week1

February 19, 2021

```
[2]: import pandas as pd
     import numpy as np
     import matplotlib.pyplot as plt
[3]: original_data = pd.read_excel("Cell-Cycle-Set.xlsx")
     df = original_data.dropna()
     #view the head so we can determine the column names and get a feel for the data
     df.head()
     #each of the columns detail the concentration of RNA/protein during one of the
     →3 phases
     #G1 phase is first growth phase/post mitotic gap phase
     #S phase is DNA replication phase
     #G2 phase is growth phase
     #GOBP indicates the biological process
     #GOMF indicates the molecular function
     #GDCC indicates the location in the cell
[3]:
      Gene_Name mean_RNA_G1 mean_RNA_S mean_RNA_G2 mean_protein_G1 \
                    10.330107
                                10.396423
     1
          RBM47
                                             10.677257
                                                              24.748020
     2
          ADAM9
                    12.321340
                                12.203630
                                             12.233293
                                                              19.083593
     3
           UBA6
                    10.827333
                                10.758463
                                             10.685847
                                                              24.614467
     5
           SHTN1
                    10.845517
                                10.824347
                                             10.634980
                                                              26.112690
           SIL1
                    9.042438
                                 8.924093
                                             9.035878
                                                              22.750520
       mean_protein_S mean_protein_G2 \
     1
            22.426777
                              24.651200
     2
            16.248873
                              19.281277
     3
            21.356450
                              25.207883
     5
                              26.138843
            22.905927
            20.598227
                              23.093443
```

1 base conversion or substitution editing; biolog...

GOBP \

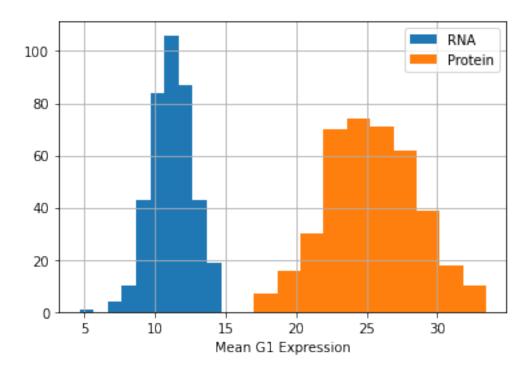
```
2 activation of MAPKK activity; activation of pro...
3 catabolic process; cellular catabolic process; c...
5 axon guidance; chemotaxis; locomotion; response t...
6 cellular macromolecule metabolic process; cellu...
                                                   GOMF \
1 binding; nucleic acid binding; nucleotide bindin...
2 binding; catalytic activity; cation binding; coll...
3 adenyl nucleotide binding; adenyl ribonucleotid...
5 binding; enzyme binding; kinase binding; protein ...
   binding; protein binding; unfolded protein binding
                                                   GOCC
1 apolipoprotein B mRNA editing enzyme complex; c...
2 cell part; extracellular region part; extracellu...
               cell part; cytoplasm; intracellular part
5 axon; cell part; cell projection; neuron projection
6 cell part; cytoplasmic part; endoplasmic reticul...
```

