PHOSPHORYLATION MOTIF PREDICTOR

OVERVIEW OF THE PROJECT

1. GIVEN A LIST OF PHOSPHORYLATION SITES

2. GET THE KNOWN PHOSPHORYLATION SITES OF A GROUP OF KINASES

3. KNOW HOW SIMILAR IS ANOTHER SET OF PROTEINS

Regulatory Network in Protein Phosphorylation

Home | About | Browse | Network Analysis | Expression Profile | Prediction | Statistics | Download

Search a kinase
(Example : PKA , PKC etc.)

PKA

Human Mouse Rat Search

Search a substrate protein
(Example : CEBPB, EGFR etc.)

EGFR

Human Mouse Rat Search

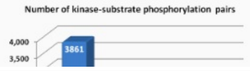
Explore phosphortlation network (A group of genes.)

RegPhos is a resource to explore the protein kinase-substrate phosphorylation networks in human and mouse. Protein phosphorylation catalyzed by kinases plays crucial regulatory roles in intracellular signal transduction. With the increasing number of in vivo phosphorylation sites has been identified by mass spectrometry-based proteomics, RegPhos (Nucl. Acids Res., 2011) was developed to construct the human phosphorylation networks between protein kinases and substrates. In this update (RegPhos 2.0), we not only integrate the experimental kinase-substrate phosphorylations from public resources and research articles, but also provide the LC-MS/MS phosphor-peptide dynamic expression data for verifying our newly discovered BCR signaling networks in mouse. The RegPhos 2.0 aims to provide a full investigation of kinase-substrate phosphorylation networks in human and mouse by integrating the information of KEGG metabolic pathways and protein-protein interactions. All of the experimental kinase-substrate data could be downloaded in **Download** page.

Statistics

Human | Mouse | Rat

Protein Kinases	518
Pseudokinases	106
Kinase Families	221
Substrate Proteins	10,257
Phosphorylation Sites	66,301
- Validated by *In vivo*	4,618
- Validated by *In vitro*	8,752
Kinase-protein Interactions	76,855
Literatures	10,976



DEPENDENCIES

BIOPYTHON

1. SeqIO Module - Fasta parsing
2. IUPAC Module - Implements "alphabets"
3. motifs Module - provides the "Motif" object

OTHER DEPENDENCIES

1. Numpy - Numeric calculations
2. Pandas - provides object "DataFrame"
3. ggplot2 - provides a nice plotting framework

PROJECT STRUCTURE

REG_PHOS_READER.PY

Program built from two smaller pandas dependant programs

- `get_kinase_group.py(source, group)`

Takes a database file and group name and returns a \nlist of the kinases that match given group.

- `get_substrates(db_source, kinase_list)`

Takes a database file and a list of uniprot ID's and returns a nested DataFrame with the kinases as a column and a data frame of data frames.

GET_WINDOWS.PY

- `fill_sequence(sequence, length, fill_right, filler)`

  Fills a string to match a length for instance 'A' for length 5 would be 'AXXXX'

- `get_windo_strings(entry, position, length)`

  gets a string, a position and a length, returns the character at given position, and the window up and downstream of given length

- `get_windows(database, identifiers, positions, fill, length)`

CALCULATE_ALLIGNMENT_SCORES.PY

Three functions used to calculate the aligment scores for strings and databases for single and multiple pssm's

- `_calculate_alignment_scores(pssm, sequence, m, n)`
- `calculate_alignment_scores(pssm, sequence)`
- `cross_score(pssms, fasta_database, start = None, end = None)`

