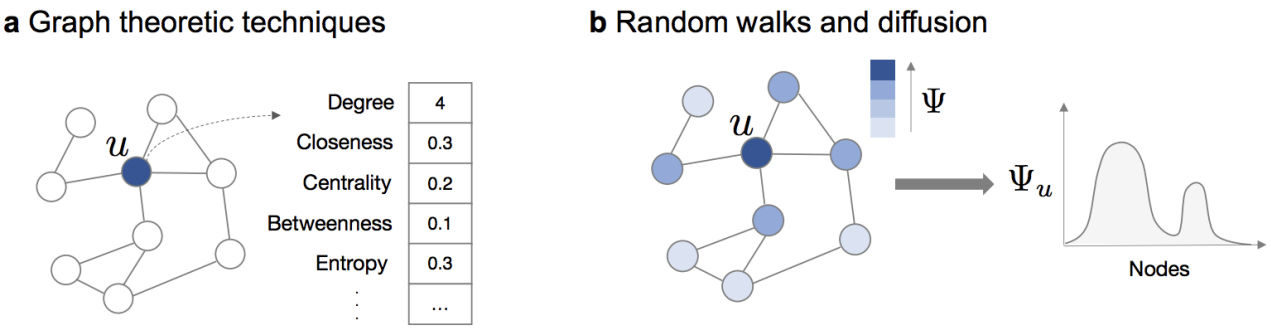


Figure: From `https://arxiv.org/abs/2104.04883`. For example. Assigning proteins to groups or people to outcomes.

Class 1: Graph Summary Statistics and Diffusion

Summary statistics and diffusion can describe patterns in the graph, importance of nodes,



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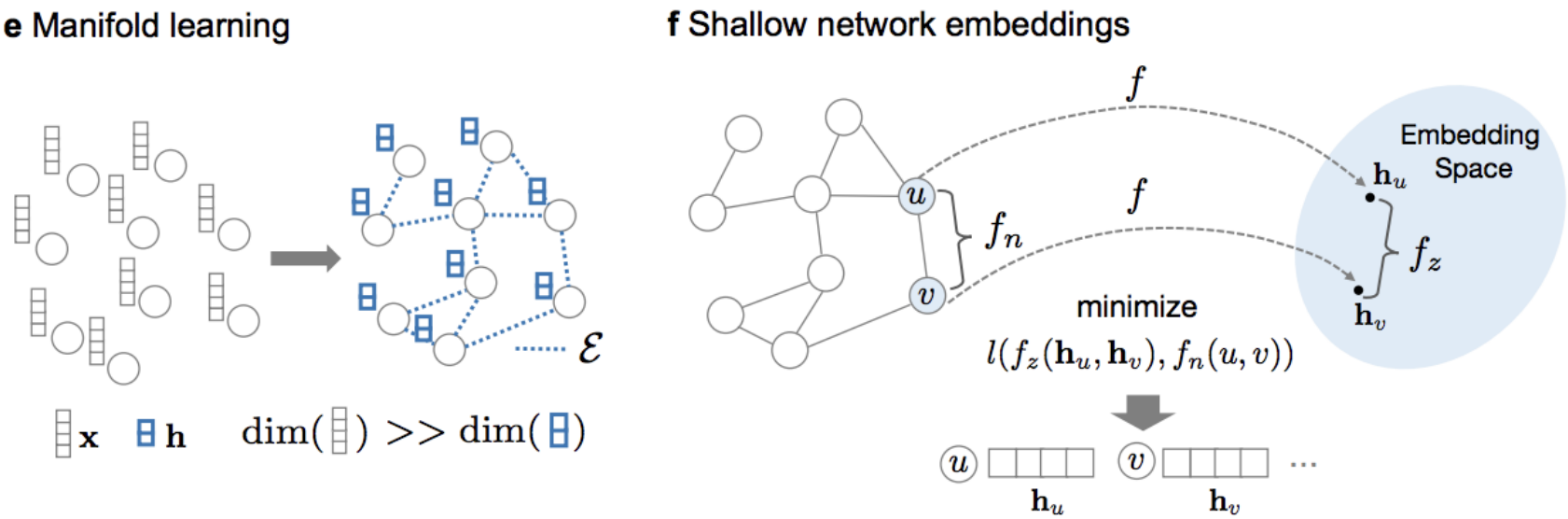
- **REGAL:** graph alignment based on structural properties

Node Embedding Theme



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- SLICER for trajectory inference (manifold)
- Grassmann Embedding for combining multiple datasets (manifold)
- Mashup for embedding nodes according to multiple relational definitions (embedding)

Class 3: Machine Learning on Graphs

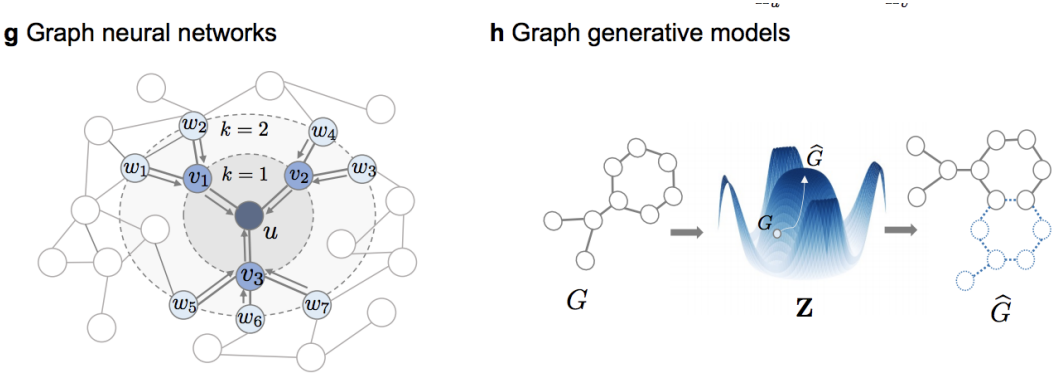

Figure: We haven't seen so much here.....

Seen in ML on Graphs

- Correct and Smooth for predicting labels of nodes based on simple base predictor for node features.

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- More next year.....