Comp683: Computational Biology

Lecture 5

January 27, 2025

Today

- Probabilistic graph partitioning
  - Stochastic block model
  - Affiliation Model
- Graph embedding with node2vec

Examples of Biological Networks

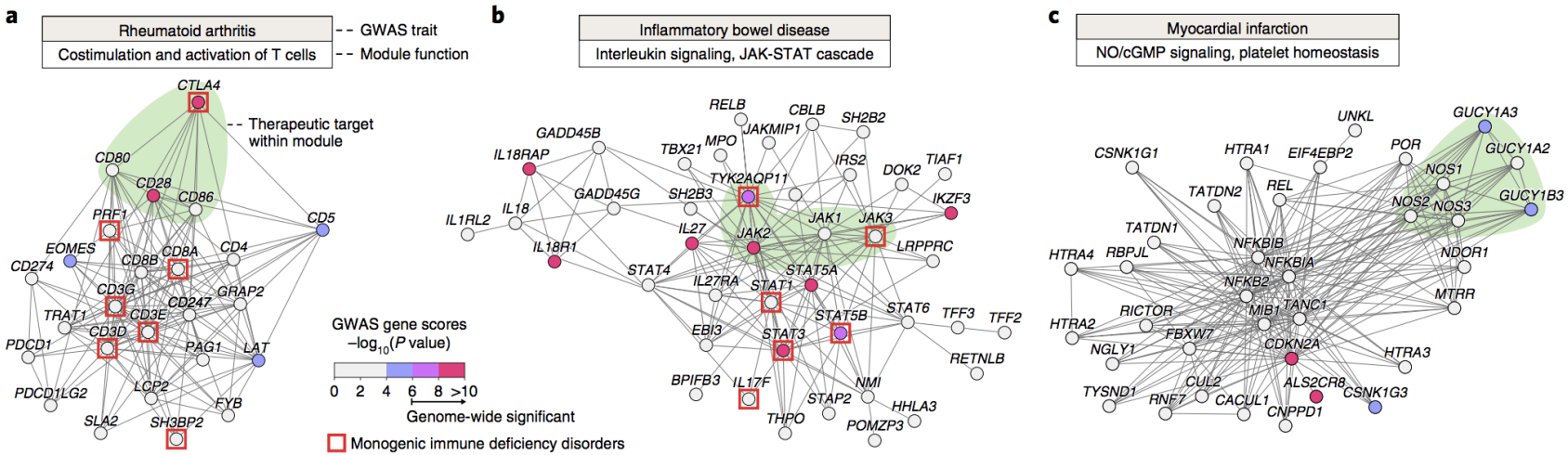


Figure: from Choodbar *et al.* Nature Methods 2018.

Transition to two probabilistic optimization approaches where a partition is optimized in a way that can best recapitulate the observed edges.

Edges as Coin Flips

- I want to grab a pair of nodes and guess whether or not there should be an edge between them
- We could use clusters assignments of nodes to make such a decision
  - An OK assumption because we assume that nodes should be more connected within a cluster than between
- We will model the probability that an edge exists between nodes based on the cluster assignments of the nodes
- issue: We at first don't know the cluster assignments for nodes!

Stochastic Block Model (SBM)

- **Intuition:** Members of a community should be connected to themselves and to members of other communities in the same way.
- **Model:** Assuming we have N nodes and K communities, we infer two main parameters
  - $\boldsymbol{\theta} \in \mathbb{R}^{K \times K}$, a matrix of between-community edge probabilities
  - $\mathbf{z} \in \mathbb{R}^{N \times 1}$, a vector of node-to-community assignments

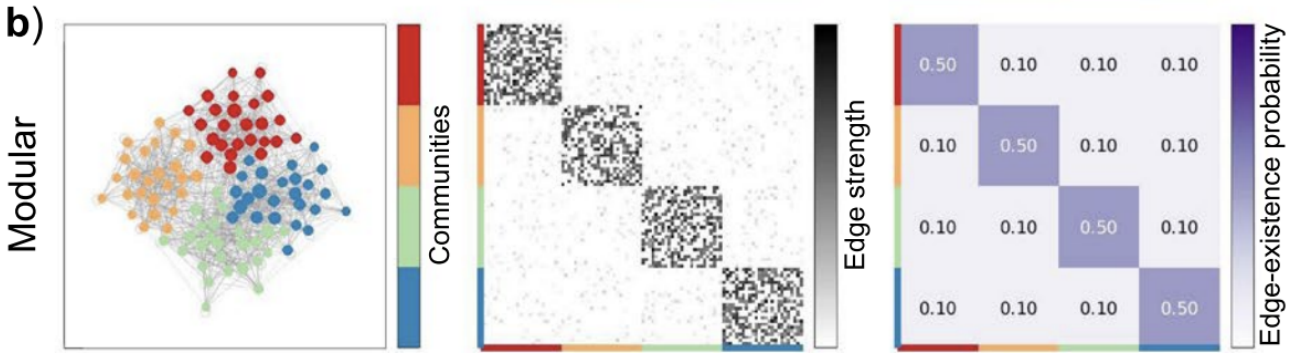


Figure: Notice the high within-edge probability on the diagonal of $\boldsymbol{\theta}$. from Fastkowitz *et al.* Scientific Reports. 2018.

