
Neuro-Integrative Connectivity (NIC)

Release 1

May 06, 2019

Table of Contents

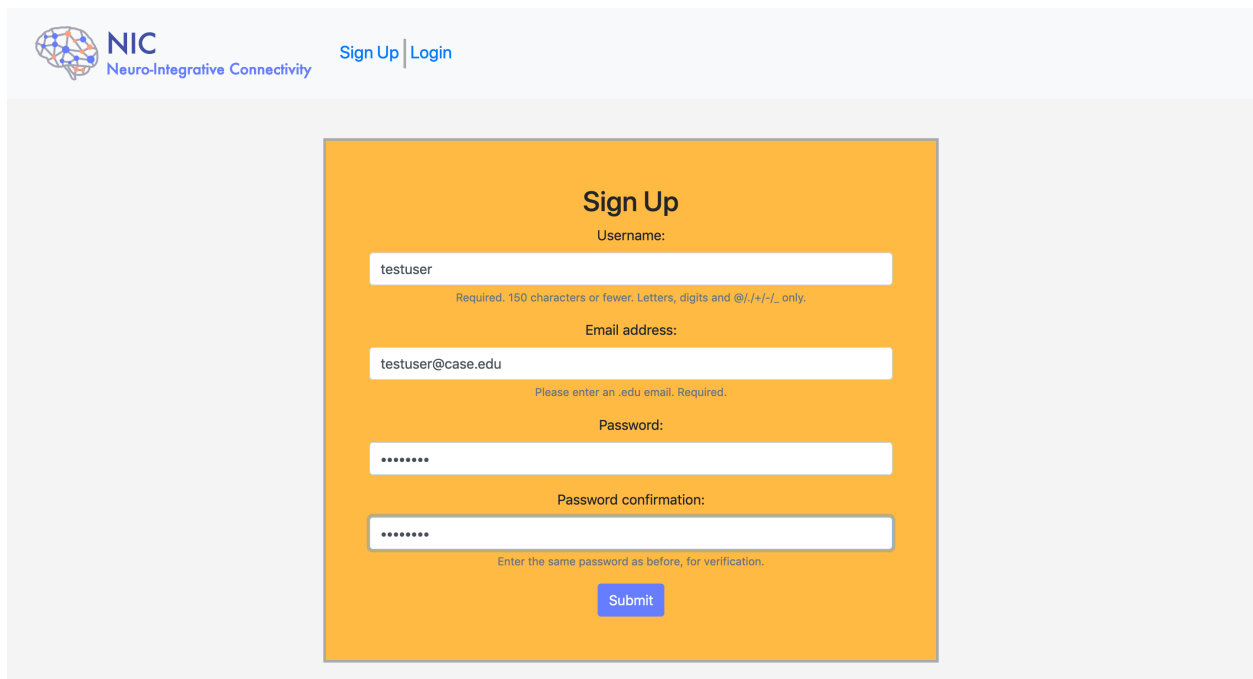
1	Create an Account	3
2	Overview of Steps	5
2.1	Conversion from EDF-CSF Files	5
2.2	Calculation of Coupling Measures	5
2.3	Calculation of Network Analysis Measures	5
3	Step 1: Entry of Patient Demographics	7
3.1	New Patient	8
3.2	Old Patient	8
4	Step 2: Conversion from EDF-CSF Files	11
5	Step 3: Calculation of Coupling Measures	15
6	Step 4: Calculation of Network Analysis Measures	17
7	Provenance and Run History	19
8	Setting up NIC on Docker	21
8.1	Installing Docker	21
8.2	Opening Kitematic (Optional)	21
8.3	Pulling the NIC Container	21
8.4	Setting up Volumes	21
8.5	Running the System	21
9	Additional Computational Background	23
9.1	Network Graph Representations	23
9.2	Summary Metrics Of Network Graphs	23
10	How to Use NIC and this Documentation	25

The Neuro-Integrative Connectivity (NIC) was developed to enable users with little computational experience to perform efficient network analysis on SEEG data to investigate epilepsy in patients. This documentation has been created to walk you through the steps necessary to calculate the supported network analysis measures and interpret the results as effortlessly as possible.

