

BCMB/CHEM 8190 Lab Exercise

Using Maple for NMR Data Processing and Pulse Sequence Design

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Introduction

Maple is a powerful collection of routines to aid in the solution of mathematical problems and the analysis of data. It is similar to MATLAB and Mathematica, some other tools frequently used in the sciences. Like these relatives, it is capable of doing both symbolic manipulations (solving equations written in terms of variables like x , y , and z) and numeric calculations. It will often default to symbolic calculations, but numeric evaluation can easily be added. To get started open a terminal window and type "xmaple". Maple 13, the version on computers in the lab at UGA, has a versatile interactive interface that allows you to write equations easily (document mode). Select Document Mode from the initial Maple screen. Note that there are many modes for entry (Text, 2D Math, etc.) By default the program will come up in document mode with 2D Math entry. You can type from the keyboard as well as insert a variety of special characters by selecting them from the pallet at the left. Use of this interactive interface is well illustrated by the ten minute tutorial (Take a Tour) found under the help menu. This is an easy way to get familiar with some of the capabilities and conventions. You can also use the search function in the Maple Help window opened using the Help tab on to the right of the second menu bar. Type any function name you might expect and activate search. To see a list of functions type 'index[function]' in the window and activate search.

Maple also operates in a worksheet mode in which commands are easily grouped in execution groups so that they can be easily repeated, strung together in more complex sequences, and saved for future reference. You can tell you are in this mode by the ">" prompt at the beginning of a line. We are going to work in this mode. To get into this mode select "New" and then "Worksheet Mode" from under the "File" menu in the upper left corner. We will go through some applications illustrating plotting of data and matrix manipulations on the first day. On the second day we will use Maple to do some algebra using product operators (the operators we use to describe NMR pulse sequences and their effect on spin systems).

Some Simple Maple Operations Using Matrices:

There are five basic rules to Maple V syntax according to one book: Maple V by Example, Abell and Braselton, Academic Press, 1994.

1. The arguments of functions are given in parentheses (...).
2. A semicolon (;) [now optional] or colon (:) must be included at the end of each command (the colon gives no output)
3. Multiplication is represented by *.
4. Powers are denoted by ^.

5. If you get no response or an incorrect response, you probably entered the command incorrectly.

We will first do some basic things to give you an idea of how MAPLE works. Open a new worksheet using the “File” menu. Let’s multiply some matrices. The operations for matrices are in a library called LinearAlgebra. We tell Maple that we will be using functions in this library by typing:

```
with(LinearAlgebra);
```

Maple will respond with a list of functions.

Define a matrix, A, by typing:

```
A:=Matrix([[1,1,0],[1,1,1],[0,1,1]]);
```

:= is the general way you define a variable.

Maple will respond with a matrix form.

Find the inverse of this matrix by typing:

```
B:=MatrixInverse(A);
```

Maple will respond with the inverse of A

Multiply A by its inverse by typing:

```
A&*B;
```

If the form is still symbolic. Try typing:

```
evalm(A&*B);
```

Note, &* denotes matrix multiplication and evalm is the matrix analog of evalf for functions. It gives the numeric representation of the result.

We can define our own functions (nmr, for example) in terms of ‘procedures’ using a series of commands like:

```
nmr:=proc(A) A&*inverse(A) end;
```

Try typing:

```
nmr(A)
```

```
nmr(B)
```

Define a new matrix C and type:

```
nmr(C)
```

Add “evalm” to the procedure if numeric values are not given and try again.

Note that Maple remembers values of functions and variables last assigned. If you need to re-establish values, put your cursor after the “;” or “:=” and hit return. You can work your way through a revised set of commands this way. You can delete (cut) code and output from the worksheet using the mouse to highlight text (hold down the left mouse button as you move it) and select cut from the right mouse button. If you need to insert a new execution prompt in the middle of the sheet, put your cursor where you want it, go to the insert option on the top menu bar, and select “execution group” followed by “before” or “after” cursor.

Reading in Data and Plotting.

