Nox SAS Detailed Scoring Commentary

Katrínartún 2
105 Reykjavík, Iceland
+354 5707170 | noxmedical.com

LBL-0400

The Nox SAS solution is a new, flexible way to record EEG, ECG and EMG data during polysomnography sleep studies conducted with the Nox A1s PSG system. The solution comes with disposable EEG electrodes that are secured to the patient's forehead, a head cable, and body cables. The Nox SAS aims to make the hookup process simple and comfortable for clinicians and patients alike.

The Nox SAS solution will be familiar to physicians and technicians experienced with the AASM rules for sleep analysis, and these guidelines can be broadly followed with a few considerations.

Nox SAS solution compared to conventional PSG:

- Nox SAS features frontal-only EEG.
- Nox SAS uses EOG instead of mastoid (M1 & M2) references.
- Nox SAS EMG is measured from the EOG electrodes on the forehead (frontalis muscle) rather than the conventional chin EMG.

Conventional AASM - EEG

- 8 EEG channels
- 2 EOG channels
- 2 EMG chin channels

Nox SAS - Frontal EEG

- 9 channels
- recording EEG and EOG (incl. EMG measures)

Nox SAS Analysis Considerations:

- Nox SAS sleep data can look both familiar and slightly different depending on the epoch. Feedback from the field recommends scrolling through a few studies to familiarise yourself with the sleep stage patterns of Nox SAS before staging in detail.
- The EEG signals available for analysis are frontal only, which means no occipital or central channels. Adjust analysis habits based on this change compared to the AASM standard configuration. The most important consideration is that occipital channels are not present for sleep onset and arousal length scoring. This analysis can be performed with ease from the frontal EEG with proper consideration.
- Nox SAS EEG features lower amplitude and power compared to conventional PSG. The Nox Medical team has developed a frontal filter (Noxturnal 6.3.2) that amplifies waveforms in the analysis range. If not using the frontal filter, adjust your expectations for sleep staging based on amplitude (e.g. N3)[1]. It is recommended to scroll through the study and familiarise yourself with the pattern of the different sleep stages.
- Nox SAS PSG can introduce eye movement into the EEG due to the reference system. This EOG could be misinterpreted for sleep physiology if not considered in context. A standard solution is to adjust the low-frequency filter when required to reduce the EOG bleed or sway artefact. When analysing Nox SAS studies, be careful not to mistake slow eyes movements for delta waves and REMs for N2 waveforms.
- Feedback from the field suggests Nox SAS EMG is not as responsive to changes in sleep stage (e.g. REM atonia). REM staging and arousals should not be based solely on the EMG. Other REM physiology

should be taken into consideration. If you have difficulty staging REM, work backwards from a definitive epoch.

With these points, the scoring of Nox SAS studies is expected to have a quick adaptation period and can be scored with the same rules as the AASM Manual for the Scoring of Sleep and Associated Events (Version 3, Feb 2023). What follows is a detailed discussion of the points mentioned above and the considerations for scoring with the established AASM rules.

Nox SAS Background

The Nox SAS solution differs from conventional PSG in a few ways.

Nox SAS is Frontal EEG only.

- For sleep staging purposes, the Nox SAS channels AF4-E3E4 and AF3-E3E4 are similar to PSG channels F4-M1 and F3-M2, though they use different references (see below). The third and fourth channels are AF7-E3E4 and AF8-E3E4.

Nox SAS replaces conventional mastoid (M1M2) with EOG reference (E3E4).

