Parallel Graph-Theoretical Analysis of Voxel-Based Brain Network

This platform(PAGANI-VBN) aims at accelerating the frequently used but time-consuming algorithms in neuroscience research. We have accelerated the process of brain network analysis (BNA) with NVIDIA GPUs (Graphic processing unit) and multi-core CPUs. The toolbox provides functions for the construction and the analysis of large networks. Network construction is intended for fMRI data using Pearson's correlation. Network analysis is general purposed and includes the calculation of clustering coefficient, characteristic path length, network efficiency, and betweenness centrality (and comparisons to Maslov random networks). We accelerate Pearson's correlation calculation, APSP and betweenness with GPUs. Other functions are implemented on multi-core CPUs. If you found the platform useful, please cite our paper published on plos one

Wang Y. et al, (2013) A Hybrid CPU-GPU Accelerated Framework for Fast Mapping of High-Resolution Human Brain Connectome. PloS one 8:e62789.

Runtime Environment

The win64 version requires a 64-bit Windows operating system, an NVIDIA GPU and the latest CUDA Toolkit (http://www.nvidia.com/content/cuda/cuda-downloads.html). We have tested all the functions on NVIDIA GTX 580 GPU or NVDIA GeForce GTX 850M with CUDA Toolkit v7.0 and Windows 7， Windows 8 and Windows 10 operating system.

The Linux version requires a Linux operating system, an NVIDIA GPU and the latest CUDA Toolkit (http://www.nvidia.com/content/cuda/cuda-downloads.html). We have tested all the functions on NVIDIA Titan GPU with CUDA Toolkit and CentOS 6.5 operating system.

To get started with CUDA, please follow
NVIDIA CUDA Getting Started Guide for Microsoft Windows
(http://docs.nvidia.com/cuda/cuda-getting-started-guide-for-microsoft-windows/index.html) or
NVIDIA CUDA Getting Started Guide for Linux
(http://docs.nvidia.com/cuda/cuda-getting-started-guide-for-linux/index.html).

Graphic User Interface

Review

We have already provide a elaborate graphic user interface(GUI) now with which researchers can quickly get started and have a better user experience. However, the instruction of command line operation is still remain for compatibility with different preference. For detail information, please see 'Function Interface' bar.

The GUI of PAGANI platform（Fig1） uses flat design concept and can be divided into three parts at first glance: Network Construction, Global Metrics, Nodal Metrics. Besides, The area out of these three parts also has some simple but important Settings which we will first introduce.

Periphery

There are two directories that need to fill at the top of the GUI. One is the path of working directory and the other is that of mask file. Click the dexter toolbutton will load the selected path. By the way, remember to fill the corresponding threshold below when loading mask file. The 'Network Type' provide the different treatment strategy when constructing network. In addition, Some algorithms currently aren't enable in weighted network such as betweenness centrality, Newman's method for modularity, etc. However, In weighted network the type setting of clustering coefficient of global metrics is accessible.

At the bottom of GUI, 'Execute and Save Script' means save all algorithms and their settings you have checked and then output corresponding function interface in command line. 'Load script' will load existing script that you used to generate.

Network Construction

The function of 'Network Construction' is constructing the correlation matrix of each .NII format file of rest-state fMRI. The specific process is to doing correlation calculation between arbitrary two time course of voxels:

The first option is whether generate group-level network. This software usually processes all files in specified folder when executing a few algorithms, so if you check the box another thread will start to average all correlation matrices in the folder and then generate a new matrix with group level. Of course you can select the strategy of average: ordinary or fisher. Thereinto, fisher represents Fisher's z-transformation and you can put cursor onto the 'fisher' to watch the displaying related tips.

The second option is whether save whole correlation matrix. For a file within raw data, after generating correlation matrix some steps will take to generate final adjacent matrix such as binarization, rarefaction, etc. The selection is intended for the purpose that whether only save final adjacent matrix or save both final adjacent matrix and original correlation matrix.

