BME 6717 Dataset 3 Timeseries Analysis

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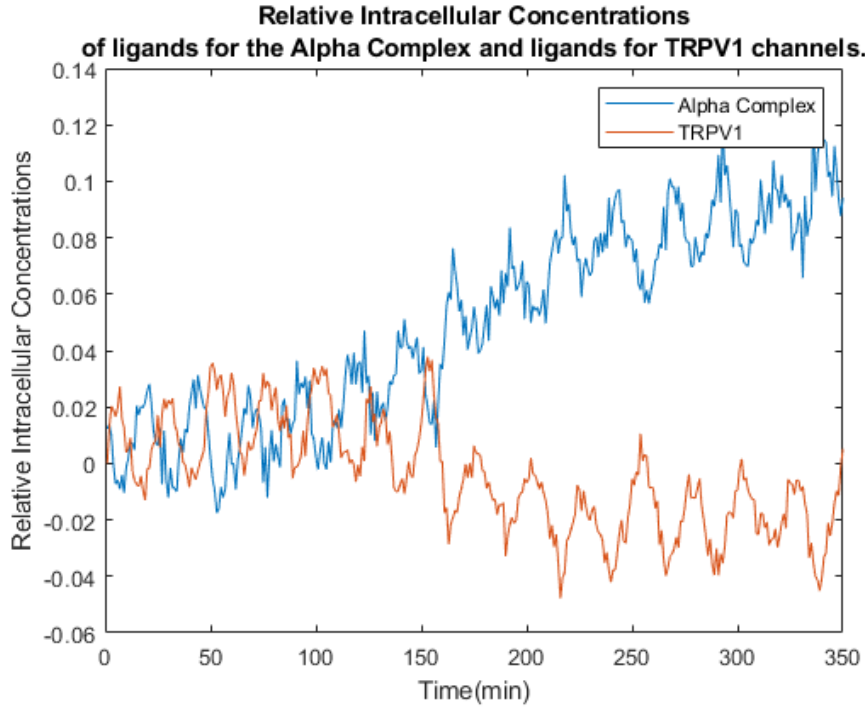We first look at the relative concentrations over time for both ligands.

Figure 1: Relative Intracellular Concentrations of ligands for the Alpha Complex and ligands for TRPV1 channels, sampled at $\frac{1}{60}$ Hz.

The plot shows an upward trend in the Alpha Complex concentrations and a downward trend in the TRPV1 concentrations. Though detrending seems plausible, it is best to check for correlation in the original dataset to observe if it is needed.
Running the correlation in MATLAB (see code) gave a *strong* negative correlation of -0.8572 between the the two processes.
The data was detrended in two ways (first difference and logarithm) *Fig. 2* to see if the correlation could be improved.
With the *crosscorr* function in the Econometrics Toolbox in Matlab, the maximum correlation was (-0.8781) between the two processes at a -2 time lag. Further analysis was carried out on the original data using the Econometrics Toolbox for two reasons:

1. plotting the corresponding detrended data against each other and comparing to the plot of the original data showed that the original data maintained semblance of a negative correlation as opposed to the others. Fig 3