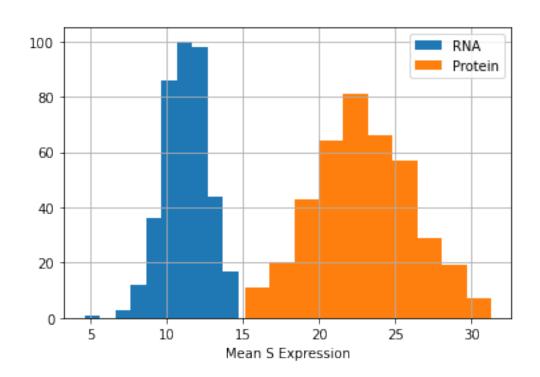
0.1 Task 1

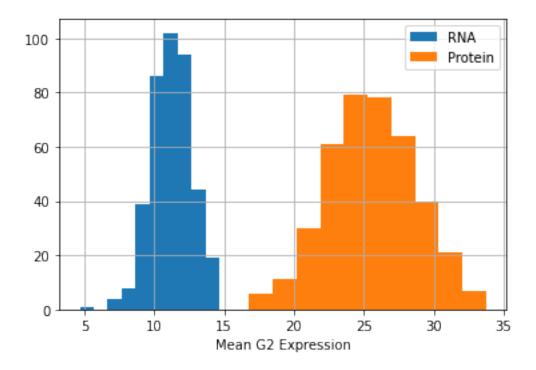
• Let's render histograms for the RNA and protein data in the G1, S and G2 phases:

```
[4]: fig1, ax1 = plt.subplots()
     #.hist draws histogram on a pandas series using matplotlib
     #default bin size is 10
     df.mean_RNA_G1.hist(ax=ax1, label='RNA', bins = 10)
     df.mean_protein_G1.hist(ax=ax1, label='Protein', bins = 10)
     #puts a colour coded legend of what each data set is
     ax1.legend()
     #set the label of the x axis
     ax1.set_xlabel('Mean G1 Expression')
     fig2, ax2 = plt.subplots()
     df.mean_RNA_S.hist(ax=ax2, label='RNA')
     df.mean_protein_S.hist(ax=ax2, label='Protein')
     ax2.legend()
     ax2.set_xlabel('Mean S Expression')
     fig3, ax3 = plt.subplots()
     df.mean RNA G2.hist(ax=ax3, label='RNA')
     df.mean_protein_G2.hist(ax=ax3, label='Protein')
     ax3.legend()
     ax3.set_xlabel('Mean G2 Expression')
```

[4]: Text(0.5, 0, 'Mean G2 Expression')







- From the above, straight away we can notice that in every phase there is a higher protein concentration than RNA. This could be due to the fact that a single mRNA strand used by ribosomes to create a protein could be used to create the same protein multiple times
- Now, if we apply a linear scalar to the RNA data from each phase and make the histogram reperesenting protein data slightly transparent in order to visualize how the distributions of the data compare, we can observe that the distributions of the RNA and protein data from each phase are similar apart from the S phase, where the RNA data is slightly more negatively skewed than in other phases.
- The negative skew of data in the S phase suggests there is a higher than normal concentration of RNA during this phase than in the other 2 phases
- See below for the scaled data:

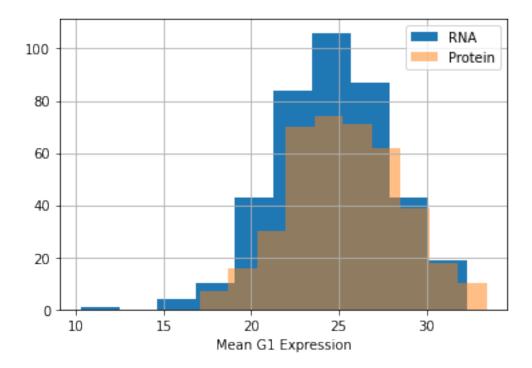
```
fig1, ax1 = plt.subplots()
df.mean_RNA_G1.map(lambda x: x * 2.2).hist(ax=ax1, label='RNA', bins = 10)
df.mean_protein_G1.hist(ax=ax1, label='Protein', bins = 10, alpha = 0.5)
ax1.legend()
ax1.set_xlabel('Mean G1 Expression')

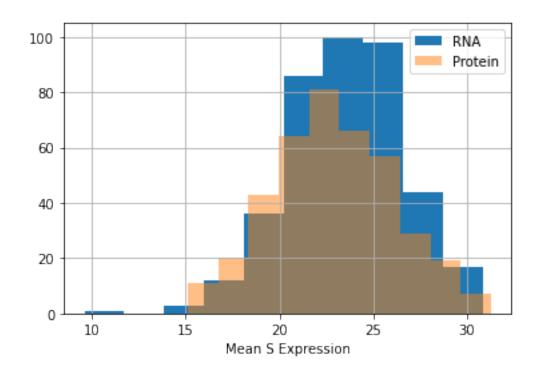
fig2, ax2 = plt.subplots()
df.mean_RNA_S.map(lambda x: x * 2.1).hist(ax=ax2, label='RNA')
df.mean_protein_S.hist(ax=ax2, label='Protein', alpha = 0.5)
ax2.legend()
ax2.set_xlabel('Mean S Expression')

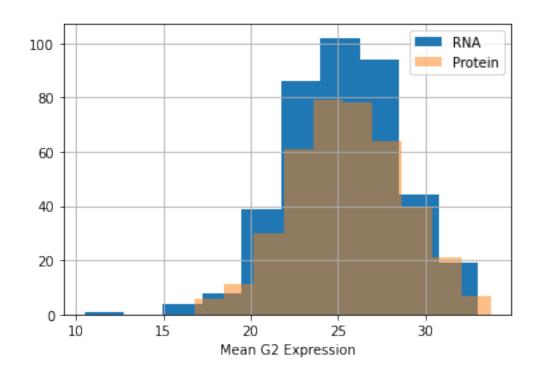
fig3, ax3 = plt.subplots()
```

```
df.mean_RNA_G2.map(lambda x: x * 2.25).hist(ax=ax3, label='RNA')
df.mean_protein_G2.hist(ax=ax3, label='Protein', alpha = 0.5)
ax3.legend()
ax3.set_xlabel('Mean G2 Expression')
```

