Neuro-Integrative Connectivity (NIC)

Release 1

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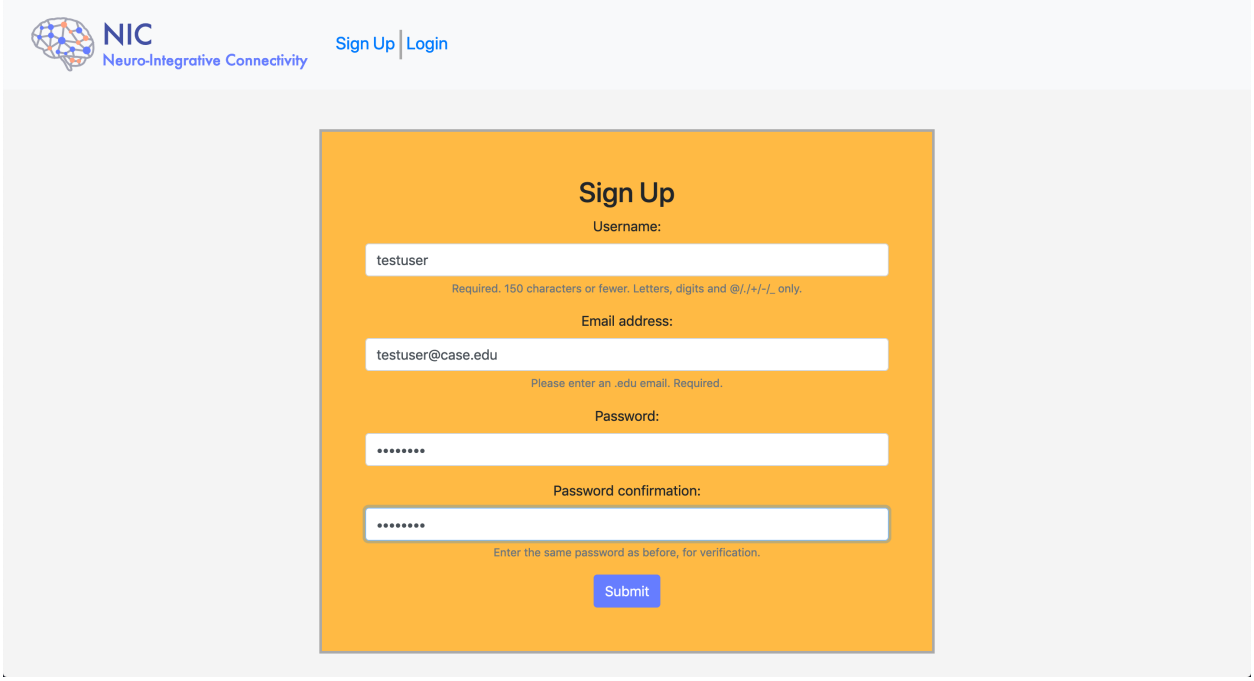
The Neuro-Integrative Connectivity (NIC) was developed to enable users with little computational experience to perform efficient network analysis on SEEG data to investigate epilepsy in patients. This documentation has been created to walk you through the steps necessary to calculate the supported network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



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 vxs215@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*.

CHAPTER 2

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 calulate coupling measures between electrodes.

For this step, please click *Step 2: Conversion from EDF-CSF Files*.