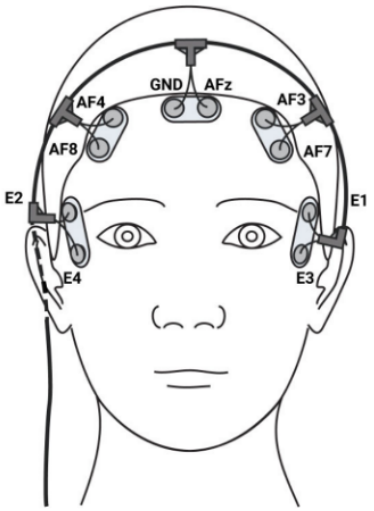
- Each of the AF-leads from the bipolar frontal montage is referenced to the average of E3 and E4 electrodes to attenuate eye movement artefacts in the EEG.

Nox SAS utilises EMG measured from the EOG signals to replace the conventional chin EMG.

- Nox SAS features EMG measured from the muscles of the forehead.
- The design means that patients with facial hair can achieve good quality EMG signals.

The table below outlines the signals available for sleep staging. Nox SAS also features ECG, nasal flow, respiratory effort (RIP), and dual limb EMG.

Nox SAS Sleep Staging Signals		
AFz	Reference	
AF3-E3E4 AF4-E3E4 AF7-E3E4 AF8-E3E4	Frontal EEG	
E2-AFZ E3-AFZ	EOG	

EMG Frontalis Left EMG Frontalis Right	EMG measured via EOG electrodes	

Nox SAS Sleep Staging Considerations

Nox SAS has already been used for research purposes involving thousands of subjects in the field[1,3]. Feedback from technicians and physicians analysing Nox SAS studies, as well as research from the Nox Medical team has outlined a few important considerations for sleep staging with Nox SAS. These include:

- Nox SAS EEG has been shown to feature lower amplitude and power across the analysed frequency range[1]. Nox Medical has developed an EEG filter (Noxturnal 6.3.2) which digitally pre-processes and amplifies the EEG signals.
- The EOG-based reference for the frontal EEG can add artefact and EOG bleed into the EEG. It is possible to adjust the low-frequency filter (LFF) to reduce or remove this EOG bleed into the EEG.
- The Nox SAS EMG is measured differently to conventional chin EMG of PSG. Other aspects of sleep physiology should be considered when staging, particularly REM, and scoring arousals.

These will all be explored in detail below.

Nox SAS EEG Amplification and Power Considerations

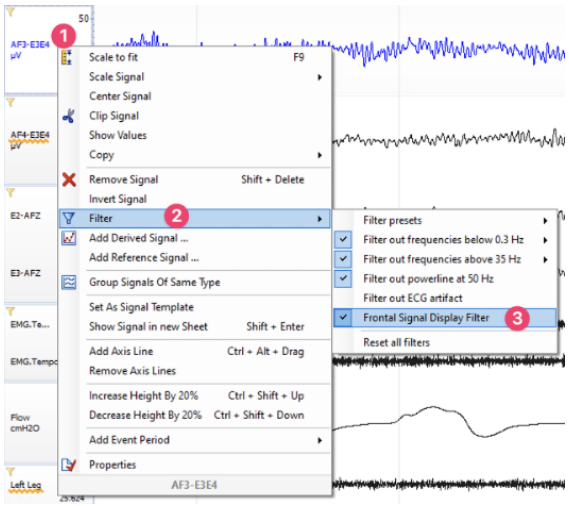
Research performed by the Nox Medical team has shown that Nox SAS EEG features lower amplitude and power across the analysed frequency range of 0.3-35Hz[1]. A Frontal filter has been developed which digitally amplifies the EEG signals in the slow wave (0-2Hz) and the alpha band (8-13Hz) frequencies to aid sleep staging.

