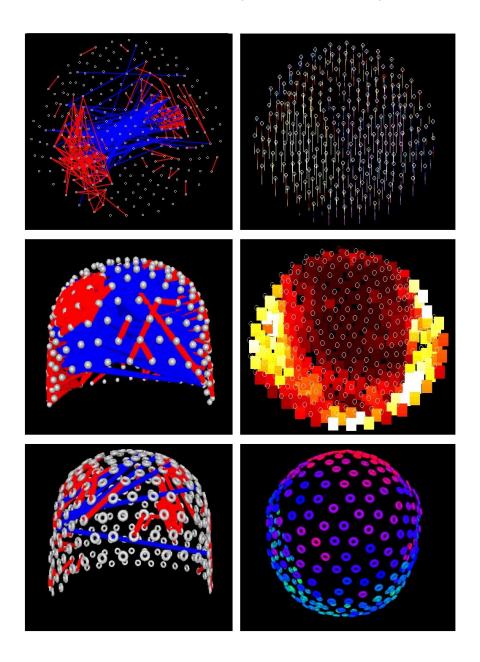
# Spectral Channel-Cross-Channel (CxC) Analyses

**Software Guide (EEG/MEG Data)** 



#### **DISCLAIMER**

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Features and specifications of this software program are subject to change without notice. This manual contains information and images about MEG (magnetoencephalography) time-frequency software and its user interface, GUI and its other signal processing algorithms, publications that may be protected by copyright.

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Thank you.

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# Warnings and Cautions

The correlation between EEG/MEG signals of time-frequency representations from two channels can be analyzed in several ways. In this manual, we frequently use the term of channel-cross-channel (CxC). "CxC" indicates operations applying to two channels or a channel-pair. An operation of two channels is a "CxC" operation that can produce many possible results. Here are some powerful usages:

- 1. Virtual time-frequency channels: similar to many software programs, EEG Studio can produce virtual channel by subtracting or adding two physical channels. Instead of manually defining a virtual channel by subtracting two physical channels or a channel-pair, "CxC" can generate all possible virtual channels by using available physical channels with a set of operations. All the operations can be done by a few clicks. Once you try it, you will the power and usefulness of the "CxC" function. It is systematic, subjective and efficient. Understandably, the computing of virtual spectral channels requires a lot of memory. Therefore, to compute virtual spectral channels, a computer with a lot memory is essential.
- 2. Coherence of time-frequency data at sensor levels: coherence, correlation and association of two-sensor can be done by simply selecting "Covariance" or "Correlation" operation. "CxC" can analyze the relationship of all possible physical channel pair according to the setting of operations.
- 3. Spectral covariance matrices for source localization: many EEG/MEG source localization algorithms require covariance matrices from sensor data. The "CxC" functions enable users to compute, preview and check spectral covariance matrices for source localization.

The coherence of two channel pair has been frequently used in the study of brain function. The study the oscillatory synchrony between two channels can be done by computing the time-frequency coherence. This can be computed in the frequency domain by normalizing the magnitude of the summed cross-spectral density between two signals by their respective power. For each frequency bin the coherence value is a number between 0 and 1. The coherence values reflect the consistency of the phase difference between the two signals at a given frequency. Unfortunately, the computing of each frequency could be time-consuming and requires a lot of memory. Therefore, it is necessary to have a powerful computer with a lot of memory to perform spectral CxC study.

This program is optimized for computing CxC for all possible pair in a group of channels, for example, all MEG sensors without reference channels. If there are N channel for computing CxC, the result will be a matrix with a size of N by N. Consequently, the results can be systematically analyzed with matrix operations.

# **Preface**

This guide describes the operation applying to the spectrograms from two channels, which is named CxC. The spectral CxC module is one of the core functions in EEG/MEG data analysis. It is used as the primary tool to determine if the signals from the spectrograms of two sensors are correlated. The spectral CxC module provides graphic user interface (GUI) for access the functions.

#### **Intended Audience**

This guide is intended for persons responsible for analyzing the correlation of sensor pair, spectral covariance and virtual channel characteristics in EEG and MEG data. This reference is useful to anyone who performs analysis techniques for EEG/MEG data. Operations of correlation and covariance analysis require some expertise to satisfy requirements of accuracy and fitness for use of the results. It is necessary to understand time-frequency transform and spectral analysis first. Technicians may use the application under review by highly trained analytical staff. The guide assumes the reader is familiar with standard EEG/MEG procedures and is familiar with the Windows operating systems.

The spectral covariance and correlation data generated by CxC operation can be used in MEG source localization.

# References

This document assumes familiarity with many terms related to computer operations and physiology. This document also assumes you are familiar with the principles of correlation coefficients, covariance and virtual channels as well as the data collection and recording process. It also assumes some knowledge of EEG/MEG analysis. The document uses terms related to computer operations and physiology as well as many acronyms.

# **Document Structure**

Documents are generally provided in both Microsoft Word® format and Adobe® Acrobat® PDF (Portable Document Format). All editions are distributed on Flash Driver, CD or websites with the related software, and include bookmarks and hyperlinks to assist navigating the document. Please feel free to send your critiques, corrections, suggestions and comments to: BrainX@live.com.

#### **Conventions**

Numeric: Numeric values are generally presented in decimal but in special circumstances may also be expressed in hexadecimal or binary. Hexadecimal values are shown with a prefix of 0x, in the form 0x3D. Binary values are shown with a prefix of 0b, in the form 0b00111101. Otherwise, values are presumed decimal.

Units: Units of measure are given in metric. Where measure is provided in imperial units, they are typically shown in parenthesis after the metric units.

A millivolt (mV) is one one-thousandth of a volt  $(0.001 \text{ V or } 1\ 10^{-3})$ . These units commonly are used in EKG, EMG, and sometimes in EEG. A microvolt (uV) is one one-millionth of a volt  $(0.000000 \text{ V or } 1\ \text{x} 10^{-6})$ . This is the commonest voltage measure in EEG. A nanovolt (nV) is one-thousandth of one-millionth of a v  $(0.000000001 \text{ V or } 1\ \text{x}\ 10^{-9})$ . This measure is used in the specific area of EEG dealing with evoked potentials.

The unit of current is the ampere (A). In EEG, typical smaller amounts are encountered. A milliampere (mA) is one one-thousandth of an ampere (0.001 A or  $1 \times 10^{-3}$ ). A microamplere (uA) is one one-millionth of an ampere (0.000000 A, or  $1 \times 10^{-6}$ ).

Magnetic signal strength is given in Teslas (T), the SI unit of flux density (or field intensity) for magnetic fields, also known as the magnetic induction. Typical signal strengths in MEG measurements are in the order of pT (picoteslas =  $10^{-12}$ ) or fT (femtoteslas =  $10^{-15}$ ).

# Changes from Previous Releases

If you used the software before, please read the ReadMeFirst.doc file for late changes that did not make it into this manual and for a list of new functions or options, changes, additions, bug fixes, frequently-asked-questions and known bugs for the application. In comparison with previous version of the software, this version of the software only provides three CxC results: Active, Control and the Results of Active and Control (Act-Ctl). The main reason for this change is to provide better user experience and minimize the use of computer memory. However, the CxC dataset can be increased for specific purposes but those modules are used only for internal tests and experienced users.

#### Introduction

This manual describes the various graphical elements that make up wave form spectral CxC analysis module and defines the CxC data throughout the software applications. There are several ways to analyze the correlations of MEG data from two sensors. In this guide, the spectral CxC operations will be discussed according to the computing of CxC data and the visualization of CxC data. The mathematic algorithms will be explained briefly. There are three major uses of the CxC data.

1. Virtual channels: similar to many software programs, EEG Studio can produce virtual channel by subtracting or adding two physical channels. Instead of manually defining a virtual channel by subtracting two physical channels or a channel-pair, "CxC" can generate all possible virtual channels by using available physical channels with a set of operations. All the operations can be done by a few clicks. Once you try it, you will the power and usefulness of the "CxC" function. It is amazing, subjective and very efficient.

2. Coherence at sensor levels: coherence, correlation and association of two-sensor can be done by simply selecting "Covariance" or "Correlation" operation. "CxC" can analyze the relationship of all possible physical channel pair according to the setting of operations.



- 3. Covariance matrices for source localization: many EEG/MEG source localization algorithms require covariance matrices from sensor data. The "CxC" functions enable users to compute, preview and check the covariance matrices for source localization.
- 4. Time-course of time-frequency representations in channel pairs: though we typically refer the time-frequency CXC as "spectral CxC" for simplicity because many EEG/MEG users of this software is familiar with spectrogram. However, this software moved one step farther by providing spectral, real, and imaginary as well as phase in the same viewer. The time-course of all those data can be viewed and analyzed as the conventional EEG/MEG waveforms.

# **Major Innovations in Spectral CxC**

The use of two physical MEG sensors or EEG electrodes to generate a new set of "virtual channels" is not new. Since an EEG voltage signal represents a difference between the voltages at two electrodes, the display of the EEG for the reading encephalographer may be set up in one of several ways. The representation of the EEG channels is referred to as a montage. The typical montages include (1) bipolar montage: Each channel (i.e., waveform) represents the difference between two adjacent electrodes. (2) referential montage: each channel represents the difference between a certain electrode and a designated reference electrode. There is no standard position for this reference; it is, however, at a different position than the "recording" electrodes. (3) average reference montage: the outputs of all of the amplifiers are summed and averaged, and this averaged signal is used as the common reference for each channel. (4) Laplacian montage: Each channel represents the difference between an electrode and a weighted average of the surrounding electrodes. Of note, each the montage represents a type of operation (typically subtraction) applied to channel pairs. The main purpose of "montages" is to highlight or better characterize certain features of the EEG/MEG data.

The major innovation in the spectral CxC is to apply operations to all possible channel pairs to generate a CxC matrix. The CxC matrix has all the possible "montages" that is going beyond the conventional one "montage" one time. Consequently, the EEG/MEG can be viewed in a systematic manner and reveal some features and characteristics that may not be able to be captured with the conventional montage that is typically selected by reviewers according their desires.

In addition, the CxC can represent the coherence at sensor levels if the operation is "correlation". The association of two-sensor can be visualized as "links" to reveal the networks of EEG/MEG data at sensor levels. "CxC" can analyze the relationship of all possible physical channel pair according to the setting of operations.

Furthermore, the spectral CxC data may include the covariance matrices for source localization. In comparison to many previous tool boxes for source localization with covariance, this software provides GUI to compute, visualize, process and edit the covariance matrix. Consequently, many EEG/MEG source localization algorithms require covariance matrices from sensor data can be refined and optimized.

Moreover, this software provides functions to track the polarity and operators in the spectral CxC data, consequently, the spectral and phase information can be adjusted, corrected and re-computed with a variety set of options for research or clinical purposes.