The third option is threshold value settings for further steps. For details see table below:

Network Type / Definition / Threshold Type	Unweighted Network	Weighted Network
Correlation	$a_{ij} = \begin{cases} 1, & c_{ij} > threshold \\ 0, & c_{ij} < threshold \end{cases}$	$a_{ij} = \begin{cases} a_{ij}, & c_{ij} > threshold \\ 0\ \ , & c_{ij} < threshold \end{cases}$
Sparsity	Calculate the number(N) of nonzero elements according to sparsity; Then get the Nth largest number of all elements, set k; Then: $a_{ij} = \begin{cases} 1, & c_{ij} > k \\ 0, & c_{ij} < k \end{cases}$	Calculate the number(N) of nonzero elements according to sparsity; Then get the Nth largest number of all elements, set k; Then: $a_{ij} = \begin{cases} a_{ij}, & c_{ij} > k \\ 0\ \ , & c_{ij} < k \end{cases}$

Metrics

Two sorts of metrics are provided: global metrics and nodal metrics. For details see table below:

Network metric	**Descriptions**	**Definitions**
Global network metrics		
Clustering coefficient (*Cp*)	A measure of local clustering and closeness of a network	Seen next table
Characteristic path length (*Lp*)	A measure of integration and global routing efficiency of a network	$Lp = \frac{n(n-1)}{2\sum_{i \neq j \in N} d_{ij}^{-1}}$ where d_{ij} is the shortest path length between *i* and *j*.
Gamma (*γ*)	The ratio of *Cp* of a network to those of random networks with identical degree distribution	$\gamma = Cp / Cp_{rand}$
Lambda (*λ*)	The ratio of *Lp* of a network to those of random networks with identical degree distribution	$\lambda = Lp / Lp_{rand}$
Sigma (*σ*)	The extent of small-world property of a network, indicating high local closeness and global communicational integration	$\sigma = \gamma / \lambda$
Modularity (*Q*)	A measure of the extent to which a network can be partitioned into tightly intra-connected and sparsely inter-connected modules.	$Q = \frac{1}{2m} \sum_{i \neq j \in N} (a_{ij} - \frac{k_i k_j}{2m}) \delta(g_i, g_j)$ where *m* is the number of network edges, g_i is the module to which node *i* belongs to, and $\delta(g_i, g_j)$ is 1 if $g_i = g_j$, and 0 otherwise.
Nodal (voxel-wise) metrics		
Degree (k_i)	The number of links connected directly to a node	$k_i = \sum_{j \in N} a_{ij}$
Efficiency (e_i)	A measure of efficiency for a node communicating with the other nodes	$e_i = \frac{1}{n-1} \sum_{j \in N, j \neq i} d_{ij}^{-1}$
Betweenness (b_i)	A centrality measure of a node in the communications between other nodes	$b_i = \frac{2}{(n-1)(n-2)} \sum_{j \neq i \neq h \in N,} \frac{\theta_{jh}(i)}{\theta_{jh}}$ where θ_{jh} is the number of shortest paths between *j* and *h*, $\theta_{jh}(i)$ is the number of shortest paths between *j* and *h* that pass through *i*.

Eigenvector Centrality(g_i)	Eigenvector centrality is a measure of the influence of a node in a network.	$g_i = \frac{1}{\lambda_{max}} \sum_{j \in N} a_{ij} g_j$ Where λ_{max} is the most positive eigenvalue of adjacent matrix of network.
Participation coefficient (p_i)	A measure of the ability of a node in keeping the communication between different modules.	$p_i = 1 - \sum_{s=1}^{N_M} \left(\frac{k_{is}}{k_i} \right)^2$ Where N_M is the number of modules, k_{is} is the degree of node i to nodes in module s.

Note: N is the set of all nodes in the network, and n is the number of nodes. a_{ij} is the element of adjacency matrices indicating the connection condition between node i and j, a_{ij}=1 if node i is directly connected to node j, otherwise a_{ij}=0.

We display the clustering coefficient at another table for reason that it is different for the definition of clustering coefficient in different environment:

Definition	Unweighted Network	Weighted Network
Global Metrics	$C_i = \frac{t_i}{C_{k_i}^2} = \frac{\sum_{j,k} a_{ij} a_{ik} a_{jk}}{C_{k_i}^2}$	$Barrat: C_i = \frac{1}{s_i(k_i - 1)} \sum_{j,k} \frac{(w_{ij} + w_{ik})}{2} a_{ij} a_{ik} a_{jk}$
		$Onnela: C_i = \frac{1}{k_i(k_i - 1)} \sum_{j,k} (w_{ij} w_{ik} w_{jk})^{\frac{1}{3}}$
Nodal Metrics	$C_a = \frac{1}{n} \sum_i C_i$	$C_a = \frac{1}{n} \sum_i C_i$

Note: a_{ij} is the element of adjacency matrices indicating the connection condition between node i and j, a_{ij}=1 if node i is directly connected to node j, otherwise a_{ij}=0. w_{ij} is the weight of the edge of network. k_i is the degree of vertex i of network. $s_i = \sum_j w_{ij}$.

