Webinar Q&A Report:

EEG and Telemetry: Best Practices for Managing Large Data Sets to Investigate Key Aspects of Epilepsy in Rodent Models

1. **How can you differentiate between motion artifacts and a true EEG signal?**

   When a goal is scored in a soccer stadium, the synchronous activity of fans is clearly distinguishable from the rest. In a similar way, brain rhythms involve large population of neurons that can be detected using EEG. This can be quantified using a fast Fourier analysis. The frequency spectral dynamics of an EEG will typically show a near-linear decrease of log power with increasing log frequency, which is characteristic of "pink" noise. The presence of artifacts in the signal will likely change the frequency spectral dynamics.

2. **What is the gold standard for artifact removal in large EEG data sets?**

   The so called "gold-standard methods" usually rely on expert human inspection of EEG epochs. In terms of semi-automatic artifact removal, there are methods based on the amplitude of the signal and others relying on features extracted from power spectra, signal entropy, independent component analysis, notch filtering, etc.

3. **How do you mitigate motion artifacts?**

   The best way to mitigate motion artifacts is to take measures to minimize them in the first place. In the case of telemetry, this can be done by inspecting the transmitter leads, because any damage can cause EMG/ECG artifacts.

   DSI's surgical services team offers free consultation to make recommendations for EMG lead placement to assist with reducing undesired skeletal muscle artifact. Contact sssurgeryteam@datasci.com to learn more.

   I also suggest using the EEGLAB, an open source MATLAB toolbox that has several tools to detect and remove artifacts.

4. **What kinds of experiments using EEG—mice, rats, maximal electroshock (MES), pentylenetetrazol (PTZ), intraperitoneal or intravenous etc.—does it take to prove the activity of new anticonvulsants?**

   It all depends on the objectives, but usually models of *status epilepticus* that can induce spontaneous recurrent seizures (SRSs) allow the quick screening of anticonvulsants and neuroprotectants. For example, intra-hippocampal pilocarpine better mimics temporal lobe epilepsy (TLE) because it doesn't cause the widespread damage when compared to the systemic model.

5. **What types of EEGgraphic seizures can be identified in animal models of epilepsy?**

   Both rat and mice can present hypersynchronous SRSs and also low voltage fast discharges SRSs. It is also known that a small proportion of animals can present spontaneous spike wave discharges during the baseline before exposure to convulsant agents.

   Please see:

   Furtado et al. 2012; Exposure to nerve agents: from status epilepticus to neuroinflammation, brain damage, neurogenesis and epilepsy. *Neurotoxicology.*

   Rossetti et al. 2012; Combined diazepam and HDAC inhibitor treatment protects against seizures and neuronal damage caused by soman exposure. *Neurotoxicology*.

6. **Do you confirm seizures detected via telemetry by checking the video footage?**

   We are currently implementing video-EEG and plan to correlate EEGgraphic seizures with behavior.

7. **In your experience, how much variability is there between each animal? We have found that some animals have excellent EEG seizures while others barely respond to the chemical.**

   Some animals won't present typical *status epilepticus* when injected with a convulsant – the proportion depends on strain, convulsant model, etc. After several experimental rounds, non-responsive animals are placed into a different control group and data from these animals is combined.

8. **How can we appropriately couple video-EEG features with measures of complexity in different models of epilepsy?**

   In terms of video-EEG features, a basic assessment is to investigate what type of

EEGgraphic seizures have behavioral correlates. Behaviors such as mastication, head myoclonus and forelimb myoclonus are likely present during hypersynchronous seizures. However, when having video-EEG capability, an analysis of behavioral sequences might be more suitable than simply indicating a "behavioral score".

Although this strategy is more time-consuming depending on the software used, this could be used in exploratory studies. Also, the analysis of behavioral sequences combined with EEG recorded in multiple sites might be ideal. For example, behavioral clusters that are associated with a given neuronal oscillation can provide some insight on the system complexity.

In terms of investigating what neural networks are involved on each type of seizures, a video-EEG setup with multiple channels (including deep brain structures) is **crucial** to understanding the neuronal dynamics encoding brain states. DSI has a solution for video-EEG (Ponemah) and up to 4 EEG channels could be used depending on the transmitter used.

Depending on your species of interest DSI has various implant options. The newest implants are the HD-X02 for mice and HD-S02 for rats, please visit datasci.com for more information.

9. **What is the difference between nominal implant and software sampling rates, and what is their relationship with transmitter bandwidth?**

Nominal Implant Sampling Rate: The rate at which data points are sampled by the implant. Higher sample rates enable accurate response to higher signal frequencies.

Software Sampling Rate: The rate at which the raw data is reconstructed in the application software (e.g. Ponemah) for plotting and feature extraction
Channel Bandwidth: The frequency range between the lowest and highest attainable frequency, measured in Hertz (Hz). For DSI products, this focuses on the range of frequencies for which the reported signal amplitude remains within an error power band of 3 dB.

10. **What kinds pre-processing do you use for your data?**

Usually, we apply a Butterworth filter and perform clipping of epochs with artifacts through automatic detection. The Butterworth filter is a type of signal processing filter created to have a frequency response as flat as possible in the passband. It was first described in 1930 by the British engineer and physicist Stephen Butterworth in his paper entitled "On the Theory of Filter Amplifiers".