Let's Try to Guess Some θs

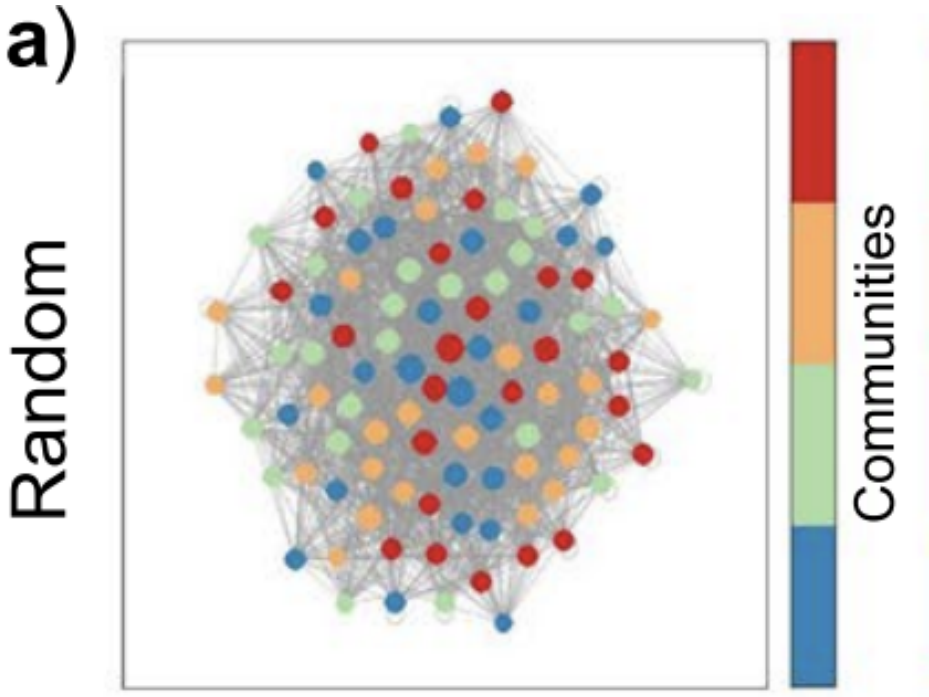


Figure: No structure (this is in fact a random graph). Connections between all kinds of nodes.

A Harder θ

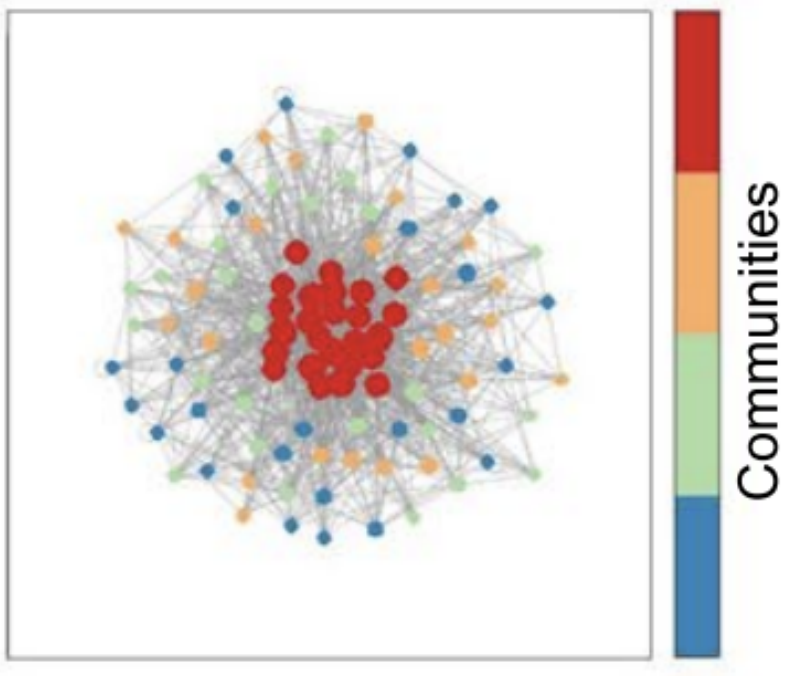
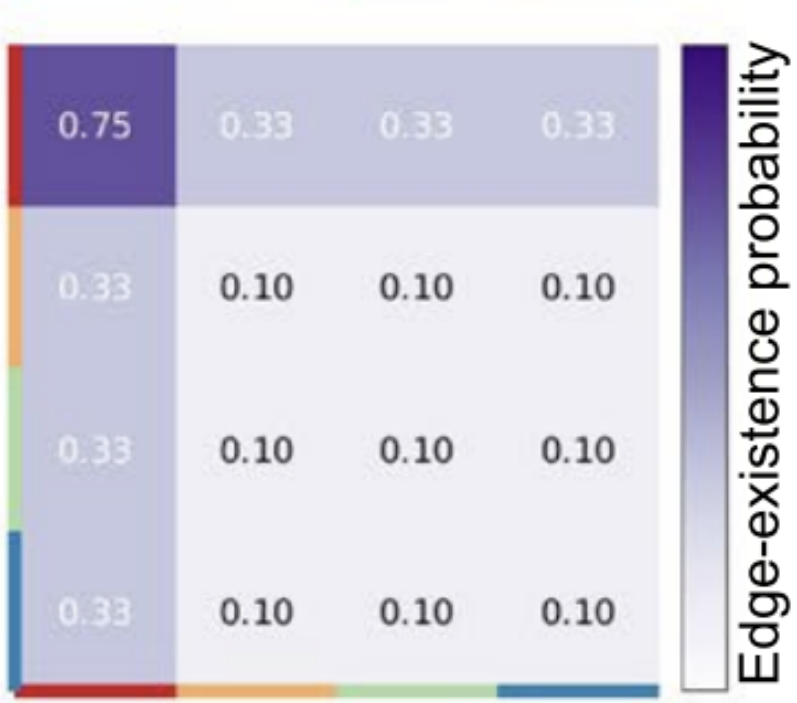


