

main

August 21, 2021

## 1 GO analysis using GOATOOLS

```
[1]: import functools
import pandas as pd
import collections as cx
from pybiomart import Dataset
# GO analysis
from goatools.base import download_go_basic_obo
from goatools.base import download_ncbi_associations
from goatools.obo_parser import GODag
from goatools.anno.genetogo_reader import Gene2GoReader
from goatools.goea.go_enrichment_ns import GOEnrichmentStudyNS
```

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[2]: @functools.lru_cache()
def get_database():
    dataset = Dataset(name="hsapiens_gene_ensembl",
                      host="http://www.ensembl.org",
                      use_cache=True)
    db = dataset.query(attributes=["ensembl_gene_id",
                                  "external_gene_name",
                                  "entrezgene_id"],
                       use_attr_names=True).dropna(subset=['entrezgene_id'])
    return db

@functools.lru_cache()
def get_deg():
    fn = '../_m/genes/diffExpr_EAvsAA_FDR05.txt'
    return pd.read_csv(fn, sep='\t')

@functools.lru_cache()
def convert2entrez():
    df = get_deg()
    if 'EntrezID' in df.columns:
        return df.rename(columns={'EntrezID': 'entrezgene_id'})
    else:
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        return df.merge(get_database(), left_on='ensemblID',
                        right_on='ensembl_gene_id')

@functools.lru_cache()
def get_upregulated():
    df = convert2entrez()
    return df.loc[(df['t'] > 0)]

@functools.lru_cache()
def get_downregulated():
    df = convert2entrez()
    return df.loc[(df['t'] < 0)]

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[3]: def obo_annotation(alpha=0.05):
    # database annotation
    fn_obo = download_go_basic_obo()
    fn_gene2go = download_ncbi_associations() # must be gunzip to work
    obodag = GODag(fn_obo) # downloads most up-to-date
    anno_hs = Gene2GoReader(fn_gene2go, taxids=[9606])
    # get associations
    ns2assoc = anno_hs.get_ns2assoc()
    for nspc, id2gos in ns2assoc.items():
        print("{NS} {N:,} annotated human genes".format(NS=nspc, N=len(id2gos)))
    goeaobj = GOEnrichmentStudyNS(
        get_database()['entrezgene_id'], # List of human genes with entrez IDs
        ns2assoc, # geneid/GO associations
        obodag, # Ontologies
        propagate_counts = False,
        alpha = alpha, # default significance cut-off
        methods = ['fdr_bh'])
    return goeaobj

def run_goea(direction):
    if direction == "Up":
        df = get_upregulated()
    elif direction == "Down":
        df = get_downregulated()
    else:
        df = convert2entrez()
    geneids_study = {z[0]:z[1] for z in zip(df['entrezgene_id'], df['Symbol'])}
    goeaobj = obo_annotation()
    goea_results_all = goeaobj.run_study(geneids_study)
    goea_results_sig = [r for r in goea_results_all if r.p_fdr_bh < 0.05]

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ctr = cx.Counter([r.NS for r in goea_results_sig])
print('Significant results[{TOTAL}] = {BP} BP + {MF} MF + {CC} CC'.format(
    TOTAL=len(goea_results_sig),
    BP=ctr['BP'], # biological_process
    MF=ctr['MF'], # molecular_function
    CC=ctr['CC'])) # cellular_component

if direction == "Up":
    label = "upregulated"
elif direction == "Down":
    label = "downregulated"
else:
    label = "allDEG"
goeobj.wr_xlsx("GO_analysis_%s.xlsx" % label, goea_results_sig)
goeobj.wr_txt("GO_analysis_%s.txt" % label, goea_results_sig)

```

## 1.1 Gene ontology

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[4]: for direction in ["All", "Up", "Down"]:
    run_goea(direction)

```

```

requests.get(http://purl.obolibrary.org/obo/go/go-basic.obo, stream=True)
WROTE: go-basic.obo

```

```

FTP RETR ftp.ncbi.nlm.nih.gov gene/DATA gene2go.gz -> gene2go.gz
gunzip gene2go.gz
go-basic.obo: fmt(1.2) rel(2021-08-18) 47,217 GO Terms
HMS:0:00:04.446010 330,313 annotations, 20,685 genes, 18,684 GOs, 1 taxids READ:
gene2go
BP 18,505 annotated human genes
MF 18,190 annotated human genes
CC 19,422 annotated human genes

```

```

Load BP Gene Ontology Analysis ...
70% 20,236 of 29,107 population items found in association

```

```

Load CC Gene Ontology Analysis ...
74% 21,428 of 29,107 population items found in association

```

```

Load MF Gene Ontology Analysis ...
70% 20,354 of 29,107 population items found in association