USAGE EXAMPLE

IMPORT ALL NECESARRY FUNCTIONS AND PACKAGES

```
from reg_phos_reader import get_kinase_group, get_substrates
from get_windows import get_windows
from fasta_tools import get_relevant_db
from calculate_alignment_scores import cross_score

from Bio import SeqIO
from Bio.Alphabet import IUPAC
from Bio import motifs

import pandas as pd

from ggplot import *
```

```
my_kinases = get_kinase_group("./regPhos/RegPhos_kinase_human.txt",
                              "CMGC")

In [3]: my_kinases[0:5]
Out[16]:
['CCRK', 'CDC2', 'CDK2', 'CDK3', 'CDK10']
```

```
my_substrates = get_substrates("./regPhos/RegPhos_Phos_human.txt",
                               my_kinases)
In [17]: my_substrates[0:5]
Out[27]:

  kinase                                          substrates
0   CCRK                ID      AC  position       descr...
1   CDC2                 ID      AC  position       desc...
2   CDK2                 ID      AC  position       desc...
3   CDK3                ID      AC  position    descript...
4  CDK10  Empty DataFrame
Columns: [ID, AC, position, de...
```

```
In [32]: my_substrates['substrates'][0]
Out[32]:

              ID      AC  position       description catalytic kinas
2715  CDK2_HUMAN  P24941       160  Phosphothreonine             CCR

                                                 reference            r
2715  1396589;14597612;16325401;17095507;17192257;17...  Swiss-Prot

     code
2715    T
```

```
my_windows = []

for i in (my_substrates['substrates'].tolist()):
    fasta_db = SeqIO.parse("./ModelOrganisms/UP000005640_9606.fasta"
                           "fasta", IUPAC.extended_protein)
    relevant_db = get_relevant_db(fasta_db, i['AC'])
    my_windows.append(
        get_windows(
            relevant_db,
            i['AC'],
            i['position']))
my_windows[1:5]
```

```
In [47]: my_windows[0:2]
Out[47]:

[  aminoacid               upstream            downstream  \
 0       (T)  (G, V, P, V, R, T, Y)  (H, E, V, V, T, L, W)

                                          window
 0  (G, V, P, V, R, T, Y, T, H, E, V, V, T, L, W)  ,
     aminoacid               upstream            downstream  \
 0         (S)  (P, A, A, A, P, A, S)  (S, D, P, A, A, A, A)
 1         (S)  (G, T, E, E, K, C, G)  (P, Q, V, R, T, L, S)
 2         (S)  (P, I, P, I, M, P, A)  (P, Q, K, G, H, A, V)
 3         (S)  (K, V, S, N, L, Q, V)  (P, K, S, E, D, I, S)
 4         (T)  (S, A, A, S, N, T, G)  (P, D, G, P, E, A, P)
 5         (S)  (D, F, I, D, A, F, A)  (P, V, E, A, E, G, T)
 6         (T)  (L, T, R, Y, T, R, P)  (P, V, Q, K, H, A, I)
```

```
my_motifs = [[] if len(window['window']) == 0 else
             motifs.create(window['window']) for
             window in my_windows]
```

```
In [63]: my_motifs[1].consensus
Out[63]:
Seq('SGGSSPSSPVKPSPP', ExtendedIUPACProtein())
```

```
my_pwm = [[] if (len(m) == 0) else m.counts.normalize(pseudocounts=1
          m in my_motifs]

In [64]: my_pwm[1]
Out[64]:

{'A': (0.05851063829787234,
  0.07446808510638298,
  0.05851063829787234,
  0.0425531914893617,
  0.05319148936170213,
  0.0797872340425532,

  ...

 'Y': (0.026595744680851064,
```

```
In [65]: my_pssm[1]
Out[66]:

{'A': [0.605282485100752,
  0.9532057885210588,
  0.605282485100752,
  0.14585086646345455,
  0.467778961350817,
  1.0527414620719733,

...

 'Y': [-0.532221038649183,
  -0.8541491335365455,
  -0.046794211478941264,
  -0.8541491335365455,
```

```
model= "./ModelOrganisms/UP000000625_83333.fasta"

score_lists=cross_score(my_pssm, model, start=1, end=100)

score_lists[0].head()["scores"]

In [67]: score_lists[0]
Out[70]:



scores
```

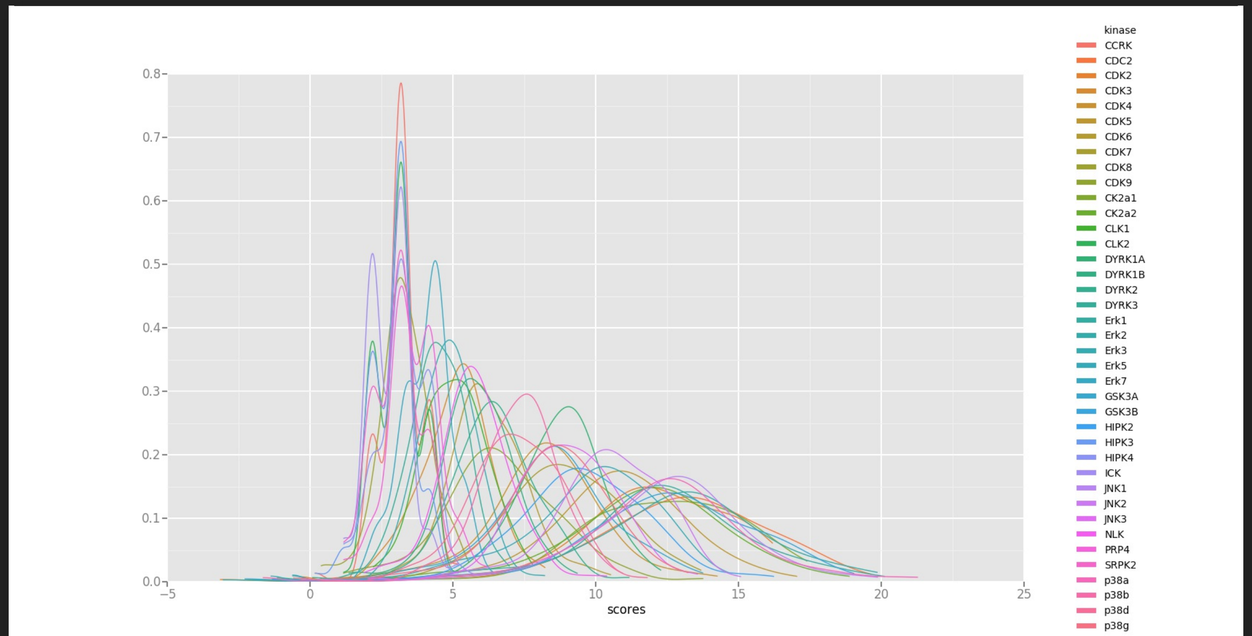
```
my_data_frame = pd.DataFrame()
my_data_frame['kinase'] = [None if isinstance(i, list) else
 str(i) for i in
my_kinases]
```