Figure: One cluster with lots of connections within and to which many nodes connect

Answer


0.75
0.33
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0.10
Edge-existence probability

Learning Parameters

Let $\mathbf{Z}$ by an $N \times K$ indicator matrix with $Z_{ik} = 1$ if a node is assigned to community k and $Z_{ik} = 0$ otherwise [1]. $\mathbf{A}$ is our binary $N \times N$ adjacency matrix.

$$A_{ij} \sim \text{Bernoulli}(\boldsymbol{\theta}_{z_i, z_j}) \tag{1}$$

The complete data log-likelihood of the observed graph ($\mathbf{A}$) and the node-to-community assignments ($\mathbf{Z}$) can be written as,

$$\log P(\mathbf{A}, \mathbf{Z}) = \log P(\mathbf{Z}) + \log P(\mathbf{A} \mid \mathbf{Z}) \tag{2}$$

[1] $\mathbf{z}_i$ gives the cluster assignment of node i.

SBM Complete Data Log Likelihood

$$\log P(\mathbf{A}, \mathbf{Z}) = \sum_i \sum_q Z_{iq} \log \alpha_q + \frac{1}{2} \sum_{i \neq j} \sum_{q,l} Z_{iq} Z_{jl} \log b(A_{ij}, \theta_{ql}) \qquad (3)$$

- α_q is the probability (in general) of being in community q.
- $b(a, \pi) = \pi^a (1 - \pi)^{1-a}$

SBM Complete Data Log Likelihood, Continued

$\sum_i \sum_q Z_{iq} \log \alpha_q + \frac{1}{2} \sum_{i \neq j} \sum_{q,l} Z_{iq} Z_{jl} \log b(A_{ij}, \theta_{ql})$ can be written completely as,

$$\sum_i \sum_q Z_{iq} \log \alpha_q + \frac{1}{2} \sum_{i \neq j} \sum_{q,l} Z_{iq} Z_{jl} \underbrace{[A_{ij} \log(\theta_{ql})}_{\text{edges}} + \underbrace{(1 - A_{ij}) \log(1 - \theta_{ql}))]}_{\text{no edges}} \tag{4}$$

Fitting Parameters

- I will not go through it here, but you can either use expectation maximization (EM), belief propagation, or MCMC methods.
  - See → `https://arxiv.org/abs/1207.2328` for EM and BP
  - See → `https://journals.aps.org/pre/abstract/10.1103/PhysRevE.89.012804` for MCMC
- The fastest implementation of SBM model parameters that is most readily scalable to large graphs can be found in GraphTool → `https://graph-tool.skewed.de`

Issue

The presented approach is most appropriate for unweighted graphs. Currently, it is more challenging to accommodate edge-weights well without assuming some kind of a distribution on edge weights.

- Any ideas about this?