# Menu for Launching Spectral CxC Windows

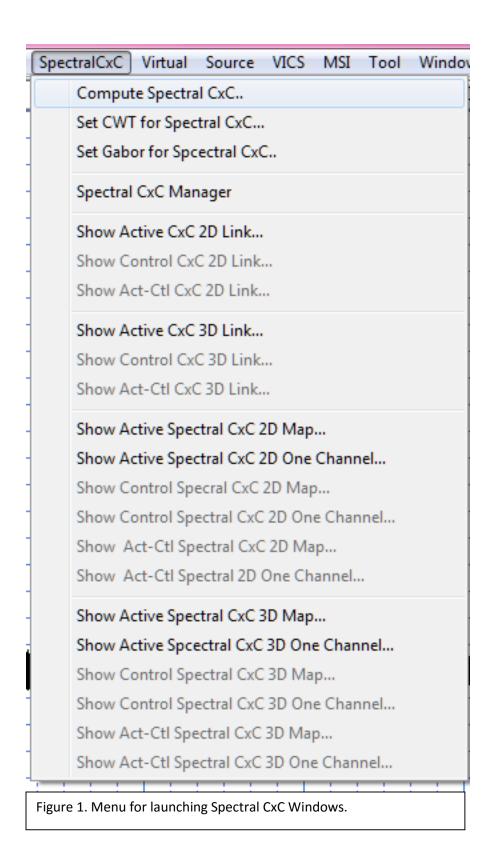
The menu for launching Spectral CxC windows is in the Main Frame of the EEG Studio program, which is under the "SpectralCxC" menu (Figure 1). EEG/MEG data for CxC analysis can be spectrograms, raw waveform data and/or pre-processed data.

The uses of raw or pre-processed waveforms for spectral CxC analysis will compute the spectral CxC internally, it is typically slow and lacks the flexibility to inspect and verify the spectral data. However, it will minimize the use of computer memory.

The uses of spectral data for spectral CxC analysis typically require a huge amount of memory. However, this approach provides the opportunity to check, verify and edit the spectral data for a variety of purposes.

Currently, we have not found a good solution to solve all the problems. We are hoping the development of computer technology will eventual solve those problems.

This manual describes the various graphical elements that make up spectral CxC computing, analyzing and visualizing modules throughout the software application.



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# **Compute Spectral CxC with Spectral Data**

Selection of "Compute Spectral CxC" menu launches the main window for computing spectral CxC with spectral data, which are matrices with multiple time-frequency slices. The Window GUI application allows you to configure parameters and processing options for spectral CxC computing as well as other kinds of analysis.

Spectral CxC is performed after spectrograms from a dataset has been acquired and reviewed. Here is the recommended procedure for a standard analysis using Spectral CxC programs:

- a) Check and verify that you have the correct dataset and trials in the spectral Viewer (see the EEG Studio Main Frame Guide).
- b) If spectral data accumulating (similar to averaging) is necessary or required, do the accumulating first.
- c) Check and analyze the EEG/MEG data to determine the interest of time-frequency window. Though there is no standardized way, it is a good idea to use both topographic and "single channel viewer" to determine the interest of time-frequency windows.
- d) If the spectral CxC main window has not been launched. Select "Compute Spectral CxC" in the Menu (see "Menu for Launching Spectral CxC Windows")
- e) During the launching of the window for Settings for computing spectral CxC data, the program gets the selected time-frequency window or the entire time-frequency window as the Active Window. The program also checks the integrity and sanity of the data and may report warning/error messages if necessary.
- f) Use the window for "for Settings for Computing spectral CxC data" to inspect the dataset as well as suitable parameters. If required or necessary, change the data selections.

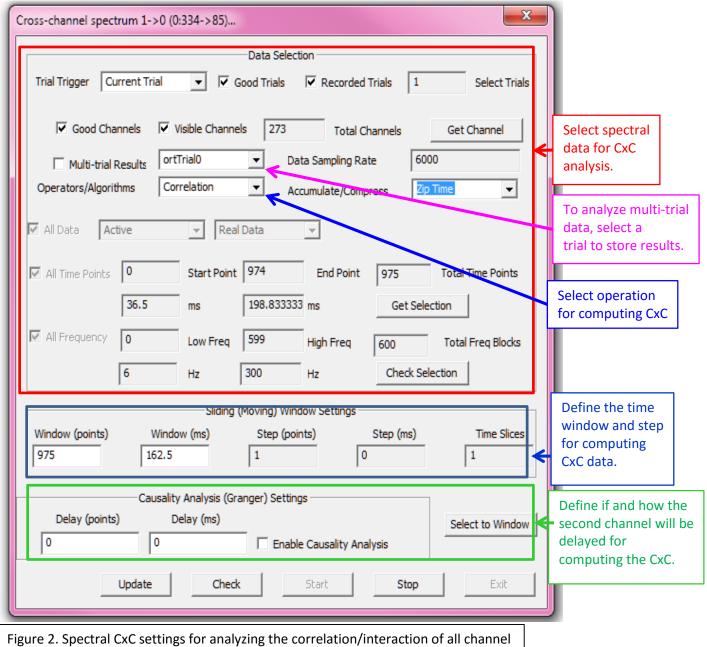


Figure 2. Spectral CxC settings for analyzing the correlation/interaction of all channe pairs.

# Main Modules in Spectral CxC Computing

The full suite of CxC computing comprises the following components.

- Spectral Data Selection (by default, the program will select all spectral classes and data types)
- Pre-processing for CxC computing
- Window and step
- Causality Analysis (Granger)

#### Start CxC computing

# Target data (Time-frequency windows)

The data selection specifies the trial, channels to be used for spectral CxC computing. By default, by default, the program will select all spectral classes and data types. In professional version of the software, the time-frequency window parameters specify active- and control-state time-frequency windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the "Get Selection" button to get the selection for either active or control time-frequency window. You may also change or add the parameters by typing in the edit controls (fields) manually.

The computing spectral CxC data largely depends on the spectral data. If there are active and control spectral data, spectral CxC computing can use both data to compute spectral CxC. Otherwise, the program will use whatever spectral data available to compute Spectral CxC data.

#### To define spectral data:

- 1) Select the correct trial or trials based on triggers.
- 2) If multi-trials will be used to compute spectral CxC, select a trial to store the multi-trials results.
- 3) Since spectral CxC uses a huge amount of memory, use "Zip Time" or Zip Frequency" or both to minimize the use of memory.
- 4) Define the time range.
- 5) Define the frequency range.

#### Pre-processing for Spectral CxC

Spectral data can be preprocessed by using spectral processing tools (see Time-Frequency Analyses Guide). The data time-points and latency (milliseconds, ms) are shown to help with the pre-processing of spectral data.

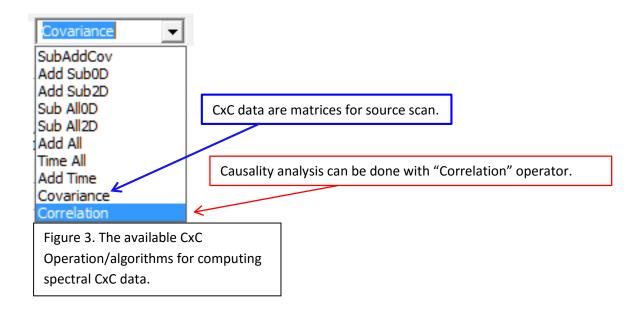
#### Storage of CxC data

For source images based on one trial, the results are typically stored with that trial. For spectral CxC based on multiple trials, the results, which are typically referred as "sum-CxC", are stored in a selected trial. It is necessary to define the targeted trial for storing the results before computing spectral CxC.

#### **CxC Operators**

There are increasing operators for the CxC computing for a variety of purposes. For example, the conventional covariance matrix can be computed with "Covariance". However, instead computing one single matrix, this program can compute a set of covariance matrices with many time slices. The number of time-slices can increase if necessary, the only limitation is probably the computer memory that may limit the number of time-slices.

The "Correlation" operator can be used to compute the correlation of very channel pair. By using time-delay, the Granger Causality can be computed by a few mouse clicks.



# **Sliding Time Window**

To generate a CxC dataset for each sensor pair, the parameters in the Spectral CxC Settings will be used to compute CxC matrices for all sensors. In other words, the time-frequency window and step in time will be applied to all CxC data sets. Since the size of the CxC in the sensor array is the same, many operations/statistical analysis can be applied to the CxC data.

To define an appropriate time window, it is necessary to check the sampling rate so as to define data points (samples) and time (latency).

- 1) "Window (points)" indicates how many data points for a window. The minimum is 1; the maximum is the selection of the data size.
- 2) "Window (ms)" indicates how many milliseconds (ms) for a window. For example, in auditory evoked neuromagnetic activation, a window of 16-26 ms may reliably reveal the correlation between the left and right temporal activation.
- 3) "Step (points)" indicates the interval between two consecutive windows. The minimum is 1; the maximum is the half of the window size.
- 4) "Step (ms)" indicates the interval between two consecutive windows in milliseconds.
- 5) "Time Slice" indicates the number of time-slices in the final CxC datasets or the results of CxC data.

# Single-state or Dual-state CxC Matrix

The single-state option generates spectral CxC based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates CxC that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state



data. To generate a dual-state CxC, you must have both active and control spectral data for computing CxC data.

## **Causality Analysis**

The causality analysis (Granger) is a statistical hypothesis test for determining whether one time series is useful in forecasting another or cause events in another. Specifically, a time series channel A is said to Granger-cause channel B if it can be shown, usually through a series of t-tests and F-tests on lagged values of A (and with lagged values of B also included), that those A values provide statistically significant information about future values of B.

A long held belief about neural function maintained that different areas of the brain were task specific; that the structural connectivity local to a certain area somehow dictated the function of that piece. Collecting work that has been performed over many years, there has been a move to a different, network-centric approach to describing information flow in the brain. Explanation of function is beginning to include the concept of networks existing at different levels and throughout different locations in the brain. The behavior of these networks can be described by non-deterministic processes that are evolving through time. That is to say that given the same input stimulus, you will not get the same output from the network. The dynamics of these networks are governed by probabilities so we treat them as stochastic (random) processes so that we can capture these kinds of dynamics between different areas of the brain.

Waveform CxC can reflect and reveal information flow from the firing activities of a neuron. When the causality is not turn on, the CxC results are limited in the kinds of conclusions you can draw and tell you little about the directional flow of information, to what degree, and how it can change with time. By using time-delay, a kind of Granger causality analysis, the results may show the direction of information flow in the brain.

#### Running Spectral CxC

Click the "Start" button will start to run the Spectral CxC computing. Once it is started, the window title bar will show the progress of the computing.

The Spectral CxC calls several internal dynamically linked libraries to perform a variety of operations. Here are some steps:

- 1) Check and select the spectral data for CxC Computing.
- 2) Perform pre-processing, if necessary.
- 3) Compute coefficients and estimate the necessary memory, if necessary
- 4) Compute spectral CxC data for each channel and each trial
- 5) Compute the summary of all sensor pairs, if necessary
- 6) As usual, the resulting spectral CxC are available to be viewed using spectral CxC Viewer.

# **Set CWT for Spectral CxC**

Selection of "Set CWT for Spectral CxC" menu launches the main window for computing spectral CxC with waveform data, which are matrices with multiple time-frequency slices. The Window GUI application allows you to configure parameters and processing options for spectral CxC computing as well as other kinds of analysis.

Spectral CxC is performed after a dataset has been acquired and reviewed. Here is the recommended procedure for a standard analysis using Spectral CxC programs:

- a) Check and verify that you have the correct dataset and trials in the Waveform Viewer (see the EEG Studio Main Frame Guide).
- b) If data averaging is necessary or required, do the averaging first. Once multiple trials have been averaged successfully, there is at least one averaged trial ("virtual trial") will be added to the MEG dataset, which is available in the main Frame for waveform viewer.
- c) Filtering and/or removing DC-offset is typically required or necessary. If you do think so, apply the filtering/DC-offset to the targeted trial;
- d) Check and analyze the EEG/MEG data to determine the interest of time-window. Though there is no standardized way, it is a good idea to use "Overlay" viewer to determine the interest of time-window with all "sensors".
- e) If the Set CWT for Spectral CxC main window has not been launched. Select "Set CWT for Spectral CxC" in the Menu (see "Menu for Launching Spectral CxC Windows")
- f) During the launching of the window for Settings for Computing Spectral CxC data, the program gets the selected time-window as the Active Window. The program also checks the integrity and sanity of the data and may report warning/error messages if necessary.
- g) Use the window for "CWT Settings" to inspect the dataset as well as suitable parameters. If required or necessary, change the data selections.
- h) Click the "CxC Settings" to define the parameters for computing spectral CxC.