Maple has some good tools for manipulating, plotting and analyzing data. Of course, NMR spectrometers, as well as other analytical instruments, come with software

that does much of this. However, new procedures come on the scene periodically and appropriate software to use these may not be in your current software. There is no reason one should be bound by what the instrument manufacturers think one should do. This section and the following explore ways of looking at the time evolution of NMR spectra (simple 1D spectra collected at successive time point as a sample evolves). The system is glucose dissolved in $^2\text{H}_2\text{O}$ at time zero. 1D proton spectra are collected every few seconds thereafter. Glucose tends to crystallize as the α anomer. In the pyranose ring form of glucose this has the anomeric hydroxyl in an axial position and the anomeric proton (H1) in an equatorial position. This proton is coupled only to the H2 proton which is in an axial position. The resulting dihedral angle of 60° results in a small coupling for the downfield doublet. As time progresses the α anomer equilibrates to a mixture of α and β anomers with the β anomer (dihedral angle of 180°) having a doublet further upfield, having a larger coupling. The spectra are supplied in a file that should be in your Maple directory:

glucose_anomeric_021008.txt

The file contains 40 lines with 80 floating points per line. The lines are ASCII representations of 1D spectra, truncated to show only the anomeric region and truncated to remove the residual water resonance that sits between the α and β anomeric resonances.

To simplify the exercise, a Maple worksheet has been stored in the Maple directory as well:

Plotting_NMR_spectra.mw

You can load this worksheet by selecting “open” from the file menu and hitting the appropriate .mw file. A copy of this worksheet with output included is attached in appendix A. The file you open has had output removed so that you can see the effect of executing commands. As indicated above, you can execute commands by placing your cursor after a “;” or “:” and hitting the enter key. Work your way down the worksheet to observe various operations. Experiment with loading different rows to see the time evolution of spectra. If you want to see the output of specific commands try changing some “:” to “;”.

Calculating and Plotting Correlation Spectra.

One useful procedure that has come on the NMR scene recently is the use of 2D correlation spectra based on covariance matrices. These rely on a statistical procedure for establishing whether lines in a spectrum are correlated in their evolution under some parameter variation (time, samples from different animals, etc). Two lines from the same compound will obviously vary in the same way from spectrum to spectrum (positively correlated); two lines from different compounds that are related as reactant and product will vary in opposite ways from spectrum to spectrum (negatively correlated); two lines from different compounds that vary in concentration randomly from sample to sample will not be correlated (zero correlation). A plot of a covariance matrix looks very much

like a 2D spectrum in which evolution in two dimensions is connected by spin-physics. A statistical TOCSY spectrum has cross-peaks that connect all resonances belonging to a single compound much like a normal TOCSY spectrum, but their presence does not depend on scalar coupling between spins (Cloarec et al. 2005. Statistical total correlation spectroscopy: An exploratory approach for latent biomarker identification from metabolic H-1 NMR data sets. *Analytical Chemistry* **77**: 1282-1289). It also has the interesting property of transferring the resolution seen in the direct dimension to the indirect dimension (Zhang, F.L., and Bruschweiler, R. 2007. Robust deconvolution of complex mixtures by covariance TOCSY spectroscopy. *Angewandte Chemie-International Edition* **46**: 2639-2642).

In the following exercise we will use a Maple worksheet to calculate a covariance matrix for the evolving set of spectra examined above. We would expect to see positive crosspeaks connecting the doublet components of α and β anomers since they belong to the same species and negative crosspeaks connecting the doublet for the α anomer to the doublet for the β anomer since the β anomer arises from the α anomer. To get started open the worksheet entitled:

correlation_spectrum_021008_b.mw

A copy is attached as Appendix B. As in the previous example, work your way through the worksheet a command at a time watching the output and trying to understand what the calculation is doing.

Appendix A

Maple Worksheet for Plotting Spectra

```
> # This is an exercise in reading data and making 2D plots
from lists the data set has 40 lines with 80 elements in
each line. Note the : suppresses printing the data to the
screen
```

```
> A := readdata ("glucose_anomeric_021008.txt"80) :
```

```
> #` Now make the library with plot options accessible
```

```
> with(plots);
```

```
[animate, animate3d, animatecurve, arrow, changecoords ,
complexplot, complexplot3d, conformal, conformal3d ,
contourplot, contourplot3d, coordplot, coordplot3d, densityplot,
display, fieldplot, fieldplot3d, gradplot, gradplot3d ,
graphplot3d, implicitplot, implicitplot3d, inequal, interactive,
interactiveparams, intersectplot, listcontplot, listcontplot3d,
listdensityplot, listplot, listplot3d, loglogplot, logplot, matrixplot,
multiple, odeplot, pareto, plotcompare, pointplot, pointplot3d,
polarplot, polygonplot, polygonplot3d, polyhedra_supported ,
polyhedraplot, rootlocus, semilogplot, setcolors, setoptions,
setoptions3d, spacecurve, sparsematrixplot, surfdata, textplot,
textplot3d, tubeplot ]
```