SBM Applied To Spatial Transcriptomics Dataset

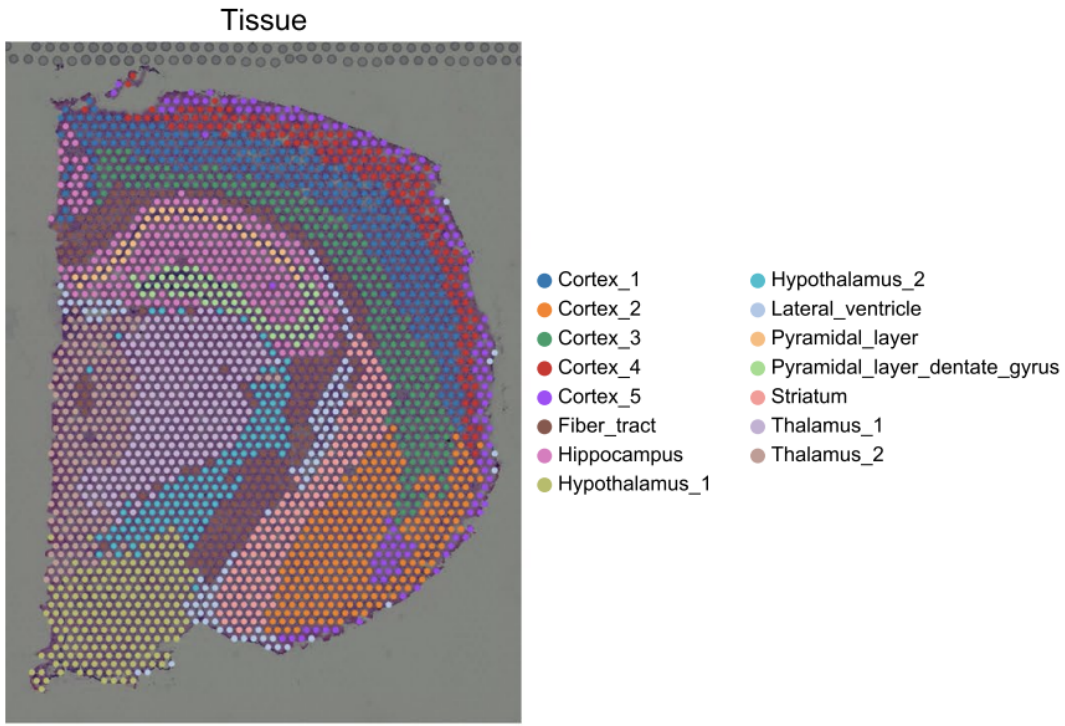
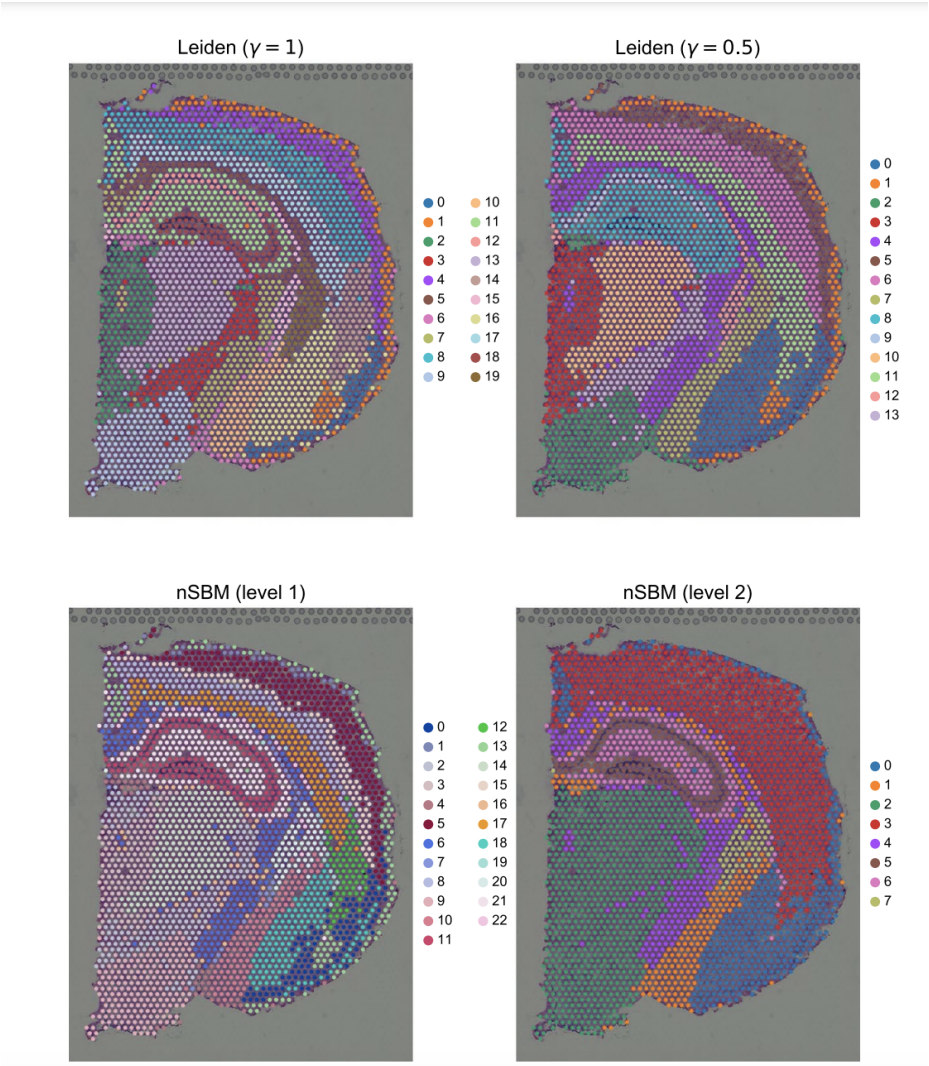


Figure: ground-truth annotation of cells within a coronal section of a mouse-brain from `https://link.springer.com/article/10.1186/s12859-021-04489-7`

Leiden vs SBM



Affiliation Model for Community Structure

- This is a *soft* clustering approach where overlapping communities are allowed
- Instead of learning a hard node-to-community partition, we learn a node-to-community *propensity*

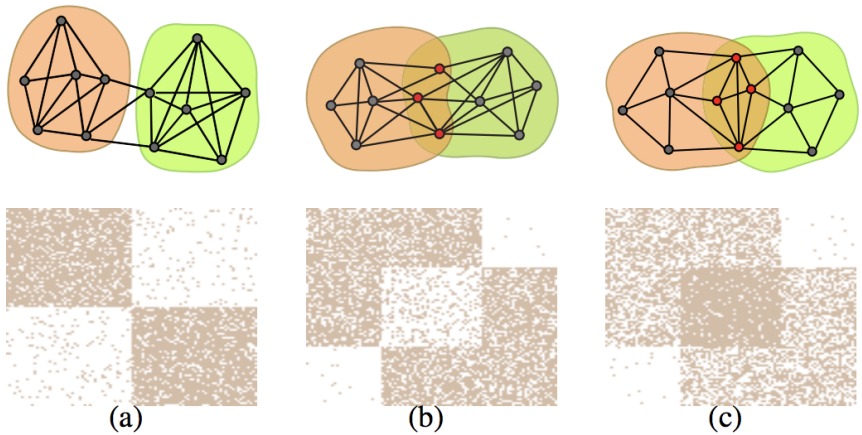


Figure: from Yang *et al.* ICDM. 2012

'BigClam' Approach to Overlapping Communities

Model the existence of an edge between nodes u and v based on the inner product of propensities, F_u and F_v.

DEFINITION 1. *Let F be a nonnegative matrix where F_{uc} is a weight between node $u \in V$ and community $c \in C$. Given F, the* BIGCLAM *generates a graph $G(V, E)$ by creating edge (u, v) between a pair of nodes $u, v \in V$ with probability $p(u, v)$:*

$$p(u, v) = 1 - \exp(-F_u \cdot F_v^T), \tag{1}$$

where F_u is a weight vector for node u ($F_u = F_{u\cdot}$).

Figure: from Yang and Leskovec. WSDM. 2013.

Finding the Optimal F_u

The log-likelihood of the graphs given the learned propensities, $\mathbf{F}_u$ can be expressed as follows. The authors optimize each $\mathbf{f}_u$ by fixing $\mathbf{f}_v$.

$$l(F_u) = \sum_{v \in \mathcal{N}_u} \log(1 - \exp(-F_u F_v^T)) - \sum_{v \notin \mathcal{N}(u)} F_u F_v^T \tag{5}$$

See their paper for more details. `https://cs.stanford.edu/people/jure/pubs/bigclam-wsdm13.pdf`.

Edge Probability vs Number of Shared Memberships

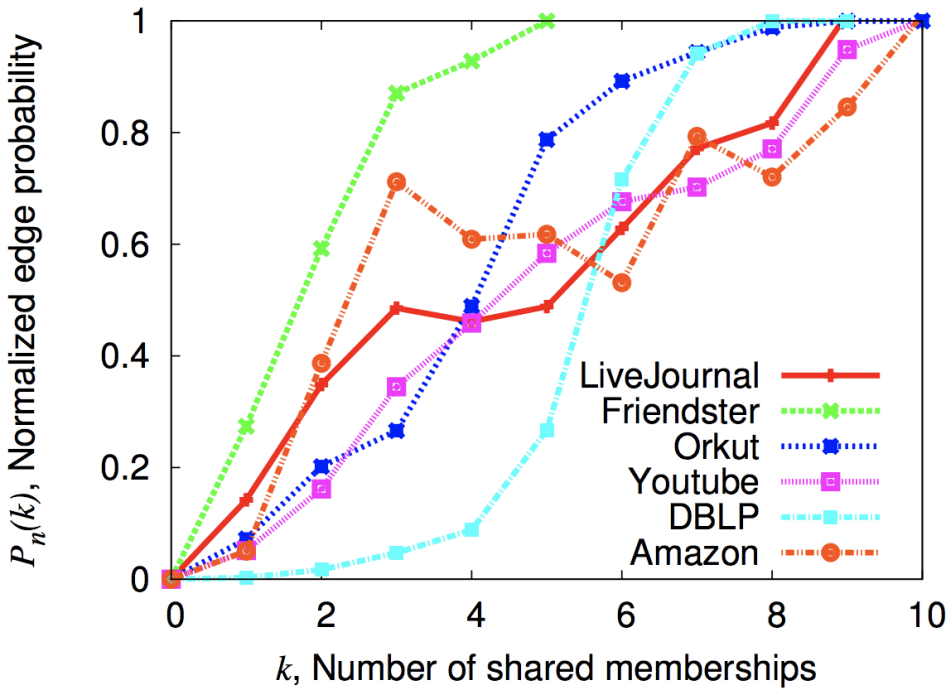


Figure: from Yang and Leskovec. WSDM. 2013.

Graph Representation Learning

- There is a lot of recent hype in the graph world about feature learning from graphs or learning a representation for each node in a continuous vector space
- For a particular node, u, the objective is to learn some representation in d dimensions, $f(u)$, with $f(u) \in \mathbb{R}^d$

