

UCSC, Entrez, KEGG, and Reactome

UCSC genome database is very informative and offers a lot of options that narrow down our search. The genome browser is easy to use and provides good user interface that allows users to look into details by simply clicking a specific locus on the chromosome.

Entrez allows users to search information in cross databases. It reduces works when users try to compare data in different databases. It allows users to select and sort datas in python, which simplifies data manipulation. However, it stores uncurated data, therefore it could provide undesirable information.

KEGG presents the pathways graphically and also allows users to interact with the graph. It clarifies the interaction among pathways. The pathways are categorized.

Reactome also presents pathways in colorful graphs that makes easier to see. It's easy to zoom in and out.

I prefer Reactome because of its simplicity, but Entrez seems to be the most complete because it has info in all databases.

```
In [1]: from Bio import Entrez
        from Bio import SeqIO
        Entrez.email = 'jinghuawu@berkeley.edu'
```

```
In [2]: orgs = ['Drosophila', 'E.coli', 'human']

        glycolysis = ['pyruvate kinase', 'enolase',
                      'Phosphoglycerate mutase', 'phosphofructokinase']

        TCA = ['malate dehydrogenase', 'citrate synthase',
               'aconitase', 'isocitrate dehydrogenase']

        pentose_phosphate = ['glucose 6-phosphate dehydrogenase', 'ribose 5-phosphat
                             'transketolase', 'transaldolase']

        all_enzymes = glycolysis + TCA + pentose_phosphate
```

Data retrieval

Variables "organism", "ids", "enzyme", "path", "description" and "ntsql" are lists that store the categorized information, which can be converted to tuples later.

```

In [3]: #gene data
organism = []
ids = []
enzyme = []
path = []

for o in orgs: #for each organism
    for e in all_enzymes:
        if e in glycolysis:
            path.append("glycolysis")
        elif e in TCA:
            path.append("TCA")
        elif e in pentose_phosphate:
            path.append("pentose phosphate pathway")

    organism.append(o)
    enzyme.append(e)
    handle = Entrez.esearch(db='nucleotide', #can be anything on Entrez
                           term= o + '[Orgn]' + ' AND ' + e + '[Prot]',
                           sort='relevance',
                           idtype='acc', #types of record IDs are re
                           retmax=1)
    for i in Entrez.read(handle)['IdList']:
        ids.append(i)

```

```

In [4]: description = []
ntseq = []
for i in ids:
    handle = Entrez.efetch(db='nucleotide',
                           id=i, #the first one is the most relevant one
                           rettype='gb', #Retrieval type.
                           retmode='text')
    record = SeqIO.read(handle, "gb")
    description.append(str(record.description))
    ntseq.append(str(record.seq[:30]))

```

Turn data into tuples for later use.

```

In [5]: gene_tuple = []
for n in range(len(ids)):
    gene_tuple.append(tuple([ids[n], description[n], organism[n], enzyme[n], path[n]]))

```

Import data to sqlite

```

In [6]: import sqlite3 #provide interface
conn = sqlite3.connect('my.db') #create a Connection object that represents
c = conn.cursor() #create cursor object for method calls later.

```

Gene table (36 different genes)

```
In [7]: #gene table
c.execute(
    """CREATE TABLE gene (id INT,
                           name TEXT,
                           description TEXT,
                           organism TEXT,
                           enzyme TEXT,
                           pathway TEXT,
                           ntseq VARCHAR(20));""")
```

Out[7]: <sqlite3.Cursor at 0x104d69880>

```
In [8]: for i in gene_tuple:
        temp = i
        c.execute("""INSERT INTO gene (id, description, organism, enzyme, path
conn.commit()
```

Pathway table (3 pathways total)

```
In [9]: c.execute("""CREATE TABLE pathway (name TEXT, description TEXT)""")
conn.commit()
```

```
In [10]: c.execute("""INSERT INTO pathway (name, description) VALUES ('glycolysis
c.execute("""INSERT INTO pathway (name, description) VALUES ('TCA', 'a me
c.execute("""INSERT INTO pathway (name, description) VALUES ('pentose_ph
conn.commit()
```