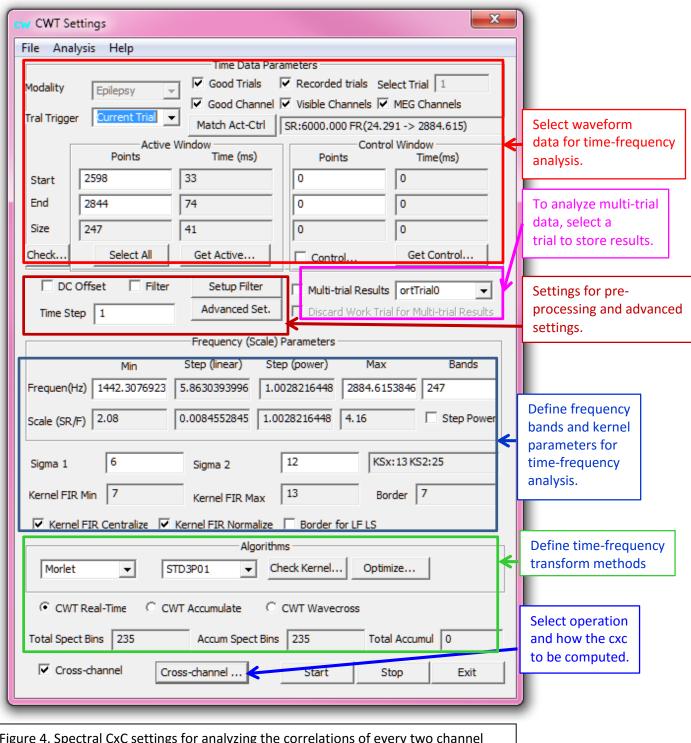


Figure 4. Spectral CxC settings for analyzing the correlations of every two channel pairs in time-frequency domains.

## Main Modules in CxC Computing

The full suite of spectral CxC computing comprises the following components.

- ❖ Wave Data Selection
- Pre-processing for time-frequency transform
- Parameters for time-frequency analysis
- Parameters for CxC computing
- Causality Analysis (Granger)
- Start Spectral CxC computing

# Target data (Time windows)

The data selection specifies the trial, channels to be used for spectral CxC. The time window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the "Get..." button to get the selection for either active or control time window. You may also change or add the parameters by typing in the edit controls (fields) manually.

Time windows are defined relative to some event in the data — either the beginning of the trial (time zero) or a marker. Triggers (one group of Markers) are added automatically by the Data Acquisition application during the recording of data. Typical markers are added by the adding Marker programs. They can also be added manually to mark an event of interest using the Selection Mark application.

If you are generating a single-state image, only active-state windows can be defined. If you are generating a dual-state image, both active- and dual-state windows can be defined.

#### To define a window:

- Click the "Get Active" or "Get Control" button (Active States or Control States) to get the selection in the waveform viewer window.
- You may click the "Select All..." to select all data points.
- To use the control data, you must select "Compute Control" checkbox.
- The Check Select will check the selection of the data.
- The Match Act-Ctl (Active-Control) will match the size of the active and control selection so that they have the same length.

# Pre-processing for Spectral CxC

Wave form data can be preprocessed by using DC-offset, Filter and more advanced settings. Raw sampling rate is shown to help define the parameters such as low and high pass filter as well as the time-window and steps.

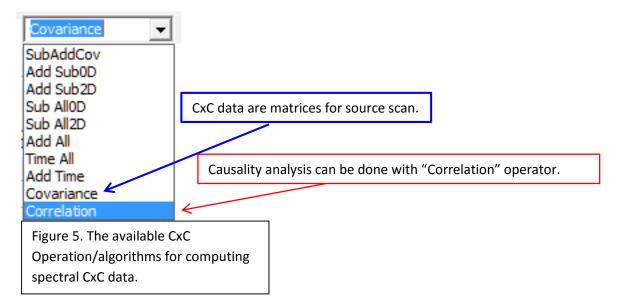
## Storage of CxC data

For source images based on one trail, the results are typically stored with that trial. For spectrograms based on multiple trials, the results, which are typically referred as "sum-spectrograms", are stored in a selected trial. It is necessary to define the targeted trial for storing the results before time-frequency analysis.

# **CxC Operators**

This function is available in the CxC Setting Dialog. There are increasing operators to be used in the CxC computing for a variety of purposes. For example, the conventional waveform covariance matrix can be computed with "Covariance". However, instead computing one single matrix, this program can compute a set of covariance matrices with many time slices as the computer memory can help.

The "Correlation" operator can be used to compute the correlation of very channel pair. By using time-delay, the Granger Causality can be computed by a few mouse clicks.



# **Sliding Time Window**

To generate a CxC matrix for each sensor pair, the parameters in the spectral CxC Settings will be used to compute CxC matrices for all sensors. In other words, the time window and step will be applied to all CxC data sets. Since the size of the CxC in the sensor array is the same and many operations/statistical analysis can be applied to the spectral CxC data.

To define an appropriate time window, it is necessary to check the sampling rate so as to define data points (samples) and time (latency).

1) "Window (points)" indicates how many data points for a window. The minimum is 1; the maximum is the selection of the data size.



- 2) "Window (ms)" indicates how many milliseconds (ms) for a window. For example, in auditory evoked neuromagnetic activation, a window of 16-26 ms may reliably reveal the correlation between the left and right temporal activation.
- 3) "Step (points)" indicates the interval between two consecutive windows. The minimum is 1; the maximum is the half of the window size.
- 4) "Step (ms)" indicates the interval between two consecutive windows in milliseconds.
- 5) "Time Slice" indicates the number of time-slices in the final CxC datasets or the results of CxC data.

# Target Frequency Range

The Frequency (Scale) Parameters panel provides options for specifying which frequency ranges to use when computing spectrogram. The "Min" (minimum) and "Max" (maximum) values in the "frequen" (frequency, Hz) group defines the frequency range. The "Bands" specifies the frequency resolution, which define the number of frequency bands or frequency-bins in the spectrogram.

# **Target Time Slices**

The "Total Spect Bins" specifies the total spectral time bins (or slices) in the spectrogram. There are at least three types of spectrograms can be generated.

- "CWT Real-Time" will generate a spectrogram that keeps all the temporal information by using a sliding window.
- "CWT Accumulate" will generate a spectrogram that accumulates a long-time window into a short-time window for keeping the frequency information without tracking all the temporal information. This type of spectrogram requires a small amount of memory/hard disk to characterize a huge amount of data.
- "CWT Wave Cross" will generate a spectrogram that keeps all the temporal information as well as frequency information by using two sigma values.

# **Dimension of Spectrograms**

To generate a spectrogram for each sensor, the parameters in the CWT Settings will be used to compute spectrograms for all sensors. In other words, the region of time window for time-frequency analysis defines the dimensions of all sensors' spectrograms. In other words, the size of the spectrograms in the sensor array is the same and many operations/statistical analysis can be applied to the spectral data.

To define an appropriate size for spectrogram:

- Ensure the "Bands" and "Spect Bins" are not too big or too small.
- Although it is possible that the entire data can be used to compute spectrogram with a high frequency resolution, a large spectrogram may take a lot memory.
- Low-frequency components will significantly increase computation time. If necessary, use "Resampling" technique to decrease the computation time (see "EEG Studio Main Frame Guide").
- The meaning of the "spectrogram" depends on the time-frequency algorithms.

## Single-state or Dual-state CxC Matrix

The single-state option generates spectrograms based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates spectrograms that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control data for time-frequency analysis.

The spectral computing depends on the settings of time-frequency transform. For example, if dual-state option is selected and the program will generate spectrograms that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. Consequently, dual-state CxC data will be computed.

# **Causality Analysis**

The causality analysis (Granger) is a statistical hypothesis test for determining whether one time series is useful in forecasting another or cause events in another. Specifically, a time series channel A is said to Granger-cause channel B if it can be shown, usually through a series of t-tests and F-tests on lagged values of A (and with lagged values of B also included), that those A values provide statistically significant information about future values of B.

A long held belief about neural function maintained that different areas of the brain were task specific; that the structural connectivity local to a certain area somehow dictated the function of that piece. Collecting work that has been performed over many years, there has been a move to a different, network-centric approach to describing information flow in the brain. Explanation of function is beginning to include the concept of networks existing at different levels and throughout different locations in the brain. The behavior of these networks can be described by non-deterministic processes that are evolving through time. That is to say that given the same input stimulus, you will not get the same output from the network. The dynamics of these networks are governed by probabilities so we treat them as stochastic (random) processes so that we can capture these kinds of dynamics between different areas of the brain.

Waveform CxC can reflect and reveal information flow from the firing activities of a neuron. When the causality is not turn on, the CxC results are limited in the kinds of conclusions you can draw and tell you little about the directional flow of information, to what degree, and how it can change with time. By using time-delay, a kind of Granger causality analysis, the results may show the direction of information flow in the brain.

## Running Spectral CxC

Click the "Start" button will start to run the Spectral CxC computing. Once it is started, the window title bar will show the progress of the computing.

The Spectral CxC calls several internal dynamically linked libraries to perform a variety of operations. Here are some steps:

- 1) Check and select the waveform data for CxC Computing.
- 2) Perform filtering and removing DC-offset, if necessary.
- 3) Compute coefficients and estimate the necessary memory, if necessary
- 4) Perform time-frequency transform
- 5) Check and verify the spectral data for CxC computing
- 6) Compute CxC data for each channel and each trial
- 7) Compute the summary of all sensor pairs, if necessary
- 8) As usual, the resulting CxC are available to be viewed using Spectral CxC Viewers.

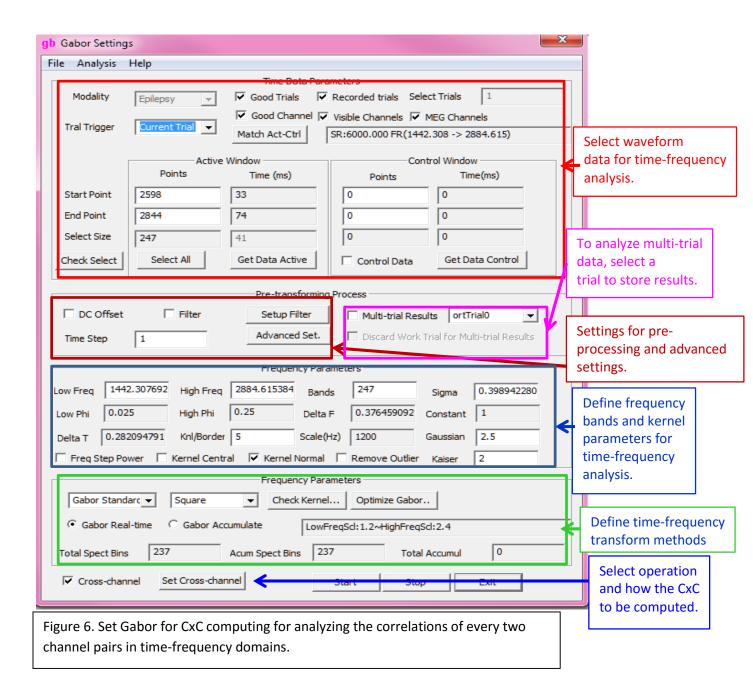
# **Set Gabor for Spectral CxC**

Selection of "Set Gabor for Spectral CxC" menu launches the main window for computing spectral CxC data, which are matrices with multiple time-frequency slices. The Window GUI application allows you to configure parameters and processing options for spectral CxC computing as well as other kinds of analysis.