CHAPTER 1

Create an Account

The first step is to create an account. If you are using the server edition of NIC, you will have to create an account on the signup page shown below.



The screenshot shows the NIC (Neuro-Integrative Connectivity) website's sign-up page. At the top left is the NIC logo, a stylized brain with a network of connections, followed by the text "NIC Neuro-Integrative Connectivity". To the right of the logo are links for "Sign Up" and "Login". The main content area is a large orange rectangle with the title "Sign Up" at the top. Below the title are four input fields: "Username:" with the value "testuser", "Email address:" with the value "testuser@case.edu", "Password:" with masked characters "*****", and "Password confirmation:" with masked characters "*****". Each input field has a small red error message below it: "Required. 150 characters or fewer. Letters, digits and @,./+/-/_ only." for the username, "Please enter an .edu email. Required." for the email, and "Enter the same password as before, for verification." for the password confirmation. A blue "Submit" button is at the bottom of the orange box.

Once you sign up, you will see a confirmation message like the one below.

Thank you for signing up! We will contact you shortly when your account has been verified.

Please wait while we verify your account. You should hear from us within a day or two. If not, please contact vx215@case.edu.

Once your account is verified, you'll be able to move on to the next step. You should start with *Step 1: Entry of Patient Demographics*.

Overview of Steps

Here, we will briefly outline the *major* steps that will be discussed in greater detail in further sections. Before these steps, we ask that you enter the **patient demographics** identified by the patient ID into our secure system.

2.1 Conversion from EDF-CSF Files

In this **first** step, we convert the conventional _European Data Format (EDF)_ files that you probably have to our defined _Cloudwave Signal Format (CSF)_ files.

For this step, please click [*Step 1: Entry of Patient Demographics*](#).

2.2 Calculation of Coupling Measures

In this **second** step, once you have created and outputted CSF files, we can calculate coupling measures between electrodes.

For this step, please click [*Step 2: Conversion from EDF-CSF Files*](#).

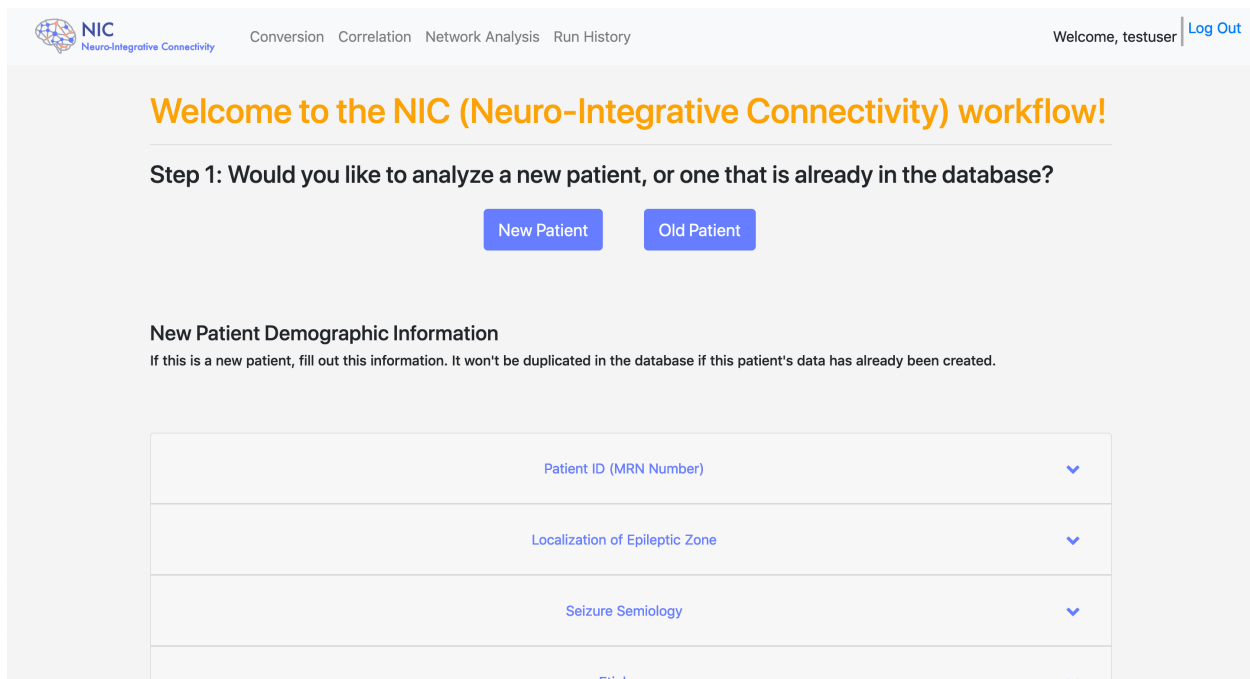
2.3 Calculation of Network Analysis Measures

