

Please note that codes and reports of Q1 and Q3 were written together in Jupyter Notebooks. It is advised to view the reports for these two questions in the notebooks rather than this PDF. (except for Q3 part 1 which is on page 19)

bio-hw4-q1-new

December 22, 2017

1 Intro to Bioinformatics

1.1 Homework Assignment 4

1.2 Question 1: Feedback, Robustness & Bifurcation

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1.4.1 Developed by Python 3.6

```
In [1]: import numpy as np
        from matplotlib import pyplot as plt
        import seaborn as sb

        import scipy
        import scipy.optimize

        %matplotlib inline
        %config InlineBackend.figure_format = 'retina'

        import sympy as sp
        sp.init_printing()
```

1.5 Finding the initial densities & defining the equations

I use *SymPy* to represent the density change rates in Python. First, I define the densities by using *symbols*.

```
In [2]: X, Y, Z = sp.symbols('X Y Z')
```

One by one, I find the initial densities. As the system is said to be stable at the start of the experiment, the density change rates should be zero. Also, alpha is 1.6 at the start.

```
In [3]: X0 = sp.solve(1 - 1.6 * X)
        x0 = X0[0]
        x0
```

Out [3] :

0.625

Y and Z equations have multiple real and complex solutions. I choose the real solutions as the initial densities.

```
In [4]: Y0 = sp.solve(0.5 + 1 / (Y**4 + 1) - 1.6 * Y)
        y0 = Y0[0]
        Y0
```

Out [4] :

[0.773037438345376, -0.805422290186745 - 0.735072417370233i, -0.805422290186745 + 0.735072417370233i,

As it can be seen above, there are multiple solutions for the equation. I only use the first one which is real. If there were two solutions that would be a case of bifurcation.

```
In [5]: Z0 = sp.solve(0.5 + ( Z**4 / (Z**4 + 1)) - 1.6 * Z)
        z0 = Z0[0]
        z0
```

Out [5] :

0.318897592409502

The protein density at each minute is computed by finding the density change in the previous minute and adding that change to the previous density. Below, I define the functions that compute the density change.

```
In [6]: dx = lambda x, alpha: (1 - alpha * x)
        dy = lambda y, alpha: (0.5 + 1 / (y**4 + 1) - alpha * y)
        dz = lambda z, alpha: (0.5 + (z**4) / (z**4 + 1) - alpha * z)
```

The value of alpha in every minute of the 48 hours is generated.

```
In [7]: alpha_48 = np.tile(np.concatenate((np.arange(1.6, 0.4, -0.1 / 60)[: -1], np.arange(0.4, 1
```

```
In [8]: x_densities = [x0]
        y_densities = [y0]
        z_densities = [z0]
```

Now, for every minute the density of each protein is calculated. New values are found by adding the density change to the previous density.

But, this method produced bad results for Y densities, so I used SciPy's *fsolve* to actually setting the left side of Y's equation to zero and solving the equation each time.

Also if the density falls below zero in a time step, it is set to zero in the density lists.

```

In [9]: %%time
        i = 1
        for alpha in alpha_48[:2880]:
            prev_x_density = x_densities[i-1]
            prev_y_density = y_densities[i-1]
            prev_z_density = z_densities[i-1]

            new_x_density = prev_x_density + dx(prev_x_density, alpha)

            new_y_density = scipy.optimize.fsolve(
                lambda y: 0.5 + 1 / (y**4 + 1) - alpha * y, float(prev_y_density))[0]

            new_z_density = prev_z_density + dz(prev_z_density, alpha)

            x_densities.append(new_x_density)
            y_densities.append(new_y_density)
            z_densities.append(new_z_density)

            i += 1

```

CPU times: user 2.48 s, sys: 28.5 ms, total: 2.51 s
 Wall time: 2.5 s

```

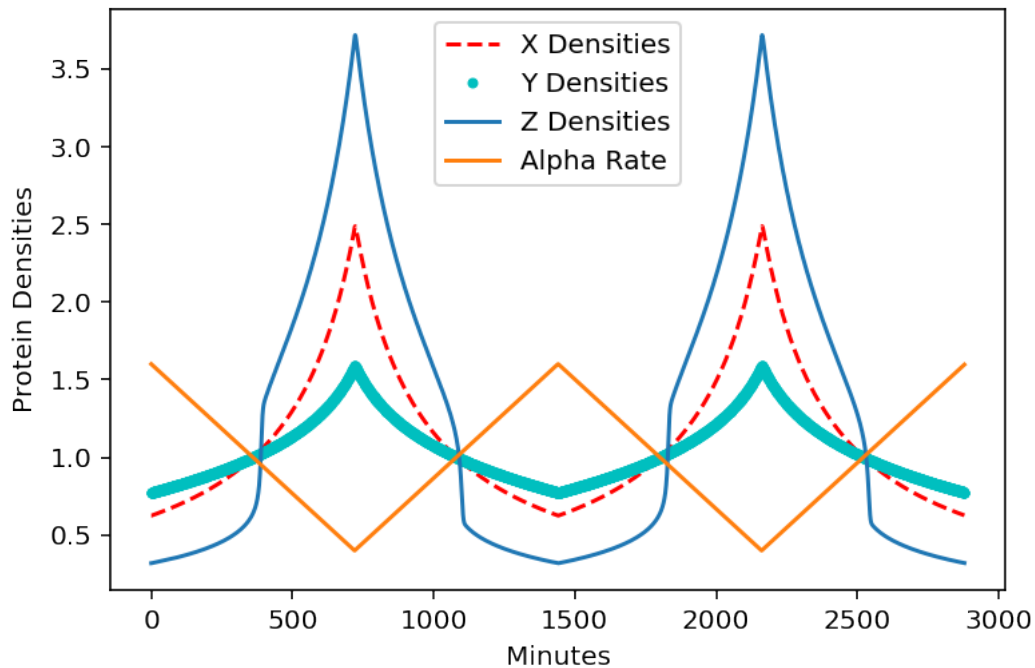
In [10]: # The x values for the plots
         minutes = list(range(60*48))