11. In your experience, what are the most useful tools for EEG analysis?

The use of FFT is relatively simple, reliable and fast. A fast Fourier transform (FFT) is an algorithm that calculates the discrete Fourier transform (DFT) of a sequence, or its inverse (IDFT). A Fourier analysis converts a signal from its time domain (in the case of EEG) to a representation in the frequency domain.

DSI offers FFT analysis capabilities in NeuroScore software. This software offers analysis and nice visualization tools to assist with identifying seizures and scoring sleep.

The use of wavelets (particularly the Morlet wavelet because it is more suitable for EEG seizure detection.) and Artificial Neural Networks can also be very useful.

12. What platform do you use for the Morlet transform?

The MATLAB signal processing toolbox has a wavelet Morlet function (morlet.m).

For details on the use of wavelet-based time frequency and coherence analysis, I suggest reading:

> Romcy-Pereira et al. 2008; A semi-automated algorithm for studying neuronal oscillatory patterns: a wavelet-based time frequency and coherence analysis. *J Neurosci Methods.*

13. How did you perform bandwidth analysis as shown in your slides?

The signal is filtered through a Butterworth filter (pass band of 0.1–125 Hz; notch filter of 60 Hz; de Araujo et al. 2009). Usually, a 60-s window is chosen to give a good spectral and time resolution when pairing EEG recordings and important experimental.

The power (calculated using the MATLAB function fft.m) is averaged in 60-s windows with 50% overlap to obtain the power spectrum density (μV^2/Hz) in the following frequency bands: delta (0.1–4.0 Hz), theta (4.1–8.0 Hz), alpha (8.1–12 Hz), beta (12.1–25 Hz), and gamma (25.1–50 Hz).

14. What is the role of machine learning-based analysis of physiology data such as EEG?

Machine learning is an application of Artificial Intelligence based on the concept that we should be able to input data to machines which in turn will learn for themselves. Artificial Neural Networks are a subset of Machine Learning methods.

Basically, a Neural Network is a computer system designed to function by classifying

information similar to neuronal networks in the human brain (obviously, networks in the human brain have much more complexity). They can be trained to recognize, for example, images, and categorize them according to elements or features that they contain. The features used to train a neural network should be determined by you.

In the case of EEG, someone can, for example, identify key features of a seizure and use it to train a neuronal network to recognize specific types of seizures or brain patterns (such as the ones present during sleep cycle).

15. How would you establish criteria to detect seizures since they are so variable? And how do you address differences in amplitude that might derive from electrode implantation?

Usually, we calculate the power average during baseline and used as a threshold. In that way, we normalize changes in amplitude due to subject variation, electrode placement, etc.

Please see:

Furtado et al. 2009; Analyzing large data sets acquired through telemetry from rats exposed to organophosphorous compounds: An EEG study. *J Neurosci Methods.*

16. Do you find spectral analysis to be an effective solution?

Yes, but combined with seizure duration. It is useful to split power spectrum in different bands depending on the objective.

17. How do you determine the limits for spontaneous seizures if spikes have a very low amplitude?

The power average during baseline used as one threshold. We set 10s as min duration. Also, it needs to match EEGgraphic signature. Other models might require setting a shorter seizure duration.

18. Can epileptic seizures be predicted in real time?

It is possible when a sampling rate higher than what we currently use in implantable telemetry is used. Also, it is necessary to record EEG in multiple brain sites and use non-linear analysis strategies. In other words, both spatial and temporal resolution must be increased. For example, high frequency oscillations (>100 Hz) can be identified near the time of seizure onset.

Still, seizure prediction is a big challenge and most of times it is very difficult for several reasons, including the presence of artifacts (particularly when recording scalp EEG) that can cause false positives or false alarms.

19. Which type of analysis is suitable for EEG signals during ictal period: linear, non-linear, or hybrid features?

The use of hybrid features is more suitable since it might improve seizure detection.

20. How would you use EEG plus brain stimulation over motor cortex to stimulate the brain and monitor the EEG at the same time?

Transcranial direct current stimulation or TDCS is currently being used for the treatment of motor impairment following TBI or traumatic brain injury and EEG has been used to evaluate the effect of transcranial Direct Current Stimulation (tDCS).

Usually, most studies are limited to studying the EEG before and after stimulation due to the presence of artifacts. The superposition of moving averages and also adaptive filtering can potentially be used to remove not only second order artifacts such as respiration related oscillations but also first order stimulation artifacts.

21. With regards to the management of large sets of data, can you provide some advice as to what data formats, recommended software and computer characteristics are ideal?

For customized solutions, it's recommended to use a binary format such as EDF or EDF+. The use of data in .txt format is only appropriate for small data sets. In terms of software, you can use the OS of your choice. For example, MATLAB and SciLab are compatible with Windows, Linux and Mac.

In terms of hardware, having at least a quad-core processor and a top GPU or multi-GPU setup will help to accelerate processing, particularly if you are modeling/training neural networks. Please feel free to contact me at support@biosead.comfor more details.

DSI offers FFT and amplitude analysis capabilities in NeuroScore software. This software offers analysis and nice visualization tools to assist with identifying seizures and scoring sleep. Please visit datasci.com email sales@datasci.com for more information.

If you have additional questions for Data Sciences International (DSI) regarding content from this webinar or wish to receive additional information about their products and laboratory services, please contact them by phone or email:

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