2. the Econometrics Toolbox proved to capture the best correlation regardless of the nature of the data.
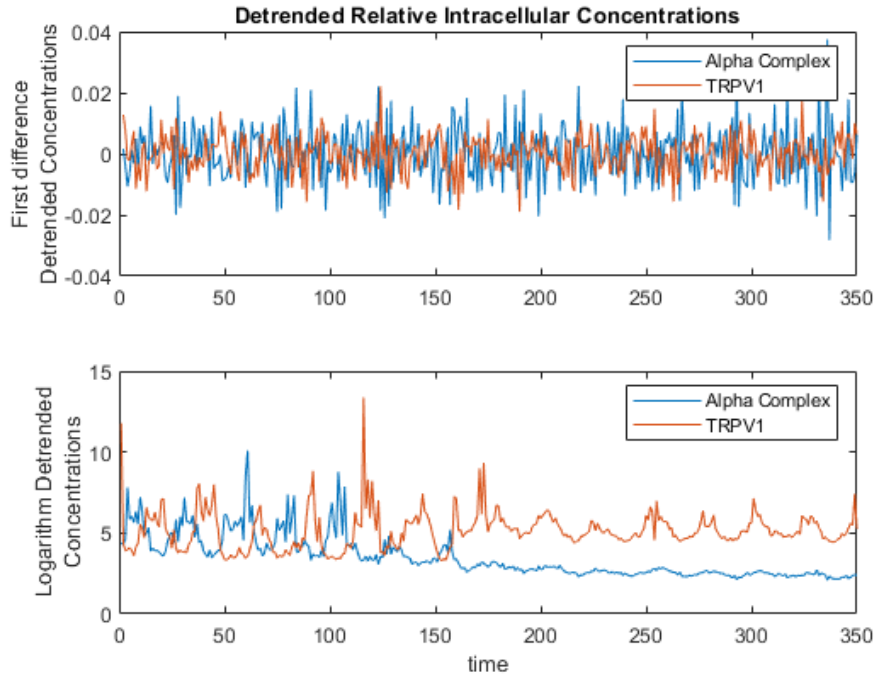
Figure 2: Detrended Relative Intracellular Concentrations of ligands for the Alpha Complex and ligands for TRPV1 channels. Top plot: 1st difference; Bottom plot: Log

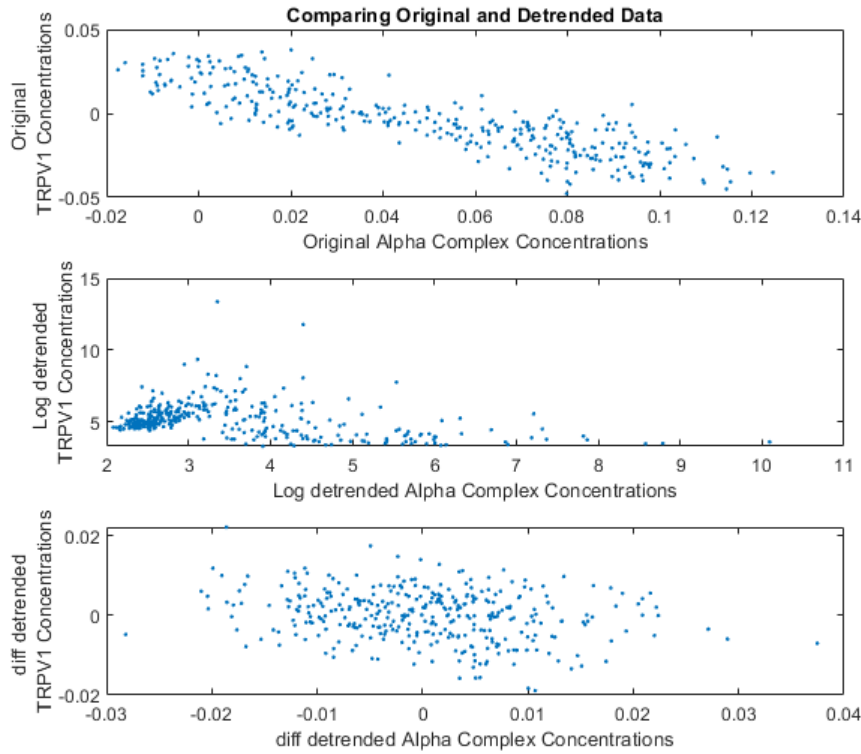Figure 3: Comparing Original and Detrended Data

With an assumption that the processes are autoregressive, an order of 2 was chosen after increasing beyond this order provided parameters that were statistically insignificant ($p > 0.05$). Fig 4.

