**NITP Summer 2014**
**Network Analysis Lab**
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**NOTE: This lab requires Matlab and the functions in the Brain Connectivity Toolbox (BCT). This will be included with the lab data. Make sure to add the folder with this lab to your matlab path ('add with subfolders').**

In the lectures, we covered different methods for obtaining a connectional graph using diffusion weighted MRI and fMRI. Here we're going to start with the connectivity matrices and explore different properties of them using the BCT. **Make sure to check the reference functions at the end of this doc for help with the exercises!**

**Background**:
The data for these connectivity matrices were downloaded from the NKI/ Rockland publicly available sample on INDI (fcon_1000.projects.nitrc.org/indi/pro/ nki.html). The data were DTI and resting state fMRI for 196 subjects. After standard data preprocessing, regions of interest were defined from the fMRI data using a spatially constrained clustering method. For each ROI, the mean timeseries was calculated and correlated with all other regions to get the 188x188 fMRI connectivity matrix. These were then averaged across subjects to obtain the matrix used in this lab. These same ROIs were registered to the DTI data and used to count the number of fibers connecting any pair of ROIs to get the 188x188 DTI connectivity matrix. Again, these were averaged across subjects. For more details on the methods, you can see: http:// www.ncbi.nlm.nih.gov/pmc/articles/PMC3508475/

**Files**:
dti_matrix.txt, fmri_matrix.txt: the connectivity matrices (tab delimited text files)
regions_188.txt: list of the brain region names for each region in the network
regions/mask*.nii.gz: the nifti mask files for each region in the network
regions/MNI152_T1_4mm_brain.nii.gz: the standard space brain (use with the region mask files)

Open Matlab. First, load in the matrices and view them. Get a sense of the range and distribution of connectivity strengths in the two matrices.
```
>> cd ~/Desktop/NITP_network_lab_2014/
>> load('dti_matrix.txt')
>> load('fmri_matrix.txt')
>> figure; imagesc(dti_matrix)
>> figure; imagesc(fmri_matrix)
```

Binarize the matrices, thresholding to keep the strongest 20% of connections:
```
>> dti_matrix_bin=adjmatrix(dti_matrix,.2,false);
>> fmri_matrix_bin=adjmatrix(fmri_matrix,.2,false);
```

How many components are in each graph after thresholding? (check the reference functions for help)
Which nodes, if any, are disconnected?
At what threshold do the networks fragments into multiple components?

Calculate the modules in the DTI graph using the Louvain algorithm:
 >> [Comm_index_dti Q]=modularity_louvain_und(dti_matrix_bin)
>> [x i]=sort(Comm_index_dti');
>> dti_matrix_bin_sort=dti_matrix_bin(i,i);
What brain regions comprise the different modules?

Do the same for the fMRI graph.  What brain regions comprise the different modules? Do these correspond to any known functional networks? How do the fMRI modules compare to the DTI modules? Which network has a higher Q value (more distinct modules)? Why might this be?
*Note: you can threshold the network at a higher level (e.g. only 5% of connections) to see how that might change the module membership.*

Optional:
If you want to visualize the regions forming the different modules in anatomical space, you can do the following:
In matlab, call the function to create a nii file with the different regions labeled according to the module they belong to. The function takes three arguments, the community index, the output filename, and the path where the regional mask files live:
>> make_nii_modules(Comm_index_dti,'dti_modules',' ~/Desktop/NITP_network_lab_2014/regions')
Then view the result in the terminal:
>> cd ~/Desktop/NITP_network_lab_2014/regions
>> fslview MNI152_T1_4mm_brain.nii.gz test.nii.gz -l "Random-Rainbow" &

**Regional measures**
Look at different measures of regional connectivity. Calculate the degree, clustering coefficient, betweenness centrality, and participation coefficient:
>> d=degrees_und(dti_matrix_bin);
>> cc=clustering_coef_bu(dti_matrix_bin);
>> bc=betweenness_bin(dti_matrix_bin);
>> P = participation_coef(dti_matrix_bin,Comm_index_dti);

Call the function *region_sorted_ranks* to create a 188x4 matrix called *sorted_ranks* that has each region as a row and that region's rank for degree, clustering, betweenness, and participation. Remember the region names are identities are in regions_188.txt.
>> sorted_ranks_dti=region_sorted_ranks(d,cc,bc,P)

Which regions are the highest for each measure? Take a look at these regions in fslview if you're interested. Look at the relationship between different measures in different brain regions.
*Advanced: which nodes are provincial hubs? Which regions are connector hubs?*

Do the same for the fMRI graph.
>> d=degrees_und(fmri_matrix_bin);
>> cc=clustering_coef_bu(fmri_matrix_bin);
>> bc=betweenness_bin(fmri_matrix_bin);
>> P = participation_coef(fmri_matrix_bin,Comm_index_fmri);
>> sorted_ranks_fmri=region_sorted_ranks(d,cc,bc,P)

How similar are the measures between DTI and fMRI?

**Global measures**
Check out some of the global network measures. First, calculate the *distance matrix* for the graph:
>> dti_matrix_bin_distmat=distance_bin(dti_matrix_bin);
Calculate the characteristic path length and global efficiency:
>> [cpl_dti,eglob_dti]=charpath(dti_matrix_bin_distmat)
The mean clustering coefficient is just the mean of the regional clustering coefficients:
>> mcc_dti=mean(clustering_coef_bu(dti_matrix_bin))

Think about what the actual numerical values for cpl, eglob, and mcc mean.

Calculate a random network with the same number of connections as the true graph and calculate its distance matrix:
>> sim_dti_matrix=randmio_und(dti_matrix_bin,10);
>> sim_dti_distmat=distance_bin(sim_dti_matrix);

Determine the characteristic path length and mean clustering coefficient for the random network. How do they compare to the real network? If the values for real and random networks are different, why is that the case?
>> [sim_cpl_dti,sim_eglob_dti]=charpath(sim_dti_distmat)
>> sim_mcc_dti=mean(clustering_coef_bu(sim_dti_matrix))

Calculate the small worldness (sigma). The formula is:
Gamma = real cc/random cc
Lambda = real cpl/random cpl
Sigma = Gamma/Lambda
A network with Sigma > 1.2 is roughly considered "small world". Is this network a small world network?
*Note: the value of sigma will differ each time it is calculated because the network is randomly rewired in a different way each time. In practice, it's best to calculate a large number of sigma values (1000 or more) and average them.*

Do the same for the fMRI network. Is it more or less small world than the DTI network?

**Reference functions**
To view a set of regions (based on region number) in fslview, go to terminal (or whatever your command line program is) and cd to the *regions* directory:
cd regions
Then call the bash script *fslview_regions.sh* with the region numbers separated by spaces:
./fslview_regions.sh 4 10 145

To get the different components and component sizes of a graph:
[comps,comp_sizes]=get_components(dti_matrix_bin)