In this **third** step, we can calculate network analysis measures from the coupled electrodes in step 3.

For this step, please click [*Step 3: Calculation of Coupling Measures*](#).

Step 1: Entry of Patient Demographics

Once you create an account and login, you will be taken to a page where you'll enter your patient demographics. It will look like this:



The screenshot shows the NIC (Neuro-Integrative Connectivity) workflow page. At the top, there is a navigation bar with the NIC logo and the text "Neuro-Integrative Connectivity". To the right of the logo, there are links for "Conversion", "Correlation", "Network Analysis", and "Run History". Further right, it says "Welcome, testuser" and a "Log Out" link. Below the navigation bar, there is a large orange heading that says "Welcome to the NIC (Neuro-Integrative Connectivity) workflow!". Underneath this, there is a step indicator that says "Step 1: Would you like to analyze a new patient, or one that is already in the database?". Below the step indicator, there are two blue buttons: "New Patient" and "Old Patient". Below the buttons, there is a section titled "New Patient Demographic Information" with a subtext that says "If this is a new patient, fill out this information. It won't be duplicated in the database if this patient's data has already been created." Below this text, there is a form with four rows, each with a label and a dropdown arrow. The labels are "Patient ID (MRN Number)", "Localization of Epileptic Zone", "Seizure Semiology", and "Etiology".

The page will guide you through the steps. There are two options that you can choose. You can start analysis about a *New Patient* or an *Old Patient*.

3.1 New Patient


If you select the *New Patient* button, you need to fill out the form and upload a discharge summary file. All fields are required. This information is stored in the database for later use. The patient ID you enter will then be automatically pre-filled in both the Conversion and Correlation steps.

Localization of Epileptic Zone	▼
Seizure Semiology	▼
Etiology	▼
Related Medical Conditions	▼
Seizure Frequency	▼
Patient Gender and Patient Gender	▼
Upload Patient Discharge Summary	▲

No file selected.

3.2 Old Patient

If you select the *Old Patient* button, you will be presented with a table where you can select from all your previously entered users. The patient ID you select will then be automatically pre-filled in both the Conversion and Correlation steps.

 **NIC**
Neuro-Integrative Connectivity

Conversion Correlation Network Analysis Run History

Welcome, testuser [Log Out](#)

Old Patient Demographics

Please select an old patient to move on to conversion of EDF to CSF files, calculating coupling measures, or network analysis.

Patient ID	Patient Age	Patient Gender
84894	23	gender
7379290	38	female
494843	24	male
837323	38	male
420482	48	fm
594945	59	male
1838383	43	mf
2394299	23	male
3333333	20	asdfasd
11111	23223	asdfasd
22222	232	asdfasd

Finally, the buttons at the bottom will allow you to move on to the next step. As the tooltip states, generally, for newly processed patient, you will need to create CSF files from EDF files before performing further analysis on them.