Figure 5 shows a pvalue of $1.4649e^{-80}$ for the influence of TRPV1 on the Alpha Complex as compared to a pvalue of $1.1183e^{-53}$ for the opposite influence.

```
>> Mdl = regARIMA(3,0,0);
Alpha_Mdl = estimate(Mdl,Alpha');

    ARMA(3,0) Error Model (Gaussian Distribution):

                  Value        StandardError      TStatistic        PValue

                _____      _____      _____      _____

    Intercept      0.06424        0.025841           2.486          0.01292
    AR{1}          0.56018        0.055475          10.098        5.6425e-24
    AR{2}          0.44114        0.057461           7.6773       1.6247e-14
    AR{3}         -0.021006       0.056685          -0.37057        0.71096
    Variance     7.1869e-05      4.9161e-06         14.619        2.1148e-48

>> Mdl = regARIMA(4,0,0);
Alpha_Mdl = estimate(Mdl,Alpha');

    ARMA(4,0) Error Model (Gaussian Distribution):

                  Value        StandardError      TStatistic        PValue

                _____      _____      _____      _____

    Intercept     0.062175        0.023628           2.6314        0.0085041
    AR{1}         0.55887         0.055523          10.066        7.8366e-24
    AR{2}         0.46753         0.064539           7.2441       4.3541e-13
    AR{3}         0.011902        0.060712           0.19605        0.84457
    AR{4}        -0.059357        0.057217          -1.0374         0.29955
    Variance    7.1621e-05       4.9258e-06         14.54         6.7413e-48
```

Figure 4: Comparing Different Model Orders. The third and fourth coefficients have insignificant p-values

This implies that TRPV1 has a greater influence (causation) on Alpha Complex. This is corroborated by the 1 response from the *gctest* function which suggests that TRPV1 process granger-causes the Alpha Complex process, whereas the reverse is not true.

```
    ARMA(2,0) Error Model (Gaussian Distribution):

                  Value        StandardError      TStatistic        PValue

                _____      _____      _____      _____

    Intercept     0.064958        0.026644           2.438          0.01477
    AR{1}         0.55121         0.050311          10.956        6.2057e-28
    AR{2}         0.42957         0.048907           8.7833       1.588e-18
    Variance    7.1901e-05       4.8912e-06         14.7         6.4447e-49


    Regression with ARMA(2,0) Error Model (Gaussian Distribution):

                  Value        StandardError      TStatistic        PValue

                _____      _____      _____      _____

    Intercept     0.042213        0.0034931         12.085        1.2717e-33
    AR{1}         0.69038         0.056856          12.143        6.2773e-34
    AR{2}         0.13174         0.055073           2.3922        0.016748
    Beta(1)      -1.5708          0.082638         -19.008        1.4649e-80
    Variance    0.00012734       1.1903e-05         10.697        1.0459e-26

reject null    pvalue      stat      cvalue
   1.0000      0.0000    44.4673     3.0220
```

Figure 5: Does TRPV1 Granger-cause/cause Alpha Complex

```
ARMA(2,0) Error Model (Gaussian Distribution):

                Value        StandardError     TStatistic       PValue
              _____      _____     _____      _____

Intercept     -0.0043888       0.0067085        -0.65422         0.51297
AR{1}          0.87209         0.059514         14.653        1.2796e-48
AR{2}          0.078431        0.060929          1.2873          0.198
Variance       3.8214e-05      2.6908e-06       14.202        8.9538e-46


Regression with ARMA(2,0) Error Model (Gaussian Distribution):

                Value        StandardError     TStatistic       PValue
              _____      _____     _____      _____

Intercept      0.018582        0.0023254         7.9912       1.3368e-15
AR{1}          0.73369         0.060217         12.184        3.7816e-34
AR{2}          0.053796        0.057115          0.9419         0.34625
Beta(1)       -0.46778         0.030327        -15.425        1.1183e-53
Variance       4.1042e-05      3.3743e-06       12.163        4.8788e-34

reject null    pvalue     stat      cvalue
       0       0.9841    0.0161     3.0220
```