enzyme table (12 enzymes total)

```
In [11]: #enzyme table
c.execute("""CREATE TABLE enzyme (name TEXT, function TEXT, enzyme_commis
conn.commit()
```

```
In [12]: c.execute("""INSERT INTO enzyme (name, function, enzyme_commission, path
VALUES ('pyruvate kinase', 'catalyzes the final step of gly
('enolase', 'metalloenzyme responsible for the cata
('Phosphoglycerate mutase', 'any enzyme that catalyz
('phosphofructokinase', 'a kinase enzyme that phosph
('malate dehydrogenase', 'an enzyme that reversibly
('citrate synthase', 'pace-making enzyme in the first
('aconitase', 'an enzyme that catalyses the stereo-s
('isocitrate dehydrogenase', 'an enzyme that catalyz
('glucose 6-phosphate dehydrogenase', 'a cytosolic e
('ribose 5-phosphate isomerase', 'catalyzes the conv
('transketolase', 'catalyzes two important reactions
('transaldolase', 'an enzyme (EC 2.2.1.2) of the non

conn.commit()
```

```
In [13]: c.execute("SELECT * FROM gene;")
print(c.fetchall())
```

```
[('XM_023317917.1', None, 'PREDICTED: Drosophila hydei pyruvate kinase
(LOC111601379), mRNA', 'Drosophila', 'pyruvate kinase', 'glycolysis',
'TTTCAATACTTAAAAAAACAAAGTTAATA'), ('XM_023310563.1', None, 'PREDICTED
: Drosophila hydei enolase (LOC111596366), mRNA', 'Drosophila', 'enola
se', 'glycolysis', 'TTATTTTGTGATATATTCAATTCTTAGTTTA'), ('NT_033777.3',
None, 'Drosophila melanogaster chromosome 3R', 'Drosophila', 'Phosphog
lycerate mutase', 'glycolysis', 'NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN'), ('N
T_033778.4', None, 'Drosophila melanogaster chromosome 2R', 'Drosophil
a', 'phosphofructokinase', 'glycolysis', 'NNNNNNNNNNNNNNNNNNNNNNNNNNNN
NN'), ('NT_033779.5', None, 'Drosophila melanogaster chromosome 2L', '
Drosophila', 'malate dehydrogenase', 'TCA', 'NNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNN'), ('NC_004354.4', None, 'Drosophila melanogaster chromosome X',
'Drosophila', 'citrate synthase', 'TCA', 'NNNNNNNNNNNNNNNNNNNNNNNNNNNN
NN'), ('NT_033779.5', None, 'Drosophila melanogaster chromosome 2L', '
Drosophila', 'aconitase', 'TCA', 'NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN'), ('
LC058675.1', None, 'Drosophila nasuta Idh gene for isocitrate dehydrog
enase, partial cds, strain: G7', 'Drosophila', 'isocitrate dehydrogena
se', 'TCA', 'CTCATTCTGCCATTCCTCGACATTGAGTTG'), ('AY364534.1', None, 'D
rosophila mojavensis strain MJS 71 glucose-6-phosphate dehydrogenase (
G6pd) gene, exon 4 and partial cds', 'Drosophila', 'glucose 6-phosphat
e dehydrogenase', 'pentose phosphate pathway', 'GGCTGGAATCGCGTGATCGTCG
AGAAGCCC'), ('XM_023305862.1', None, 'PREDICTED: Drosophila hydei ribo
se-5-phosphate isomerase (LOC111593212), mRNA', 'Drosophila', 'ribose
5-phosphate isomerase', 'pentose phosphate pathway', 'TTTCAAATAGATGTCA
AATTCACCTGTGAAA'), ('NT_033777.3', None, 'Drosophila melanogaster chrom
osome 3R', 'Drosophila', 'transketolase', 'pentose phosphate pathway',
'NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN'), ('XM_002005838.2', None, 'Drosophil
a mojavensis uncharacterized protein (Dmoj\GI18849), mRNA', 'Drosophi
la', 'transaldolase', 'pentose phosphate pathway', 'GTCCAGACTAAAGATTTA
GTTGCACCGGGT'), ('NZ_CP009050.1', None, 'Escherichia coli NCCP15648, c
omplete genome', 'E.coli', 'pyruvate kinase', 'glycolysis', 'NNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN'), ('NZ_CP009050.1', None, 'Escherichia coli NCC
P15648, complete genome', 'E.coli', 'enolase', 'glycolysis', 'NNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN'), ('PDAC01000032.1', None, 'Escherichia coli s
```