```

```

Run BP Gene Ontology Analysis: current study set of 786 IDs ... 81%    472 of
580 study items found in association
74%    580 of    786 study items found in population(29107)
Calculating 12,429 uncorrected p-values using fisher
12,429 GO terms are associated with 17,848 of 29,107 population items
2,280 GO terms are associated with    472 of    786 study items

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METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) ( 0 enriched + 0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run CC Gene Ontology Analysis: current study set of 786 IDs ... 87%    505 of
580 study items found in association
74%    580 of    786 study items found in population(29107)
Calculating 1,753 uncorrected p-values using fisher
    1,753 GO terms are associated with 18,711 of 29,107 population items
    408 GO terms are associated with    505 of    786 study items
METHOD fdr_bh:
    5 GO terms found significant (< 0.05=alpha) ( 5 enriched + 0
purified): statsmodels fdr_bh
    324 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run MF Gene Ontology Analysis: current study set of 786 IDs ... 85%    491 of
580 study items found in association
74%    580 of    786 study items found in population(29107)
Calculating 4,420 uncorrected p-values using fisher
    4,420 GO terms are associated with 17,838 of 29,107 population items
    690 GO terms are associated with    491 of    786 study items
METHOD fdr_bh:
    1 GO terms found significant (< 0.05=alpha) ( 1 enriched + 0
purified): statsmodels fdr_bh
    325 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)
Significant results[6] = 0 BP + 1 MF + 5 CC
    6 items Wrote: GO_analysis_allDEG.xlsx
    6 GOEA results for    424 study items. Wrote: GO_analysis_allDEG.txt
EXISTS: go-basic.obo
EXISTS: gene2go
go-basic.obo: fmt(1.2) rel(2021-08-18) 47,217 GO Terms
HMS:0:00:04.536116 330,313 annotations, 20,685 genes, 18,684 GOs, 1 taxids READ:
gene2go
BP 18,505 annotated human genes
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Load BP Gene Ontology Analysis ...
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Load MF Gene Ontology Analysis ...

```

```

70% 20,354 of 29,107 population items found in association

Run BP Gene Ontology Analysis: current study set of 404 IDs ... 79%    215 of
273 study items found in association
  68%    273 of    404 study items found in population(29107)
Calculating 12,429 uncorrected p-values using fisher
  12,429 GO terms are associated with 17,848 of 29,107 population items
  1,437 GO terms are associated with    215 of    404 study items
  METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) ( 0 enriched + 0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run CC Gene Ontology Analysis: current study set of 404 IDs ... 86%    235 of
273 study items found in association
  68%    273 of    404 study items found in population(29107)
Calculating 1,753 uncorrected p-values using fisher
  1,753 GO terms are associated with 18,711 of 29,107 population items
  280 GO terms are associated with    235 of    404 study items
  METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) ( 0 enriched + 0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run MF Gene Ontology Analysis: current study set of 404 IDs ... 82%    225 of
273 study items found in association
  68%    273 of    404 study items found in population(29107)
Calculating 4,420 uncorrected p-values using fisher
  4,420 GO terms are associated with 17,838 of 29,107 population items
  392 GO terms are associated with    225 of    404 study items
  METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) ( 0 enriched + 0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)
Significant results[0] = 0 BP + 0 MF + 0 CC
  0 items. NOT WRITING GO_analysis_upregulated.xlsx
  0 GOEA results. NOT WRITING GO_analysis_upregulated.txt
  EXISTS: go-basic.obo
  EXISTS: gene2go
go-basic.obo: fmt(1.2) rel(2021-08-18) 47,217 GO Terms
HMS:0:00:04.499649 330,313 annotations, 20,685 genes, 18,684 GOs, 1 taxids READ:
gene2go
BP 18,505 annotated human genes
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```

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Load BP Gene Ontology Analysis ...
  70% 20,236 of 29,107 population items found in association

Load CC Gene Ontology Analysis ...
  74% 21,428 of 29,107 population items found in association

Load MF Gene Ontology Analysis ...
  70% 20,354 of 29,107 population items found in association

Run BP Gene Ontology Analysis: current study set of 382 IDs ... 84%    257 of
307 study items found in association
  80%    307 of    382 study items found in population(29107)
Calculating 12,429 uncorrected p-values using fisher
  12,429 GO terms are associated with 17,848 of 29,107 population items
  1,298 GO terms are associated with    257 of    382 study items
METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) (  0 enriched +  0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run CC Gene Ontology Analysis: current study set of 382 IDs ... 88%    270 of
307 study items found in association
  80%    307 of    382 study items found in population(29107)
Calculating 1,753 uncorrected p-values using fisher
  1,753 GO terms are associated with 18,711 of 29,107 population items
  277 GO terms are associated with    270 of    382 study items
METHOD fdr_bh:
    0 GO terms found significant (< 0.05=alpha) (  0 enriched +  0
purified): statsmodels fdr_bh
    0 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)

Run MF Gene Ontology Analysis: current study set of 382 IDs ... 87%    266 of
307 study items found in association
  80%    307 of    382 study items found in population(29107)
Calculating 4,420 uncorrected p-values using fisher
  4,420 GO terms are associated with 17,838 of 29,107 population items
  456 GO terms are associated with    266 of    382 study items
METHOD fdr_bh:
    1 GO terms found significant (< 0.05=alpha) (  1 enriched +  0
purified): statsmodels fdr_bh
    176 study items associated with significant GO IDs (enriched)
    0 study items associated with significant GO IDs (purified)
Significant results[1] = 0 BP + 1 MF + 0 CC
  1 items WROTE: GO_analysis_downregulated.xlsx
  1 GOEA results for    176 study items. WROTE: GO_analysis_downregulated.txt

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[ ]: