Decorrelation Within Pathways

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In this notebook, I show that decorrelation could help order a pathway. The approach I will take is as follows:

- Calculate primary pairwise correlations between each mutant transcriptome
- Weight all correlations by the number of isoforms that are DE in both transcriptomes, divided by the total number of isoforms in either transcriptome.
- Plot

There's a lot of untidy code here, for which I apologize. This is probably the most poorly documented notebook in this project...

```
In [1]: # important stuff:
        import os
        import pandas as pd
        import numpy as np

        import morgan as morgan
        import genpy
        import gvars

        # Graphics
        import matplotlib as mpl
        import matplotlib.pyplot as plt
        import seaborn as sns
        from matplotlib import rc
        rc('text', usetex=True)
        rc('text', usetex=True)
        rc('text.latex', preamble=r'\usepackage{cmbright}')
        rc('font', **{'family': 'sans-serif', 'sans-serif': ['Helvetica']})

        # Magic function to make matplotlib inline;
        %matplotlib inline

        # This enables SVG graphics inline.
        %config InlineBackend.figure_formats = {'png', 'retina'}

        # JB's favorite Seaborn settings for notebooks
        rc = {'lines.linewidth': 2,
              'axes.labelsize': 18,
              'axes.titlesize': 18,
              'axes.facecolor': 'DFDFE5'}
        sns.set_context('notebook', rc=rc)
        sns.set_style("dark")

        mpl.rcParams['xtick.labelsize'] = 16
        mpl.rcParams['ytick.labelsize'] = 16
        mpl.rcParams['legend.fontsize'] = 14
```

```
In [2]: genvar = gvars.genvars()
```

```
In [4]: # Specify the genotypes to refer to:
        single_mutants = ['b', 'c', 'd', 'e', 'g']

        # Specify which genotypes are double mutants
        double_mutants = {'a' : 'bd', 'f':'bc'}

        # initialize the morgan.hunt object:
        thomas = morgan.hunt('target_id', 'b', 'tpm', 'qval')

        # input the genmap file:
        thomas.add_genmap('../input/library_genotype_mapping.txt', comment='#')

        # add the names of the single mutants
        thomas.add_single_mutant(single_mutants)

        # add the names of the double mutants
        thomas.add_double_mutants(['a', 'f'], ['bd', 'bc'])

        # set the q-value threshold for significance to its default value, 0.1
        thomas.set_qval()

        # Add the tpm files:
        kallisto_loc = '../input/kallisto_all/'
        thomas.add_tpm(kallisto_loc, '/kallisto/abundance.tsv', '')

        # Make all possible combinations of WT, X
        combs = {}
        for gene in thomas.genmap.genotype.unique():
            if gene != 'wt':
                combs[gene] = 'WT_'+gene+'/'

        # load all the beta values for each genotype:
```

```
        sleuth_loc = '../sleuth/kallisto/'
        for file in os.listdir("../sleuth/kallisto"):
            if file[:4] == 'beta':
                letter = file[-5:-4].lower()
                thomas.add_beta(sleuth_loc + file, letter)
                thomas.beta[letter].sort_values('target_id', inplace=True)
                thomas.beta[letter].reset_index(inplace=True)
        thomas.filter_data()
```

```
In [5]: barbara = morgan.mcclintock('bayesian', thomas, True)
```

```
starting comparison of d, c
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.7 sec
starting comparison of d, e
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.9 sec
starting comparison of d, b
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.9 sec
starting comparison of d, g
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.9 sec
starting comparison of c, e
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 2.1 sec
starting comparison of c, b
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.8 sec
starting comparison of c, g
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.7 sec
starting comparison of e, b
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 2.6 sec
starting comparison of e, g
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 2.1 sec
starting comparison of b, g
Applied log-transform to lam and added transformed lam_log_ to model.
 [-----------------100%-----------------] 2000 of 2000 complete in 1.9 secd d
d c
Applied log-transform to lam and added transformed lam_log_ to model.
d e
Applied log-transform to lam and added transformed lam_log_ to model.
d b
Applied log-transform to lam and added transformed lam_log_ to model.
```

```
d g
Applied log-transform to lam and added transformed lam_log_ to model.
c c
c e
Applied log-transform to lam and added transformed lam_log_ to model.
c b
Applied log-transform to lam and added transformed lam_log_ to model.
c g
Applied log-transform to lam and added transformed lam_log_ to model.
e e
e b
Applied log-transform to lam and added transformed lam_log_ to model.
e g
Applied log-transform to lam and added transformed lam_log_ to model.
b b
b g
Applied log-transform to lam and added transformed lam_log_ to model.
g g
```

Next, I define some functions that will help me clean up the matrix I just generated with the above command and place it into a tidy dataframe.

```
In [6]: def tidy_df(df, corr='corr', morgan_obj=thomas):
            """
            A function that returns a tidied up dataframe.

            Dataframe provided must be the result of morgan.robust_regression()
            or morgan.robust_regression_secondary()

            df - dataframe to tidy up
            corr - a string indicating whether to use 'corr' or 'outliers'

            outputs:
            df - a tidied dataframe with columns 'corr_wit', 'variable',
                'fraction' and 'pair'
            """
            # make a copy of the df
            df = df.copy()
            # append a column called corr_with
            if 'corr_with' not in df:
                df['corr_with'] = morgan_obj.single_mutants
            # melt it so that each row has a single correlation
            df = pd.melt(df, id_vars='corr_with')
            # drop any observations where the correlated letters are the same
            df = df[df.corr_with != df.variable]

            def calculate_fraction(x, fraction='corr'):
```

```
            """Fraction of genes that participate in a given interaction."""
            if (x.corr_with, x.variable) in barbara.correlated_genes.keys():
                dd = barbara.correlated_genes[(x.corr_with, x.variable)]
                outliers = len(dd['outliers'])
                corr = len(dd['corr'])
                total = outliers + corr
                if fraction == 'corr':
                    return corr/total
                else:
                    return outliers/total
            else:
                return np.nan

        # calculate the fraction of genes participating in any interaction
        df['fraction'] = df.apply(calculate_fraction, args=(corr,), axis=1)
        # generate a new variable 'pair' that is
        df['pair'] =  df.variable + df.corr_with
        # return the damned thing:
        return df

In [7]: def different(x, d):
        """
        Returns an indicator variable if the primary regression
        is different in sign from the secondary.
        """
        # extract the pair in question:
        p = x.pair
        # search for the primary interaction in the dataframe
        primary = d[(d.pair == p) &
                    (d.regression == 'primary')].value.values[0]
        # search for the secondary
        secondary = d[(d.pair == p) &
                      (d.regression == 'secondary')].value.values[0]

        # if the interactions are 0, return 0
        if primary == 0 or secondary == 0:
            return 0
        # if they have the same sign, return -1
        elif (primary*secondary > 0):
            return -1
        # otherwise return 1
        else:
            return 1

In [8]: def special_add(x):
        """
        If the primary and secondary have the same sign,
        returns the addition of both.
```

```
    """
    # if the current row is a secondary row
    # and the primary and secondary rows are the same
    # then return np.nan since we will want to ignore
    # the secondary correlation
    # if they are different in sign, return the current value
    if x.regression == 'secondary':
        if x.different == -1:
            return np.nan
        else:
            return x.value

    # if the regression is primary,
    # then add the values if the correlations have the same sign
    # otherwise just return the current value:
    check = d[(d.regression=='secondary') & \
         (d.pair == x.pair)].different.values
    if check == -1:
        to_add = d[(d.regression=='secondary') &
                   (d.pair == x.pair)].value.values[0]
        return x.value + to_add
    else:
        return x.value
```

tidy up the dataframes:

```
In [9]: # tidy up the dataframe w/bayesian primary interactions:
        d_pos = tidy_df(barbara.robust_slope)
        d_pos['regression'] = 'primary'
        # tidy up the secondary interactions
        d_minus = tidy_df(barbara.secondary_slope, corr='outliers')
        d_minus['regression'] = 'secondary'

        frames = [d_pos, d_minus]
        d = pd.concat(frames)

        # identify whether primary and secondary
        # interactions have different signs
        d['different'] = d.apply(different, args=(d,), axis=1)
        # drop any fractions that are NAN
        d.dropna(subset=['fraction'], inplace=True)
        # calculate corrected coefficients
        d['corrected'] = d.apply(special_add, axis=1)
        # drop any NAN corrected columns
        d.dropna(subset=['corrected'], inplace=True)

        # sort the pairs according to functional distance
        d['sort_pairs'] = d.pair.map(genvar.sort_pairs)
        d.sort('sort_pairs', inplace=True)

        # add the labels for plotting:
        d['genes'] = d.pair.map(genvar.decode_pairs)
```

```
In [10]: # extract the standard error for each correlation
         e_plus = tidy_df(barbara.errors_primary)

         # add a sort pairs column
         e_plus['sort_pairs'] = e_plus.pair.map(genvar.sort_pairs)
         # decode the gene pairs
         e_plus['genes'] = e_plus.pair.map(genvar.decode_pairs)
         # sort
         e_plus.sort('sort_pairs', inplace=True)
         # drop nonnumeric values
         e_plus.dropna(inplace=True)

         # repeat for secondary errors
         e_minus = tidy_df(barbara.errors_secondary)
         e_minus['sort_pairs'] = e_minus.pair.map(genvar.sort_pairs)
         e_minus['genes'] = e_minus.pair.map(genvar.decode_pairs)
         e_minus.sort('sort_pairs', inplace=True)
         e_minus.dropna(inplace=True)
```

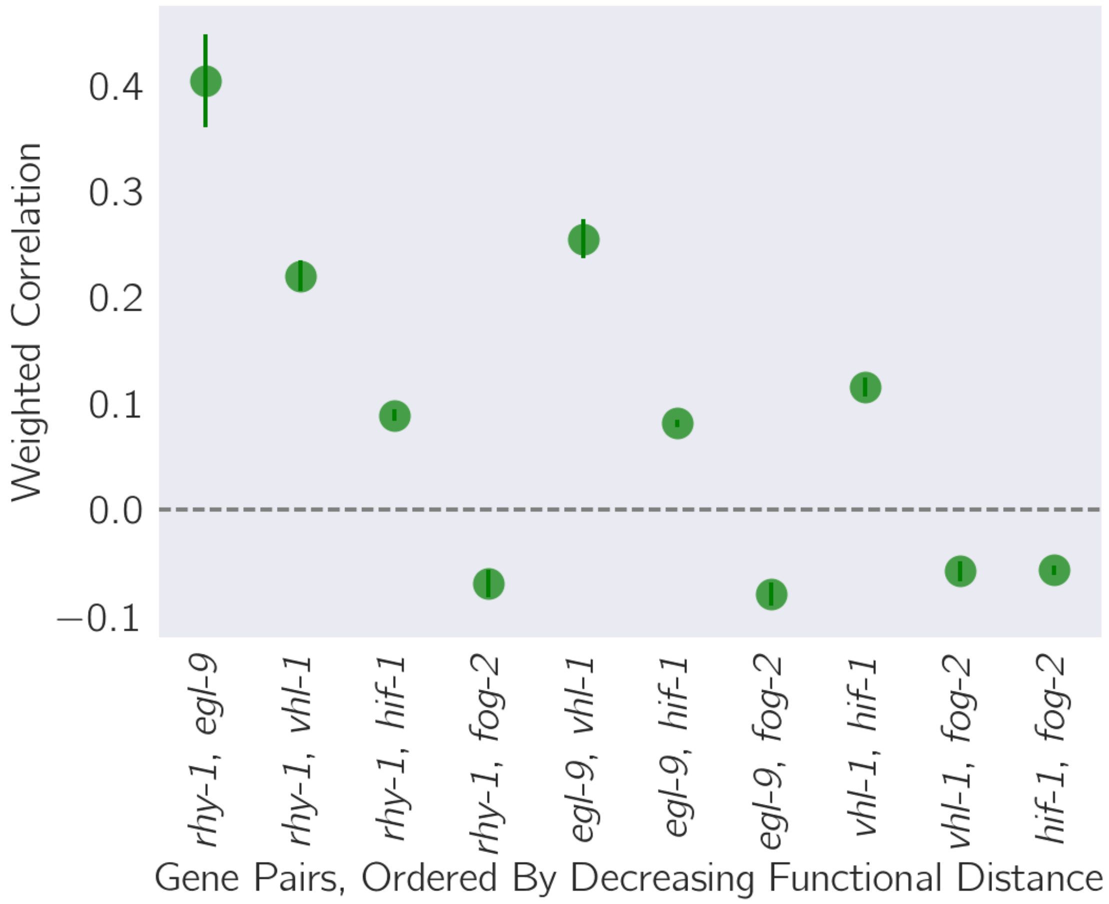
2 Figure 7

```
In [11]: # generate a stripplot with all the
         sns.stripplot(x='genes', y='corrected',
                       data=d[d.regression=='primary'], size=15,
                       color='g', alpha=0.7)

         # add errorbars:
         # for each xtick and xticklabel
         for x, xlabel in zip(plt.gca().get_xticks(),
                              plt.gca().get_xticklabels()):
             # get the data
             temp = d[d.regression=='primary']
             # get the gene ID
             f = temp.genes == xlabel.get_text()
             # get the error bar gene ID
             f2 = e_plus.genes == xlabel.get_text()
             # plot the errorbar
             plt.gca().errorbar(np.ones_like(temp[f].corrected.values)*x,
                                temp[f].corrected.values,
                                yerr=e_plus[f2].value.values,
                                ls='none', color='g')
```

```
# prettify:
plt.xticks(rotation=90, fontsize=20)
# plt.yticks([-0.1, 0, 0.5], fontsize=20)
plt.yticks(fontsize=20)
plt.axhline(0, lw=2, ls='--', color='gray')
plt.xticks(fontsize=20)
plt.yticks(fontsize=20)
plt.xlabel('Gene Pairs, Ordered By Decreasing Functional Distance', fontsize=20)
plt.ylabel('Weighted Correlation', fontsize=20)

# save
plt.savefig('../output/weighted_corr_decreases_w_distance.svg')
```



Secondary correlations do not seem to have this property. That may be a result of the low number of genes (we should have sequenced deeper) or a result of other things that may be occurring. I don't really know.