2.3 Calculation of Network Analysis Measures

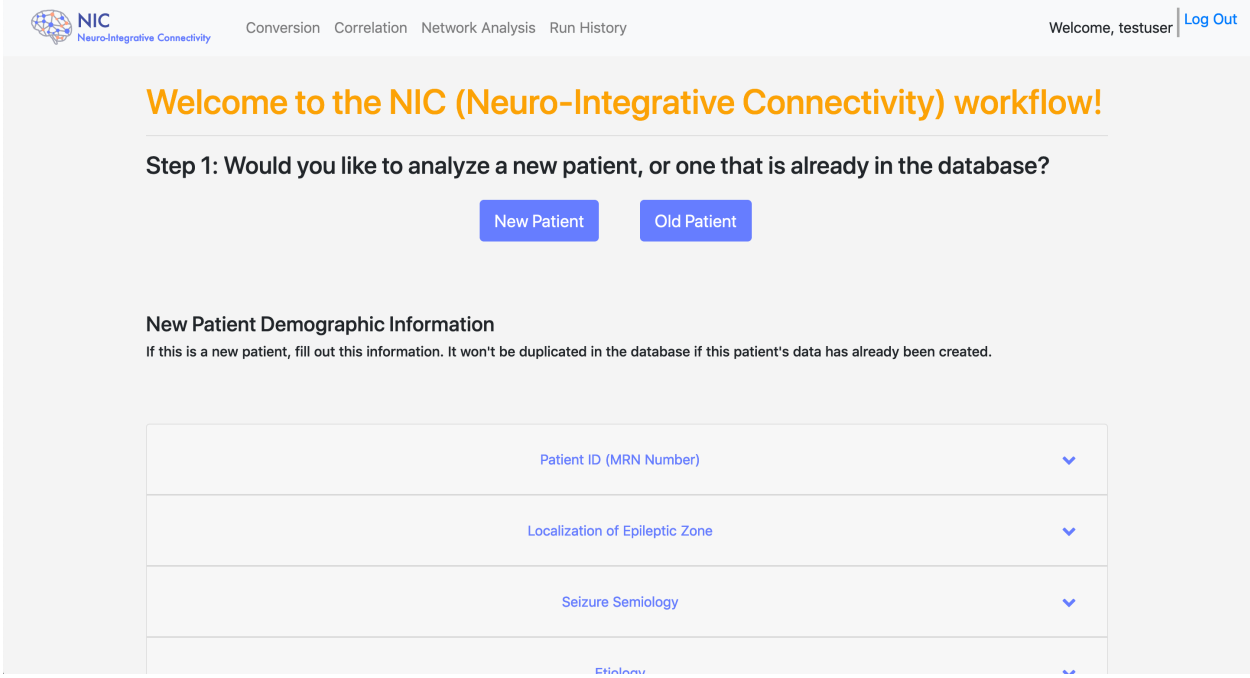
In this **third** step, we can calculate network analysis measures from the coupled electrodes in step 3.

For this step, please click *Step 3: Calculation of Coupling Measures*.