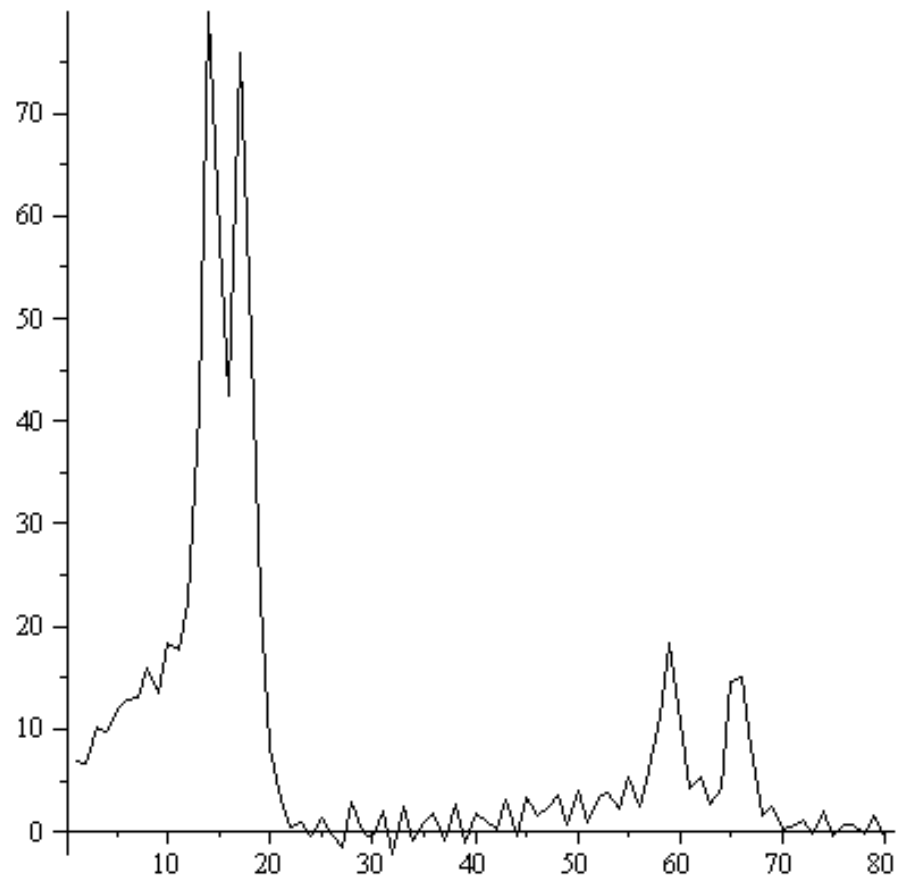
```
> #` now list all the elements in a particular row
```

```
> A[1, 1..80];
```