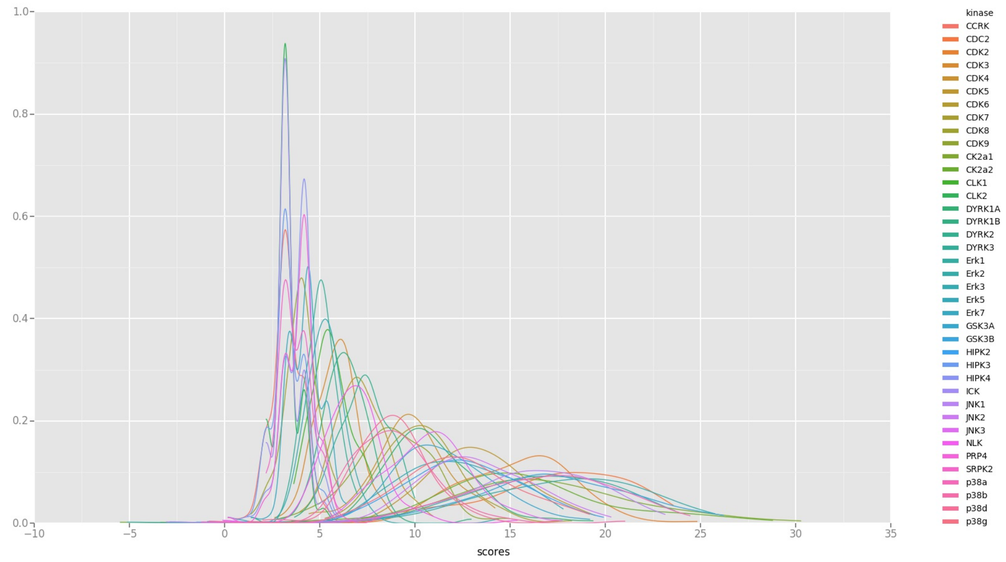
```
In [88]: my_data_frame['matches'][0]
Out[88]:

      scores                    id
0   2.183283   sp|P0AB43|YCGL_ECOLI
1   3.183283   sp|P33644|YFIH_ECOLI
2   2.183283   sp|P76656|YQII_ECOLI
3   2.183283   sp|P46887|YECH_ECOLI
4   3.183283   sp|P00452|RIR1_ECOLI
5   3.183283   sp|P75933|FLGA_ECOLI
```

```
In [89]: concat.head()
Out[90]:

  kinase    scores                    id
0   CCRK  2.183283  sp|P0AB43|YCGL_ECOLI
1   CCRK  3.183283  sp|P33644|YFIH_ECOLI
2   CCRK  2.183283  sp|P76656|YQII_ECOLI
3   CCRK  2.183283  sp|P46887|YECH_ECOLI
4   CCRK  3.183283  sp|P00452|RIR1_ECOLI
```

```
concat = pd.concat(my_data_frame['matches'].tolist(),
                   keys = my_data_frame['kinase'])
concat.reset_index(level=0, inplace=True)
concat = concat[concat['scores'].notnull()]
```

```
ggplot(concat, aes(x = 'scores', color = 'kinase'), norm=True) + geo
```


0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
−5
0
5
10
15
20
25
scores
kinase
CCRK
CDC2
CDK2
CDK3
CDK4
CDK5
CDK6
CDK7
CDK8
CDK9
CK2a1
CK2a2
CLK1
CLK2
DYRK1A
DYRK1B
DYRK2
DYRK3
Erk1
Erk2
Erk3
Erk5
Erk7
GSK3A
GSK3B
HIPK2
HIPK3
HIPK4
ICK
JNK1
JNK2
JNK3
NLK
PRP4
SRPK2
p38a
p38b
p38d
p38g


1.0
0.8
0.6
0.4
0.2
0.0
−10
−5
0
5
10
15
20
25
30
35
scores
kinase
CCRK
CDC2
CDK2
CDK3
CDK4
CDK5
CDK6
CDK7
CDK8
CDK9
CK2a1
CK2a2
CLK1
CLK2
DYRK1A
DYRK1B
DYRK2
DYRK3
Erk1
Erk2
Erk3
Erk5
Erk7
GSK3A
GSK3B
HIPK2
HIPK3
HIPK4
ICK
JNK1
JNK2
JNK3
NLK
PRP4
SRPK2
p38a
p38b
p38d
p38g