CHAPTER 3

Step 1: Entry of Patient Demographics

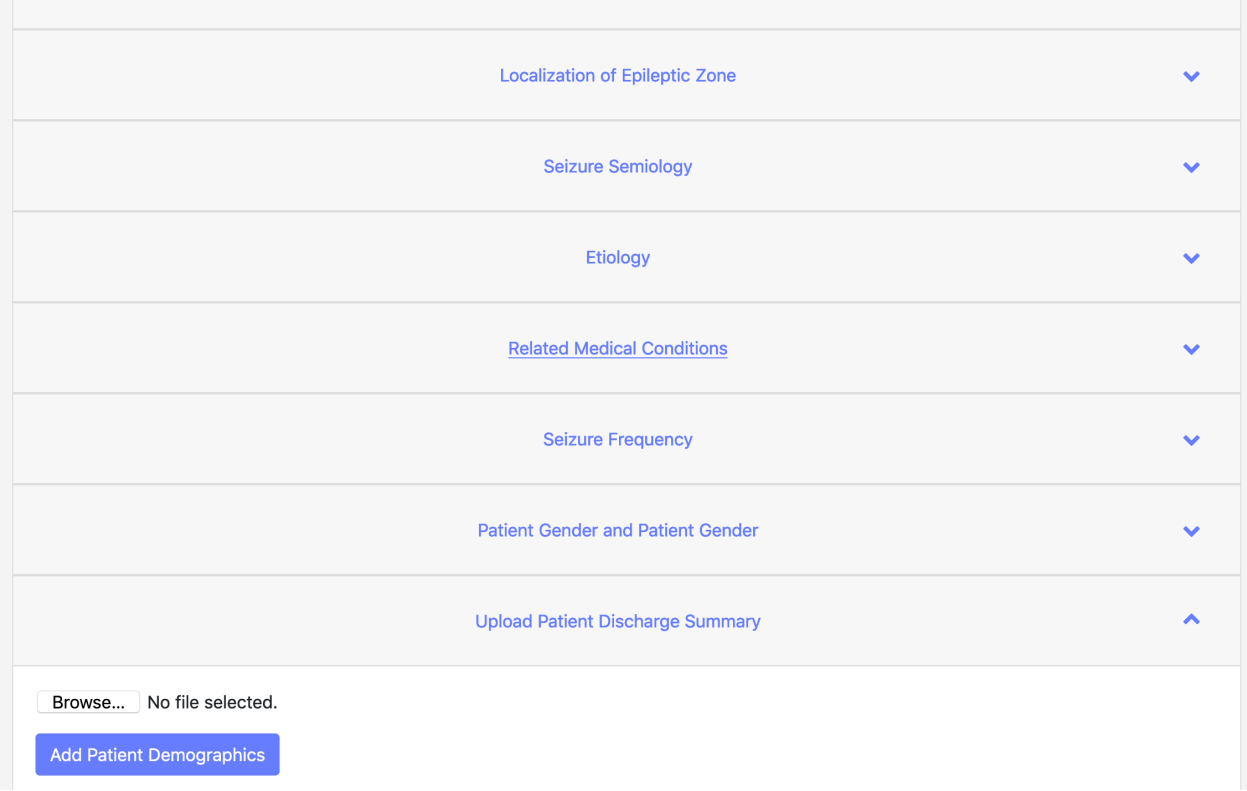
Once you create an account and login, you will be taken to a page where you'll enter your patient demographics. It will look like this:



The 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*.

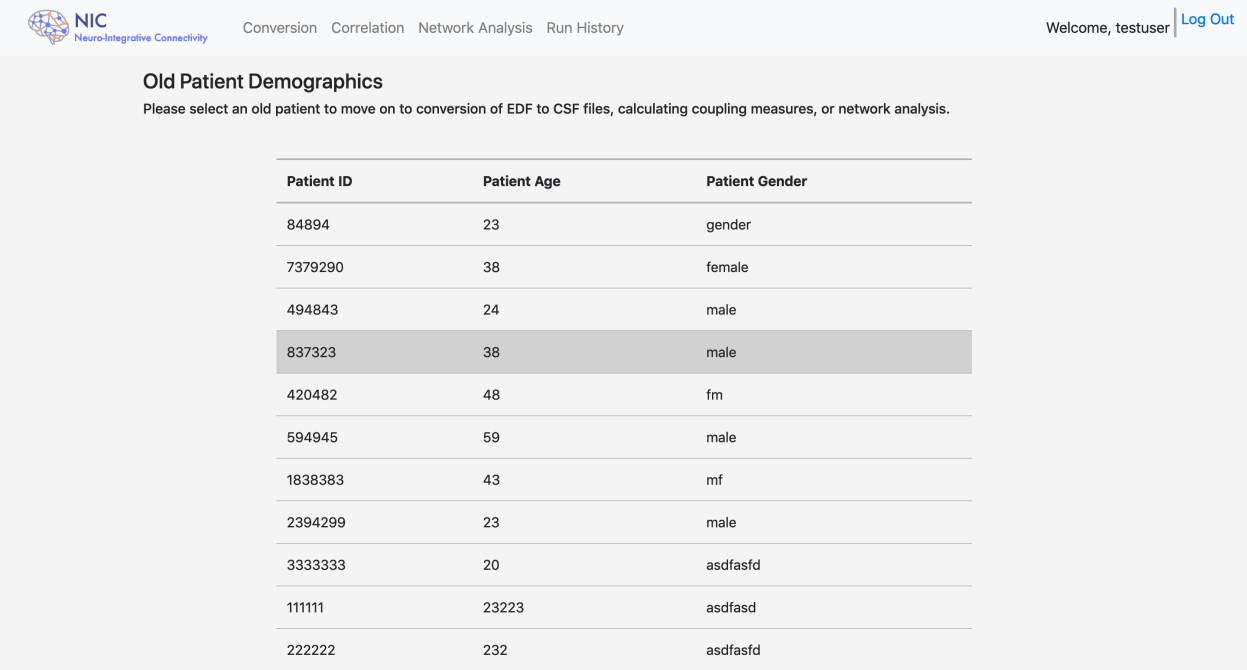
3.1 New Patient

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.