Spectral CxC is performed after a dataset has been acquired and reviewed. Here is the recommended procedure for a standard analysis using Spectral CxC programs:

- i) Check and verify that you have the correct dataset and trials in the Waveform Viewer (see the EEG Studio Main Frame Guide).
- j) If data averaging is necessary or required, do the averaging first. Once multiple trials have been averaged successfully, there is at least one averaged trial ("virtual trial") will be added to the MEG dataset, which is available in the main Frame for waveform viewer.
- k) Filtering and/or removing DC-offset is typically required or necessary. If you do think so, apply the filtering/DC-offset to the targeted trial;
- Check and analyze the EEG/MEG data to determine the interest of time-window. Though there is no standardized way, it is a good idea to use "Overlay" viewer to determine the interest of time-window with all "sensors".
- m) If the Set Gabor for Spectral CxC main window has not been launched. Select "Set Gabor for Spectral CxC" in the Menu (see "Menu for Launching Spectral CxC Windows")
- n) During the launching of the window for Settings for Computing Spectral CxC data, the program gets the selected time-window as the Active Window. The program also checks the integrity and sanity of the data and may report warning/error messages if necessary.
- o) Use the window for "Gabor Settings" to inspect the dataset as well as suitable parameters. If required or necessary, change the data selections.

p) Click the "CxC Settings" to define the parameters for computing spectral CxC.



#### Main Modules in Gabor based CxC Computing

The full suite of waveform source scan comprises the following components.

- ❖ Wave Data Selection
- Pre-processing for time-frequency transform

- Parameters for time-frequency analysis
- Parameters for CxC computing
- Causality Analysis (Granger)
- Start Spectral CxC computing

## Target data (Time windows)

The data selection specifies the trial, channels to be used for spectral CxC. The time window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the "Get..." button to get the selection for either active or control time window. You may also change or add the parameters by typing in the edit controls (fields) manually.

Time windows are defined relative to some event in the data — either the beginning of the trial (time zero) or a marker. Triggers (one group of Markers) are added automatically by the Data Acquisition application when the recording of data. Typical markers are added by the adding Marker programs. They can also be added manually to mark an event of interest using the Selection Mark application.

If you are generating a single-state image, only active-state windows can be defined. If you are generating a dual-state image, both active- and dual-state windows can be defined.

#### To define a window:

- Click the "Get Active" or "Get Control" button (Active States or Control States) to get the selection in the waveform viewer window.
- You may click the "Select All..." to select all data points.
- To use the control data, you must select "Compute Control" checkbox.
- The Check Select will check the selection of the data.
- The Match Act-Ctl (Active-Control) will match the size of the active and control selection so that they have the same length.

# Pre-processing for Spectral CxC

Wave form data can be preprocessed by using DC-offset, Filter and more advanced settings. Raw sampling rate is shown to help define the parameters such as low and high pass filter as well as the time-window and steps.

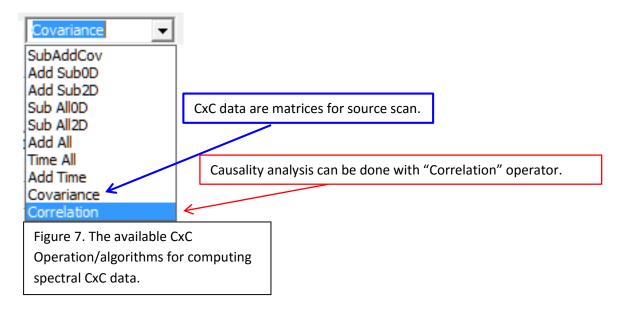
# Storage of CxC data

For source images based on one trail, the results are typically stored with that trial. For spectrograms based on multiple trials, the results, which are typically referred as "sum-spectrograms", are stored in a selected trial. It is necessary to define the targeted trial for storing the results before time-frequency analysis.

## **CxC Operators**

This function is available in the CxC Setting Dialog. There are increasing operators to be used in the CxC computing for a variety of purposes. For example, the conventional waveform covariance matrix can be computed with "Covariance". However, instead computing one single matrix, this program can compute a set of covariance matrices with many time slices as the computer memory can help.

The "Correlation" operator can be used to compute the correlation of very channel pair. By using time-delay, the Granger Causality can be computed by a few mouse clicks.



#### **Sliding Time Window**

To generate a CxC matrix for each sensor pair, the parameters in the spectral CxC Settings will be used to compute CxC matrices for all sensors. In other words, the time window and step will be applied to all CxC data sets. Since the size of the CxC in the sensor array is the same and many operations/statistical analysis can be applied to the spectral CxC data.

To define an appropriate time window, it is necessary to check the sampling rate so as to define data points (samples) and time (latency).

- "Window (points)" indicates how many data points for a window. The minimum is 1; the maximum is the selection of the data size.
- "Window (ms)" indicates how many milliseconds (ms) for a window. For example, in auditory evoked neuromagnetic activation, a window of 16-26 ms may reliably reveal the correlation between the left and right temporal activation.
- "Step (points)" indicates the interval between two consecutive windows. The minimum is 1; the maximum is the half of the window size.
- "Step (ms)" indicates the interval between two consecutive windows in milliseconds.

• "Time Slice" indicates the number of time-slices in the final CxC datasets or the results of CxC data.

# **Target Frequency Range**

The Frequency (Scale) Parameters panel provides options for specifying which frequency ranges to use when computing spectrogram. The "Min" (minimum) and "Max" (maximum) values in the "frequen" (frequency, Hz) group defines the frequency range. The "Bands" specifies the frequency resolution, which define the number of frequency bands or frequency-bins in the spectrogram.

# **Target Time Slices**

The "Total Spect Bins" specifies the total spectral time bins (or slices) in the spectrogram. There are at least three types of spectrograms can be generated.

- "Gabor Real-Time" will generate a spectrogram that keeps all the temporal information by using a sliding window.
- "Gabor Accumulate" will generate a spectrogram that accumulates a long-time window into a short-time window for keeping the frequency information without tracking all the temporal information. This type of spectrogram requires a small amount of memory/hard disk to characterize a huge amount of data.

# **Dimension of Spectrograms**

To generate a spectrogram for each sensor, the parameters in the CWT Settings will be used to compute spectrograms for all sensors. In other words, the region of time window for time-frequency analysis defines the dimensions of all sensors' spectrograms. In other words, the size of the spectrograms in the sensor array is the same and many operations/statistical analysis can be applied to the spectral data.

To define an appropriate size for spectrogram:

- Ensure the "Bands" and "Spect Bins" are not too big or too small.
- Although it is possible that the entire data can be used to compute spectrogram with a high frequency resolution, a large spectrogram may take a lot memory.
- Low-frequency components will significantly increase computation time. If necessary, use "Resampling" technique to decrease the computation time (see "EEG Studio Main Frame Guide").
- The meaning of the "spectrogram" depends on the time-frequency algorithms.

# Single-state or Dual-state CxC Matrix

The single-state option generates spectrograms based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates spectrograms that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from

active state data. To generate a dual-state image, you must select both active and control data for time-frequency analysis.

The spectral computing depends on the settings of time-frequency transform. For example, if dual-state option is selected and the program will generate spectrograms that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. Consequently, dual-state CxC data will be computed.

# **Causality Analysis**

The causality analysis (Granger) is a statistical hypothesis test for determining whether one time series is useful in forecasting another or cause events in another. Specifically, a time series channel A is said to Granger-cause channel B if it can be shown, usually through a series of t-tests and F-tests on lagged values of A (and with lagged values of B also included), that those A values provide statistically significant information about future values of B.

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#### Running Spectral CxC

Click the "Start" button will start to run the Spectral CxC computing. Once it is started, the window title bar will show the progress of the computing.

The Spectral CxC calls several internal dynamically linked libraries to perform a variety of operations. Here are some steps:

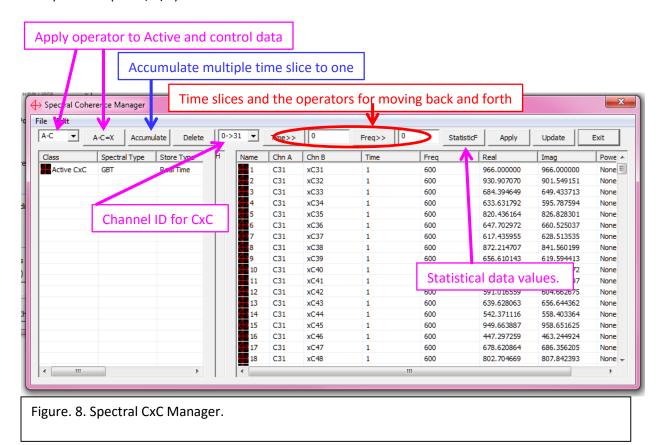
- 1) Check and select the waveform data for CxC Computing.
- 2) Perform filtering and removing DC-offset, if necessary.

- 3) Compute coefficients and estimate the necessary memory, if necessary
- 4) Perform time-frequency transform
- 5) Check and verify the spectral data for CxC computing
- 6) Compute CxC data for each channel and each trial
- 7) Compute the summary of all sensor pairs, if necessary
- 8) As usual, the resulting CxC are available to be viewed using Spectral CxC Viewers.

# **Spectral CxC Manager**

Spectral CxC data can be viewed, edited and analyzed quantitatively with Spectral CxC Manager. In the new version of this program, operation can be applied to Active CxC data and Control CxC data to generate Act-Ctl data, which is the result from the Active and control CxC data. The operations include:

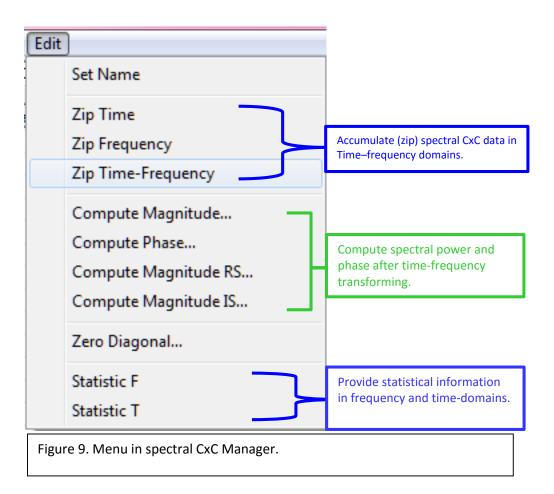
- 1) Subtraction (A-C)
- 2) Summation (A+C)
- 3) Covariance (Time, A\*C)
- 4) Divide (Ratio, A/C)



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# Menu in Spectral CxC Manager

Spectral CxC data can have many time-slices. Multi-time slice data may reveal dynamic changes of every channel pair. To quantify the characteristics of all channel paired during the entire period of time, a function ("Zip Time") has been designed to accumulate multiple time slices to one time-slice. The one slice may reveal the stationary correlations of all channel pairs.



# **Accumulating Multi-Time Slices to One Time-Slice (Zip-Time)**

Spectral CxC data can have many time-slices. Multi-time slice data may reveal dynamic changes of every channel pair. To quantify the characteristics of all channel paired during the entire period of time, a function ("Zip Time") has been designed to accumulate multiple time slices to one time-slice. The one slice may reveal the stationary correlations of all channel pairs.