train TVS 353 NODE_32_length_28275_cov_33.7839, whole genome shotgun s
equence', 'E.coli', 'Phosphoglycerate mutase', 'glycolysis', 'AGAAAGGC
AGTCCGCTGCATAAATCTACGC'), ('CP026473.1', None, 'Escherichia coli strai
n KBN10P04869 chromosome, complete genome', 'E.coli', 'phosphofructoki
nase', 'glycolysis', 'CCAGCATGGCGCGCCGGGTGGAGGATTATA'), ('NZ_CP009050.
1', None, 'Escherichia coli NCCP15648, complete genome', 'E.coli', 'ma
late dehydrogenase', 'TCA', 'NN'), ('NZ_PD
AP01000234.1', None, 'Escherichia coli strain 2016C-3325 NODE_234_leng
th_464_cov_0.697329_ID_21090, whole genome shotgun sequence', 'E.coli'
, 'citrate synthase', 'TCA', 'NN'), ('QREF
01000006.1', None, 'Escherichia coli strain 333 Ga0213564_106, whole g
enome shotgun sequence', 'E.coli', 'aconitase', 'TCA', 'CTTGAGACTTGGA
TTCATTTTTCTGTCTTG'), ('NZ_NDCE01000057.1', None, 'Escherichia coli stra
in 39913 39913_NODE_70.ctg_1, whole genome shotgun sequence', 'E.coli'
, 'isocitrate dehydrogenase', 'TCA', 'NN'), ('NZ_CP009050.1', None, 'Escherichia coli NCCP15648, complete genome', 'E.coli', 'glucose 6-phosphate dehydrogenase', 'pentose phosphate pathway', 'NN'), ('NZ_CP009050.1', None, 'Escherichia coli NCCP15648, complete genome', 'E.coli', 'ribose 5-phosphate isomerase', 'pentose phosphate pathway', 'NN'), ('NZ_CP009050.1', None, 'Escherichia coli NCCP15648, complete genome', 'E.coli', 'transketolase', 'pentose phosphate pathway', 'NN'), ('NZ_CP009050.1', None, 'Escherichia coli NCCP15648, complete genome', 'E.coli', 'transaldolase', 'pentose phosphate pathway', 'NN'), ('FUIG01000043.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_35, whole genome shotgun sequence', 'human', 'pyruvate kinase', 'glycolysis', 'AATTACGCGATCATGACACTAGCACGATGC'), ('FUIG01000070.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_6, whole genome shotgun sequence', 'human', 'enolase', 'glycolysis', 'GAACTTGACGCACACAACCTACAATCAGTCG'), ('FUIG01000013.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_11, whole genome shotgun sequence', 'human', 'Phosphoglycerate mutase', 'glycolysis', 'GGCCGAGAAGGCGCTGACCGCCGTCATCCA'), ('AH002936.2', None, 'Homo sapiens phosphofructokinase (PFKM) gene, partial cds', 'human', 'phosphofructokinase', 'glycolysis', 'AGTGGTTTCGCACACAGTGGCTGTGATGAAC'), ('NM_006623.3', None, 'Homo sapiens phosphoglycerate dehydrogenase (PHGDH), mRNA', 'human', 'malate dehydrogenase', 'TCA', 'GCAGGGATTTGGCAACCTCAGAGCCGCGAG'), ('FUIG01000002.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_10, whole genome shotgun sequence', 'human', 'citrate synthase', 'TCA', 'CAGAACTTGACGCACACAACCTCGAGACTGG'), ('AH007467.3', None, 'Homo sapiens chromosome 22 aconitase (ACO2) gene, complete cds', 'human', 'aconitase', 'TCA', 'GATGGCGGAGATACTAAAATTTGTTCTTG'), ('KU639670.1', None, 'Homo sapiens voucher NGX277 isocitrate dehydrogenase (IDH2) gene, partial cds', 'human', 'isocitrate dehydrogenase', 'TCA', 'TCCCAATGGAACCTATCCGGAACATCCTGGG'), ('FUIG01000013.