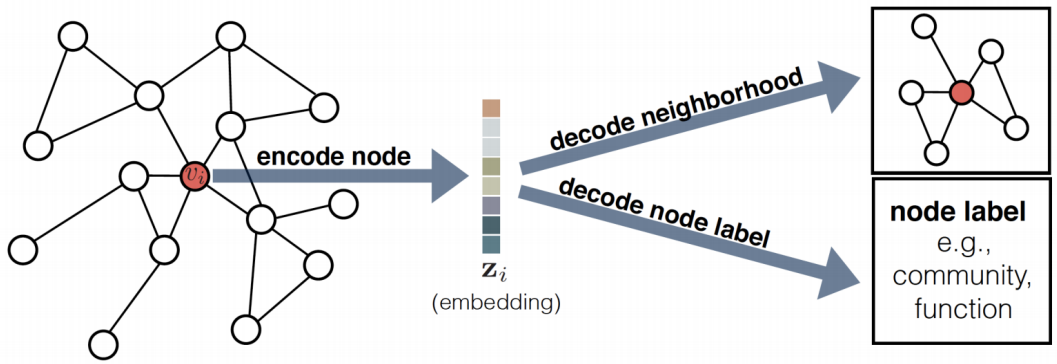


Figure: from Hamilton *et al.* ArXiv. 2018

Get Graph Partitioning for Free from Embedding

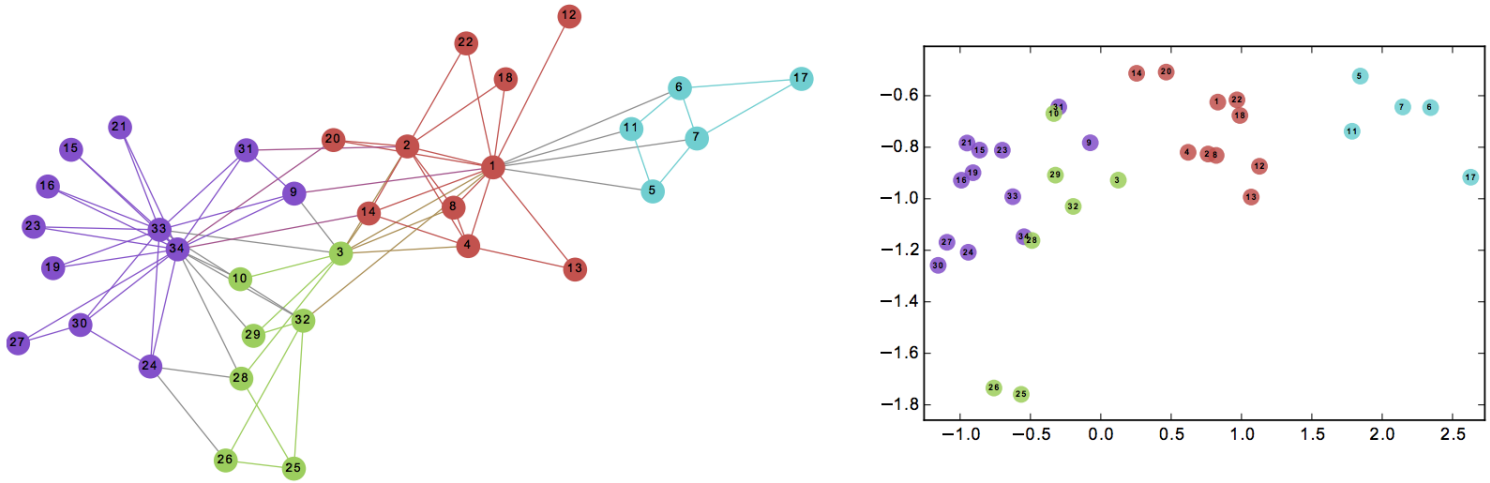
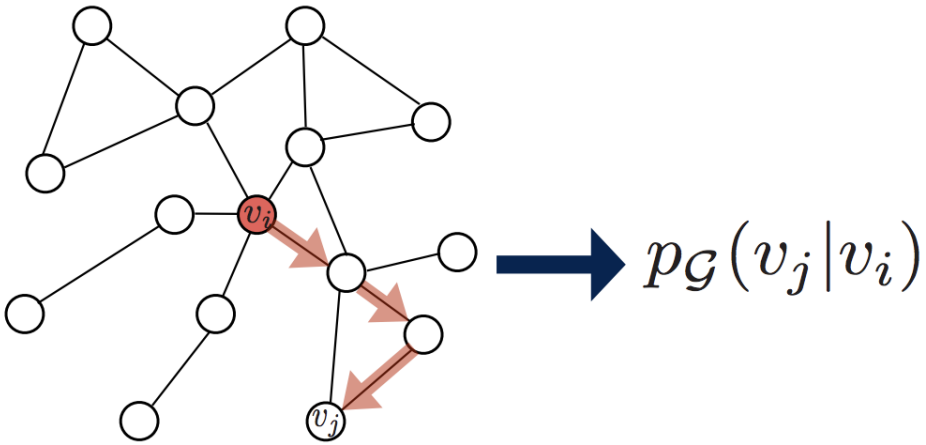
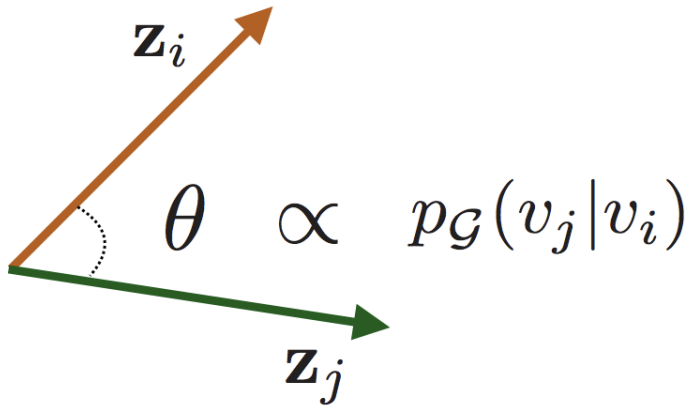


Figure: from Perozzi *et al.* KDD. 2014

The Random Walk Based Approach



1. Run random walks to obtain co-occurrence statistics.



2. Optimize embeddings based on co-occurrence statistics.

Figure: from Hamilton *et al.* ArXiv. 2018

Encoding the 'Role' of a Node with Node2Vec

- Node2Vec allows for control of whether the embedding captures between-node structural similarity (neighborhoods) or role (the types of nodes in connection with)

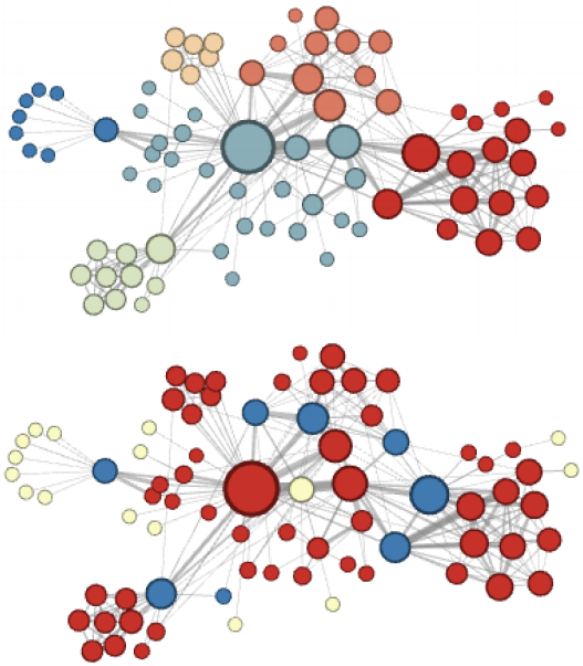


Figure: from Grover and Leskovec. KDD. 2016

Other Similar Approaches

- LINE → `https://arxiv.org/abs/1503.03578`
- DeepWalk → `https://arxiv.org/abs/1403.6652`
- Node2Vec → `https://arxiv.org/abs/1607.00653`
- Splitter → `https://arxiv.org/pdf/1905.02138.pdf`

Flexible Notion of Neighborhood (Breadth First)

When defining a neighborhood set N_s of some node u, there are two possible strategies. The following example assumes sampling $k = 3$ nodes.