Scoring with the Nox SAS Frontal Filter recommendations:

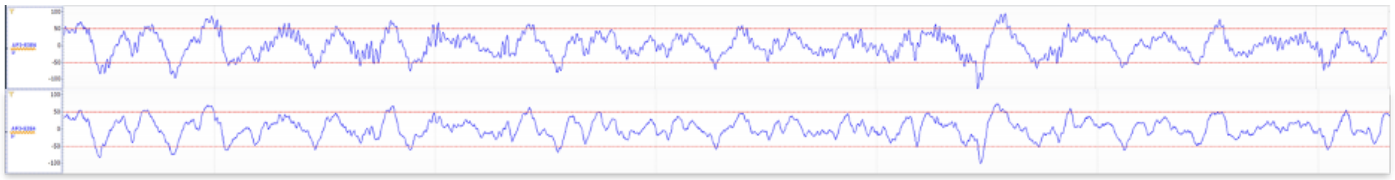
- Familiarise yourself with the EEG pattern by scrolling through and adjusting the epoch time between 30s and 1 minute to get a feel for the amplitude and frequency of the EEG

- The Frontal Filter is *optional* but comes activated as standard in the built in Nox SAS worksheet.
- If using the SAS Frontal Filter, maintain the normal AASM rules for scoring N3 (75Hz delta waves).
- If using the standard PSG filter with SAS, consider lowering the threshold for delta based on a review of the overall PSG pattern.

The Nox SAS Filter is used in addition to the standard (or adjusted) filter settings for EEG. The image below shows the standard AASM EEG filters (LFF 0.3Hz and HFF 35Hz) plus the addition of the frontal filter to amplify the signals. The Nox SAS Frontal filter can be turned on and off for EEG signals in the filter settings.



The screenshots below compare N3 with and without the frontal signal filter. The top signal is with the frontal filter and the bottom is without. Notice the increased amplitude of the delta waves and more prominent alpha waveforms that are amplified by the filter.



When using the frontal filter, it is important to consider what is being amplified. The frontal filter can enhance wake and NREM waveforms, but feedback from the field suggests it can also create an alpha-like intrusion onto the EEG. It is recommended to familiarise yourself with the EEG waveform patterns with the frontal filter turned on and off.

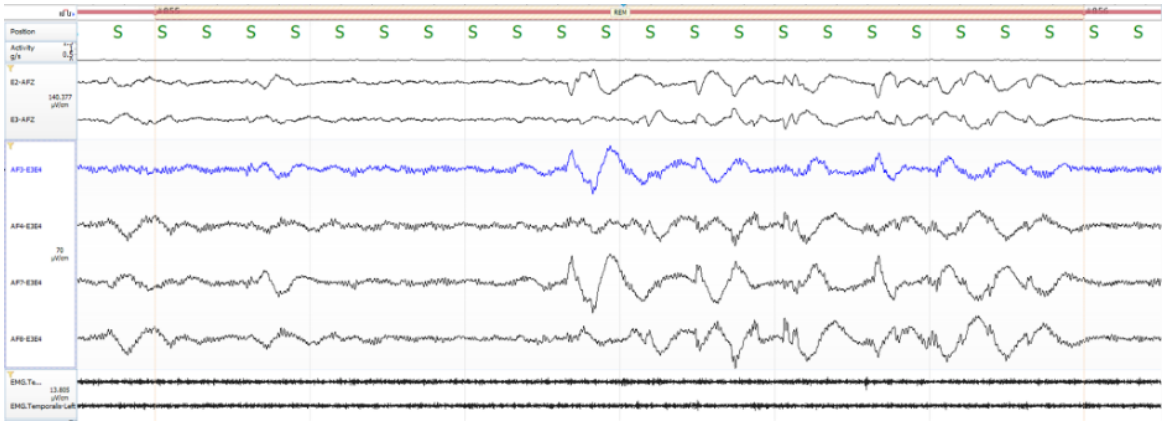
Nox SAS EOG-based reference considerations

Nox SAS replaces the conventional mastoid reference for the unipolar channels with references from sourced from the EOG electrodes. This results in a few changes to the EEG. Nox SAS uses the average of EOG (E3E4) as the reference instead of M1M2. As a result, eye movements can be seen in the EEG. This EOG bleed should not be misinterpreted for other characteristics of EEG, including:

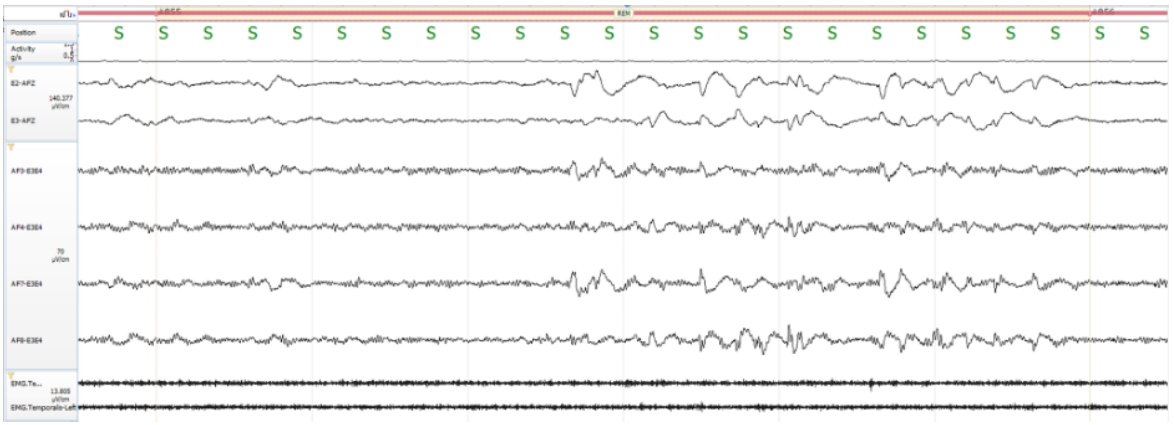
- Slow eyes movements of sleep as delta waves or N3
- Wake eye movements for delta waves
- REMs for NREM waveforms (K-complexes or delta waves)

Adjustments to the low frequency filter (LFF; also known as high pass filter) can help reduce the EOG bleed into the EEG. Feedback from the field suggests increasing the LFF from 0.3Hz to 0.5Hz for periods of the study that feature EOG bleed can aid in sleep analysis. It is important to consider that increasing the LFF will impact the amplitude of the signals. Play around with the filter settings to understand what is best for you without compromising the overall signal quality.

Below shows a Nox SAS with EOG bleed from REMs into the EEG. This waveform deviation should not be considered when staging the EEG.



Now with the LFF set to 0.5Hz, the EOG bleed into the EEG is less pronounced and the usual low-amplitude, mixed-frequency (LAMF) characteristics of REM is more obvious.