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_11, whole genome shotgun sequence', 'human', 'glucose 6-phosphate dehydrogenase', 'pentose phosphate pathway', 'GGCCGAGAAGGCGCTGACCGCCGTCATCCA'), ('NM_144563.2', None, 'Homo sapiens ribose 5-phosphate isomerase A (RPIA), mRNA', 'human', 'ribose 5-phosphate isomerase', 'pentose phosphate pathway', 'CGGGGGCGGGACTTCAGCGGAGGCCGAGC'), ('BC009970.2', None, 'Homo sapiens transketolase, mRNA (cDNA clone MGC:15349 IMAGE:4310396), complete cds', 'human', 'transketolase', 'pentose phosphate pathw

```
ay', 'GCCTGTCGCCGCGGGAGCAGCCGCTATCTC'), ('NM_006755.1', None, 'Homo sa  
piens transaldolase 1 (TALDO1), mRNA', 'human', 'transaldolase', 'pent  
ose phosphate pathway', 'CGCGCCCGTCCCGTCGCCGCGCGCCGCCGCC')]
```

```
In [14]: c.execute("SELECT * FROM pathway;")  
print(c.fetchall())
```

```
[('glycolysis', 'a metabolic process that occurs during aerobic and an  
aerobic respiration of living organisms within the cytoplasm.'), ('TCA  
, 'a metabolic process that occurs during aerobic and anaerobic respi  
ration of living organisms within the cytoplasm.'), ('pentose_phosphat  
e_pathway', 'hexose monophosphate shunt) is a metabolic pathway parall  
el to glycolysis.')] ]
```

```
In [15]: c.execute("SELECT * FROM enzyme;")  
print(c.fetchall())
```

```
[('pyruvate kinase', 'catalyzes the final step of glycolysis', '2.7.1.  
40', 'glycolysis'), ('enolase', 'metalloenzyme responsible for the cat  
alysis of the conversion of 2-phosphoglycerate (2-PG) to phosphoenolpy  
ruvate (PEP)', '4.2.1.11', 'glycolysis'), ('Phosphoglycerate mutase',  
'any enzyme that catalyzes step 8 of glycolysis', '5.4.2.11', 'glycoly  
sis'), ('phosphofructokinase', 'a kinase enzyme that phosphorylates fr  
uctose 6-phosphate in glycolysis', '2.7.1.11', 'glycolysis'), ('malate  
dehydrogenase', 'an enzyme that reversibly catalyzes the oxidation of  
malate to oxaloacetate', '1.1.1.37', 'TCA'), ('citrate synthase', 'pac  
e-making enzyme in the first step of the citric acid cycle', '2.3.3.1'  
, 'TCA'), ('aconitase', 'an enzyme that catalyses the stereo-specific  
isomerization of citrate to isocitrate via cis-aconitate in the tricar  
boxylic acid cycle', '4.2.1.3', 'TCA'), ('isocitrate dehydrogenase', '  
an enzyme that catalyzes the oxidative decarboxylation of isocitrate',  
'1.1.1.42', 'TCA'), ('glucose 6-phosphate dehydrogenase', 'a cytosolic  
enzyme that catalyzes D-glucose 6-phosphate', '1.1.1.49', 'pentose_pho  
sphate_pathway'), ('ribose 5-phosphate isomerase', 'catalyzes the conv  
ersion between ribose-5-phosphate (R5P) and ribulose-5-phosphate (Ru5P  
)', '5.3.1.6', 'pentose_phosphate_pathway'), ('transketolase', 'cataly  
zes two important reactions, which operate in opposite directions in t  
hese two pathways', '2.2.1.1', 'pentose_phosphate_pathway'), ('transal  
dolase', 'an enzyme (EC 2.2.1.2) of the non-oxidative phase of the pen  
tose phosphate pathway', '2.2.1.2', 'pentose_phosphate_pathway')]
```

