# Methods

## Grid search of random walk embeddings

We performed grid searches to identify the optimal combination of hyperparameters in node2vec and edge2vec that returns the best predictive performance of known gene-AD connections.

We explored the following set of hyperparameters for node2vec:

1. the return parameter *p*, [2.0, 1.0, 0.5], which controls the likelihood of returning to a visited node;
2. the in-out parameter *q*, [2.0, 1.0, 0.5], which controls whether the walk explores locally;
3. *walk length*, [5, 10], which determines the length of a random walk.

Additionally, *the number of random walks* initiated from each node was set to 5. This hyperparameter accounted for the probabilistic process of random walks. In total, there were eighteen combinations of hyperparameters for node2vec. In addition to the above hyperparameters, we also explored different *numbers of Expectation-Maximization (EM) iterations*, [3, 5], a hyperparameter specific to edge2vec used to learn the transition matrix of edge types. As a result, we examined a total of thirty-six combinations of hyperparameters for edge2vec. Word2vec was instructed to learn 128-dimensional embeddings using a context window of two and five epochs of stochastic gradient descent.

The learned embeddings were evaluated for their representativeness of graph features by testing how well embeddings could predict gene-AD connections in Hetionet using XGBoost. The input to the XGBoost classifier was the concatenated embedding of each gene-disease pair. Positive edges were the known gene–disease links in Hetionet, while the same number of negative edges were randomly sampled. Edges in Hetionet were randomly split into training (80%) and testing (20%). The XGBoost prediction accuracy was evaluated by the AUROC.

# Results

## Random walk performance

The best configuration was selected based on the gene-disease link prediction accuracy using XGBoost, which indicated how well the embeddings captured the network structural features relevant to downstream tasks. Node2vec achieved a mean test prediction accuracy of 60.72% with a standard deviation of 3.90%. The highest accuracy for node2vec reached a test prediction accuracy of 67.62% with *p*=2, *q*=2, and *walk length* = 10. Edge2vec obtained a mean test prediction accuracy of 52.77% with a standard deviation of 7.71%. The highest accuracy for edge2vec achieved a test prediction accuracy of 72.03% with *p*=1, *q*=0.5, and *walk length* = 10.