```

```

In [11]: plt.plot(minutes, x_densities[:2880], 'r--', label='X Densities')
         plt.plot(minutes, y_densities[:2880], 'c.', label='Y Densities')
         plt.plot(minutes, z_densities[:2880], label='Z Densities')
         plt.plot(minutes, alpha_48[:2880], label='Alpha Rate')
         plt.xlabel('Minutes')
         plt.ylabel('Protein Densities')
         plt.legend(loc='upper center')
         plt.show()

```



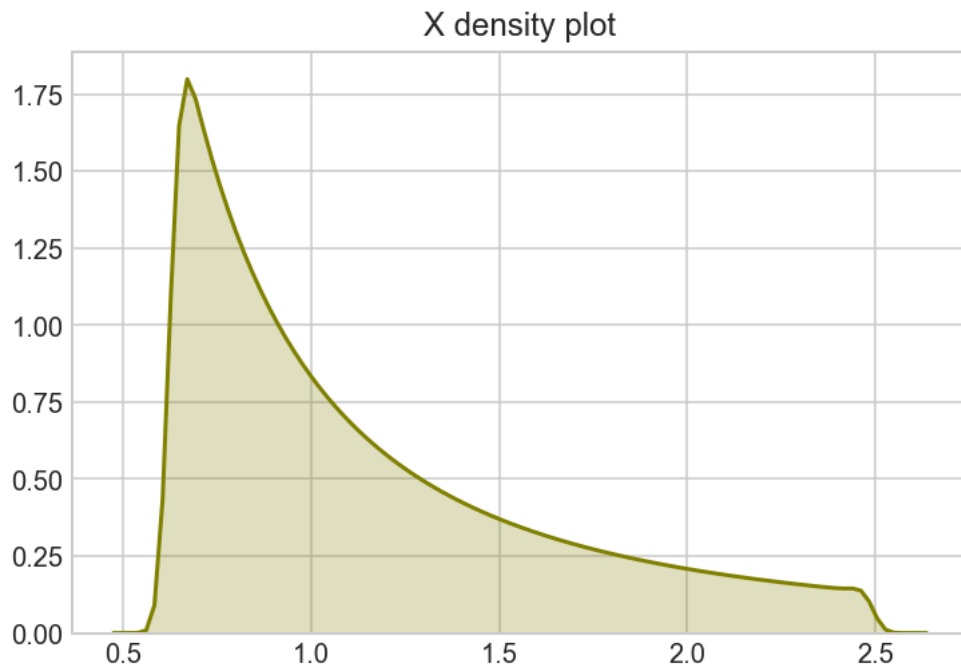
Each protein's density increases as alpha decreases and vice versa.
Z has the highest variance in density while Y changes the least.

1.5.1 Drawing the density plots

In the previous step, the densities of each protein through the 48 hours are stored in different lists. Using these lists and *Seaborn's kdeplot*, the density plot for each protein is drawn.

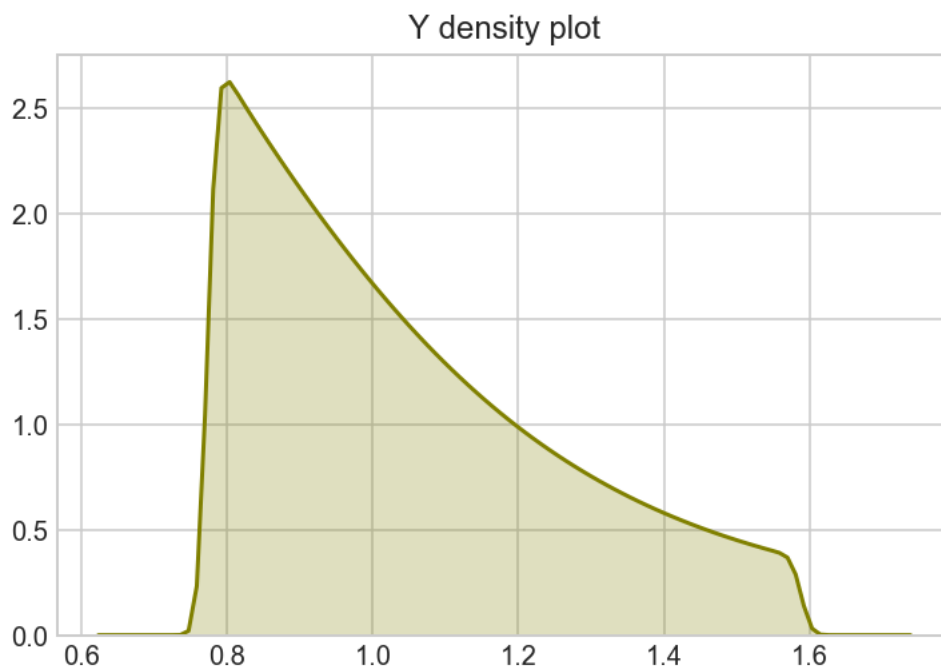
```
In [12]: sb.set_style('whitegrid')
         sb.kdeplot(np.array(x_densities), shade=True, bw=.05, color="olive").set_title('X densi
```

```
Out[12]: Text(0.5,1,'X density plot')
```



```
In [13]: sb.set_style('whitegrid')
          sb.kdeplot(np.array(y_densities), shade=True, bw=.05, color="olive").set_title('Y density plot')

Out[13]: Text(0.5,1,'Y density plot')
```



```
In [14]: sb.set_style('whitegrid')
         sb.kdeplot(np.array(z_densities), shade=True, bw=.05, color="olive").set_title('Z density plot')

Out[14]: Text(0.5,1,'Z density plot')
```



Density plots of X and Y are quite similar. X's plot has a steeper slope in the beginning which decrease in higher densities, while Y's plot has a more consistent slope. We can argue that Y is more robust than X and Z.

Compared to other proteins, Z's densities are concentrated in a small range(between 0.2 and 0.7). Z also has the steepest slope among these 3 proteins.