Associative Table

- gene table x pathway table x enzyme table *

```
In [16]: c.execute("""
CREATE TABLE assoc AS
SELECT gene.id, gene.name AS gene_name, gene.description AS gene_descript
        pathway.name AS pathway, pathway.description AS pathway_descriptio
        enzyme.name AS enzyme, enzyme.function AS function, enzyme.enzyme_
FROM gene, pathway, enzyme
WHERE gene.pathway == pathway.name AND gene.enzyme == enzyme.name AND pat
conn.commit()
```

In []:

Comments:

1. To avoid crashing the website, I only limited the sequence to 30 nucleotides here.
2. As one of the disadvantages of Entrez, the search results from Entrez are inconsistent, therefore some sequences (especially those in e.coli) do not contain useful information.

1. There are relationships between enzymes and pathways—some enzymes belong to certain pathways. Do any belong to multiple pathways? Is this a one-to-many or many-to-many relationship?

To my knowledge, the enzymes I found here belong to only one pathway, therefore it's a one-to-one relationship. But if there are, it will be a many-to-many relationship because some enzymes might belong to many pathways and a pathway might contain enzymes that are also in its parental table.

2. There is an order to enzymes within pathways. How can the order be represented in a table?

Assigning enzymes a name or index, then sort the table by names or index.

3. Genes in the gene table encode enzymes in the enzyme table. How can this be represented? Is this a one-to-one, one-to-many, or many-to-many relationship, and in which direction?

This can be represented by adding a columns that indicates the pathway(s) the enzyme involved to the end of the gene table, and use boolean statement to filter the rows. Gene to enzyme is a one-to-one relationship because one gene corresponds to one enzyme.

Some manual modifications on the table

```
In [17]: c.execute("""UPDATE assoc SET gene_name = "AC02" WHERE id == 'AH007467.3
c.execute("""UPDATE assoc SET gene_name = "G6pd" WHERE id == 'AY364534.1
c.execute("""UPDATE assoc SET gene_name = "PFKM" WHERE id == 'AH002936.2
c.execute("""UPDATE assoc SET gene_name = "PHGDH" WHERE id == 'NM_006623
c.execute("""UPDATE assoc SET gene_name = "IDH2" WHERE id == 'KU639670.1
c.execute("""UPDATE assoc SET gene_name = "TALDO1" WHERE id == 'NM_006751
conn.commit()
```

Comment: Due to the inconsistency of Entrez search results, not all given sequences are mRNA sequence, thus not all have gene_name.

```
In [18]: c.execute("SELECT * FROM assoc;")
          print(c.fetchall())
```

[illegible]

[illegible]

isocitrate', '1.1.1.42'), ('FUIG01000043.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_35, whole genome shotgun sequence', 'human', 'AATTACGCGATCATGACACTAGCACGATGC', 'glycolysis', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'pyruvate kinase', 'catalyzes the final step of glycolysis', '2.7.1.40'), ('FUIG01000070.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_6, whole genome shotgun sequence', 'human', 'GAACTTGACGCACACAACTACAATCAGTCG', 'glycolysis', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'enolase', 'metalloenzyme responsible for the catalysis of the conversion of 2-phosphoglycerate (2-PG) to phosphoenolpyruvate (PEP)', '4.2.1.11'), ('FUIG01000013.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_11, whole genome shotgun sequence', 'human', 'GGCCGAGAAGGCGCTGACCGCCGTCATCCA', 'glycolysis', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'Phosphoglycerate mutase', 'any enzyme that catalyzes step 8 of glycolysis', '5.4.2.11'), ('AH002936.2', 'PFKM', 'Homo sapiens phosphofructokinase (PFKM) gene, partial cds', 'human', 'AGTGGTTCGCACACAGTGGCTGTGATGAAC', 'glycolysis', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'phosphofructokinase', 'a kinase enzyme that phosphorylates fructose 6-phosphate in glycolysis', '2.7.1.11'), ('NM_006623.3', 'PHGDH', 'Homo sapiens phosphoglycerate dehydrogenase (PHGDH), mRNA', 'human', 'GCAGGGATTTGGCAACCTCAGAGCCGCGAG', 'TCA', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'malate dehydrogenase', 'an enzyme that reversibly catalyzes the oxidation of malate to oxaloacetate', '1.1.1.37'), ('FUIG01000002.1', None, 'Homo sapiens genome assembly, contig: BQ8482_Contig_10, whole genome shotgun sequence', 'human', 'CAGAACTTGACGCACACAACTCGAGACTGG', 'TCA', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'citrate synthase', 'pace-making enzyme in the first step of the citric acid cycle', '2.3.3.1'), ('AH007467.3', 'AC02', 'Homo sapiens chromosome 22 aconitase (AC02) gene, complete cds', 'human', 'GATGGCGGAGATAACTAAAATTTGTTCTTG', 'TCA', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'aconitase', 'an enzyme that catalyses the stereo-specific isomerization of citrate to isocitrate via cis-aconitate in the tricarboxylic acid cycle', '4.2.1.3'), ('KU639670.1', 'IDH2', 'Homo sapiens voucher NGX277 isocitrate dehydrogenase (IDH2) gene, partial cds', 'human', 'TCCCAATGGAACATATCCGGAA CATCCTGGG', 'TCA', 'a metabolic process that occurs during aerobic and anaerobic respiration of living organisms within the cytoplasm.', 'isocitrate dehydrogenase', 'an enzyme that catalyzes the oxidative decarboxylation of isocitrate', '1.1.1.42')]