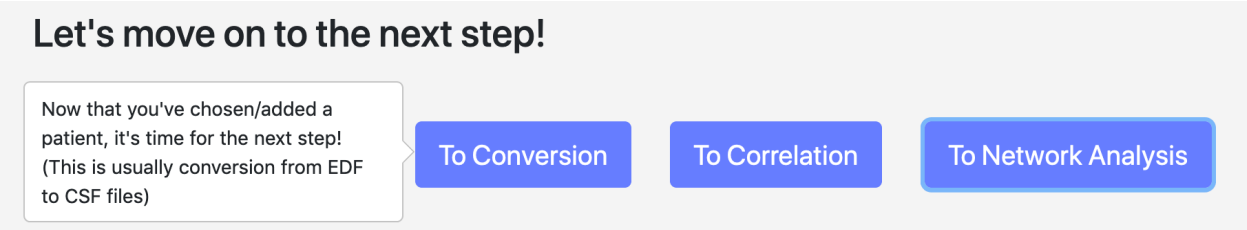


3.2 Old Patient

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.



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.



CHAPTER 4

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:

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.

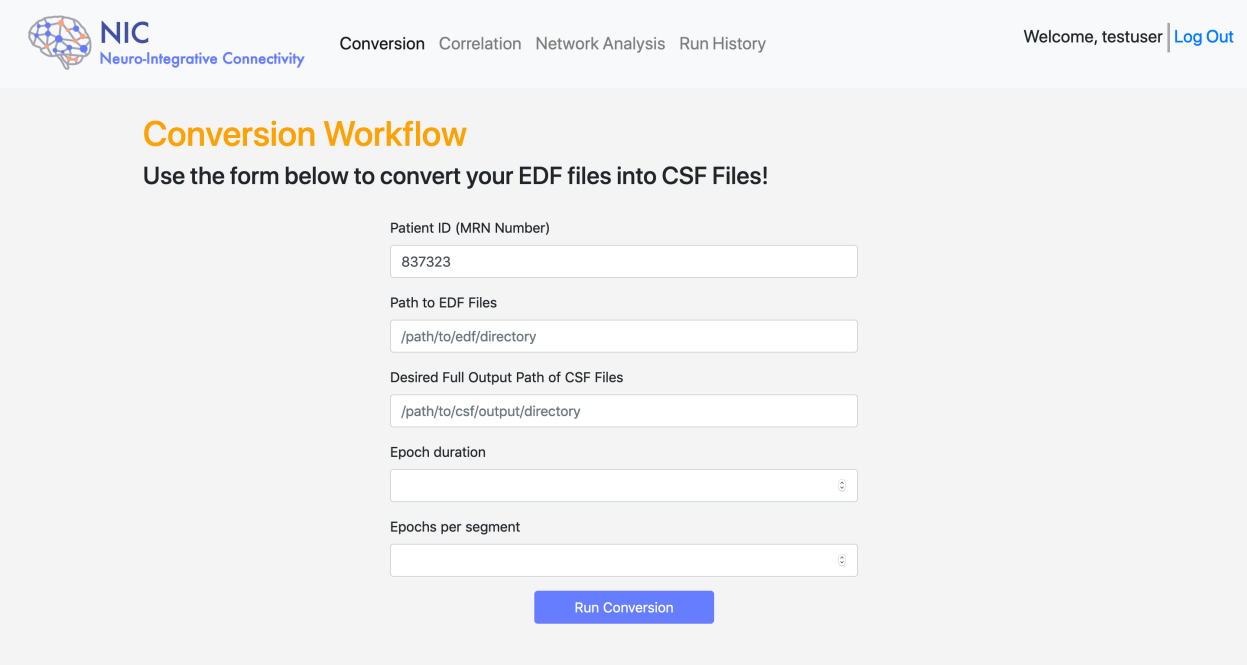
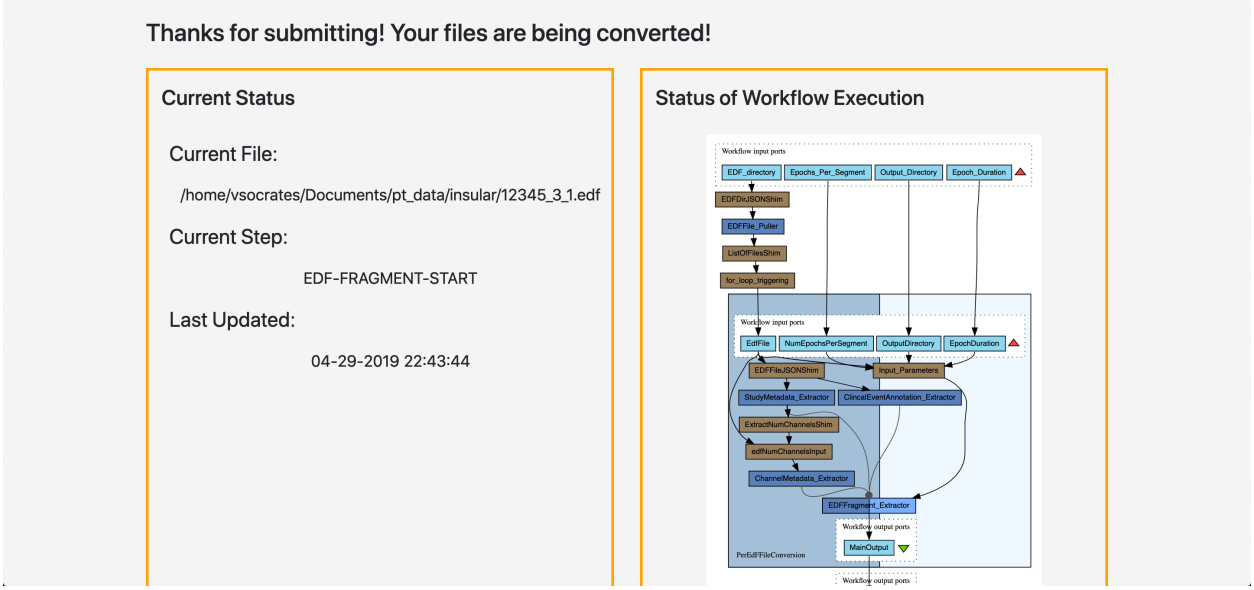