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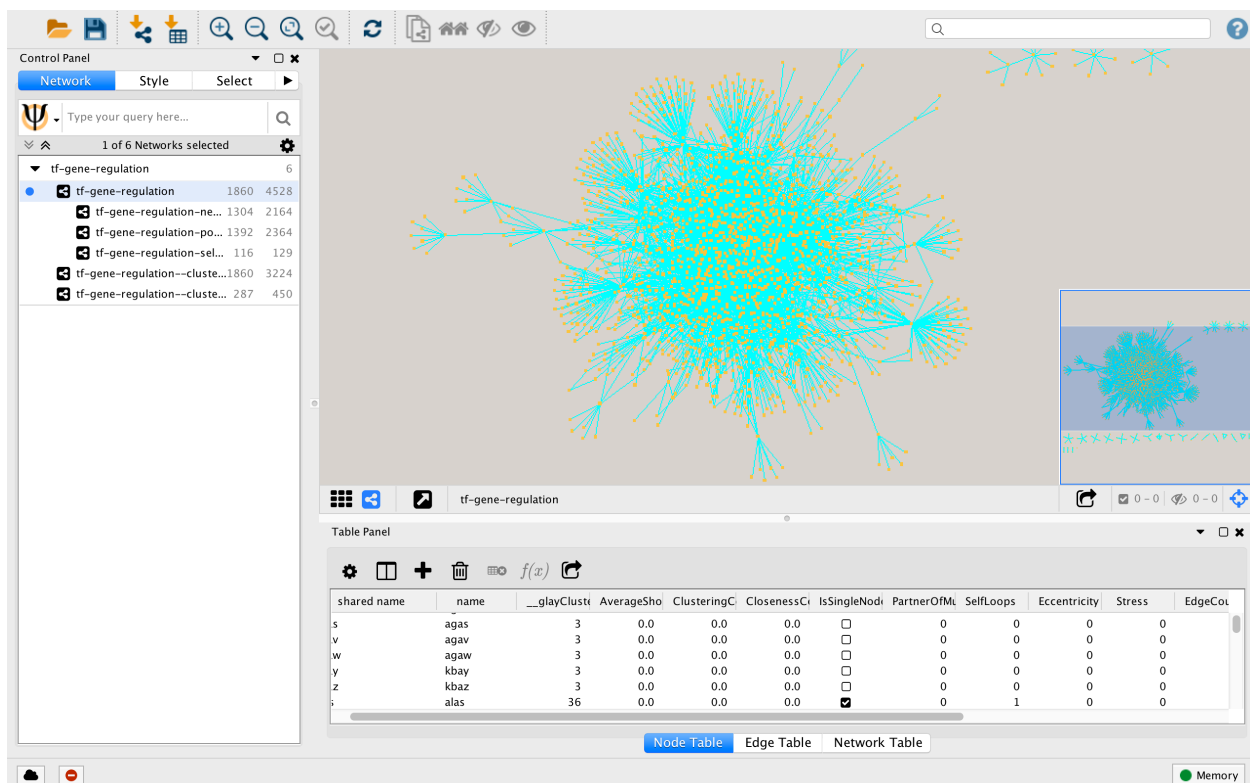
Intro to Bioinformatics

Homework Assignment 4 - Question 2

After downloading the TF-Gene file from RegulonDB, I read the text file with python and split each line to different entries. Then, I saved the list of split lines in a Pandas dataframe.

Next, I cleaned up the data by setting names for each column, setting all gene and TF names to lowercase and removing entries whose Evidence-Type was null or Regulatory-Effect was ?.

At last, for each row whose Regulatory-Effect was +-, I duplicated that row and changed the Regulatory-Effects so for each such row there is two rows. One with + and the other with - for Regulatory-Effect. At last I saved the dataframe in an Excel file. Screen shots of the code is attached to the end of this document.



Then, I imported the clean data into Cytoscape, setting the Regulatory-Effect as the interaction type of each edge.

A) Using the NetworkAnalyzer, I found the following facts about the network

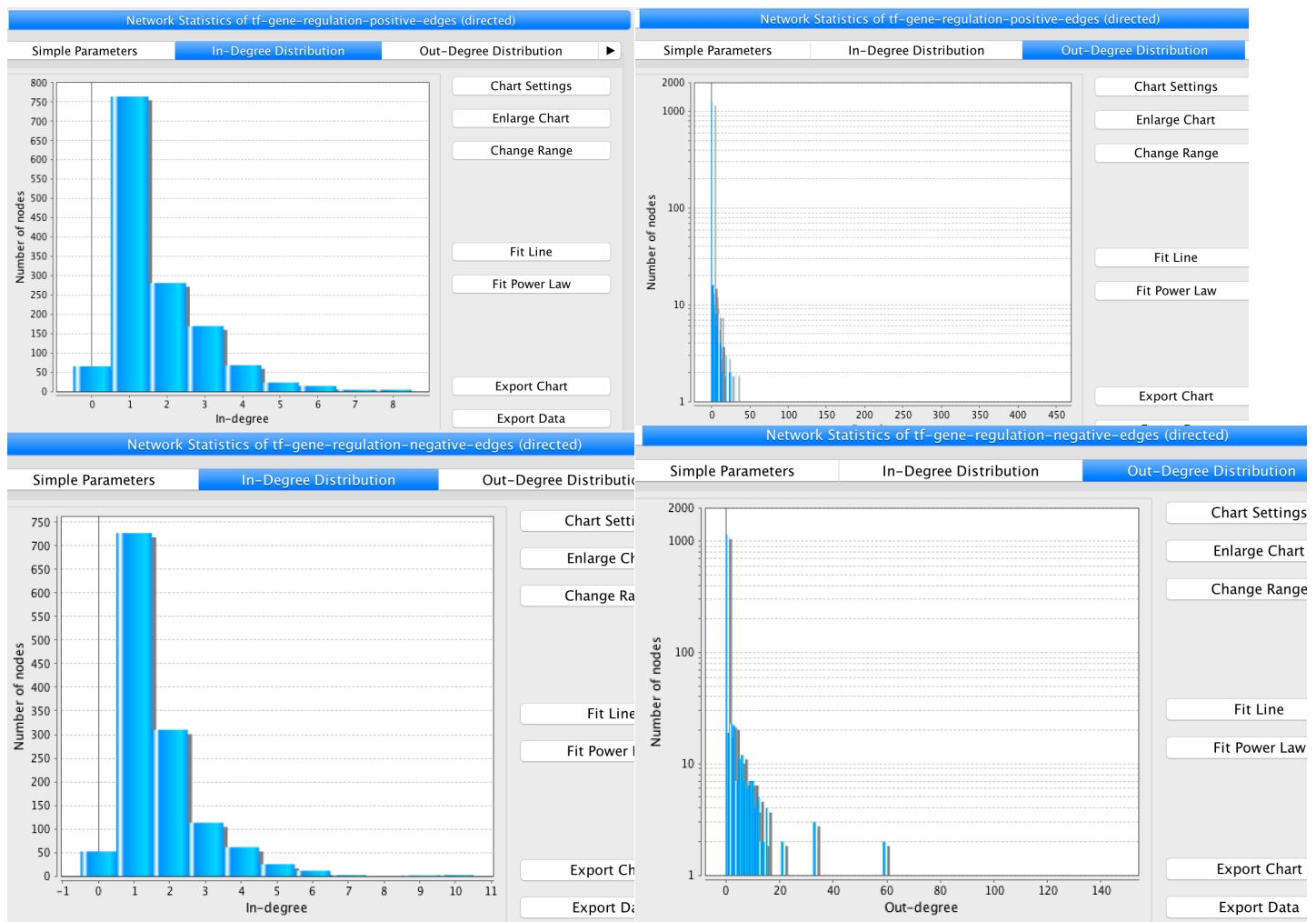
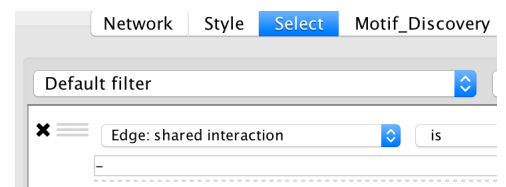
Number of Nodes: 1860

Number of Edges: 4528

Clustering coefficient : 0.113	Number of nodes : 1860
Connected components : 25	Network density : 0.0
Network diameter : 10	Isolated nodes : 1
Network radius : 1	Number of self-loops : 129
Shortest paths : 19443 (0%)	Multi-edge node pairs : 208
Characteristic path length : 2.957	Analysis time (sec) : 2.705
Avg. number of neighbors : 4.452	

In-Degree & Out-Degree distributions for positive and negative edges:

I used Cytoscape's filtering ability to select negative and positive edges and create different networks for each edge type. Then, I ran the NetworkAnalyzer on each network to find the distributions. (Out-Degree Y axis is logarithmic)

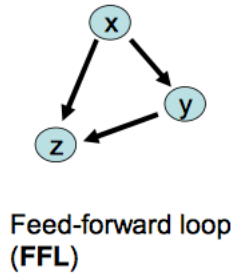


B)

Negative Auto Regulatory are Nodes that are self-looping and their loop's edge type is -

Positive Auto Regulatory are Nodes that are self-looping and their loop's edge type is +

Feed Forward Loops are subgraphs which look like the picture below.



First, I selected self-looping nodes with the filter below made a new network from them.

✕ ☰ Node: SelfLoops is between 1 and 3 inclusive.

and inclusive.

Then I deleted the non-looping edges from this network. I selected all edges whose shared interaction name was a string that contained the same gene name with a (+) or a (-) between them. I achieved this by using a regex pattern.

✕ ☰ Edge: shared interaction matches regex

And now I had a network of self-looping nodes and their looping edges. Again I used the filters to find out how many of these looping edges were + or -.

PAR or + looping edge count: 40

NAR or - looping edge count: 89

In order to find the FFL subgraphs I installed the Motif-Discovery app on Cytoscape. I set the motif size to 3 and the motif type to Directed. after running the app I chose the motif which was of the feed forward loop type and clicked on it so it was drawn.

The screenshot shows the Cytoscape Motif-Discovery app interface. The Control Panel on the left displays the following settings:

- Motif Size: 3
- Motif Type: Directed
- # Random Network: 0

A "Run" button is visible below these settings. Below the settings, the text indicates: "Different Types of Subgraphs Found [Original Network]: 11", "Subgraph Occurrences Found [Original Network]: 320892", and "Computing Time: 0 second and 158 milliseconds".

Below the text, there are three visual representations of subgraphs: a red directed feed-forward loop (FFL), a vertical column of three green nodes, and a vertical column of three red nodes.

At the bottom of the Control Panel, a table lists subgraph occurrences. The table has three columns: Subgraph, Frequency, and Z-Score. The row for the FFL motif (000100110) is highlighted with a red box, showing a frequency of 1322.

Subgraph	Frequency	Z-Score
011000000	310504	0
000100100	3998	0
000000000	3555	0
000100110	1322	0
011100000	1105	0
011101000	244	0

The main network visualization area shows a large, complex network of nodes and edges. A small inset window on the right shows a zoomed-in view of a specific part of the network.

Below the network visualization, a "Table Panel" is visible, showing a table with columns: PartnerOfMultiEdgedNodePairs, SelfLoops, Eccentricity, Stress, EdgeCount, Indegree, and Outd. The table contains several rows of data.

At the bottom of the interface, there are tabs for "Node Table", "Edge Table", and "Network Table". A status bar at the very bottom indicates "Total Number of VS in VMM = 18" and "Memory".

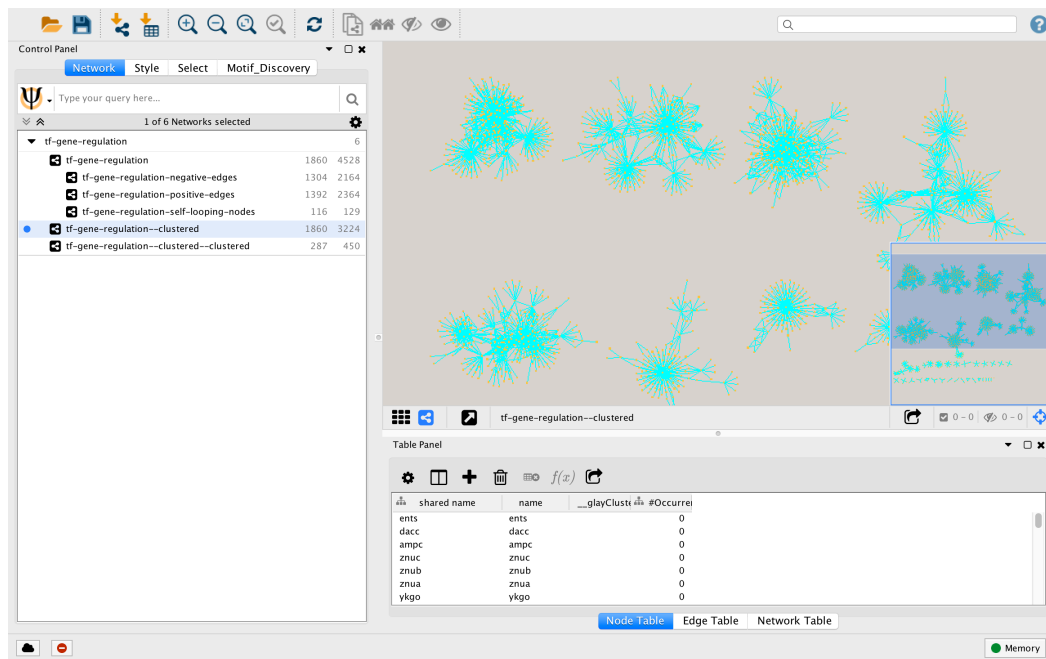
As it can be seen above, there were 1322 FFLs in the network.

C)

Number of Nodes in the second cluster: 287

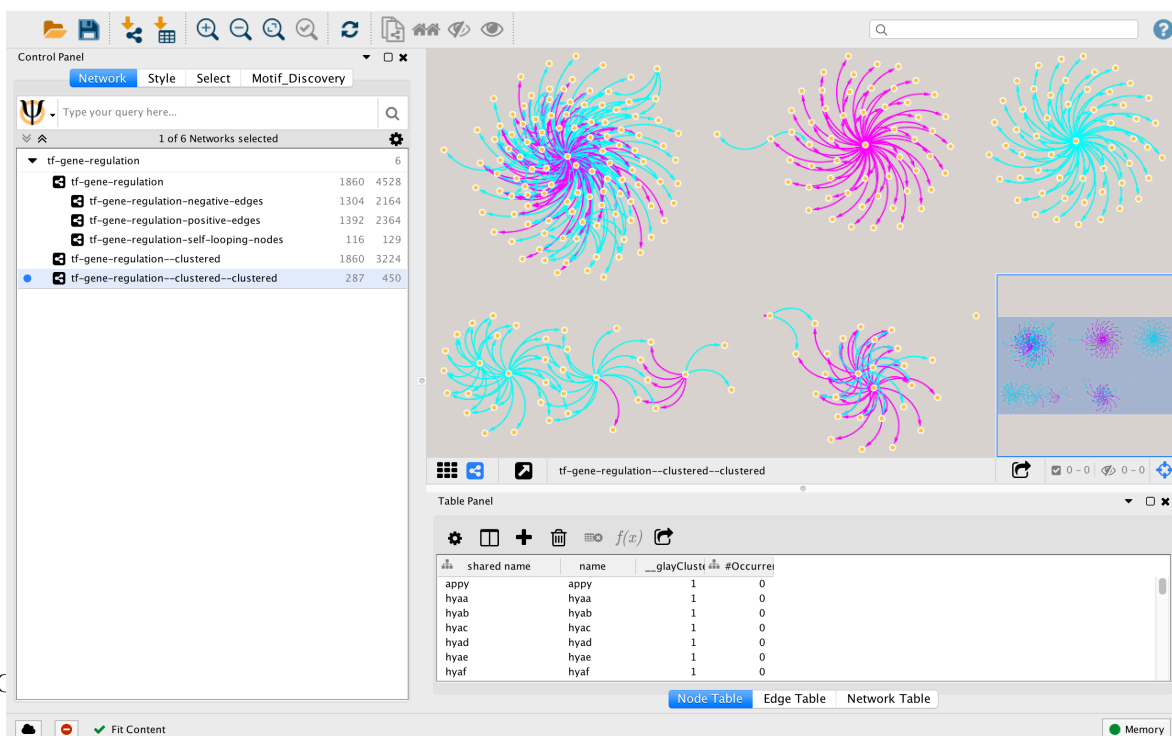
Number of Edges in the second cluster: 450

First Clustering:



Second Clustering:

Neon Blue edges are + and purple edges are -.



D)

First, I exported the table of the second cluster to a CSV file. Then, I opened this file in Excel and copied all the gene names in it and pasted these names in DAVID. I chose the OFFICIAL-GENE_SYMBOL setting and submitted the list.

Then, DAVID showed a list of possible species from which I chose the first one.

Select to limit annotations by or more species [Help](#)

- Use All Species -
Escherichia coli str. K-12 substr. MG1655
Escherichia coli UMN026(270)
Escherichia coli IAI39(260)

Select Species

Step 1: Enter Gene List

A: Paste a list

appy
hyaa
hyab
hyac

Clear

Or

B: Choose From a File

Choose File no file selected

☐ Multi-List File ?

Step 2: Select Identifier

OFFICIAL_GENE_SYMBOL

Step 3: List Type

Gene List ☒
Background ☐

Step 4: Submit List

Submit List

From the Functional Categories list, DAVID drew charts for UP_KEYWORDS and UP_SEQ_FEATURE. I sorted the charts by the number of genes to see what functional annotation most of the genes had.

Annotation Summary Results

[Help and Tool Manual](#)

Current Gene List: List_2

276 DAVID IDs











Current Background: Escherichia coli str. K-12 substr. MG1655







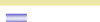
Check Defaults

Clear All

☒ Functional_Categories (3 selected)



<input checked="" type="checkbox"/> COG_ONTOLOGY	7.2%	20	Chart	<div></div>
<input type="checkbox"/> PIR_SEQ_FEATURE	31.2%	86	Chart	<div></div>
<input type="checkbox"/> SP_COMMENT_TYPE	95.3%	263	Chart	<div></div>
<input checked="" type="checkbox"/> UP_KEYWORDS	99.3%	274	Chart	<div></div>
<input checked="" type="checkbox"/> UP_SEQ_FEATURE	99.3%	274	Chart	<div></div>

Category	Term	RT	Genes	Count	%	P-Value	Benjamini
UP_KEYWORDS	Membrane	RT		92	33.3	3.6E-2	1.8E-1
UP_KEYWORDS	Cell membrane	RT		88	31.9	7.8E-3	4.7E-2
UP_KEYWORDS	Metal-binding	RT		84	30.4	3.1E-11	5.0E-10
UP_KEYWORDS	Cell inner membrane	RT		80	29.0	1.8E-3	1.2E-2
UP_KEYWORDS	Transmembrane	RT		73	26.4	7.4E-2	3.1E-1
UP_KEYWORDS	Transmembrane helix	RT		71	25.7	5.4E-2	2.5E-1
UP_KEYWORDS	Transport	RT		69	25.0	8.4E-4	5.8E-3
UP_KEYWORDS	Oxidoreductase	RT		62	22.5	2.8E-13	6.7E-12
UP_KEYWORDS	Iron	RT		61	22.1	2.9E-22	2.1E-20
UP_KEYWORDS	Iron-sulfur	RT		47	17.0	8.5E-2	9.1E-1

Category	Term	RT	Genes	Count	%	P-Value	Benjamini
UP_SEQ_FEATURE	transmembrane region	RT		70	25.4	4.9E-2	7.8E-1
UP_SEQ_FEATURE	topological domain:Cytoplasmic	RT		47	17.0	8.5E-2	9.1E-1
UP_SEQ_FEATURE	mutagenesis site	RT		37	13.4	8.8E-3	2.8E-1
UP_SEQ_FEATURE	metal ion-binding site:Iron-sulfur 2 (4Fe-4S)	RT		19	6.9	5.5E-12	2.5E-9
UP_SEQ_FEATURE	metal ion-binding site:Iron-sulfur 1 (4Fe-4S)	RT		17	6.2	1.8E-10	4.1E-8
UP_SEQ_FEATURE	domain:4Fe-4S ferredoxin-type 1	RT		16	5.8	4.6E-10	6.9E-8
UP_SEQ_FEATURE	domain:4Fe-4S ferredoxin-type 2	RT		16	5.8	4.6E-10	6.9E-8

It can be seen that these genes affect the cell membrane, iron-binding proteins and in general how the cell transports metals like iron through the membrane.

As for the pathway lists, DAVID shows that these genes affect the two component system and the flagellar assembly which forms the flagellum organelle which helps E.coli bacteria to move around.

Category	Term	RT	Genes	Count
KEGG_PATHWAY	Two-component system	RT		34
KEGG_PATHWAY	Flagellar assembly	RT		22

Pathways (1 selected)				
<input type="checkbox"/> EC_NUMBER	37.7%	104	Chart	
<input checked="" type="checkbox"/> KEGG_PATHWAY	48.2%	133	Chart	

bio-hw4-q2-GRN

December 22, 2017

```
In [1]: import pandas as pd
import numpy as np
```

```
In [2]: tf_gene_pd = pd.read_pickle('tf-gene-dataframe.pickle')
```

```
In [3]: tf_gene_pd.head(5)
```

```
Out[3]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence	\
0	AccB	accB	-		[]
1	AccB	accC	-		[]
2	AcrR	acrA	-	[BCE, BPP, GEA, HIBSCS]	
3	AcrR	acrB	-	[BCE, BPP, GEA, HIBSCS]	
4	AcrR	acrR	-	[AIBSCS, BCE, BPP, GEA, HIBSCS]	

	Evidence-Type
0	null
1	null
2	Weak
3	Weak
4	Weak

```
In [4]: ev_col = tf_gene_pd['Evidence']
```

```
In [5]: new_col = [r.replace('[', '').replace(']', '') for r in ev_col]
```

```
In [6]: new_col[:5]
```

```
Out[6]: ['',
'',
'BCE, BPP, GEA, HIBSCS',
'BCE, BPP, GEA, HIBSCS',
'AIBSCS, BCE, BPP, GEA, HIBSCS']
```

```
In [7]: tf_gene_pd['Evidence'] = new_col
```

```
In [8]: tf_gene_pd.head(10)
```

```
Out[8]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence \
0	AccB	accB	-	
1	AccB	accC	-	
2	AcrR	acrA	-	BCE, BPP, GEA, HIBSCS
3	AcrR	acrB	-	BCE, BPP, GEA, HIBSCS
4	AcrR	acrR	-	AIBSCS, BCE, BPP, GEA, HIBSCS
5	AcrR	flhC	-	GEA, HIBSCS
6	AcrR	flhD	-	GEA, HIBSCS
7	AcrR	marA	-	BPP, GEA, HIBSCS
8	AcrR	marB	-	BPP, GEA, HIBSCS
9	AcrR	marR	-	BPP, GEA, HIBSCS

```
Evidence-Type
0      null
1      null
2     Weak
3     Weak
4     Weak
5     Weak
6     Weak
7   Strong
8   Strong
9   Strong
```

```
In [9]: tf_gene_pd.to_excel('tf-gene-cleaned.xlsx', sheet_name='tf-gene-regulation', index=False)
```

```
In [10]: tf_gene_pd['TF-Name'] = tf_gene_pd['TF-Name'].str.lower()
         tf_gene_pd['Regulated-Gene'] = tf_gene_pd['Regulated-Gene'].str.lower()
```

```
In [11]: tf_gene_pd.to_excel('tf-gene-lowered-cleaned.xlsx', sheet_name='tf-gene-regulation', index=False)
```

```
In [12]: np.unique(tf_gene_pd['Evidence-Type'])
```

```
Out[12]: array(['Strong', 'Weak', 'null'], dtype=object)
```

```
In [13]: np.unique(tf_gene_pd['Regulatory-Effect'])
```

```
Out[13]: array(['+', '+-', '-', '?'], dtype=object)
```

```
In [14]: # Remove ?s and nulls
         na_less = tf_gene_pd[tf_gene_pd['Regulatory-Effect'] != '?']
         na_less = na_less[na_less['Evidence-Type'] != 'null']
```

```
In [15]: na_less.head(10)
```

```
Out[15]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence \
2	acrr	acra	-	BCE, BPP, GEA, HIBSCS
3	acrr	acrb	-	BCE, BPP, GEA, HIBSCS
4	acrr	acrr	-	AIBSCS, BCE, BPP, GEA, HIBSCS

5	acrr	flhc	-	GEA, HIBSCS
6	acrr	flhd	-	GEA, HIBSCS
7	acrr	mara	-	BPP, GEA, HIBSCS
8	acrr	marb	-	BPP, GEA, HIBSCS
9	acrr	marr	-	BPP, GEA, HIBSCS
10	acrr	micf	-	AIBSCS
11	acrr	soxr	-	BPP, GEA, HIBSCS

	Evidence-Type
2	Weak
3	Weak
4	Weak
5	Weak
6	Weak
7	Strong
8	Strong
9	Strong
10	Weak
11	Strong