The accumulating or zipping of CxC time-frequency data may significantly minimize the use of computer memory. In addition, it can provide an unique view of the data in time or frequency domain.

# Accumulating Multi-Frequency Slices CxC to One Frequency-Slice (Zip-Frequency)

Spectral CxC data can have many frequency-slices. Multi-frequency slice data may reveal dynamic changes of every channel pair. To quantify the characteristics of all channel pairs across the entire frequency bands, a function ("Zip Frequency") has been designed to accumulate multiple frequency slices to one slice.

The accumulating or zipping of CxC time-frequency data may significantly minimize the use of computer memory. In addition, it can provide an unique view of the data in time or frequency domain.

# Accumulating Multi-Time-Frequency Slices CxC to One Slice (Zip-Time-Frequency)

Spectral CxC data can have many time-frequency-slices. To quantify the characteristics of all channel pairs during the time window and across the entire frequency bands, a function ("Zip Time-Frequency") has been designed to accumulate multiple time-frequency slices to one slice.

The accumulating or zipping of CxC time-frequency data may significantly minimize the use of computer memory. In addition, it can provide an unique view of the data in time or frequency domain.

# **CxC Diagonal**

The diagonal values in Spectral CxC data have some special meanings. For example, in covariance matrix of EEG/MEG data, the diagonal values may reflect the sensor noise. In correlation matrix, the diagonal values may be 1. This program has designed function to zero diagonal value. To zero diagonal values, launch the Spectral CxC Manager, then select the Edit Menu-> Zero Diagonal.

# Statistic of Spectral CxC

In spectral CxC manager, there are two functions can provide statistical information about the minimum, maximum, mean and RMS values of the Spectral CxC data.

The "Statistic F" provides the statistical information about the spectral CxC data in frequency domain (each frequency band or bin) while the "Statistic T" provide the statistical information about the spectral CxC data in time domain (each time point or slice).

# Visualization of Spectral CxC Data

CxC data can be visualized in both 2D and 3D. In either 2D or 3D visualization, CxC data of EEG/MEG data can be plotted as link view and topographic (contour map) view.

The link view is designed for viewing the correlation or interaction to two channels. The topographic view is designed for viewing a group of sensors with one central channel for a specified time interval. Of note, there are several ways of graphically representing the data. The visualization of the CxC data varies slightly among the versions of the software.

# **Launching Spectral CxC Link Viewers**

Since this program computes the correlation or interaction of channel pairs in several ways, the data visualization windows may be different from the conventional coherence viewers.

Importantly, this program provides three classes of 2D viewers and three classes of 3D Viewers. The spectral data can be displayed as links, map and single plate. For example, the viewers include:

- ✓ Active Spectral CxC 2D Link Viewer;
- ✓ Control Spectral CxC 2D Link Viewer;
- ✓ Act-Ctl Spectral CxC 2D Link Viewer;
- ✓ Active Spectral CxC 3D Link Viewer;
- ✓ Control Spectral CxC 3D Link Viewer;
- ✓ Act-Ctl Spectral CxC 3D Link Viewer;

In some cases, the time courses of the correlation and interaction in channel pairs are important. The program has also designed three viewers to the CxC waveforms.

- Active Spectral CxC 2D Map Viewer;
- Control Spectral CxC 2D Map Viewer;
- Act-Ctl Spectral CxC 2D Map Viewer;
- Active Spectral CxC 2D One Channel Viewer;
- Control Spectral CxC 2D One Channel Viewer;
- Act-Ctl Spectral CxC 2D One Channel Viewer;
- Active Spectral CxC 3D Map Viewer;
- Control Spectral CxC 3D Map Viewer;
- Act-Ctl Spectral CxC 3D Map Viewer;
- Active Spectral CxC 3D One Channel Viewer;
- Control Spectral CxC 3D One Channel Viewer;
- Act-Ctl Spectral CxC 3D One Channel Viewer;

Please see the "Classification of CxC Data" for explanation about Active, Control and Act-Ctl CxC data.

# **CxC 2D Link Viewer**

Spectral CxC 2D Link Viewers are commonly used to analyze the spatial correlation of spectral data in all sensors in a specified time-frequency range. In this program, one link shows a link of one channel pair. If color is used, red color is typically used to represent positive correlation or interaction (plus), while blue color is typically used to represent negative correlation or interaction (minus). One circle is typically used to represent the sensor location. This is kind of "coherence" plots of all channels, in a quasi-topographical layout in a specified time interval.

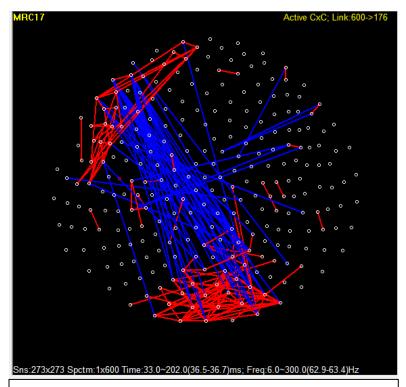


Figure 10. Spectral CxC Link Viewer.

#### Display Controls for Spectral CxC 2D Link

The Spectral CxC 2D Link Viewer provides a set of options and controls for appropriately displaying the CxC data in all sensors or a group of selected sensors. All the options and the controls are on the top-left of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The Spectral CxC 2D Map shows the details about the display items and their controls.

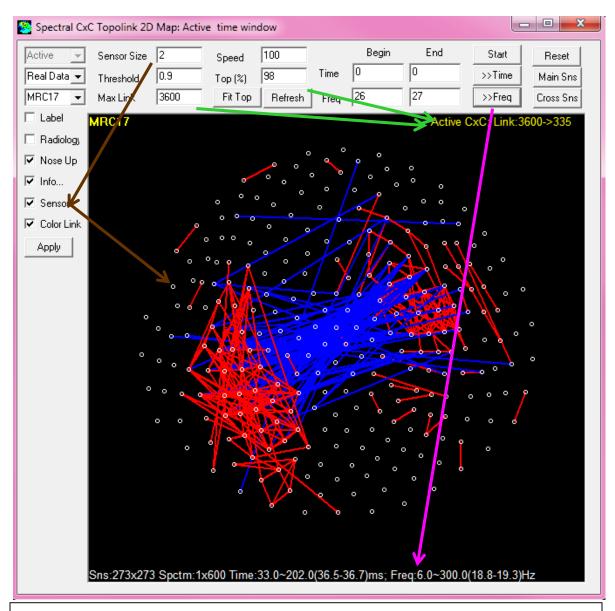


Figure 11. Controls for wave CxC 2D link viewer.

## Operations in Spectral CxC 2D Link Viewer

The 2D Link Viewer provides a set of options and controls for appropriately displaying the CxC data. All the options and the controls are on the top of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The following figure shows the details about the display items and their controls.

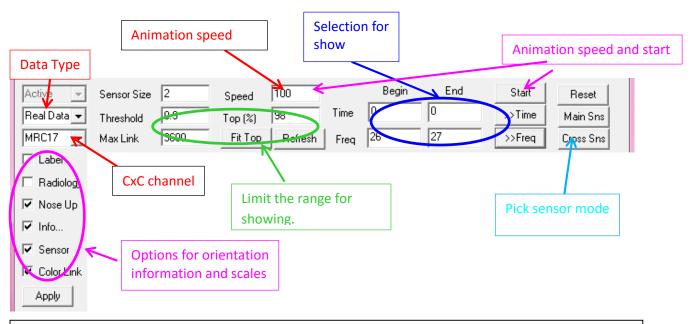


Figure 12. Controls and options in Spectral CxC 2D Link Viewer for a group of sensors.

# Spectral CxC 3D Link Viewer

Spectral 3D Link Viewers are commonly used to analyze the spatial correlation of spectral data in all sensors in a specified time range. In this program, one link shows a link of one channel pair. If color is used, red color is typically used to represent positive correlation or interaction (plus), while blue color is typically used to represent negative correlation or interaction (minus). One torus (cube or ball) is typically used to represent the sensor location. This is kind of "coherence" plots of all channels in 3D coordinate in a specified time interval.

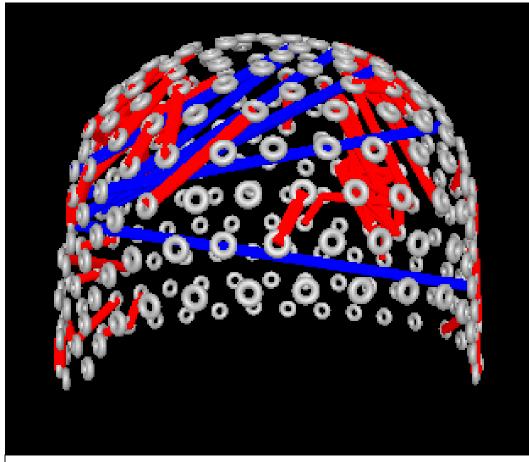


Figure 13. Visualization of wave CxC data in 3D.

# Display Controls for CxC 3D Viewer

The 2D Single Channel Viewer provides a set of options and controls for appropriately displaying the spectral data. All the options and the controls are on the top of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The following figure shows the details about the display items and their controls.

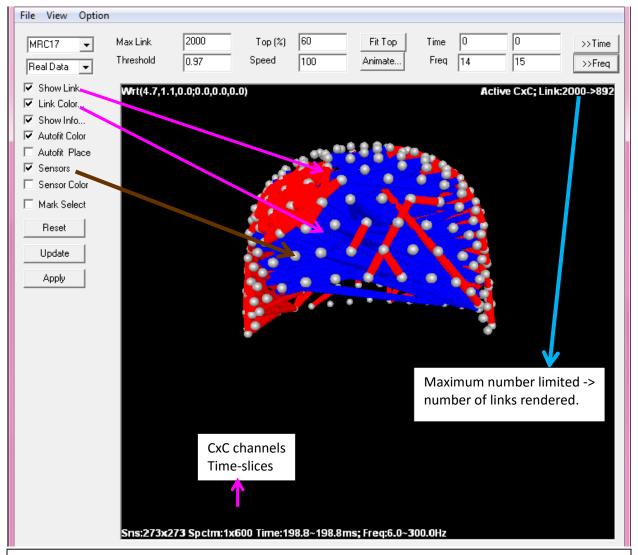
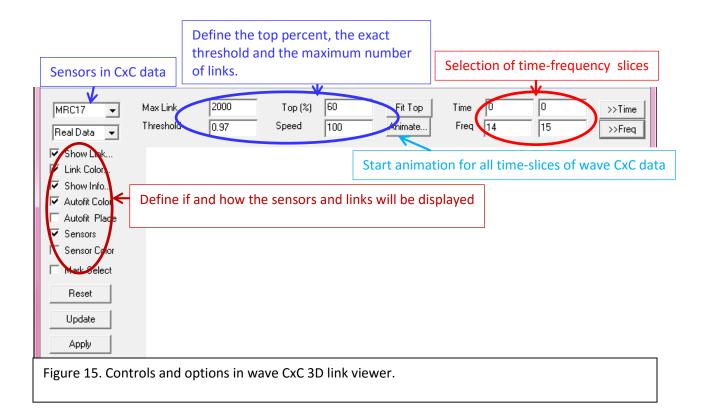


Figure 14. The options and controls of Spectral CxC 3D Link Viewer for all channel pairs.

#### Operations in Spectral CxC 3D Viewer

The Spectral CxC 3D link viewer provides a set of tools to operate and analyze waveform CxC data. If the 3D links is computed with multiple time slices, you may select to show the correlation or interaction of sensor pairs in certain latency range or interval.