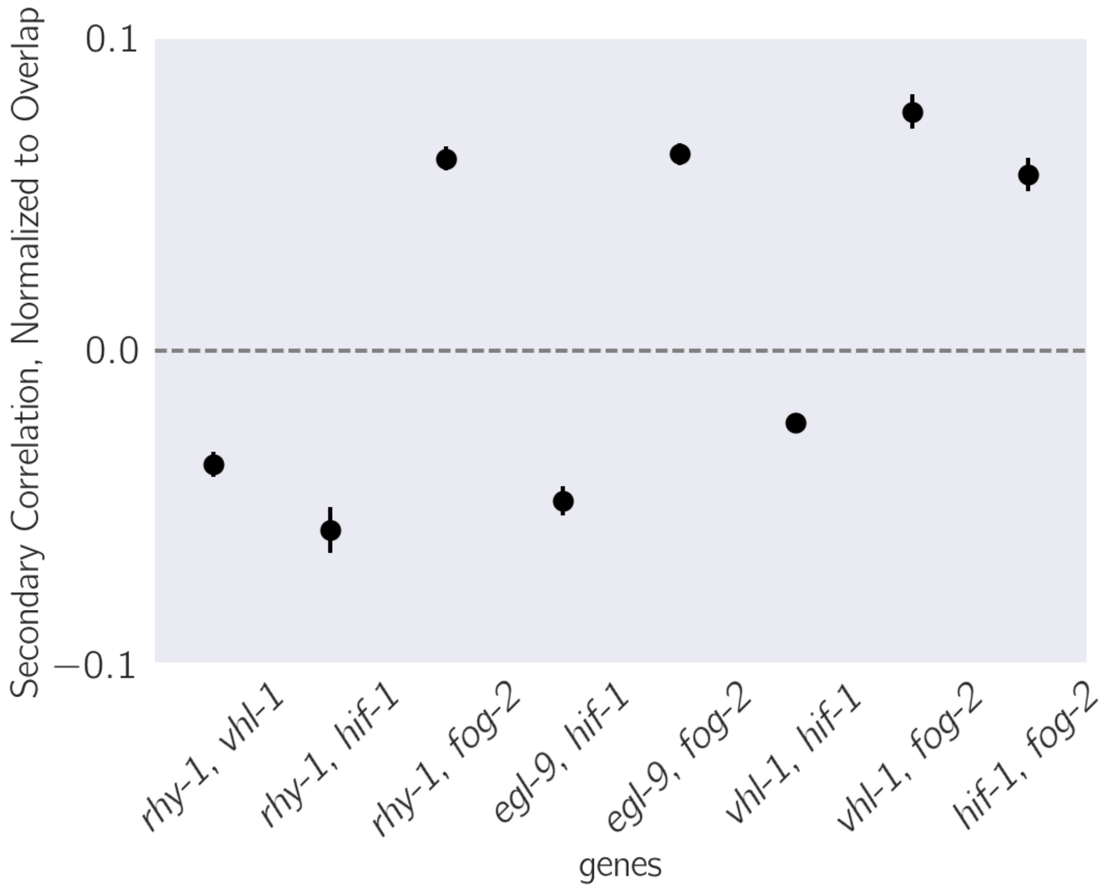
```
In [12]: # plot secondary interactions
         sns.stripplot(x='genes', y='corrected',
                       data=d[(d.regression=='secondary') &
```

```
                        (d.different == 1)],
                 size=10, color='k')

    # add errorbars:
    for x, xlabel in zip(plt.gca().get_xticks(),
                         plt.gca().get_xticklabels()):
        temp = d[d.regression=='secondary']
        f = temp.genes == xlabel.get_text()
        f2 = e_minus.genes == xlabel.get_text()
        plt.gca().errorbar(np.ones_like(temp[f].corrected.values)*x,
                           temp[f].corrected.values,
                           yerr=e_minus[f2].value.values,
                           ls='none', color='k')

    # prettify
    plt.axhline(0, ls='--', color='0.5')
    plt.xticks(rotation=45, fontsize=20)
    plt.yticks([-0.1, 0, 0.1], fontsize=20)
    plt.axhline(0, lw=2, ls='--', color='gray')
    plt.ylabel('Secondary Correlation, Normalized to Overlap')
```

```
Out[12]: <matplotlib.text.Text at 0x13737d978>
```



```
In [ ]:
```