```
In [16]: na_less.to_excel('tf-gene-nullCleaned-lowered-cleaned.xlsx', sheet_name='tf-gene-regula
```

```
In [17]: duals = na_less[na_less['Regulatory-Effect'] == '+-']
```

```
In [18]: len(na_less)
```

```
Out[18]: 4457
```

```
In [19]: cnt = 0
lind = duals.index[-1]
dd = pd.DataFrame(columns=list(duals.columns))
news = []
for ind, row in duals.iterrows():
    nr = pd.DataFrame(
        [[row['TF-Name'], row['Regulated-Gene'], '-', row['Evidence'], row['Evidence
        dd = dd.append(nr)
        row['Regulatory-Effect'] = '+'
        cnt += 1
        lind += 1

dual_fixed = pd.concat([duals, dd])
```

```
In [20]: df_full = pd.concat([na_less[na_less['Regulatory-Effect'] != '+-'], dual_fixed])
```

```
In [25]: df_full.to_excel('tf-gene-final.xlsx', sheet_name='tf-gene-regulation', index=False)
```

```
In [21]: np.unique(df_full['Regulatory-Effect'])
```

```
Out[21]: array(['+', '-'], dtype=object)
```

```
In [24]: df_full.head(10)
```

```
Out[24]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence
2	acrr	acra	-	BCE, BPP, GEA, HIBSCS
3	acrr	acrb	-	BCE, BPP, GEA, HIBSCS
4	acrr	acrr	-	AIBSCS, BCE, BPP, GEA, HIBSCS
5	acrr	flhc	-	GEA, HIBSCS
6	acrr	flhd	-	GEA, HIBSCS
7	acrr	mara	-	BPP, GEA, HIBSCS
8	acrr	marb	-	BPP, GEA, HIBSCS
9	acrr	marr	-	BPP, GEA, HIBSCS
10	acrr	micf	-	AIBSCS
11	acrr	soxr	-	BPP, GEA, HIBSCS

	Evidence-Type
2	Weak
3	Weak
4	Weak
5	Weak
6	Weak
7	Strong
8	Strong
9	Strong
10	Weak
11	Strong

```
In [22]: pd.DataFrame(
[[row['TF-Name'], row['Regulated-Gene'], '-', row['Evidence'], row['Evidence-Type']]
```

```
Out[22]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence
0	ompr	ompf	-	AIBSCS, BCE, BPP, GEA, HIBSCS, SM

	Evidence-Type
0	Weak

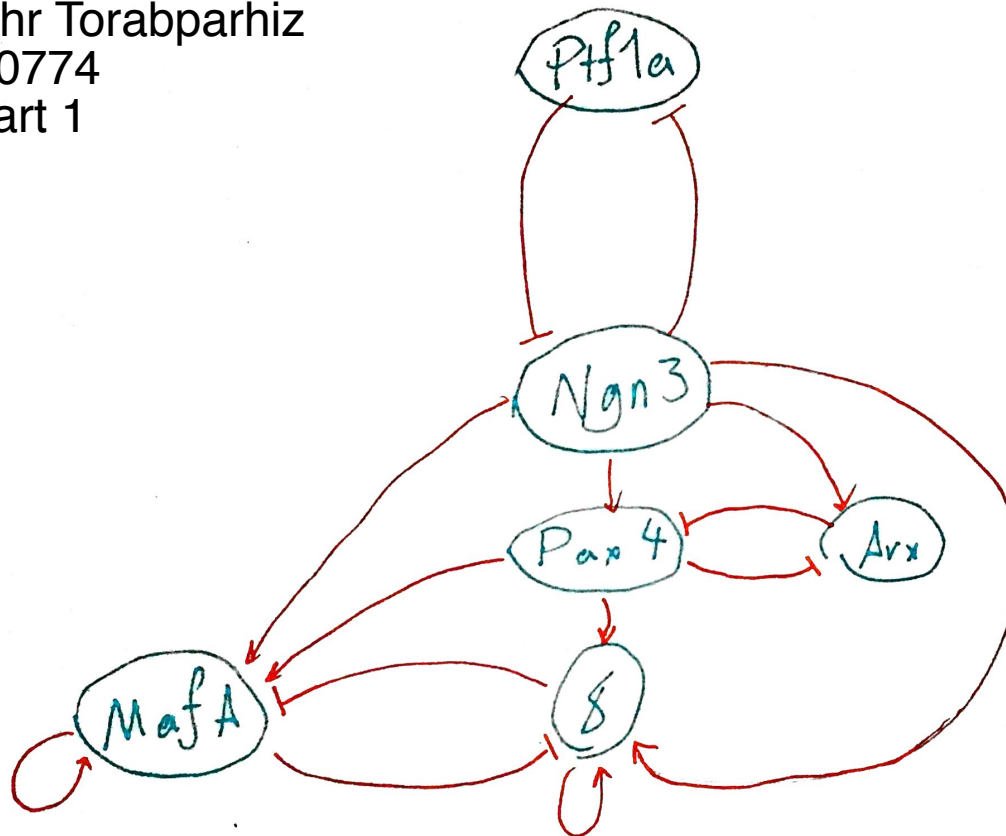
```
In [23]: nr
```