[5]: Text(0.5, 0, 'Mean G2 Expression')







0.2 Task 2

• We can see that when we look at the pairwise correlations accurate to 3 significant figures, there is only at most a difference of 0.01 in the spearmans rank score between any two phases in the pairwise correlation between RNA and protein concentration, hence the change in timestep has little effect on the relationship between the concentration amounts of RNA and protein

```
[6]: #pairwise correlation

print("G1 correlation:", "%0.3f" % df.mean_RNA_G1.corr(df.mean_protein_G1,

→method = "spearman"))

print("S correlation:", "%0.3f" % df.mean_RNA_S.corr(df.mean_protein_S, method

→= "spearman"))

print("G2 correlation:", "%0.3f" % df.mean_RNA_G2.corr(df.mean_protein_G2,

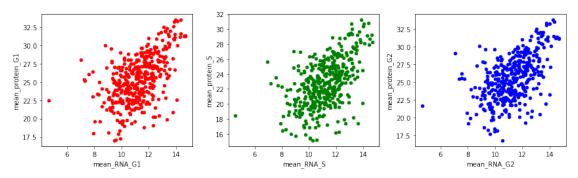
→method = "spearman"))
```

G1 correlation: 0.513 S correlation: 0.523 G2 correlation: 0.526

0.3 Task 3

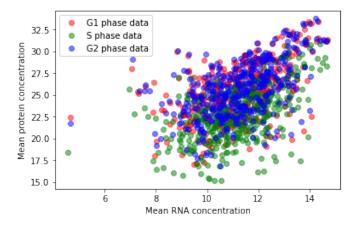
• Let's generate scatterplots of the RNA vs protein concentration for each stage:

Scatterplots of the RNA/protein concentration in each of the 3 phases



• Now, as before let's observe how the data look when overlayed onto one another:

Overlayed scatterplots of the RNA/protein concentration in each of the 3 phases



- As before, we can see that the distribution of data from each phase is fairly similar
- Now, let's use scikit-learn to train a linear regression models for each of the data sets from each phase:

```
[9]: from sklearn.linear_model import LinearRegression
from sklearn.model_selection import train_test_split
from sklearn.metrics import mean_squared_error, r2_score
```

• We can see that the data in question is a Pandas Series object of floats:

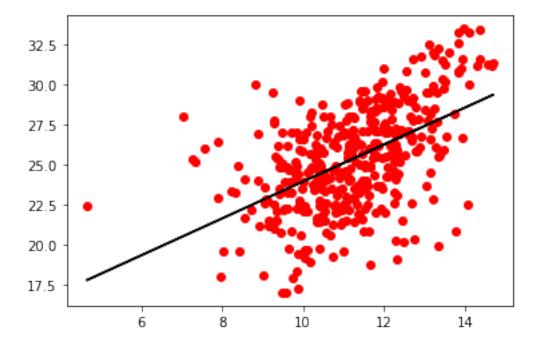
```
[10]: df.mean RNA G1
\lceil 10 \rceil : 1
               10.330107
      2
               12.321340
      3
               10.827333
      5
               10.845517
               9.042438
      494
               11.115773
      495
               11.251870
      496
               13.013263
      497
               9.048456
      498
               13.525467
      Name: mean_RNA_G1, Length: 397, dtype: float64
```

- We know that the data is actually just a 1D list, so let's flatten the pandas series into a numpy array which is suitable for feeding to a scikit-learn model.
- Let's train 3 linear regression models on the data for each cell stage which predicts protein concentration from RNA concentration, and plot the "line of best fit" that is found by the model, and also print the coefficient of determination score that is found between the predicted protein concentrations generated by the model and the actual protein concentrations:

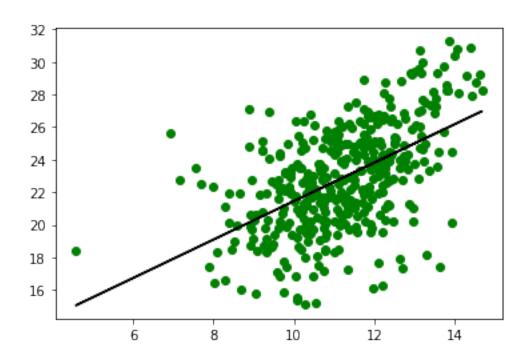
```
[11]: def process_column(col):
    return col.to_numpy().reshape(-1,1)
```

```
print(g1_score)
```

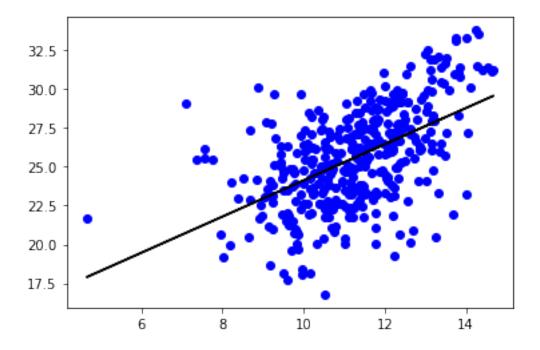
0.2731711059314553



0.28750000422102284



0.28362549895654476



- The coefficient of determination scores aren't huge, but that is to be expected as a score near to 1 would indicate a high correlation and would mean the data are in a near perfect straight line shape which they are not, they are fairly spread out around the "line of best fit"
- Visually looking at the data above we can see that most of the data points with RNA concentration values of less than 8 or so are sort of outliers and are not representative of the general distribution of the data and are perhaps "skewing" our "line of best fit", so let's see if filtering out these data points can improve our coefficient of determination score at all:

S_model = LinearRegression().fit(S_rna, S_protein)

```
S_protein_predictions = S_model.predict(S_rna)
print("S filtered score:",r2_score(S_protein, S_protein_predictions))
print("S original score:", s_score)
```

S filtered score: 0.318061690581281 S original score: 0.28750000422102284

```
[18]: G2_rna, G2_protein = process_column(G2_filtered.mean_RNA_G2),

→process_column(G2_filtered.mean_protein_G2)

G2_model = LinearRegression().fit(G2_rna, G2_protein)

G2_protein_predictions = G2_model.predict(G2_rna)

print("G2_filtered_score:",r2_score(G2_protein, G2_protein_predictions))

print("G2_original_score:", g2_score)
```

G2 filtered score: 0.32148617805391766 G2 original score: 0.28362549895654476

- By removing outliers, we can see that the predictions of protein concentration now have a slightly higher correlation with the actual reference values
- However, as mentioned before the correlation between the predictions and actual values are not strong enough for a linear model alone to be used for accurate prediction of protein concentration from RNA concentration. Perhaps a deep learning approach may produce more accurate predictions

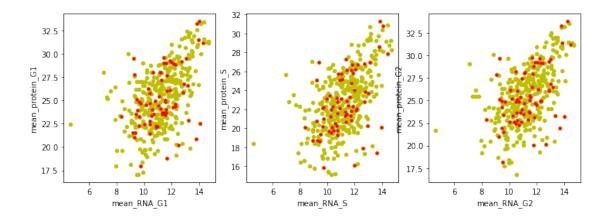
1 Week 2

1.1 Task 1

First plot the points where the string "cell cycle" is contained in the GOBP term for each phase G1, G2 and S and colour it red so we can clearly see how the data differs from the unfiltered data:

```
[19]: gobp = df[df.GOBP.str.contains('cell cycle')]
  fig4,ax4 = plt.subplots(ncols=3, figsize=(12,4))
  df.plot.scatter('mean_RNA_G1', 'mean_protein_G1', ax=ax4[0], color='y')
  ax4[0].scatter(gobp.mean_RNA_G1, gobp.mean_protein_G1, color='r', s=10.)
  df.plot.scatter('mean_RNA_S', 'mean_protein_S', ax=ax4[1], color='y')
  ax4[1].scatter(gobp.mean_RNA_S, gobp.mean_protein_S, color='r', s=10.)
  df.plot.scatter('mean_RNA_G2', 'mean_protein_G2', ax=ax4[2], color='y')
  ax4[2].scatter(gobp.mean_RNA_G2, gobp.mean_protein_G2, color='r', s=10.)
  print(len(gobp))
```