Function Interface

1. CUCorMat()

Note that this new version of CUCorMat() has made a few changes of parameters.

```
CUCorMat Dir_for_BOLD threshold_for_mask(0~1) to_average(yf/yn/bf/bn/n)
    to_save_cormatrix(y/n) threshold_type(r/s) threshold_for_correletaio
n_coefficient(s)(0~1)
```

This function constructs correlation matrices from BOLD signals on GPU. There are at least six inputs: 1) a directory containing NII files of BOLD signals and a gray matter mask file named "mask.nii" (data type: float or boolean, can be recognized automatically), 2) a threshold to select valid voxels, 3) a flag indicating whether or not the correlation matrices are to be averaged, and 4) a flag indicating whether or not the original results are to be saved, 5)threshold_type indicates the binary_threshold is for correlation values or sparsities, 6) at least one threshold for binarizing the correlation coefficients. The outputs are adjacency matrices in .csr files and upper-triangle matrices in .cormat files, if enabled.

Both weighted and unweighted networks are supported for function CUCorMat. Note that the output directory is different with different type of network. For detail information see following table and example.

Parameter	**Meaning**
Dir_for_BOLD	The input directory containing NII files of BOLD signals. In the directory, there has to be a file named 'mask.nii', which gives the probability of each voxel belonging to the gray matter. All the NII files must be **little-endian (ieee-le)** and the data type must be **32-bit real** (single-precision floating point numbers).
threshold_for_mask	A threshold to select valid voxels from 'mask.nii'. Data type: float or boolean, which be recognized automatically. If data type of mask.nii is Boolean or unsigned char, this value can be arbitrary from 0~1.
to_average	A flag indicating whether or not the correlation matrices are to be averaged. If average_flag = 'yf' or 'yn', all correlation matrices are averaged and only one adjacency matrix is generated; If average_flag = 'n', each NII file for BOLD signals corresponds to an adjacency matrix; If average_flag = 'bf' or 'bn', both the individual adjacency matrices and the average adjacency matrix are generated. The second character 'f' or 'n' indicates whether fisher transformation is used in the process of averaging.
to_save_cormatrix	A flag indicating whether or not the original correlation matrices are to be saved. If to_save_cormatrix='y', both the original correlation matrices and the binarized csr results will be saved under input directory (Dir_for_BOLD). If to_save_cormatrix='n', only binarized csr results will be saved. These matrices are stored in *.cormat* files.
threshold_type	A parameter indicating all correlation matrices are thresholded by the same correlation value or the same sparsity. For correlation threshold, threshold_type = "r"; For sparsity threshold, threshold_type = "s".
threshold_for_ correletaion_coefficient	A set of thresholds for binarizing the correlation coefficients. Each threshold will generate a set of outputs.

Example :

The following command

```
./CUCorMat ../../data/ 0.2 yn n r 0.25 0.3 0.35
```

generates the output files in the directory ../../data/unweighted for unweighted network and the directory ../../data/weighted for weighted network.

2. CUBFW_Lp(), CUBFS_Lp(), BFS_MulCPU()

```
CUBFS_Lp input_dir num_of_random_networks  parameter_type
#This function is not recommended as it is not stable.
BFS_MulCPU input_dir num_of_random_networks parameter_type
CUBFW_Lp input_dir num_of_random_networks parameter_type
```

These three functions calculate the characteristic path length (Lp) of the network and compare with K (user specified) random networks on GPU and multi-core CPU. The input is 1) a directory containing .csr files, and 2) the number of random networks for comparison. 3)The output type of parameter. The corresponding parameter sets is：g, n, l, gn, gl, nl, gnl. Thereinto, ‘g’ represents the global metric ‘characteristic path length’, ‘n’ represents the nodal metric ‘nodal efficiency’, ‘l’ represents the global metric ‘lambda’. ‘gn’, ‘gl’, ‘nl’, ‘gnl’ are used on behalf of the combination of these three basic output method above. For instance, ‘gnl’ indicates all the three output are printed. The functions will calculate Lp for each network in the input directory. The output is a text file for each input network, storing the Lp results of the brain network and K random networks (one file for each .csr network).