- **Breadth-first Sampling:** Find the most immediate neighbors of node u and sequentially sample additional nodes according to their distance from u. In the image below, if we are selecting k neighbors, this selects s_1, s_2, s_3.

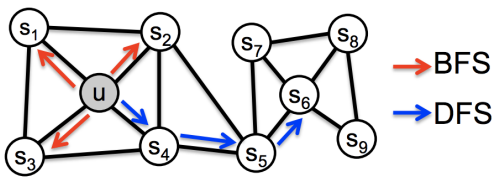


Figure 1: BFS and DFS search strategies from node u ($k = 3$).

Figure: from Leskovec and Grover. KDD. 2016

Flexible Notion of Neighborhood (Depth First)

- **Depth-first Sampling:** Select nodes sampled at sequentially further distances from the source node, u. According to the example below, nodes s_4, s_5, s_6 are selected.

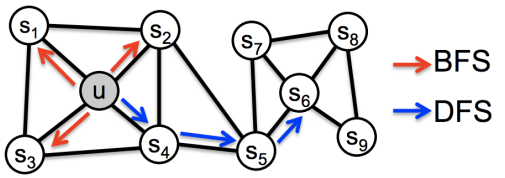


Figure 1: BFS and DFS search strategies from node u ($k = 3$).

Figure: from Leskovec and Grover. KDD. 2016

Node2Vec Objective

Starting with a graph, G with $G = (V, E)$, then the task if to learn a mapping function, f with $f : V \to \mathbb{R}^d$. Here, d is the number of dimensions of of f. Ultimately, f is a matrix of size $|V| \times d$. $\mathcal{N}_s(u)$ is further defined as the nodes that are sampled in the walk from u. Then the objective is to find an f such that,

$$\sum_{u \in V} \log P(\mathcal{N}_s(u) \mid f(u)) \tag{6}$$

is as large as possible. Here, $\mathcal{N}_s(u)$ is conditioned on the feature representation of u, $f(u)$.

Conditional Independence Assumption

$$P(\mathcal{N}_S(u)|f(u)) = \prod_{n_i \in \mathcal{N}_s(u)} P(n_i \mid f(u)). \tag{7}$$

Conditional Likelihood for each Source, Neighborhood Pair

To model each source (u), neighborhood pair and given the conditional independence assumption introduced on the previous slide,

$$P(n_i \mid f(u)) = \frac{\exp(f(n_i) \cdot f(u))}{\sum_{v \in V} \exp(f(v) \cdot f(u))} \tag{8}$$

Varying Neighborhood According to DFS or BFS

As we have pointed out, $\mathcal{N}_S(u)$ is not restricted to the immediate neighbors of u. The authors define a flexible notion of a random walk on the graph that allows for sampling in either a DFS or BFS way. Assuming the random walk has just traversed edge (t, v) and now resides at node v. The transition probability from v to x (π_{vx}) can be written as,

$$\pi_{vx} = \alpha_{pq}(t, x) \cdot w_{vx} \tag{9}$$

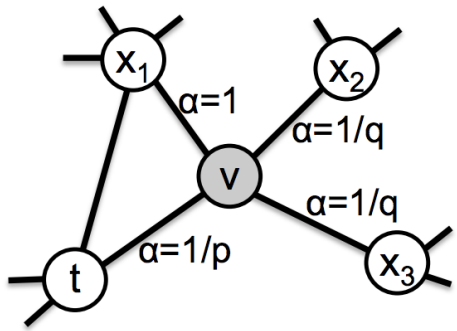


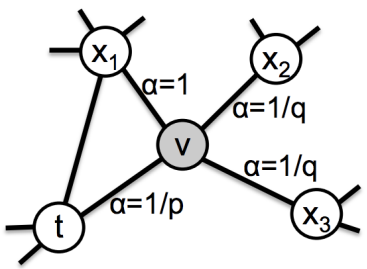
Figure: from Grover and Leskovec, KDD. 2016

Varying Neighborhood According to DFS or BFS

$$\pi_{vx} = \alpha_{pq}(t, x) \cdot w_{vx} \tag{10}$$

Here w_{vx} is the edge weight between nodes v and x or simply $\{0, 1\}$ if the graph is unweighted. d_{tx} denotes shortest path distance between t and x (we are at v). A user can specify p or q.

$$\alpha_{p,q}(t, x) = \begin{cases} 1/p & \text{if} d_{tx} = 0 \\ 1 & \text{if} d_{tx} = 1 \\ 1/q & \text{if} d_{tx} = 2 \end{cases}$$



Intuition Behind p

- p controls the likelihood of immediately revisiting a node in the walk.
  - A **low** value of p would keep the walk local, close to the starting node, u. A low value of p would encourage local walks next to a source node, u.