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Now lets see if the correlation is stronger or weaker for any of the 3 phases, lets remind ourselves of the pairwise correlation between RNA concentration and protein concentration for each of the 3 phases in the original unfiltered data:

```
[20]: print("G1 unfiltered data correlation:", "%0.3f" % df.mean_RNA_G1.corr(df.

→mean_protein_G1, method = "spearman"))

print("S unfiltered data correlation:", "%0.3f" % df.mean_RNA_S.corr(df.

→mean_protein_S, method = "spearman"))

print("G2 unfiltered data correlation:", "%0.3f" % df.mean_RNA_G2.corr(df.

→mean_protein_G2, method = "spearman"))
```

G1 unfiltered data correlation: 0.513 S unfiltered data correlation: 0.523 G2 unfiltered data correlation: 0.526

Now let's see how the pairwise correlation is in only the genes that contain the string "cell cycle" in their GOBP column

```
cell cycle GOBP G1 data correlation: 0.393 cell cycle GOBP S data correlation: 0.420 cell cycle GOBP G2 data correlation: 0.403
```

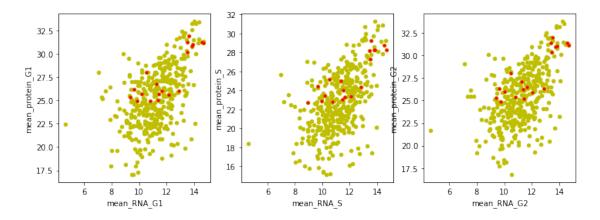
So, we can see that the correlation is weaker in the set of data that only includes genes that contain the string "cell cycle" in their GOBP field.

1.2 Task 2

Now let's do the same for only those data instances that contain the substring "ribosome" in their GOCC term:

```
[22]: gocc = df[df.GOCC.str.contains('ribosome')]
  fig5,ax5 = plt.subplots(ncols=3, figsize=(12,4))
  df.plot.scatter('mean_RNA_G1', 'mean_protein_G1', ax=ax5[0], color='y')
  ax5[0].scatter(gocc.mean_RNA_G1, gocc.mean_protein_G1, color='r', s=10.)
  df.plot.scatter('mean_RNA_S', 'mean_protein_S', ax=ax5[1], color='y')
  ax5[1].scatter(gocc.mean_RNA_S, gocc.mean_protein_S, color='r', s=10.)
  df.plot.scatter('mean_RNA_G2', 'mean_protein_G2', ax=ax5[2], color='y')
  ax5[2].scatter(gocc.mean_RNA_G2, gocc.mean_protein_G2, color='r', s=10.)
```

[22]: <matplotlib.collections.PathCollection at 0x7fd81e1079a0>



And now let's compare the correllations again:

```
print("G1 unfiltered data correlation:", "%0.3f" % df.mean_RNA_G1.corr(df.

mean_protein_G1, method = "spearman"))

print("S unfiltered data correlation:", "%0.3f" % df.mean_RNA_S.corr(df.

mean_protein_S, method = "spearman"))

print("G2 unfiltered data correlation:", "%0.3f" % df.mean_RNA_G2.corr(df.

mean_protein_G2, method = "spearman"))

print("specific GOCC G1 data correlation:", "%0.3f" % gocc.mean_RNA_G1.

corr(gocc.mean_protein_G1, method = "spearman"))

print("specific GOCC S data correlation:", "%0.3f" % gocc.mean_RNA_S.corr(gocc.

mean_protein_S, method = "spearman"))

print("specific GOCC G2 data correlation:", "%0.3f" % gocc.mean_RNA_G2.

corr(gocc.mean_protein_G2, method = "spearman"))
```

G1 unfiltered data correlation: 0.513 S unfiltered data correlation: 0.523 G2 unfiltered data correlation: 0.526 specific GOCC G1 data correlation: 0.732 specific GOCC S data correlation: 0.770 specific GOCC G2 data correlation: 0.744