The number of links can be defined by use both top percentile and absolute threshold. To avoid time-delay, you may limit the maximum number of links or connections. If the number of links meeting the threshold is larger than that of the maximum number of links, the number of links rendered in the 3D viewer will change to red.



#### Menu in Spectral CxC 3D Link

The Spectral CxC 3D link viewer can be used to visualize and analyze the correlation and interaction of all sensor pairs or a group of sensor pairs.

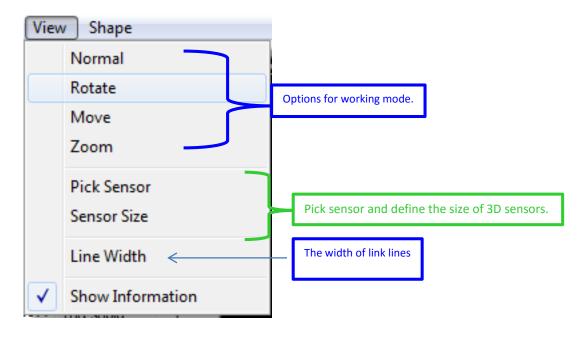


Figure 16. Menu in spectral CxC 3D Link Viewer.

#### Spectral CxC 2D Map

Spectral CxC 2D maps (topographic CxC virtual channel waveforms) are commonly used to analyze the spatial distribution of CxC data in a specified time ranges or interval. In this program, the amplitude of virtual channel waveform from a sensor can be color coded and displayed on the sensor. This is kind of time-course plots of all channel pairs, in a quasi-topographical and varies among the version due to the variation of the usage of CxC data.

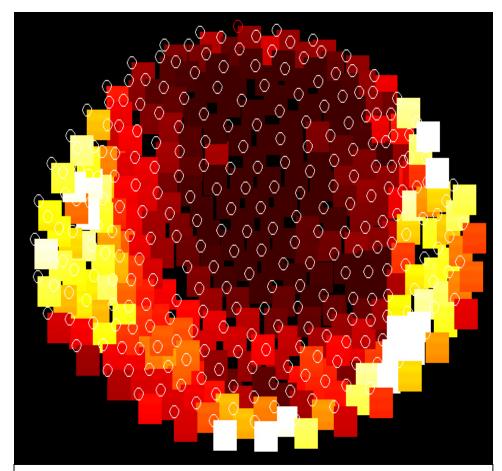


Figure 17. Visualization of spectral CxC data with 2D virtual channel spectrogram (2D topographic spectral patch). In this type of 2D map, each small torus represents a sensor. To minimize the use of memory, both time and frequency can be accumulated as one slice, which will be a vertical or horizontal line.

#### Display controls for 2D CxC Map

The 2D Contour Map Viewer or Topographic Viewer provides a set of options and controls for appropriately displaying the spectral data in all sensors or a group of selected sensors. All the options and the controls are on the top-left of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The "Controls for Contour Map" shows the details about the display items and their controls.

## **Spectral CxC**

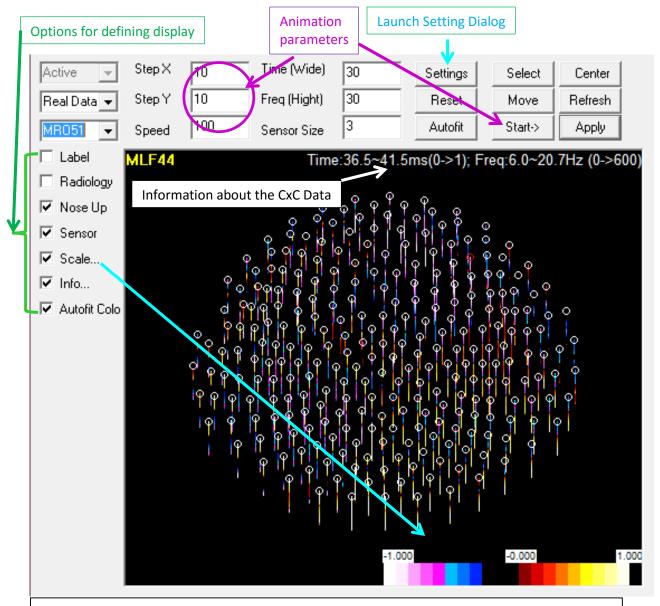


Figure 18. Controls for 2D contour map (topographic spectrogram) shows spectral CxC data with one time slice (accumulated in time domain).

# Spectral CxC 2D Time-Frequency Plate (Time-Frequency representation for one sensor)

2D spectrogram for single channel, which is typically showed as a plate, is commonly used to analyze the spectral values in a specified time-frequency ranges. In this program, one plate shows the spectrogram from on sensor.

It has to be emphasized that a spectrogram can be computed from a group of sensor. A summation (e.g. mean values, maximum values and minimum values of a group of sensor can be showed in the 2D Time-Frequency Plate by selecting it in the combo box.

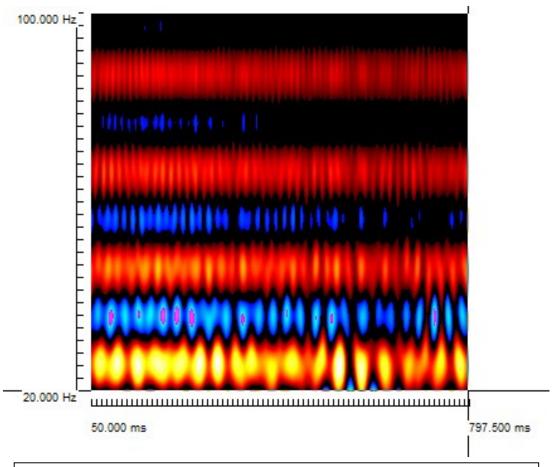


Figure 19. Visualization of the time-frequency representation for single sensor in 2D.

#### Display Controls for Spectral CxC 2D Single Channel Viewer

The Spectral CxC 2D Single Channel Viewer provides a set of options and controls for appropriately displaying the spectral data. All the options and the controls are on the top of the window (or Dialog).

The Dialog provides a lot of flexibility and power for you to control the display. The following figure shows the details about the display items and their controls.

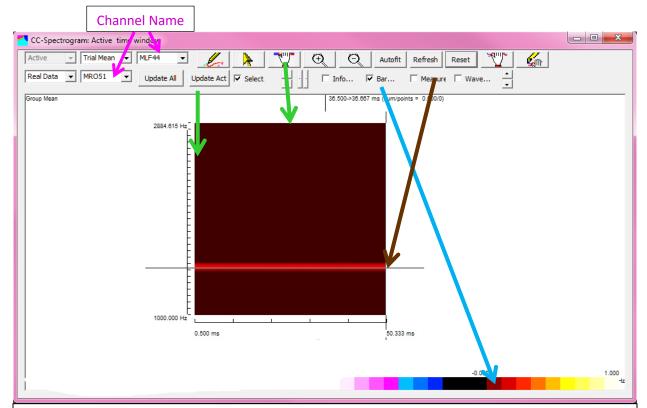


Figure 20. The options and controls of Spectral CxC 2D Viewer for Single Channel or a summation of spectrograms from a group of sensors. If the summation of spectrograms is from all sensors within a MEG dewar or a EEG array, the summation is also called global spectrogram.

#### Operations in 2D Single Channel Viewer

The 2D Single Channel Viewer also provides a set of tools to operate and analyze the time-frequency representations of oscillatory data. To measure the latency, frequency and spectral values, please make sure that the "Select" and the "Measure..." check boxes are checked. The select lines will show the location of the measuring point or area.

If the spectrogram is computed with waveform data from one sensor, the waveform can also be displayed with the matched time-window by checking the "Wave..." check box. Of course, the waveforms can be moved up-down, left-right to give a best display for both spectrogram and waveforms.

The easiest way to find a suitable display is to click "Autofit" and "Reset" Buttons if the spectrogram appears unfavorable.

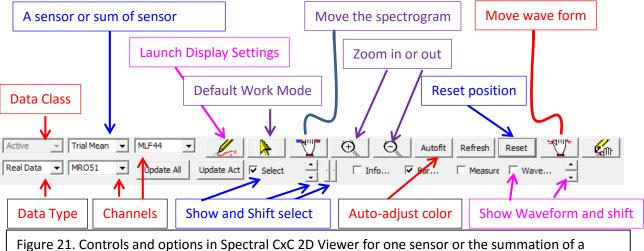


Figure 21. Controls and options in Spectral CxC 2D Viewer for one sensor or the summation of a group of sensors.

#### Global and group spectrogram in 2D Viewer

The 2D Single Channel Viewer can also be used to visualize and analyze the summation of spectrograms computed from a group of sensors. If the group sensors are the entire sensor array (or MEG dewar), the summation of the spectrograms is also called global spectrogram. The summation of group spectrograms can be described as a few sub-types:

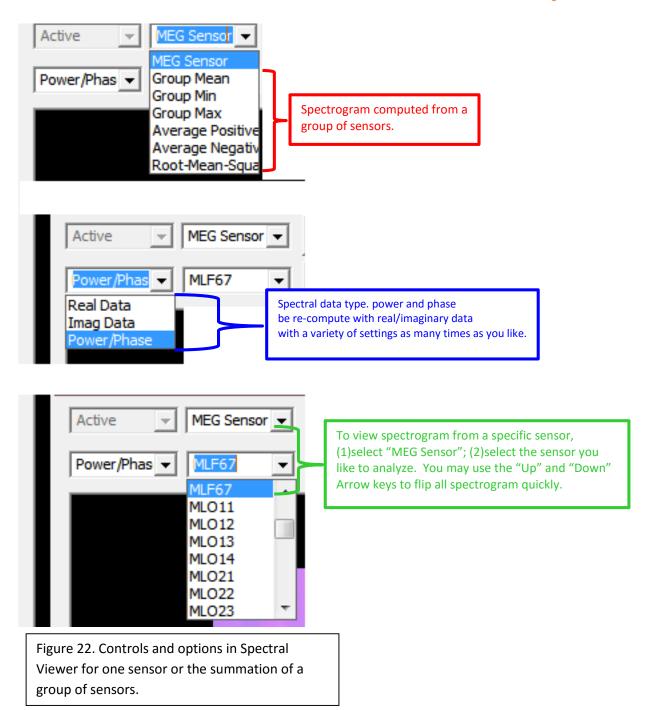
- 1) Group Mean
- 2) Group Min (minimum, negative)
- 3) Group Max (maximum, positive)
- 4) Averaged Positive (magnetic goes out/in)
- 5) Averaged Negative (magnetic goes in/out)
- 6) Root-Mean-Square (RMS)

To view the summation type of spectrogram, select and specify it from the corresponding Combo box as following figure. Specifically, to view spectrogram from a specific sensor:

- (1) select "MEG Sensor";
- (2) select the sensor you like to analyze.

You may use the "Up" and "Down" Arrow keys to flip all spectrogram quickly.

It is important to point it out that spectral data type "Power/Phase) can be re-compute with real/imaginary data with a variety of settings as many times as you like.



## 2D View Parameters for Displaying Spectral CxC Data

The spectral values may vary among algorithms for time-frequency transforms. To appropriately display spectrum, the ranges of low and high limits of the spectral data are important. To enable users to easily and appropriately adjust the parameters, a window (dialog) has been designed to visually set or change the parameters.