Let's move on to the next step!

Now that you've chosen/added a patient, it's time for the next step!
(This is usually conversion from EDF to CSF files)

[To Conversion](#)[To Correlation](#)[To Network Analysis](#)

Step 2: Conversion from EDF-CSF Files

The NIC system assumes that you start with **EDF** files from an epilepsy patient that you have collected data for. The first step is to convert these EDF files to our defined CSF file format.

Our system only supports CSF files and we encourage their use as they provide support for human-readability and better management of your metadata (e.g. clinical seizure event annotations, EEG instrument and electrode details, study details). If you'd like to learn more information, please visit <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4360820/>

This step is pretty simple. You will see a form that accepts a number of inputs described below:

<p>Caution: This form assumes that the input EDF folder pertains to only one patient and contains both the EDF files and the clinical annotations in .txt format.</p>
--

Conversion Workflow

Use the form below to convert your EDF files into CSF Files!

Patient ID (MRN Number)

Path to EDF Files

Desired Full Output Path of CSF Files

Epoch duration

Epochs per segment

[Run Conversion](#)

Table 1: Conversion Input Parameters

Input	Description
Patient ID	The patient ID from the patient demographics page
Path to EDF Files	The path to the EDF Files. This would be the server path on NIC Server Edition and the bound container path on NIC Docker Edition (<i>Refer to Docker documentation</i>)
Output Path of CSF Files	The full path of your output CSF Files
Epoch Duration	The length of each fragment in your CSF file in seconds
Epochs Per Segment	The number of fragments to each CSF file

Once you click *Run Conversion* you will be taken to a status page that looks like this:

Thanks for submitting! Your files are being converted!

Current Status

Current File:

/home/vsocrates/Documents/pt_data/insular/12345_3_1.edf

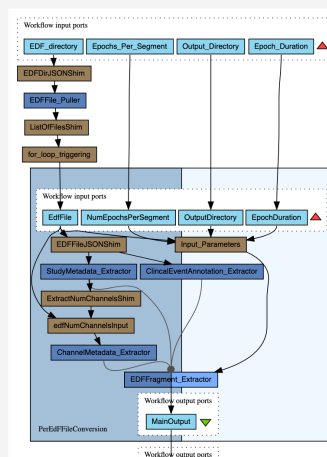
Current Step:

EDF-FRAGMENT-START

Last Updated:

04-29-2019 22:43:44

Status of Workflow Execution



This page will continue to update every few minutes with a status update. Eventually, you will see a popup that takes you to the next step, Calculation of Correlation Measures.

Step 3: Calculation of Coupling Measures

In this step, we will be calculating coupling measures between electrodes to determine any temporal correlations.

This allows us to create an adjacency matrix representation of a network graph that we can calculate network summary statistics on. For more information regarding network graph representations, please check [Network Graph Representations](#).

We support three different correlation measures: the linear Pearson's Correlation, and non-linear mean phase coherence correlation, and the non-linear correlation coefficient (Pijn's Measure).

When you get to the Correlation page, you will see the following form. This page works very similarly to the conversion page.

Step 1: Select the location of your CSF Files for the selected patient.

Patient ID (MRN Number)

Full Path of CSF Files

Step 2: Select the coupling measures you would like to calculate.

☐ PIJN Correlation

☐ Pearson Correlation

☐ Phase Coherence Correlation

Step 3: Enter the event windows for the given patient.