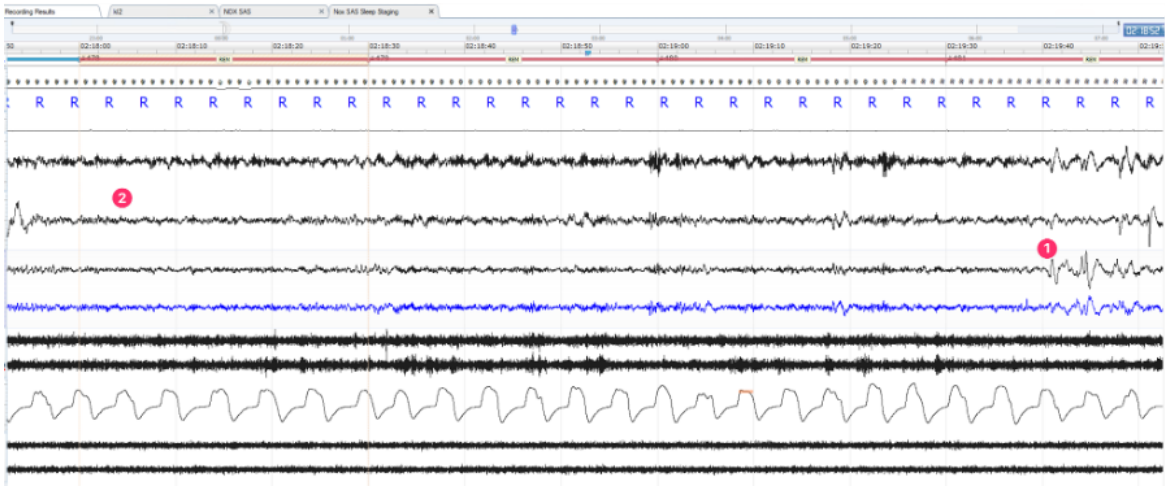
Nox SAS EMG Considerations

As mentioned, Nox SAS streamlines the PSG set-up and replaces chin EMG with EMG measured from the electrodes used for EOG. Feedback from the field suggests the EMG tone (amplitude) changes with sleep stages and arousals is not as prominent as conventional PSG. This is like using adhesive instead of gold-cup electrodes for Chin EMG in conventional PSG. As a result, it is recommended to use all the data available in Nox SAS PSGs for sleep staging and arousal detection, particularly when staging REM.

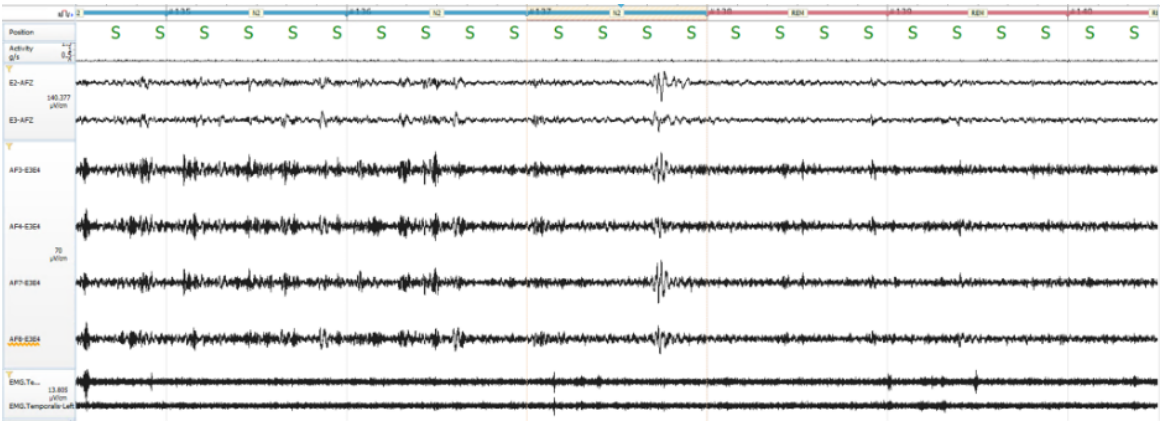
The AASM defines low chin EMG tone as “baseline EMG activity in the chin derivation no higher than in any other sleep stage and usually at the lowest level of the entire recording” (Section I, 1.1)[2]. In Nox SAS, the chin EMG tone has not been seen to be higher than wake or NREM but is often not at the lowest level seen in the recording. It is recommended to find definite REM epochs through the study as a baseline for the REM EMG tone.

In REM, consider the EEG for low-amplitude, mixed-frequency (LAMF) waveform, rapid eye movements in the EOG, and other characteristics of REM, such as variable respiration and heart rate, and reduced or no activity (EMG, limb EMG, and activity signal). As mentioned previously, it is important not to mistake EOG bleed for NREM waveforms in REM.

When determining the onset of REM, stage REM at the first obvious epoch with LAMF and rapid eye movements. Use the AASM score back rules (Section I, 1.3)[2] to score REM for contiguous epochs that feature LAMF and are missing the defining characteristics of NREM (spindles, K-complexes, and delta waves). In this example, one (1) shows the onset of rapid eye movements, and two (2) shows the score back rule for LAMF EEG without REMs.