Table 1: Conversion Input Parameters

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 (*Refer to Docker documentation*)
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:



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.

CHAPTER 5

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 calcalate 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.

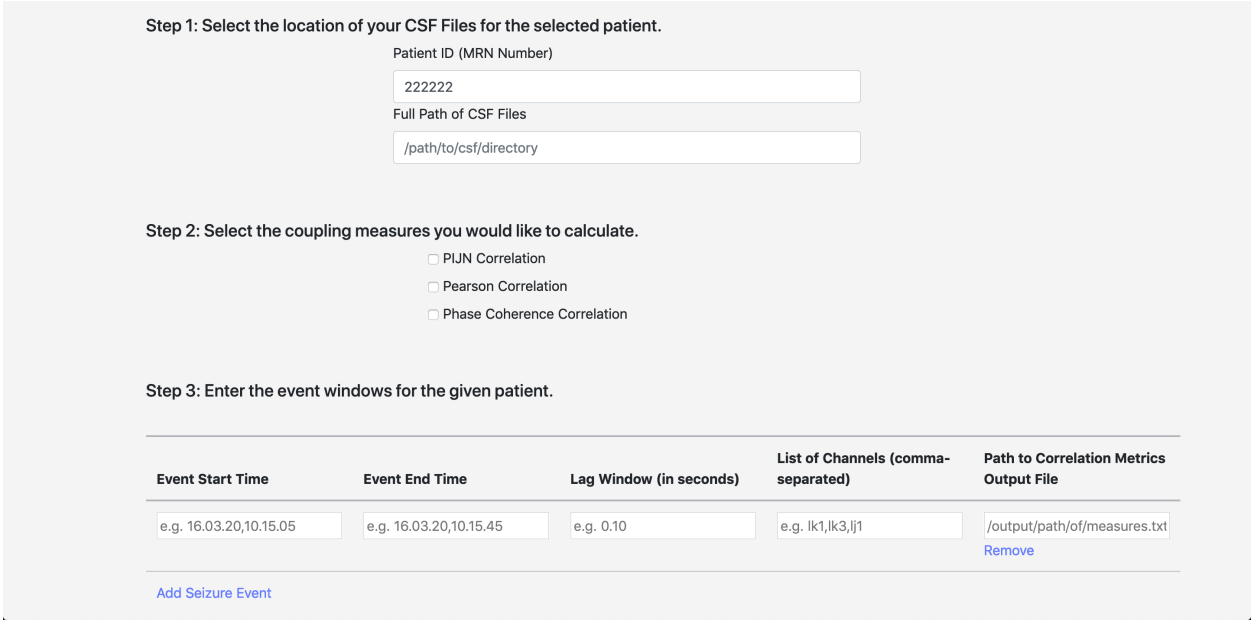


Table 1: Correlation Overall Input Parameters

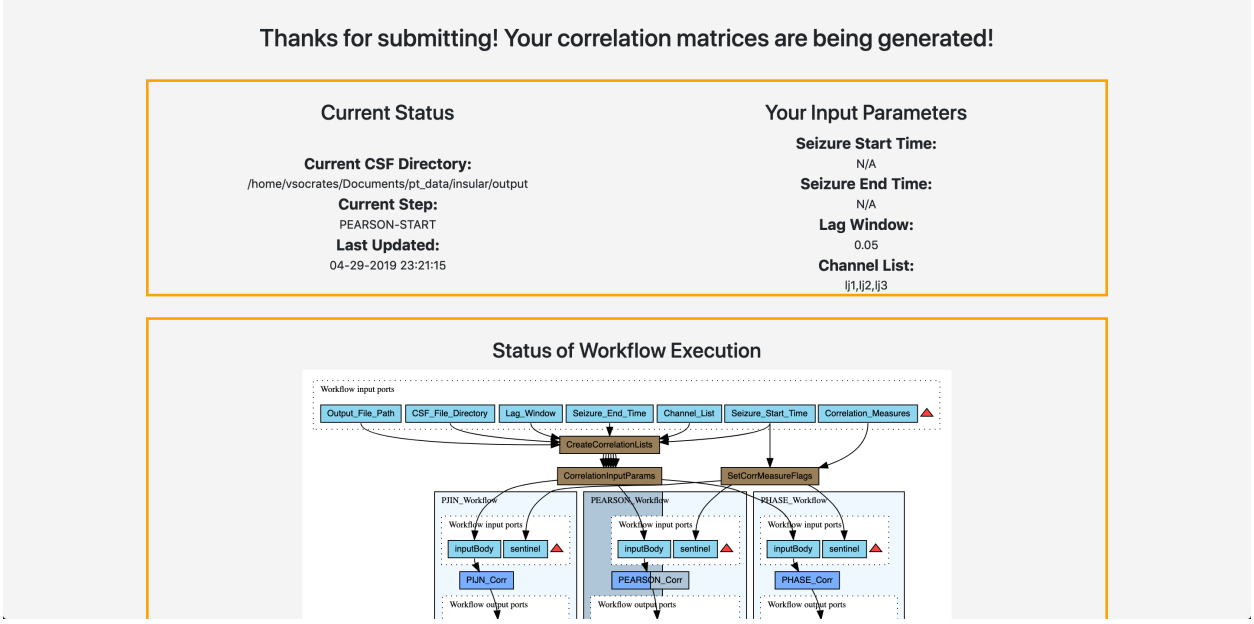
Input	Description
Patient ID	The patient ID from the patient demographics page
Path to CSF Files	The full path to the CSF fules produced in step 1.
Coupling Measures	The list of coupling measures you'd like to select

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 Start 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:



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

CHAPTER 6

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:

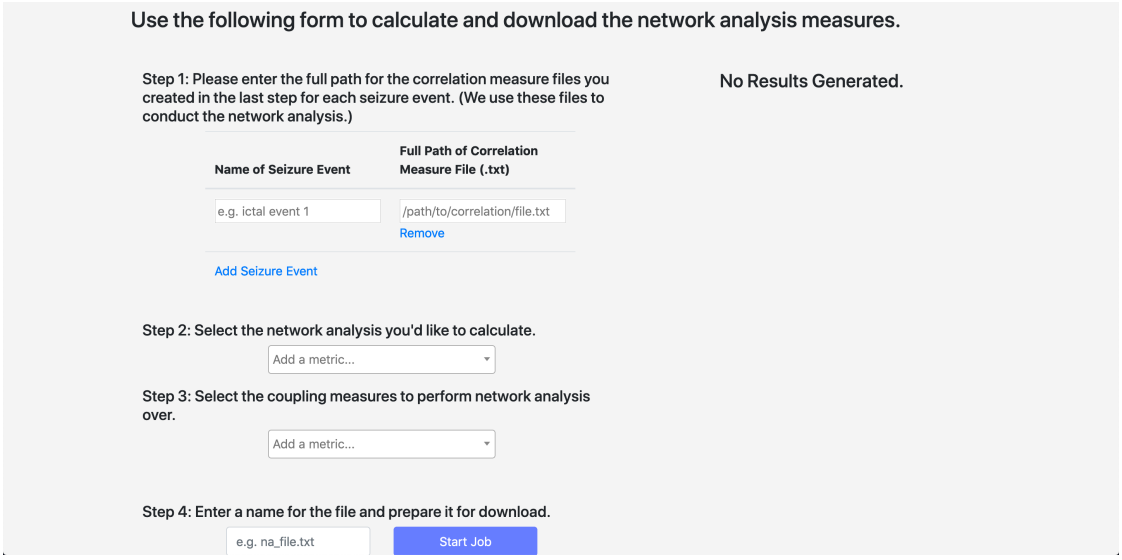


Table 1: Network Analysis Inputs

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

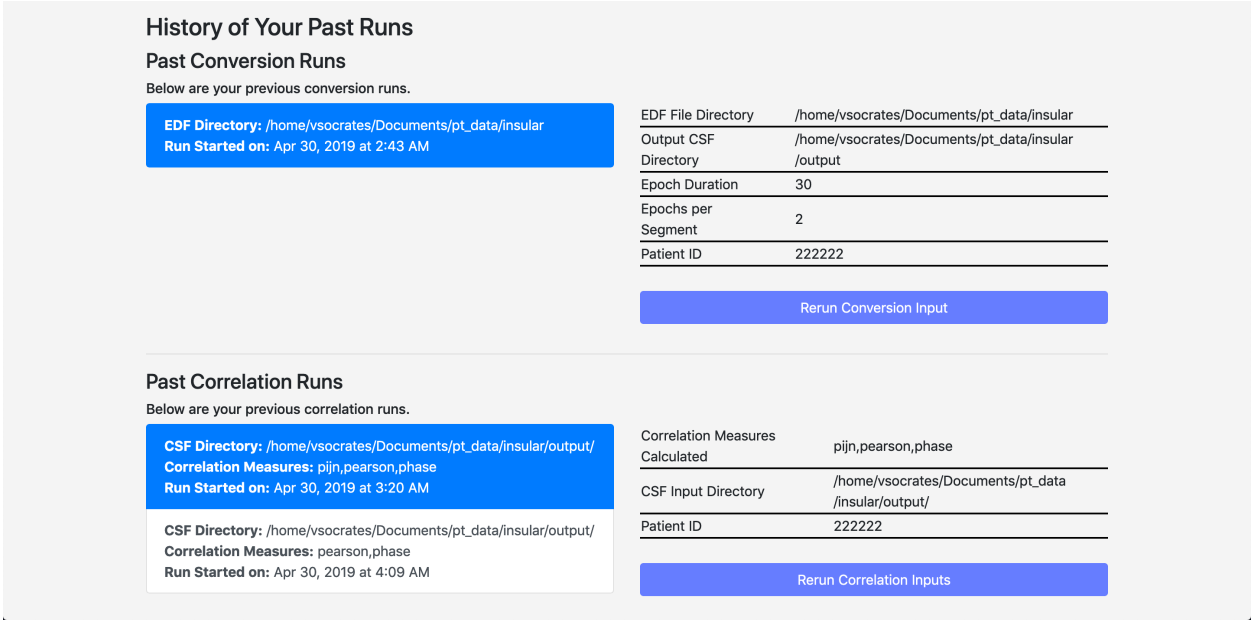
Provenance and Run History

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:



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.

CHAPTER 8

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!

CHAPTER 9

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*.