Event Start Time	Event End Time	Lag Window (in seconds)	List of Channels (comma-separated)	Path to Correlation Metrics Output File
<input type="text" value="e.g. 16.03.20,10.15.05"/>	<input type="text" value="e.g. 16.03.20,10.15.45"/>	<input type="text" value="e.g. 0.10"/>	<input type="text" value="e.g. lk1,lk3,lj1"/>	<input type="text" value="/output/path/of/measures.txt"/> Remove

[Add Seizure Event](#)

Table 1: Correlation Overall Input Parameters

Input	Description
Patient ID	The patient ID from the patient demographics page
Path to CSF Files	The full path to the CSF files produced in step 1.
Coupling Measures	The list of coupling measures you'd like to select

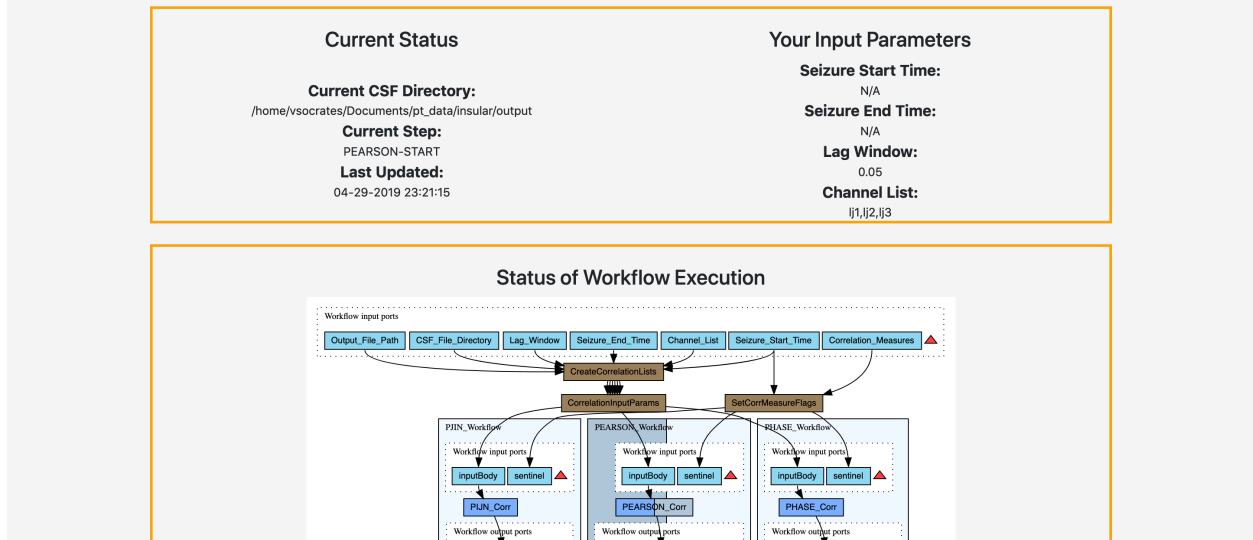
Once you have selected the location of the CSF files (**for one patient**), you can select as many event windows as you'd like by clicking *Add Seizure Event* and *Remove*.

Table 2: Correlation Event Window Input Parameters

Input	Description
Event Start Time	The start time of the event
Event End Time	The end time of the event
Lag Window	The lag window to calculate over
List of Channels	The list of electrodes over which you'd like to calculate correlations
Path to Correlation Metrics Output File	The output file path for each event (must be unique for each entry)

Once you click *Run Correlations* you will be taken to a very similar screen that allows you to view your status as shown below:

Thanks for submitting! Your correlation matrices are being generated!



Again, a popup will take you to the next step, network analysis.

Step 4: Calculation of Network Analysis Measures

Once we calculate our coupling measures, we can create an *adjacency matrix representation* to better draw conclusions about our coupled electrodes created in step 3. See more detailed information regarding these summary metrics at *Summary Metrics Of Network Graphs*.

You will be taken to a form that looks like the following:

Use the following form to calculate and download the network analysis measures.

Step 1: Please enter the full path for the correlation measure files you created in the last step for each seizure event. (We use these files to conduct the network analysis.)