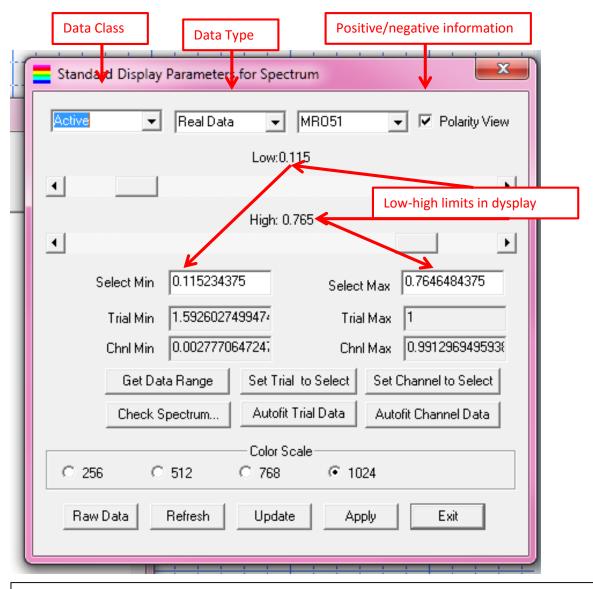


Figure 23. Standard Display Parameters for Spectral CxC 2D Spectrogram.

In the Standard Display Parameters for 2D Spectrum, there are two combo boxes, which enable you to check and get the data range of a specified data class and type. Consequently, the data display can be precisely controlled and presented.

The low and high limits of the display values are absolute values. If there are negative values, the values will be judged in absolute values. If "Magnetic Polarity View" is checked, the magnetic/electric polarity information will be displayed by using two color coding systems, one for negative numbers and one for positive numbers.

- 1) Visible range of spectral values: The "Select Low" and "Select High" can be adjusted with the horizontal scroll bars. If you know the exact values (very common for experienced researchers/clinicians), you may directly input the values in the "Select Min" and "Select Max" edit fields. The selected values define and specify the data range for spectral display.
- 2) The range of spectral data in the current trial: The "Trial Min" and "Trial Max" show the range of spectral data in the current trial that is shown in the Spectral Contour Map and Topographic Viewer. You may click the "Get Data Range" to retrieve the data ranges. The range of spectral data in the current trail is very important for Spectral Contour map.
- 3) The range of spectral data in the current channel (sensor): The "Chnl Min" and "Chnl Max" show the range of spectral data in the current channel that is shown in the single channel viewer. You may click the "Get Data Range" to retrieve the data ranges. The range of spectral data in the current trail is very important for spectrogram for single channel.
- 4) Set Trial and Channel to Select: The "Set Trial to Select" and "Set Channel to Select" get the trial and channel data and transfer the ranges to the selected minimum (low) and maximum (high). The two functions enable you to view the full range of data in either Spectral Contour Map or Spectral Single Channel Viewer easily.
- 5) Check Spectrum function: the "Check Spectrum" function checks the integrity and sanity of the spectral data in the entire trails, e.g. the data range and the size and errors.
- 6) Automatically fit Trial Data and Channel data: the "Autofit Trial Data" and "Autofit Channel Data" compute or retrieve the data range and automatically define the range for appropriate showing according to the default settings. This function is based on experience with thousands of MEG datasets (http://clinicaltrials.gov/show/NCT00600717).
- 7) Color Scale and Color Coding: There are at least 4 groups of color scale (256, 512, 768 and 1024) for coding the spectrograms. Of note, the color scale will change the dysplay of the data, it does not change the data. Therefore, you are free to try all the color scales and find the best to meet your taste and requirements.
- 8) Raw data: If you did anything wrong that may change the data, you may click the "Raw data" to get the original data that are typically stored during time-frequency transforms.
- 9) Refresh: the "Refresh" button updates all viewers.
- 10) Other buttons are self-explainable.

### **Spectral CxC 3D Time-Frequency Contour Map**

3D spectral contour maps (topographic spectrogram) are commonly used to analyze the spatial distribution of EEG/MEG data in a specified time-frequency ranges. In this program, the magnitude of spectrogram from a sensor is color coded and displayed on the sensor. A sensor can be showed as a torus, cube or ball. In this manual, we typically use a torus to represent a 3D sensor, which has the location as well as orientation. This is kind of time-frequency plots of all channels, in a quasi-topographical layout in a specified time-frequency interval.

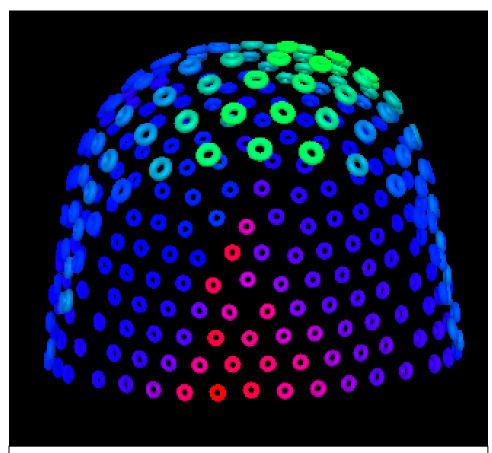


Figure 24. Visualization of time-frequency representation of MEG data with 3D spectral contour map (3D topographic spectrogram). In this type of "spectral contour map", each small torus represents a sensor. The magnitude of the spectrogram at a selected time-frequency range is color-coded in each sensor.

#### Display controls for 3D Contour Map

The 3D Contour Map Viewer or Topographic Viewer provides a set of options and controls for appropriately displaying the spectral data in all sensors or a group of selected sensors. All the options and the controls are on the top of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The "Controls for Contour Map" shows the details about the display items and their controls.

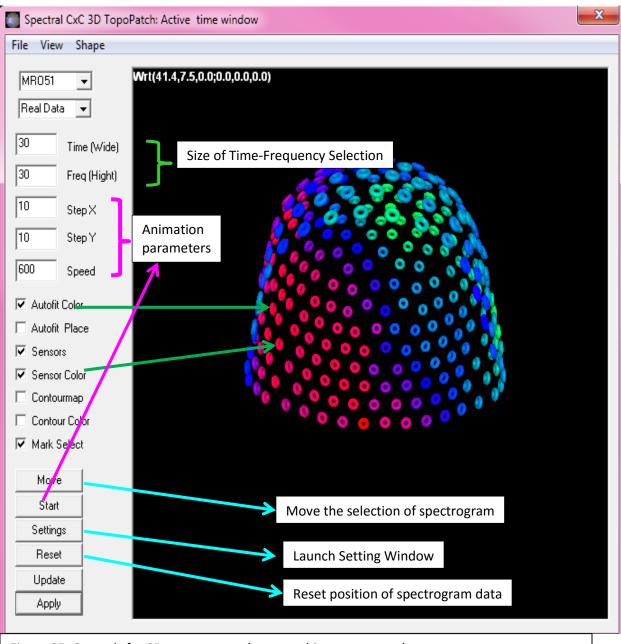


Figure 25. Controls for 3D contour map (topographic spectrogram).

#### Menu in 3D Contour Map

The Menu in 3D Single Channel Viewer provides a set of options and controls for appropriately displaying the spectral data. The options and the controls change the "working mode", which is indicated by the cursor. Once the "working mode" is set, press-the left mouse button and move the mouse will change the display. In this manner, it provides a dynamic visual feedback and has a lot of



flexibility for you to control the display. The following figure shows the details about the display items and their controls.

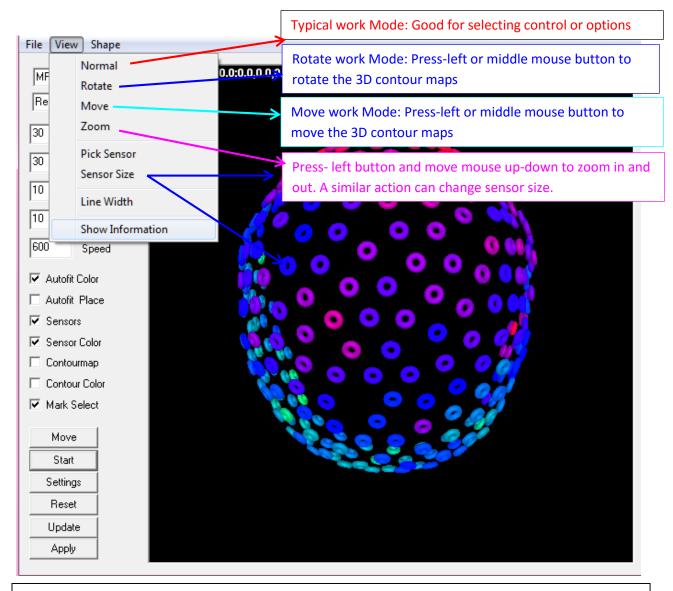


Figure 26. Menu for spectral CxC 3D contour map (topographic spectrogram).

# **CxC 3D Time-Frequency Plate (Time-Frequency representation for one sensor)**

3D spectrogram for single channel, which is typically showed as a 3D plate with peaks and troughs, is commonly used to analyze the spectral values in a specified time-frequency ranges. In this program, one plate shows the spectrogram from on sensor.

It has to be emphasized that a spectrogram can be computed from a group of sensor. A summation (e.g. mean values, maximum values and minimum values of a group of sensor can be showed in the 2D Time-Frequency Plate by selecting it in the combo box.

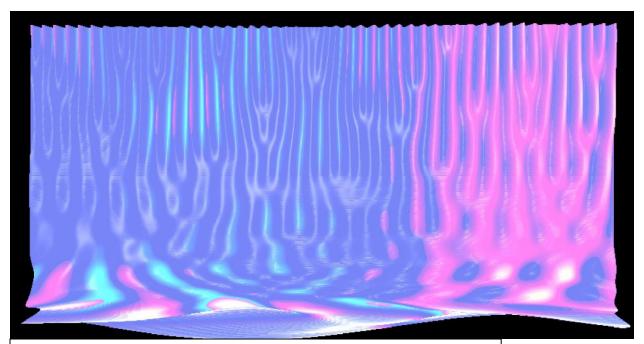


Figure 27. Visualization of the time-frequency representation for one sensor in 3D.

#### Display Controls for 3D Single Channel Viewer

The 3D Single Channel Viewer provides a set of options and controls for appropriately displaying the spectral data. All the options and the controls are on the top of the window (or Dialog). The Dialog provides a lot of flexibility and power for you to control the display. The following figure shows the details about the display items and their controls.

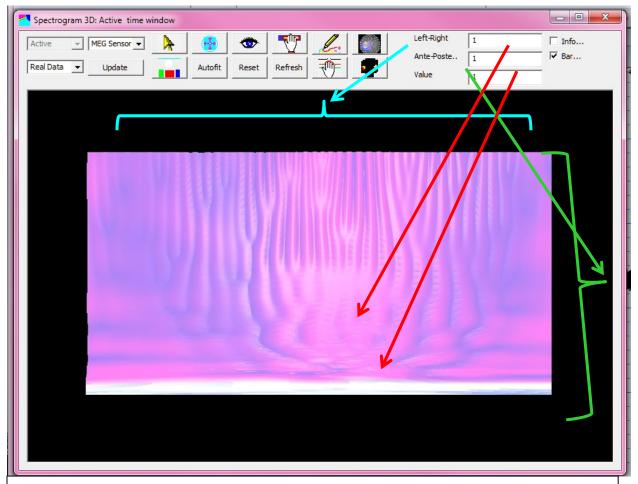


Figure 28. The options and controls of 3D Spectral Viewer for Single Channel or a summation of a group of sensors. If the summation of spectrograms is from all sensors within a MEG dewar or a EEG array, the summation is also called global spectrogram.

#### Operations in 3D Single Channel Viewer

The 3D Single Channel Viewer also provides a set of tools to operate and analyze the time-frequency representations of oscillatory data. To analyze the latency, frequency and spectral values, please make sure that the parameters are appropriate used.