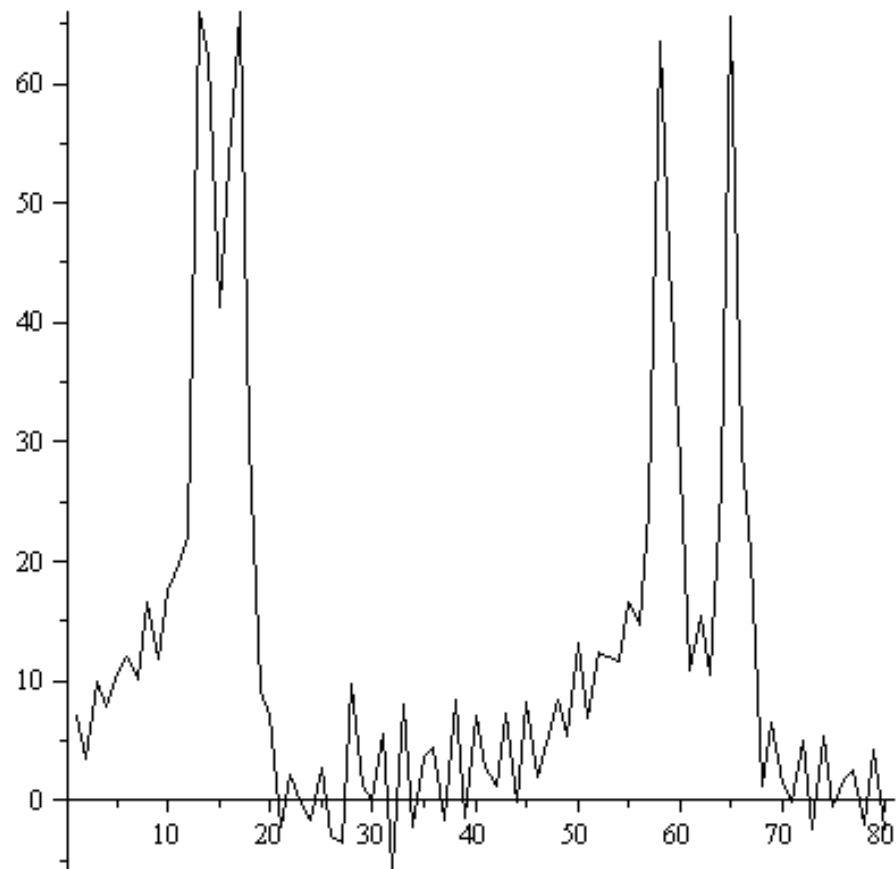
```
[6.88674 6.71932 10.1826 9.81554 12.0841 12.7721 13.0638 15.8922
13.4764 18.3412 17.7667 22.3273 41.2496 79.8992 57.6429
42.5073 75.8843 53.2645 22.8668 8.21004 3.08898 0.406383
0.965, -.35866 1.33142 -.187674 -1.59647 2.94416 0.076275
-.663215 1.97814 -2.26676 2.41783 -.786294 0.999904
1.72891, -.919743 2.75346 -1.05469 1.86125 1.23796
0.328664 3.14554 -.323768 3.452 1.65393 2.25359 3.64313
0.798591 4.09284 0.998589 3.26487 3.76633 2.18372 5.32162
2.36547 5.91841 11.2497 18.3552 10.5576 4.25486 5.23857
2.75403 4.26366 14.6109 15.0597 8.13963 1.48505 2.4092
0.165846 0.418552 1.21156 -.242511 2.06176 -.316915
0.629331 0.640378 -.281724 1.50842 -.683636]
```

```
> # now plot the list in that row - it should look like a
spectrum
```

```
> listplot(A[1, 1..80]);
```



```
> # now try plotting a row later in the acquisition  
> listplot(A[32, 1..80]);
```

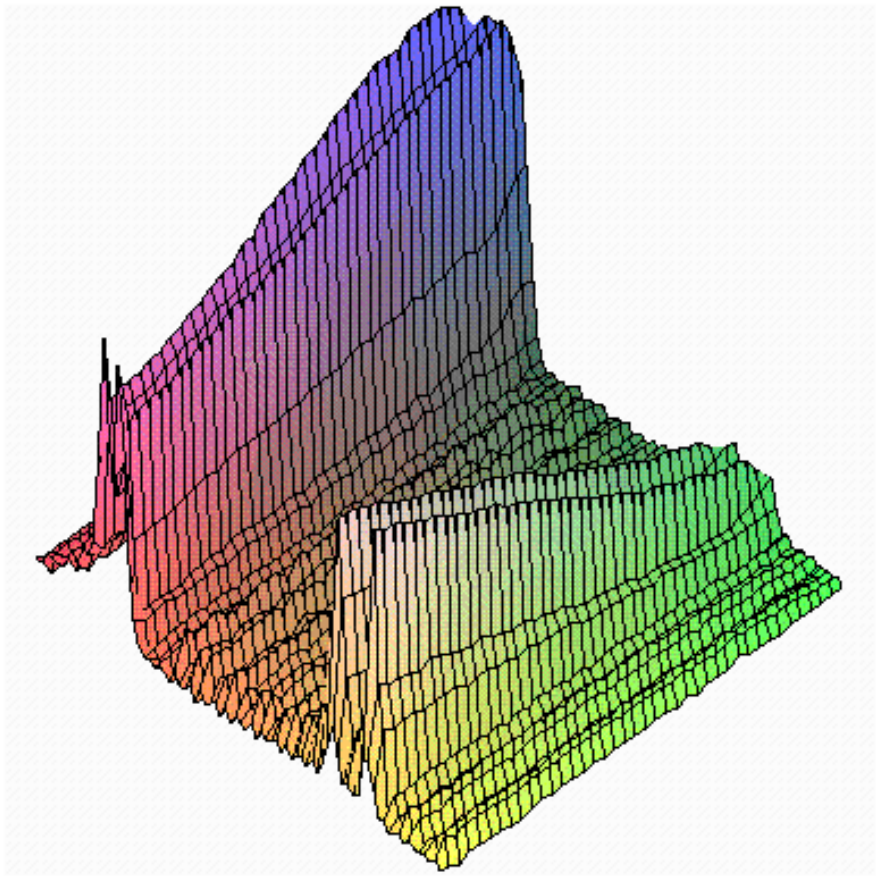


> # The peak on the right grows systematically through the set. Now lets plot the data as a matrix

> $B := \text{Matrix}(A);$

$B := \left[\begin{array}{l} 40 \times 80 \text{ Matrix} \\ \text{Data Type: anything} \\ \text{Storage: rectangular} \\ \text{Order: Fortran_order} \end{array} \right]$

> $\text{matrixplot}(A);$



>

Appendix B

Maple Worksheet for Generating and Plotting Covariance Matrices

```
> # This is an exercise in creating a 2D correlation  
spectrum from an evolving set of 1D NMR spectra  
> with(LinearAlgebra);
```

[&x, Add, Adjoint, BackwardSubstitute, BandMatrix, Basis, BezoutMatrix, BidiagonalForm, BilinearForm, CharacteristicMatrix, CharacteristicPolynomial, Column, ColumnDimension, ColumnOperation, ColumnSpace, CompanionMatrix, ConditionNumber, ConstantMatrix, ConstantVector, Copy, CreatePermutation, CrossProduct, DeleteColumn, DeleteRow, Determinant, Diagonal, DiagonalMatrix, Dimension, Dimensions, DotProduct, EigenConditionNumbers, Eigenvalues, Eigenvectors, Equal, ForwardSubstitute, FrobeniusForm, GaussianElimination, GenerateEquations, GenerateMatrix, Generic, GetResultDataType, GetResultShape, GivensRotationMatrix, GramSchmidt, HankelMatrix, HermiteForm, HermitianTranspose, HessenbergForm, HilbertMatrix, HouseholderMatrix, IdentityMatrix, IntersectionBasis, IsDefinite, IsOrthogonal, IsSimilar, IsUnitary, JordanBlockMatrix, JordanForm, LA_Main, LUDecomposition, LeastSquares, LinearSolve, Map, Map2, MatrixAdd, MatrixExponential, MatrixFunction, MatrixInverse, MatrixMatrixMultiply, MatrixNorm, MatrixPower, MatrixScalarMultiply, MatrixVectorMultiply, MinimalPolynomial, Minor, Modular, Multiply, NoUserValue, Norm, Normalize, NullSpace, OuterProductMatrix, Permanent, Pivot, PopovForm, QRDecomposition, RandomMatrix, RandomVector, Rank, RationalCanonicalForm, ReducedRowEchelonForm, Row, RowDimension, RowOperation, RowSpace, ScalarMatrix, ScalarMultiply, ScalarVector, SchurForm, SingularValues, SmithForm, StronglyConnectedBlocks, SubMatrix, SubVector, SumBasis, SylvesterMatrix, ToeplitzMatrix, Trace, Transpose, TridiagonalForm, UnitVector, VandermondeMatrix, VectorAdd, VectorAngle, VectorMatrixMultiply, VectorNorm, VectorScalarMultiply, ZeroMatrix, ZeroVector, Zip]

```
> # First read in the data, calculate the average value at
each point and subtract this from each point in each
spectrum
```

```
> A := readdata ("glucose_anomeric_021008.txt"80) :
```

```
for j from 1 to 80 do
```

```
    s := 0:
```

```
    for i from 1 to 40 do
```

```
        s := (A[i,j]+s)
```

```
    end do:
```

```
    for i from 1 to 40 do
```

```
        A[i,j] := A[i,j]-s/40
```

```
    end do:
```

```
end do:
```

```
> # Now convert this list of data to a matrix, calcualte
its transpose and multiply the matrices
```

```
> A := Matrix(A):
```

```
B := Transpose(A):
```

```
C := B &* A;
```