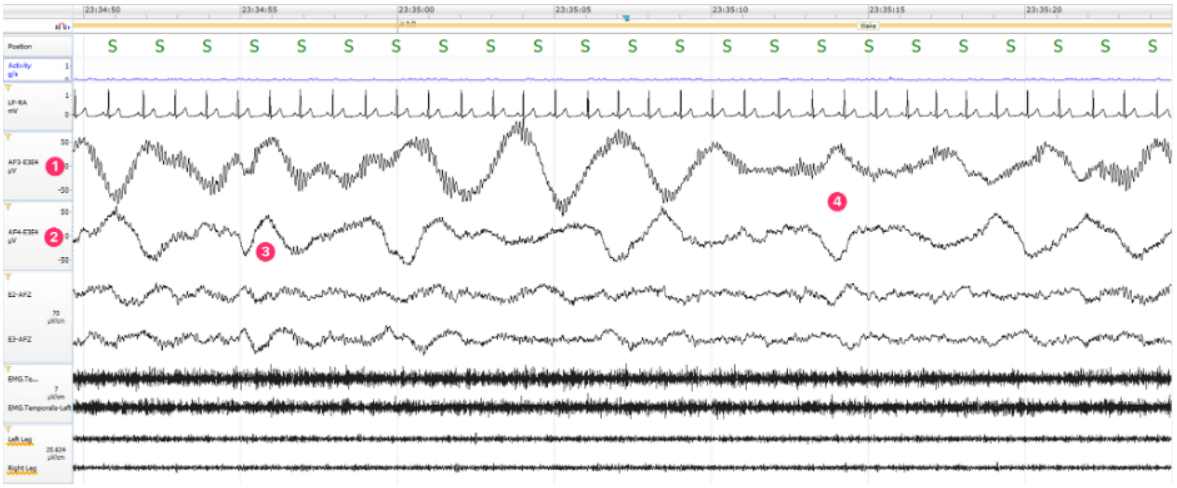


This second example again shows the change from the N2 waveform into the LAMF waveform of REM. Changing the time signature for the EEG can help when determining REM onset when EMG changes are not definitive.

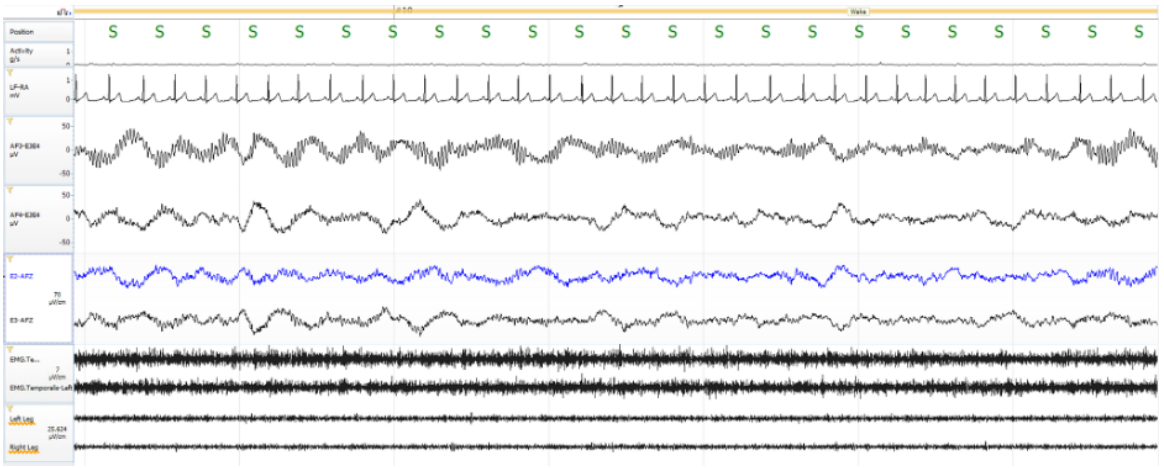


Detailed Nox SAS Examples:

Stage Wake

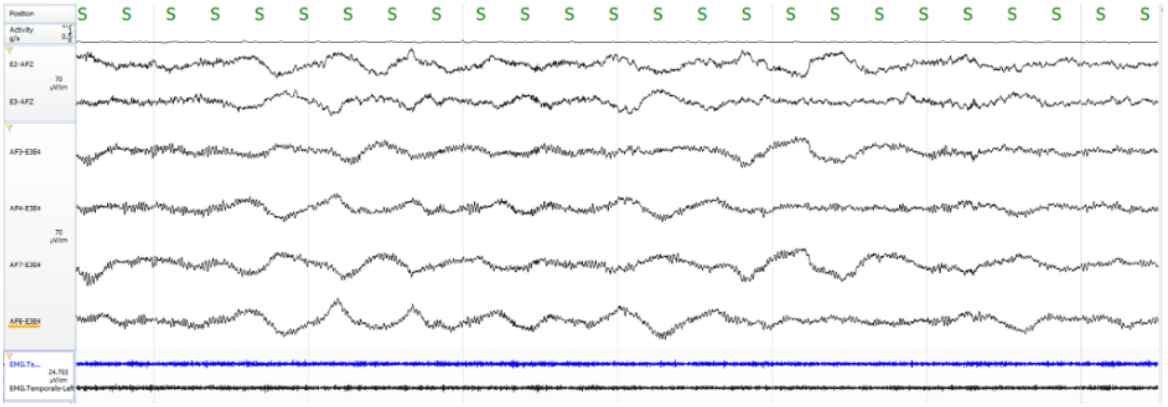


This example shows stage wake just prior to the transition to N1. Signal 1 features the frontal filter and shows strong alpha rhythm. The slow rolling eye movements of N1 can be seen bleeding into the EEG. Below is the same epoch but the low-frequency filter (LFF) has been adjusted from 0.3 to 0.5Hz to aid in the removal of some of the slow eye movements.



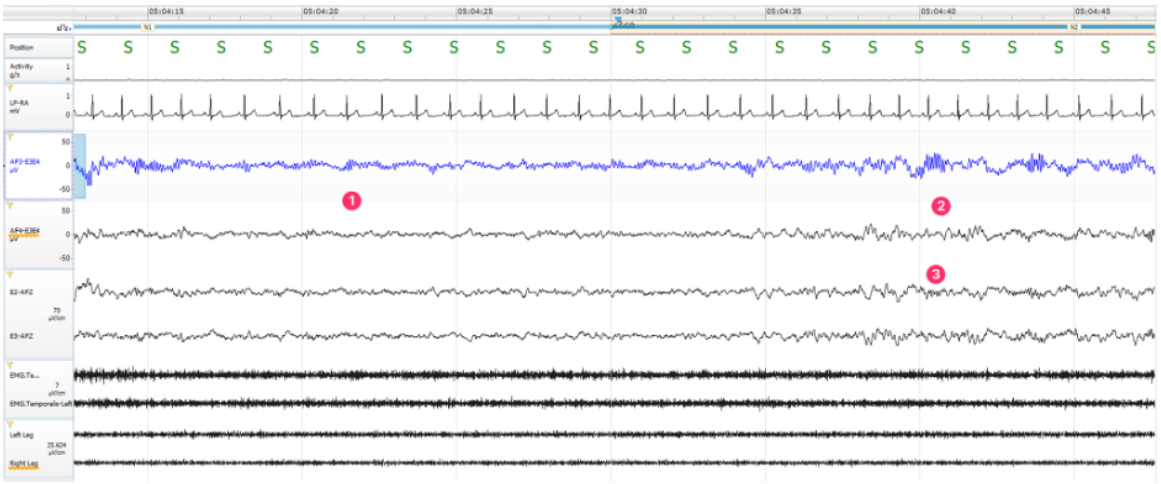
Stage N1

This example shows the transition from wake to N1 with the slower EEG frequency and the cessation of the slow eye movements. In this example, the second EEG channel that features the frontal signal turned off better features the reduction in alpha activity and onset of N1.