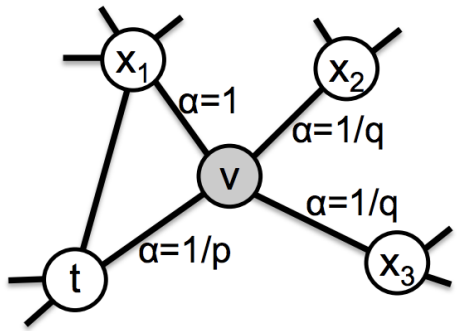


Figure: from Grover and Leskovec, KDD. 2016

Intuition Behind q

item q allows for differentiation between inward and outward nodes

- For $q < 1$, the walk is inclined to visit nodes that are further from node t. (Depth First)

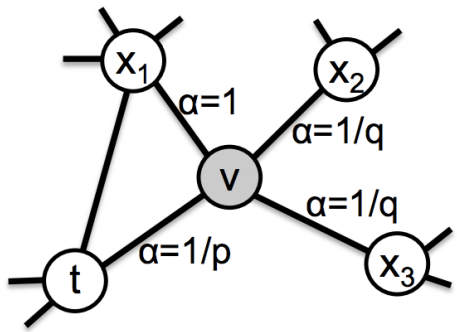
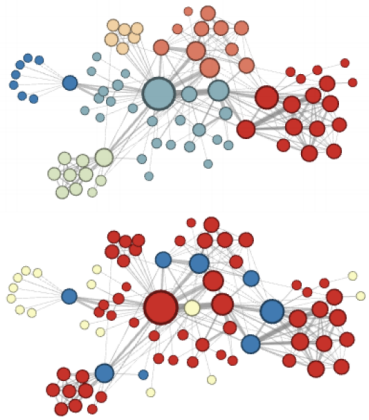


Figure: from Grover and Leskovec, KDD. 2016

Allow for Variation in What Defines Nodes as Being Similar

- **Application of Capturing Local Similarities:** Identify proteins involved in a common pathway. Or parts of the brain that are correlated to each other.
- **Usefulness of Capturing More Global Similarities:** Identify proteins that are regulators of many other proteins but are not related extensively among them selves.
- Validating a graph representation (**project idea!!!**).



Embedding as a Tool for a Variety of Tasks on Graphs

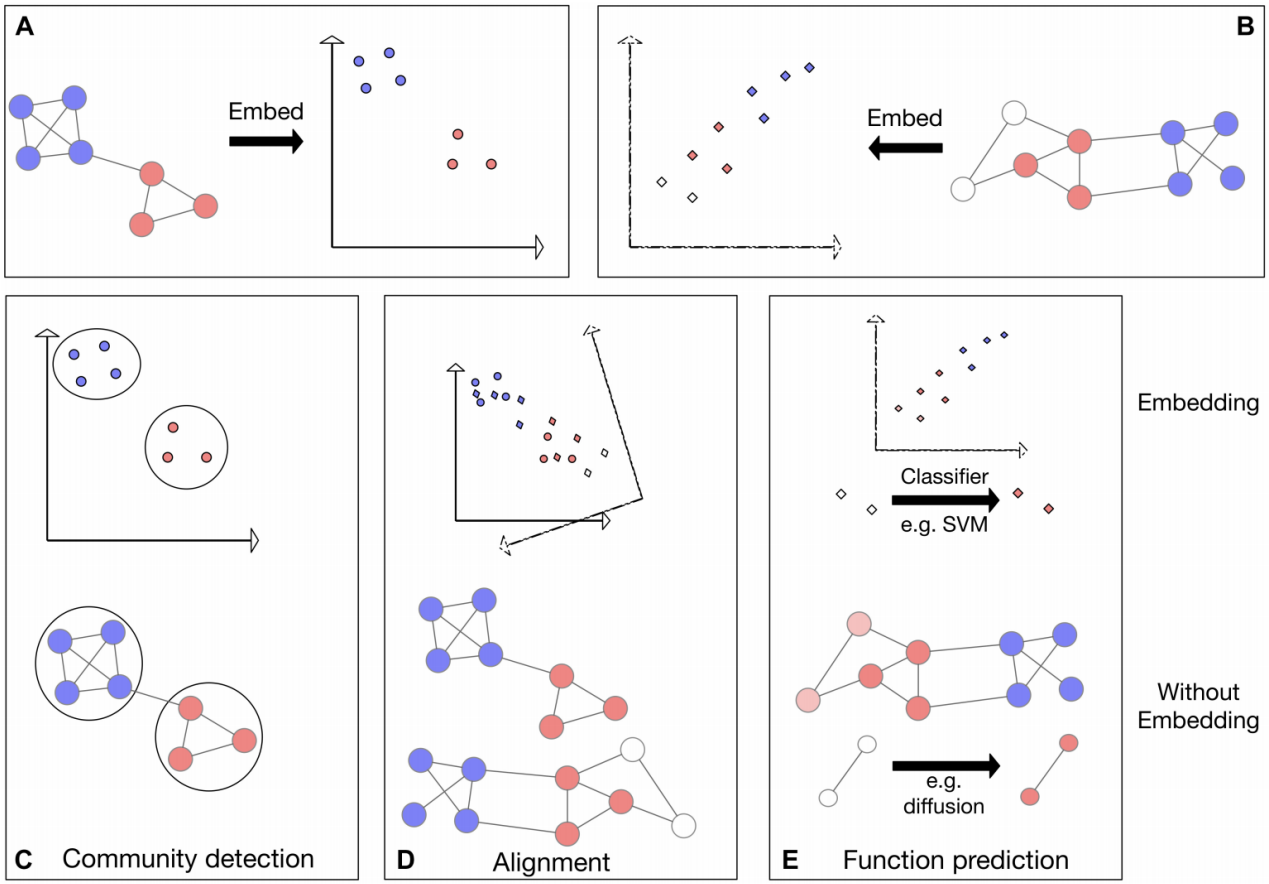


Figure: from Nelson *et al.* Frontiers in Genetics. 2019. Protein families (C). Cross-Species Alignment (D), Function Prediction (E)