

Abstract

This vignette shows how to build the ligand-target prior regulatory potential scores based on the NicheNet method but using Omnipath interactions.

Construct a ligand-target model from Omnipath ligand-receptor, signaling and gene regulatory networks

We first load the required packages and the networks generated on the previous scripts: Omnipath ligand-receptor, Omnipath signaling and Omnipath (Dorothea) gene regulatory network. These networks are used to construct the ligand-target model.

```
library(nichenetr)
library(tidyverse)

## We load the networks generated in the ParameterOptimization script
lr_network_Omnipath = readRDS("OmniNetworks_NNformat/lr_Network_Omnipath.rds")
sig_network_Omnipath = readRDS("OmniNetworks_NNformat/sig_Network_Omnipath.rds")
gr_network_Omnipath = readRDS("OmniNetworks_NNformat/gr_Network_Omnipath.rds")
```

Construct NicheNet's ligand-target model from unoptimized data source weights

The interactions available in Omnipath are well curated, and we therefore first create a model considering the same weight for all the databases. On the other hand, we use the optimized parameters for the PageRank algorithm.

```
## The interactions are weighted only based in the number of data sources that
## report them
All_sources <- unique(c(lr_network_Omnipath$source,
  sig_network_Omnipath$source, gr_network_Omnipath$source))

my_source_weights_df <-
  tibble(source = All_sources, weight = rep(1,length(All_sources)))

weighted_networks <- construct_weighted_networks(
  lr_network = lr_network_Omnipath,
  sig_network = sig_network_Omnipath,
  gr_network = gr_network_Omnipath,
  source_weights_df = my_source_weights_df)

## We read the results of the optimization
resultsOptimization <- readRDS("Results/Optimization_results.rds")

optimized_parameters = resultsOptimization %>%
  process_mlrmbbo_nichenet_optimization(
    source_names = my_source_weights_df$source %>% unique())

weighted_networks <- apply_hub_corrections(
  weighted_networks = weighted_networks,
  lr_sig_hub = optimized_parameters$lr_sig_hub,
  gr_hub = optimized_parameters$gr_hub)
saveRDS(weighted_networks, "Results/weighted_networksNonSourceWeights.rds")
```

We now generate the matrix containing the ligand-target regulatory potential scores based on the weighted integrated networks.

```
ligands <- as.list(unique(lr_network_Omnipath$from))

ligand_target_matrix <- construct_ligand_target_matrix(
  weighted_networks = weighted_networks,
  ligands = ligands,
  algorithm = "PPR",
  damping_factor = optimized_parameters$damping_factor,
  ltf_cutoff = optimized_parameters$ltf_cutoff)
saveRDS(ligand_target_matrix, "Results/ligand_target_matrixNoweights.rds")
```

Construct NicheNet's ligand-target model from optimized data source weights

Now, we create an alternative model using the optimized weights for the different sources of data.

```
## Here we also take into account the optimized source weights
weighted_networks <- construct_weighted_networks(
  lr_network = lr_network_Omnipath,
  sig_network = sig_network_Omnipath,
  gr_network = gr_network_Omnipath,
  source_weights_df = optimized_parameters$source_weight_df)

weighted_networks <- apply_hub_corrections(
  weighted_networks = weighted_networks,
  lr_sig_hub = optimized_parameters$lr_sig_hub,
  gr_hub = optimized_parameters$gr_hub)

ligand_target_matrix = construct_ligand_target_matrix(
  weighted_networks = weighted_networks,
  ligands = ligands,
  algorithm = "PPR",
  damping_factor = optimized_parameters$damping_factor,
  ltf_cutoff = optimized_parameters$ltf_cutoff)
saveRDS(ligand_target_matrix, "Results/ligand_target_matrixWithweights.rds")
saveRDS(weighted_networks, "Results/weighted_networksWithSourceWeights.rds")
```