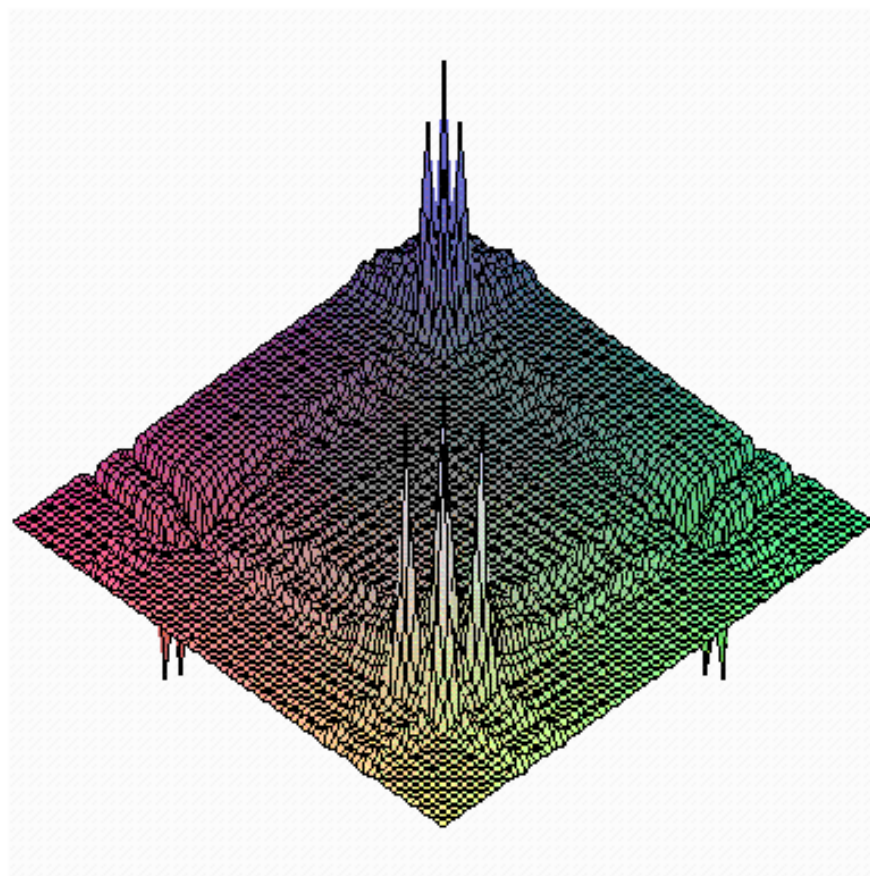
$$C := \begin{bmatrix} 80 \times 40 \text{ Matrix} \\ \text{Data Type: anything} \\ \text{Storage: rectangular} \\ \text{Order: Fortran_order} \end{bmatrix} \&* \begin{bmatrix} 40 \times 80 \text{ Matrix} \\ \text{Data Type: anything} \\ \text{Storage: rectangular} \\ \text{Order: Fortran_order} \end{bmatrix}$$

```
> # Now let's plot the data
```

```
> with(plots);
```

```
[animate, animate3d, animatecurve, arrow, changecoords ,
complexplot, complexplot3d, conformal, conformal3d ,
contourplot, contourplot3d, coordplot, coordplot3d, densityplot,
display, fieldplot, fieldplot3d, gradplot, gradplot3d,
graphplot3d, implicitplot, implicitplot3d, inequal, interactive,
interactiveparams, intersectplot, listcontplot, listcontplot3d,
listdensityplot, listplot, listplot3d, loglogplot, logplot, matrixplot,
multiple, odeplot, pareto, plotcompare, pointplot, pointplot3d,
polarplot, polygonplot, polygonplot3d, polyhedra_supported ,
polyhedraplot, rootlocus, semilogplot, setcolors, setoptions,
setoptions3d, spacecurve, sparsematrixplot, surfdata, textplot,
textplot3d, tubeplot]
```

```
> matrixplot(C);
```



> # The positive diagonal peaks represent our spectrum. The positive cross-peaks near the diagonal signify peaks belong to the same molecule. The negative cross-peaks indicate one molecule is turning into the other.