Figure 6: Does Alpha Complex Granger-cause/cause TRPV1

MATLAB

```matlab
%% BME 6717: Timeseries Analysis

% Data have been collected on two cellular processes that are suspected to
% causally related to one another. The CellProcess.mat dataset contains the
% relative intracellular concentrations (normalized difference from cell
% baseline levels (a.u.)) of two molecules: ligands for the Alpha Complex
% and ligands for TRPV1 channels, sampled once per minute.
% Analyze the Alpha Complex and TRPV1 timeseries to determine how they are
% related to one another. Estimate the potential for a causal relation
% between the processes generating these ligands,
% and justify your analysis.
%
% Suggestion: You may use any analysis methods you wish, but it may be
% useful to start with the  hypothesis that these are autoregressive
% processes.

%% IMPORTING DATA

CellProcess = importdata('CellProcess.mat');

Alpha = CellProcess.AlphaComplex;
TRPV1 = CellProcess.TRPV1;
time= CellProcess.Time;

%% VISUALIZATION

figure(1)
plot(time, Alpha, time, TRPV1)
legend('Alpha Complex','TRPV1')
xlabel('Time(min)')
ylabel('Relative Intracellular Concentrations')
title(["Relative Intracellular Concentrations";...
    "of ligands for the Alpha Complex and ligands for TRPV1 channels."])

%% CORRELATION BTWN LIGANDS
corrcoef( Alpha, TRPV1)

%% DETRENDING

%first difference
diff_Alpha = diff(Alpha);
diff_TRPV1 = diff(TRPV1);

%log
log_Alpha = abs(log(Alpha));
log_TRPV1 = abs(log(TRPV1));


figure(2)
subplot(211)
plot(time(2:end), diff_Alpha, time(2:end), diff_TRPV1)
ylabel({'First difference';'Detrended Concentrations'})
legend('Alpha Complex','TRPV1')
title("Detrended Relative Intracellular Concentrations")

subplot(212)
plot(time, log_Alpha, time, log_TRPV1)
legend('Alpha Complex','TRPV1')
ylabel({'Logarithm Detrended';'Concentrations'})
xlabel('time')

%% Comparing Original and Detrended Data
figure(3)
subplot(311)
plot(Alpha, TRPV1,'.')
title('Comparing Original and Detrended Data')
ylabel({'Original ';'TRPV1 Concentrations'})
xlabel("Original Alpha Complex Concentrations")

subplot(312)
plot(log_Alpha, log_TRPV1,'.')
ylabel({'Log detrended ';'TRPV1 Concentrations'})
```

```matlab
73   xlabel("Log detrended Alpha Complex Concentrations")
74
75   subplot(313)
76   plot(diff_Alpha, diff_TRPV1,'.')
77   ylabel({'diff detrended ';'TRPV1 Concentrations'})
78   xlabel("diff detrended Alpha Complex Concentrations")
79
80
81   %% Cross Correlation btn data
82   %original
83   [acor,lag] = crosscorr(Alpha,TRPV1);
84   [¬,I] = max(abs(acor));
85   lag(I)
86   corrcoef( Alpha(-lag(I):349), TRPV1(1:end+lag(I)))
87   %%
88   %first difference
89   [acor,lag] = crosscorr(diff_Alpha,diff_TRPV1);
90   [¬,I] = max(abs(acor));
91   lag(I)
92   corrcoef( Alpha(-lag(I):349), TRPV1(1:end+lag(I)))
93   %%
94
95   % log
96   [acor,lag] = crosscorr(log_Alpha,log_TRPV1);
97   [¬,I] = max(abs(acor));
98   lag(I)
99   corrcoef( Alpha(-lag(I):349), TRPV1(1:end+lag(I)))
100
101  %% REGRESSION MODELLING AND CAUSALITY CHECK
102
103  %% does trpv1 granger-cause alpha
104  Mdl = regARIMA(2,0,0);
105  Alpha_Mdl = estimate(Mdl,Alpha');
106  Alpha_Mdl_T = estimate(Mdl,Alpha','X',TRPV1');
107
108  [h,pvalue,stat,cvalue] = gctest(TRPV1',Alpha','NumLags',2,'Test','f');
109  disp([' reject null ',' pvalue ',' stat ',' cvalue '])
110  disp([h,pvalue,stat,cvalue])
111
112  %% does alpha granger-cause trpv1
113  Mdl = regARIMA(2,0,0);
114  TRPV1_Mdl = estimate(Mdl,TRPV1');
115  TRPV1_Mdl_A = estimate(Mdl,TRPV1','X',Alpha');
116
117  [h,pvalue,stat,cvalue] = gctest(Alpha',TRPV1','NumLags',2,'Test','f');
118  disp([' reject null ',' pvalue ',' stat ',' cvalue '])
119  disp([h,pvalue,stat,cvalue])
```