Name of Seizure Event	Full Path of Correlation Measure File (.txt)
<input type="text" value="e.g. ictal event 1"/>	<input type="text" value="/path/to/correlation/file.txt"/> Remove
Add Seizure Event	

No Results Generated.

Step 2: Select the network analysis you'd like to calculate.

Step 3: Select the coupling measures to perform network analysis over.

Step 4: Enter a name for the file and prepare it for download.

Table 1: Network Analysis Inputs

Input	Description
Name of Seizure Event	The name you'd like to output for the seizure event
Full Path of Correlation Metric File	This is the full path of the correlation metric file you produced in step 3.
Network Analysis Measures	The list of network analysis measures you'd like to calculate
Coupling Measures	The coupling measures you'd like to perform the network analysis on
Output File	This will produce a file with delimited tables for each of the network analyses and coupling measures selected.

You will fill out the network analysis form on the left side of the page and the outputs will be displayed on the right once they are calculated. You are also able to download a text/csv version of this output for your analysis later.

Tip: Congratulations! You have successfully completed use of the NIC system.

There are a few other features such as *rerunning previous runs* that you should feel free to play around with.

CHAPTER 7

Provenance and Run History

Due to the lack of scientific reproducibility in biomedicine, in general, the NIC platform has implemented several features we hope will encourage reproducible science. In addition to a PostgreSQL database that stores all inputs, we also allow the user to recreate past runs.

After you have completed a conversion and correlation run, you are able to rerun one of these runs.

Note: You will only be able to see your past runs and no one else can see your runs.

The page will look like this:

History of Your Past Runs

Past Conversion Runs

Below are your previous conversion runs.

EDF Directory: /home/vsocrates/Documents/pt_data/insular
Run Started on: Apr 30, 2019 at 2:43 AM

EDF File Directory	/home/vsocrates/Documents/pt_data/insular
Output CSF Directory	/home/vsocrates/Documents/pt_data/insular/output
Epoch Duration	30
Epochs per Segment	2
Patient ID	222222

Rerun Conversion Input

Past Correlation Runs

Below are your previous correlation runs.

CSF Directory: /home/vsocrates/Documents/pt_data/insular/output/
Correlation Measures: pijn,pearson,phase
Run Started on: Apr 30, 2019 at 3:20 AM

Correlation Measures Calculated	pijn,pearson,phase
CSF Input Directory	/home/vsocrates/Documents/pt_data/insular/output/
Patient ID	222222

Rerun Correlation Inputs

When you click either *Rerun Conversion Input* or *Rerun Correlation Inputs*, you will be taken back to those respective pages with the forms automatically populated with that run's data. Then you can follow the process described in steps 2 or 3.

Setting up NIC on Docker

Documentation coming soon!

8.1 Installing Docker

Documentation coming soon!

8.2 Opening Kitematic (Optional)

Documentation coming soon!

8.3 Pulling the NIC Container

Documentation coming soon!

8.4 Setting up Volumes

Documentation coming soon!

PostgreSQL database and data location volumne

8.5 Running the System

Documentation coming soon!

Additional Computational Background

Here is some background on the computational methods implemented by our system so that you can better interpret your results.

Documentation coming soon!

9.1 Network Graph Representations

There are a number of ways to represent a network graph.

Documentation coming soon!

9.2 Summary Metrics Of Network Graphs

Documentation coming soon!

CHAPTER 10

How to Use NIC and this Documentation

There are two editions of the NIC system.

1. NIC Server Edition (at <https://bmhinformatics.case.edu/nicworkflow>)

The Server Edition is only for use with data on the CWRU servers in the Population and Quantitative Health Sciences department and UH Epilepsy Center.

2. NIC Docker Container (at <https://hub.docker.com/r/vsocrates/nicworkflow>)

The Docker Container can be downloaded from the public repository and run on any platform with your own data. Additional instructions can be found at *Setting up NIC on Docker*.