- We can see that there is a greater amount of postive corelation between protein and RNA concentration in only those instances of data that contain the substring "ribosome" in their GOCC term compared to both the original unfiltered data and also the set consisting of only those instances with "cell cycle" in their gobp term
- This sort of makes sense as the GOCC value is "ribosome" meaning the location where the concentration data is being recorded is around the ribosome, logically a ribosome is bound to have a greater concentration of RNA around it as there is an abundance of both RNA in mRNA strands being delivered to ribosomes to synthesize proteins and also the RNA that makes up the actual ribosomes themselves. A greater correlation indicates that the RNA concentration levels are generally higher here than in other data previously in the notebook, due to the fact that the other data have smaller correlations whilst the RNA concentration was generally smaller than protein concentration, meaning there has to have been an increase in RNA concentration for the correlation to go up

1.3 Task 3

Now let's count the number of occurrences of every GOBP term across all genes:

```
[24]: print(df.GOBP.str.split(';',expand=True).stack().value_counts()[:50])
```

cellular process	377
metabolic process	273
cellular metabolic process	260
primary metabolic process	255
biological regulation	236
regulation of biological process	225
regulation of cellular process	211
macromolecule metabolic process	211
cellular macromolecule metabolic process	201
nitrogen compound metabolic process	167
cellular nitrogen compound metabolic process	166
nucleobase-containing compound metabolic process	158
response to stimulus	148
cellular component organization or biogenesis	145
nucleic acid metabolic process	144
cellular component organization	142
regulation of metabolic process	141
regulation of cellular metabolic process	130
regulation of primary metabolic process	125
regulation of macromolecule metabolic process	123
cellular component organization or biogenesis at cellular level	122
cellular component organization at cellular level	119
RNA metabolic process	119
biosynthetic process	118
cellular biosynthetic process	117

```
cellular response to stimulus
                                                                    116
protein metabolic process
                                                                    104
regulation of nitrogen compound metabolic process
                                                                    100
establishment of localization
                                                                     98
                                                                      95
transport
regulation of nucleobase-containing compound metabolic process
                                                                      95
regulation of cellular biosynthetic process
                                                                      92
regulation of gene expression
                                                                      92
regulation of biosynthetic process
                                                                      92
positive regulation of biological process
                                                                      90
organelle organization
                                                                      87
regulation of macromolecule biosynthetic process
                                                                      86
positive regulation of cellular process
                                                                      85
regulation of cellular macromolecule biosynthetic process
                                                                      85
signal transduction
                                                                      84
catabolic process
                                                                      83
cellular protein metabolic process
                                                                      82
negative regulation of biological process
                                                                      81
regulation of RNA metabolic process
                                                                      79
negative regulation of cellular process
                                                                      75
macromolecule biosynthetic process
                                                                      73
cellular macromolecule biosynthetic process
                                                                      73
small molecule metabolic process
                                                                      72
regulation of transcription, DNA-dependent
                                                                      72
cellular catabolic process
                                                                      71
dtype: int64
```

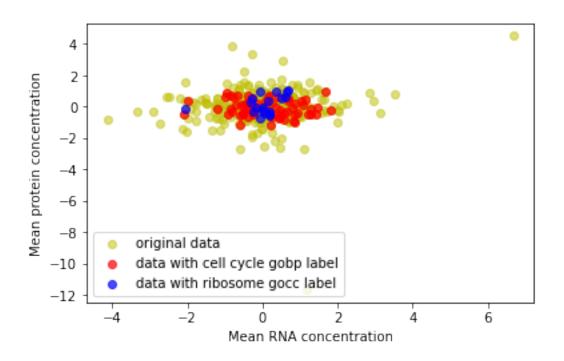
• One difficulty that arises when using these terms is that some are quite similar e.g. "cellular process", "metabolic process" and "cellular metabolic process" so perhaps they could be hard to distinguish