Lp is the harmonic average of All-Pairs-Shortest-Path (APSP), and also the reciprocal of global efficiency. The two functions use different algorithm to calculate APSP. CUBFS_Lp() and BFS_MulCPU() implement the Breadth First Search (BFS) algorithm, which performs well with sparse networks but poorly with dense ones, on GPU and multi-core CPU respectively. The performance of these two functions is comparable with each other. We suggest using the latter one if you have a more than 8 cores CPU. CUBFW_Lp() uses the blocked Floyd-Warshall algorithm (BFW), which outperforms BFS on dense networks. The transition point of the performance of the two algorithms is approximately where network density equals 3%. It means CUBFS_Lp() is recommended if the network density is lower than 3% and CUBFW_Lp() is recommended if otherwise.

Both weighted and unweighted networks are supported for function CUBFW_Lp.

Only unweighted networks are supported for BFS-based functions.

Parameter	**Meaning**
input_dir	The input directory containing *.csr* binary networks.
num_of_random_networks	The number of random networks with the same degree distribution for comparison. If num_of_random_networks == 0, no comparison is initiated.
parameter_type	The output type of parameter. The corresponding parameter sets is：g, n, l, gn, gl, nl, gnl. For detail information see text.

Example：

The commands

```
./CUBFW_Lp ../../data/ 15 gnl
./CUBFS_Lp ../../data/ 15  nl
```

generates both *.eff* files storing the nodal efficiency and *_Lp.txt* for LP.

3. Cp()

```
Cp input_dir num_of_random_networks parameter_type
```

This function calculates clustering coefficient (Cp) of the network and compare the results with K (user specified) random networks on CPU. The input is 1) a directory containing .csr files, and 2) the number of random networks for comparison. 3)The output type of parameter. The corresponding parameter sets is： g, n, k, gn, gk, nk, gnk. Thereinto, 'g' represents the global metric 'characteristic path length', 'n' represents the nodal metric 'nodal efficiency', 'k' represents the global metric 'gamma'. 'gn', 'gk', 'nk', 'gnk' are used on behalf of the corresponding combination of these three basic output method above. For instance, 'gnk' indicates all the three output are printed. The functions will calculate Cp for each network in the input directory, generating .cp files for each input network.

Both weighted and unweighted networks are supported for function Cp.

Parameter	Meaning
input_dir	The input directory containing .csr binary networks.
num_of_random_networks	The number of random networks with same degree distribution for comparison. If num_of_random_networks == 0, no comparison is initiated.
parameter_type	The output type of parameter. The corresponding parameter sets is： g, n, k, gn, gk, nk, gnk. For detail information see text.

Example:

```
./Cp ../../data/ 15 gnk
```

4. Degree()

```
Degree input_dir
```

This function calculates the degree centrality of the network on CPU. The input is a directory containing .csr files. The functions will calculate degree centrality for each network in the input directory, generating .deg files for each input network. There is only the CPU version.

Both weighted and unweighted networks are supported for function Degree.

Parameter	Meaning
input_dir	The input directory containing .csr binary networks.

Example:

```
./Degree ../../data/
```

5. CUBC()

```
CUBC input_dir
```

This function calculates the betweenness centrality of the network on GPU. The input is a directory containing .csr files. The functions will calculate betweenness centrality for each network in the input directory, generating .bc files for each input network.

Only unweighted networks are supported for CUBC functions.

Parameter	Meaning
input_dir	The input directory containing .csr binary networks.

Example:

```
./CUBC ../../data/
```

6. CUEC()

```
CUEC input_dir
```

This function calculates the eigenvector centrality of the network on GPU. The input is a directory containing .csr files. The functions will calculate eigenvector centrality for each network in the input directory, generating .ec files for each input network.

Both unweighted and weighted networks are supported for CUEC functions.

Parameter	Meaning
input_dir	The input directory containing .csr binary networks.

Example:

```
./CUEC ../../data/
```

7. ConvertNII()

```
ConvertNII  input_file  mask_file  mask_threshold
```

This function puts the .cp .eff .deg .bc results back to the 3-D matrix and converts these filesto the standard NII format. The inputs are: one of the mentioned files, a file for mask data in NII format and a threshold to select the voxels. The mask file and the mask threshold should be the same as those used in network construction with CUCorMat().

Both weighted and unweighted networks are supported for function ConvertNII.

Parameter	Meaning
input_dir	The input directory containing files to be converted to NII format.
mask.nii	The name of NII file in the input directory giving the probability of each voxel belonging to the gray matter.
mask_threshold	A threshold to select valid voxels from 'mask.nii', if the datatype of mask_nifti file is float. If the datatype is unsigned char, an

	arbitrary value from 0~1 is available.

Example:

```
./ConvertNII ../datadir ../maskdir/mask.nii 0.2
```

X.cp should exist in the specified directory. The output file X.cp.nii is generated in directory ../datadir/ .