```
Out[23]:
```

	TF-Name	Regulated-Gene	Regulatory-Effect	Evidence
0	ompr	ompf	-	AIBSCS, BCE, BPP, GEA, HIBSCS, SM

	Evidence-Type
0	Weak

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Q3 part 1



If Ngn3 wins Pax4/Arx and MafA/Delta switches have a chance to function, so Ngn3 is an activator for all of them. Same is true for Pax4 activating MafA and Delta.

For each switch, the gene pair inhibit one another as they compete.

And for MafA & delta, we can argue that they activate themselves to keep make the final cell type which the Beta or the Delta cell.

bio-hw4-q3

December 23, 2017

1 Intro to Bioinformatics

1.1 Homework Assignment 4

1.2 Question 3: Hierarchical Attractors

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1.4.1 Developed by Python 3.6

```
In [1]: import numpy as np
```

1.4.2 Computing Probabilites for each switch

```
In [2]: endocrine_progenitor_prob = lambda ngn3, ptf1a: 0.001 * (
        (ngn3**2 + ngn3) / (ngn3**2 + 1)) * (
        (ptf1a**2 + 1) / (ptf1a**2 + ptf1a + 1))

        beta_delta_progenitor_prob = lambda pax4, arx: 0.005 * (
        (pax4**3 + pax4) / (pax4**3 + 1)) * (
        (arx**3 + 2) / (arx**3 + arx + 1))

        beta_cells_prob = lambda mafa, delta: 0.003 * (
        (mafa**4 + mafa) / (mafa**4 + 1)) * (
        (delta**4 + 1) / (delta**4 + delta**2 + 1))
```

Using NumPy's *random.uniform* method, a million random densities for each of the six genes are generated. Then, probabilities of genes winning a switch is computed using the functions written above. Finally, NumPy's *random.choice* is used to find the winner according to the probabilities which are computed. A 1 means that the switch goes toward the creation beta cells.

In the Beta/Delta and Beta switches, the probability of that switch going toward beta cell creation is multiplied by probability of ending up in that switch.

```
In [3]: def markov_toar():
        # Endocrine Progenitor Sampling
        ptf1a_densities = np.random.uniform(low=0, high=1, size=10**6)
        ngn3_densities = np.random.uniform(low=0, high=1, size=10**6)
```

```

ngn3_win_probs = [
    endocrine_progenitor_prob(ngn3, ptf1a) for ngn3, ptf1a in zip(ptf1a_densities, n

endoc_prog_outcomes = [
    np.random.choice(
        [0, 1], p=[1-ngn3_win_prob, ngn3_win_prob]) for ngn3_win_prob in ngn3_win_pr

endoc_prog_prob = sum(endoc_prog_outcomes) / 1e6
print(f'Number of Ngn3 wins in a million samples without considering prior probabili
print(f'Probabilty of creation of a endocrine progenitor cell: {endoc_prog_prob}')
print('')

# Beta/Delta Progenitor Sampling
pax4_densities = np.random.uniform(low=0, high=1, size=10**6)
arx_densities = np.random.uniform(low=0, high=1, size=10**6)

pax4_win_probs = [
    beta_delta_progenitor_prob(pax4, arx) for pax4, arx in zip(
        pax4_densities, arx_densities)]

beta_delta_win_probs = [
    pax4_win_prob for pax4_win_prob in pax4_win_probs]

beta_delta_outcomes = [
    np.random.choice(
        [0, 1], p=[1-beta_delta_win_prob, beta_delta_win_prob]) for beta_delta_win_p

# the probabiltly of Pax4 winning the switch is multiplied by
# the probabiltly of endocrine progenitor winning the previous switch.
beta_delta_prob = sum(beta_delta_outcomes) / 1e6 * endoc_prog_prob

print(f'Number of Pax4 wins in a million samples without considering prior probabili
print(f'Probabilty of creation of a Beta/Delta progenitor cell: {beta_delta_prob}')
print('')

# Beta Cell Sampling
mafa_densities = np.random.uniform(low=0, high=1, size=10**6)
delta_densities = np.random.uniform(low=0, high=1, size=10**6)

mafa_win_probs = [
    beta_cells_prob(mafa, delta) for mafa, delta in zip(
        mafa_densities, delta_densities)]

beta_cell_win_probs = [
    mafa_win_prob for mafa_win_prob in mafa_win_probs]

```

```

beta_cell_outcomes = [
    np.random.choice(
        [0, 1], p=[1-beta_cell_win_prob, beta_cell_win_prob]) for beta_cell_win_prob in

# the probabiltiy of Mafa winning the switch is multiplied
# by the probabiltiy of Ngn3 and Pax4 winning the previous switches.
beta_cell_prob = sum(beta_cell_outcomes) / 1e6 * beta_delta_prob

print(f'Number of Mafa wins in a million samples without considering prior probabili
print(f'Probabilty of creation of a Beta cell: {beta_cell_prob}')
print('')

```

```

In [4]: %%time
        markov_toar()

```

```

Number of Ngn3 wins in a million samples without considering prior probabilitites: 420
Probabilty of creation of a endocrine progenitor cell: 0.00042

```

```

Number of Pax4 wins in a million samples without considering prior probabilitites: 3630
Probabilty of creation of a Beta/Delta progenitor cell: 1.5246e-06

```

```

Number of Mafa wins in a million samples without considering prior probabilitites: 1284
Probabilty of creation of a Beta cell: 1.9575864e-09

```

```

CPU times: user 1min 28s, sys: 1.35 s, total: 1min 30s
Wall time: 1min 32s

```