1.4 Task 4

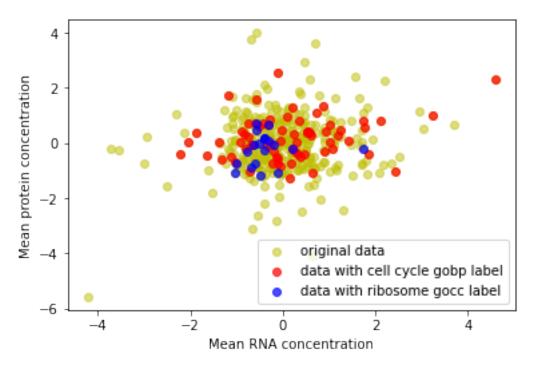
```
gocc = df[df.GOCC.str.contains('ribosome')]
g1sPlot, g1sAx = plt.subplots()
g1sAx.scatter(df.mean_RNA_g1s, df.mean_protein_g1s, color = 'y', alpha = 0.5,
→label = "original data")
g1sAx.scatter(gobp.mean RNA g1s, gobp.mean protein g1s, color = 'r', alpha = 0.
\hookrightarrow7, label = "data with cell cycle gobp label")
g1sAx.scatter(gocc.mean_RNA_g1s, gocc.mean_protein_g1s, color = 'b', alpha = 0.
→7, label = "data with ribosome gocc label")
g1sAx.legend()
g1sAx.set_xlabel("Mean RNA concentration")
g1sAx.set_ylabel("Mean protein concentration")
g1sPlot.suptitle("Standardized G1/S difference data", fontsize = 16)
g1sPlot.subplots_adjust(top=0.85)
sg2Plot, sg2Ax = plt.subplots()
sg2Ax.scatter(df.mean_RNA_sg2, df.mean_protein_sg2, color = 'y', alpha = 0.5,__
→label = "original data")
sg2Ax.scatter(gobp.mean_RNA_sg2, gobp.mean_protein_sg2, color = 'r', alpha = 0.
\hookrightarrow7, label = "data with cell cycle gobp label")
sg2Ax.scatter(gocc.mean_RNA_sg2, gocc.mean_protein_sg2, color = 'b', alpha = 0.
→7, label = "data with ribosome gocc label")
sg2Ax.legend()
sg2Ax.set_xlabel("Mean RNA concentration")
sg2Ax.set_ylabel("Mean protein concentration")
sg2Plot.suptitle("Standardized S/G2 difference data", fontsize = 16)
\#sg2Plot.subplot\_adjust(top = 0.85)
g2g1Plot, g2g1Ax = plt.subplots()
g2g1Ax.scatter(df.mean_RNA_g2g1, df.mean_protein_g2g1, color = 'y', alpha = 0.
g2g1Ax.scatter(gobp.mean_RNA_g2g1, gobp.mean_protein_g2g1, color = 'r', alpha = __
→0.7, label = "data with cell cycle gobp label")
g2g1Ax.scatter(gocc.mean_RNA_g2g1, gocc.mean_protein_g2g1, color = 'b', alpha = __
→0.7, label = "data with ribosome gocc label")
g2g1Ax.legend()
g2g1Ax.set_xlabel("Mean RNA concentration")
g2g1Ax.set_ylabel("Mean protein concentration")
g2g1Plot.suptitle("Standardized G2/G1 difference data", fontsize = 16)
#g2g1Plot.subplot_adjust(top = 0.85)
```

[27]: Text(0.5, 0.98, 'Standardized G2/G1 difference data')

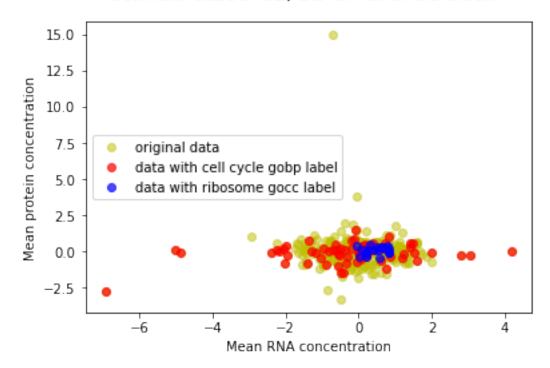
Standardized G1/S difference data



Standardized S/G2 difference data



Standardized G2/G1 difference data



Interestingly from the graph we can see that the set of data points that contain "ribosome" in their gocc label have little change in protein or RNA concentration between any of the 3 phases, this could be explained by the fact that proteins are used to carry out a large majority of tasks in a cell, so the ribosomes need to continuously produce new proteins regardless of what cell cycle stage the cell is in, and obviously the ribosome constantly needs mRNA strands to be delivered to it in order to continute producing the proteins explaining for the little change in RNA concentration.