8. Louvain_Modularity ()

```
Louvain_Modularity dir_for_csr num_of_random_networks
```

This function calculates Louvain Modularity for each of the *.csr* files in the given directory and compares each of them with several optional random networks. The outputs are *.modu* files in the date directory.

Both weighted and unweighted networks are supported for function Louvain_Modularity.

Parameter	Meaning
input_dir	The input directory containing .csr binary networks.
num_of_random_networks	The number of random networks with same degree distribution for comparison. If num_of_random_networks == 0, no comparison is initiated.

Example:

./Louvain_Modularity ../../data/ 15

9. PC_CPU()

```
PC_CPU dir_for_csr type_for_participant_coefficient
```

This function calculates participant coefficient for each subject ("*.csr*" files) in the given directory. Each "*.csr*" files should be accompanied with a "*.modu*" files, which has a same file name, in the data directory. The type of participant coefficient is original as default and is normalized by (Nm-1)/Nm where Nm is the number of modules if this option is set as 'n'. The outputs are *.pc* files in the date directory.

Both weighted and unweighted networks are supported for function PC_CPU.

Example:

./PC_CPU.exe ../../data/ #(output original participant coefficient)

./PC_CPU.exe ../../data/ n #(output normalized participant coefficient)

File Format

The input files in the first procedure CUCorMat and the output files of our platform are all standard NII files with some extra restriction. Here we also introduce the format of other related files of our platform for the convenience of some users who may want to process these intermediate results.

1. The original input

NII files for BOLD signals and mask data. Little-endian (ieee-le) NII files with single-precision floating point numbers (float) are required.

2. CSR

.csr file (Compressed Sparse Row). The first 32-bit integer indicates the length of array *R* , which is the number of voxels *N*+1, followed by *N*+1 32-bit integers of the array *R*. Next is a 32-bit integer indicating the length of array *C*, which equals the number of edges *E*, followed by *E* 32-bit integers of the array *C*. That's all for the unweighted network. If the network is weighted, the final part is a 32-bit integer indicating the length of array V, which also equals the number of edges *E,* followed by *E* 32-bit floats of the array V, indicating the weight of each edge remained after thresholding).

3. Characteristics results

.deg .cp .eff .bc .modu .ec .pc, files with the first 32-bit integer indicating the number of voxels *N*, followed by *N* integers (nodal degree (.deg), if the network is unweighted, module index (.modu)), or N float numbers (nodal degree (.deg, if the network is weighted) clustering coefficient (.cp), nodal efficiency (.eff), betweenness centrality (.bc), eigenvector centrality(.ec) or participant coefficient (.pc)) representing the corresponding characteristics of that voxel.

It is important to note that In the latest version of the PAGANI software we have already unified .cp, .deg, .eff, .bc, .pc, .ec format into .nm(represents nodal metric) format so that analysis results look more concise and straightforward.

4. Correlation matrices

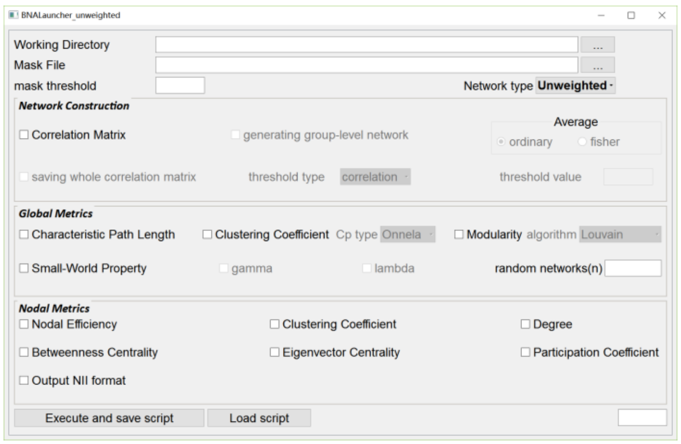
.cormat files begin with a 32-bit integer indicating the number of following numbers, which equals N(N-1)/2 if N is the number of rows or columns. These correlation indexes are 32-bit float numbers. Note that correlation matrices are symmetric and we only stores the *upper*-triangle part

5. Output NII file

All the result files *.deg .cp .eff .bc* .ec *.pc(*Note that only .nm format exists in the latest version) are converted to standard NII file using ConvertNII().

Figure Sets

Fig1



Network type Unweighted
threshold type correlation
Cp type Onnela
algorithm Louvain

Fig1. GUI of PAGANI platform