If the range of the spectral data is very large, please try to use the "Rotate" and "Zoom" to adjust the position and depth for viewing.

The easiest way to find a suitable display is to click, "Reset", "Autofit" and "Fit Peak" Buttons if the spectrogram appears unfavorable.

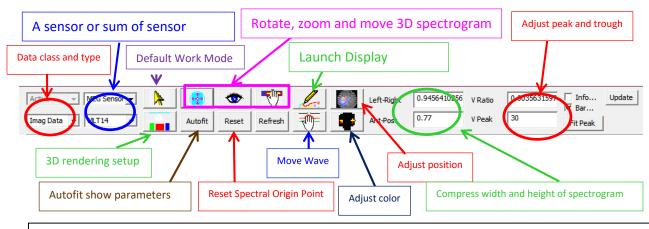


Figure 29. Controls and options in Spectral Viewer for one sensor or the summation of a group of sensors.

#### Global and group spectrogram in 3D Viewer

The 3D Single Channel Viewer can also be used to visualize and analyze the summation of spectrograms computed from a group of sensors. If the group sensors are the entire sensor array (or MEG dewar), the summation of the spectrograms is also called global spectrogram. The summation of group spectrograms can be described as a few sub-types:

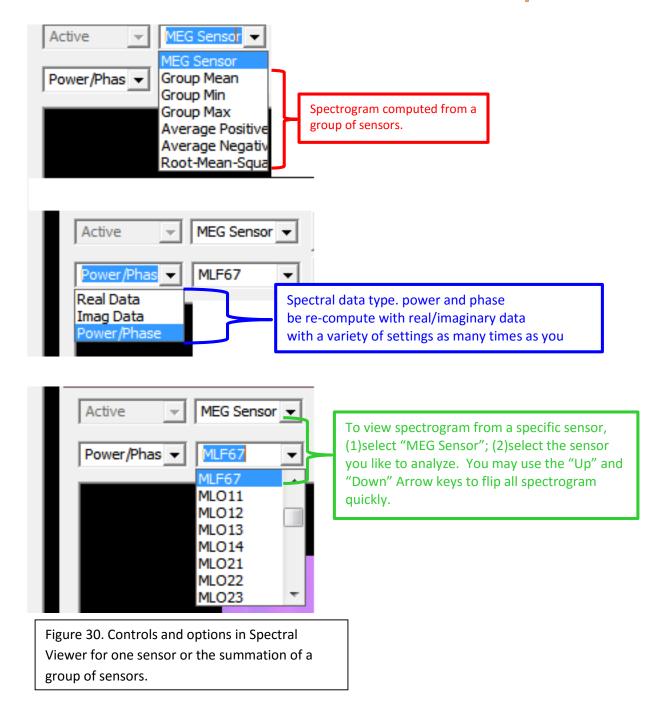
- 1) Group Mean
- 2) Group Min (minimum, negative)
- 3) Group Max (maximum, positive)
- 4) Averaged Positive (magnetic goes out/in)
- 5) Averaged Negative (magnetic goes in/out)
- 6) Root-Mean-Square (RMS)

To view the summation type of spectrogram, select and specify it from the corresponding Combo box as following figure. Specifically, to view spectrogram from a specific sensor:

- (1)select "MEG Sensor";
- (2) select the sensor you like to analyze.

You may use the "Up" and "Down" Arrow keys to flip all spectrogram quickly.

It is important to point it out that spectral data type "Power/Phase) can be re-compute with real/imaginary data with a variety of settings as many times as you like.



## 3D View Parameters for Displaying Spectral Data

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In the Standard Display Parameters for 3D Spectrum, there are two combo boxes, which enable you to check and get the data range of a specified data class and type. Consequently, the data display can be precisely controlled and presented.

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- 1) Visible range of spectral values: The "Select Low" and "Select High" can be adjusted with the horizontal scroll bars. If you know the exact values (very common for experienced researchers/clinicians), you may directly input the values in the "Select Min" and "Select Max" edit fields. The selected values define and specify the data range for spectral display.
- 2) The range of spectral data in the current trial: The "Trial Min" and "Trial Max" show the range of spectral data in the current trial that is shown in the Spectral Contour Map and Topographic Viewer. You may click the "Get Data Range" to retrieve the data ranges. The range of spectral data in the current trail is very important for Spectral Contour map.
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- 6) Automatically fit Trial Data and Channel data: the "Autofit Trial Data" and "Autofit Channel Data" compute or retrieve the data range and automatically define the range for appropriate showing according to the default settings. This function is based on experience with thousands of MEG datasets (http://clinicaltrials.gov/show/NCT00600717).
- 7) Color Scale and Color Coding: There are at least 4 groups of color scale (256, 512, 768 and 1024) for coding the spectrograms. Of note, the color scale will change the display of the data, it does not change the data. Therefore, you are free to try all the color scales and find the best to meet your taste and requirements.
- 8) Raw data: If you did anything wrong that may change the data, you may click the "Raw data" to get the original data that are typically stored during time-frequency transforms.
- 9) Refresh: the "Refresh" button updates all viewers.
- 10) Other buttons are self-explainable.

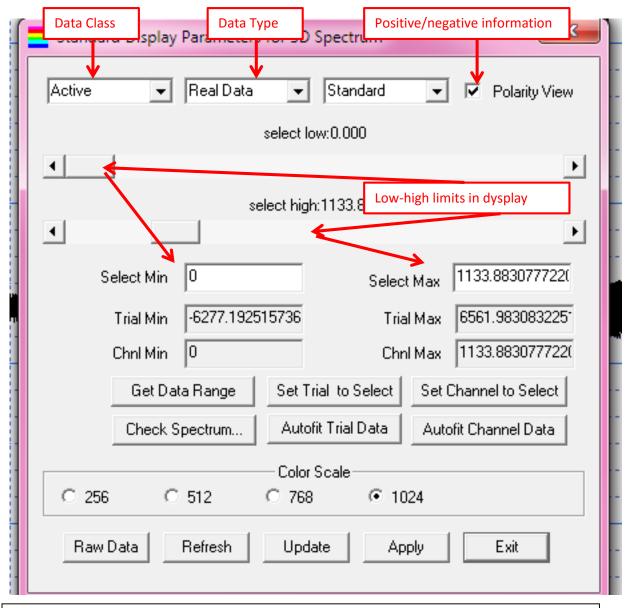
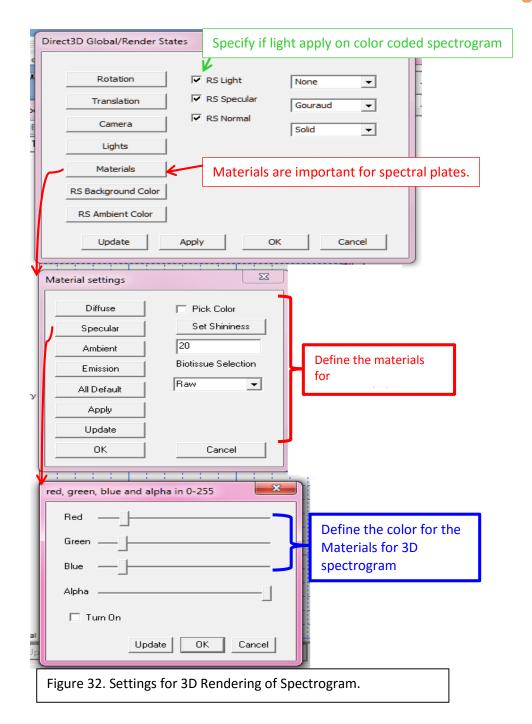


Figure 31. Standard Display Parameters for 3D Spectrogram.

## 3D Rendering for Spectral Data

This software has a powerful 3D rendering engine which supports both Direct3D and OpenGL. To appropriately display spectrum in 3D, several windows (dialogs) have been designed to enable you to adjust the 3D images.



# Normalization of Spectral Data

To better characterize EEG/MEG data, normalization of spectral data with respect to a baseline interval can be performed. There are several possibilities for normalizing: (a) subtracting, for each frequency, the average magnitude (or power) in a baseline interval from all other magnitude values. This gives, for each frequency, the absolute change in magnitude with respect to the baseline interval. (b) expressing,



for each frequency, the raw power values as the relative increase or decrease with respect to the power in the baseline interval. This means active period/baseline. Note that the relative baseline is expressed as a ratio (i.e. no change is represented by 1).

# Classification of Spectral data (Active, Control and Mixer of Active-Control)

To maximize the usability of spectral data and to provide the most flexible ways for users to explore the data, this program provides a data manager to deal with three classes of spectral data: Active state, Control State and Mixer of Active-Control. You can combine the various visualization options/functions interactively to explore your data and perform a set of post-transforming processes.

- 1) Active data typically represent the spectral data acquired during an active task
- 2) Control data typically represent the spectral data acquired during a resting state, which is not involved in responding to the task.
- 3) Mixer of Active-Control (or Mix AC or Results of Act-Ctl) represents the results of an operation applied to active and control data. We use those kinds of awkward names because there are no standardized names. We have to follow the rules in each journal, which may represent reviewers' consideration.

For example, (1) subtracting, for each frequency, the average power in a baseline interval from all other power values. This gives, for each frequency, the absolute change in power with respect to the baseline interval. (b) dividing, for each frequency, the raw power values as the relative increase or decrease with respect to the power in the baseline interval. This means active period/control period. Of note, the mixer of active-control may be the results of active data subtracted/divided by control data.

## **Granger Causality and Multivariate Autoregressive Model**

The program can compute spectrally resolved Granger causality. Though the program can do many other frequency-domain directional measures of connectivity, the results from autoregressive model of the data are still under internally testing. The results seemed to be variable among subjects.

The program can also compute the spectral transfer function using non-parametric spectral factorization of the cross-spectral density matrix. In this case, Gabor transformation seemed to be suitable for the decomposition of the data.

### Physical sensor and virtual sensor

Physical sensor can reveal a clear directed connectivity, or a pick-up of a common source in two channels. We will now continue with connectivity analysis on real MEG data. In addition, physical sensor may be affected by volume conduction. Consequently, data from physical sensors/electrodes may not be well for connectivity analysis.

Virtual sensor can minimize the effect of volume conduction. Virtual sensor signals are typically computed with beamformers or spatial filters. A typical beamformer is applied to the whole brain using

a regular 3-D grid or using a triangulated cortical sheet. To compute virtual sensor signals, a location of a single or multiple points of interest are typically pre-defined. Consequently, beamformer will simply be performed at the location of interest. The beamformer spatial filter for the location of interest will pass the activity at that location with unit-gain, while optimally suppressing all other noise and other source contributions to the virtual signals.

### **CxC versus Coherency (Coherence) Analysis**

Coherence analysis has been frequently used in EEG/MEG research. One frequently asked question is the relationship between CxC and Coherency analysis. The program provides a window for computing channel-cross-channel (CxC) analysis, which generates coefficients/data to describe the relationship among every two-channel pairs. We use CxC instead of typically used "Coherence Analysis" because several nonlinear relationship/association analysis algorithms have been implemented in the software, which enables users to investigate the correlation/coherence or interdependency of EEG/MEG signals in time, with the use of moving (shifting or sliding) time-windows. In a simple words, the program provide coherency analysis and plus.

The CxC data can be directly used for additional data analysis. For example, covariance Matrix computed with MEG sensor data can be used for source localization. Therefore, the selections of trial, sensor, data range (points and time), active and control status are very important.

# **Spectral CxC**

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