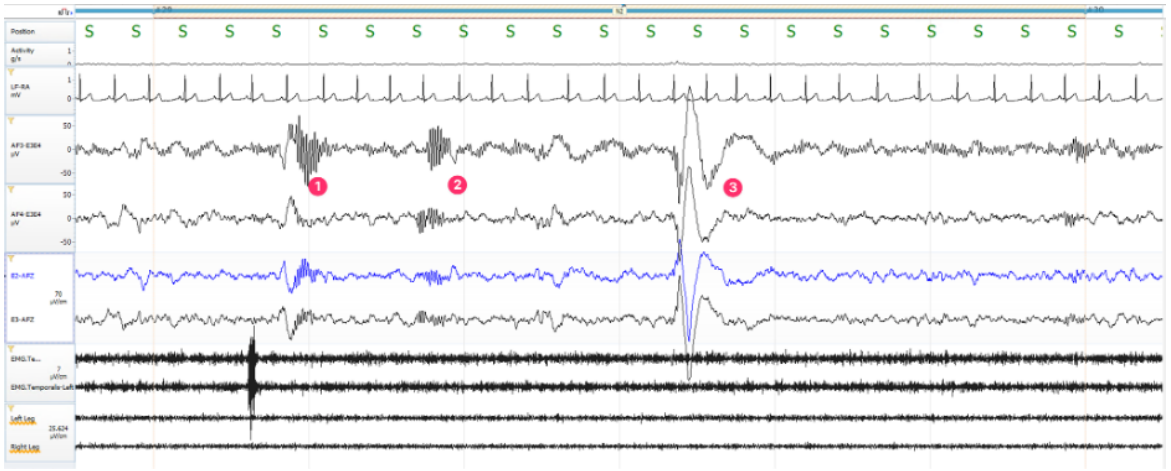


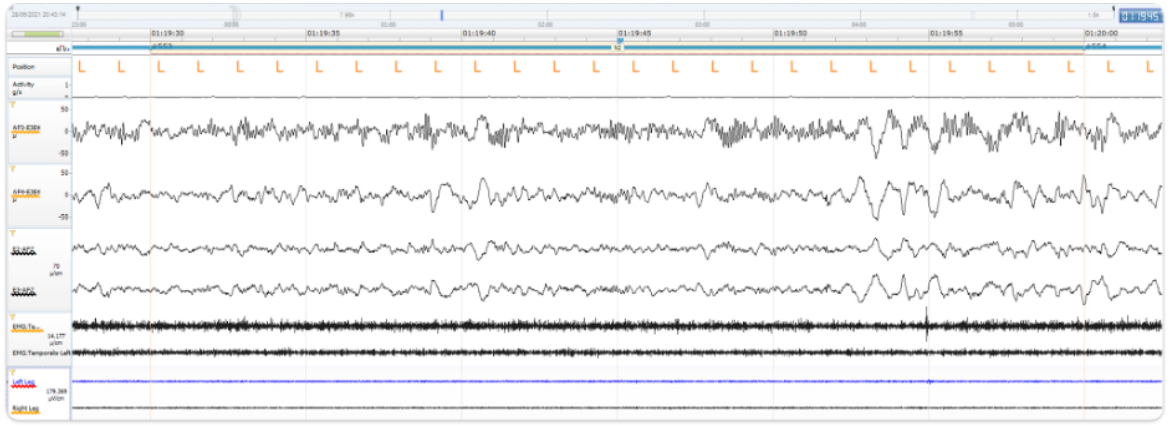
Stage N2

This example shows the transition from N1 to N2 with the Nox SAS PSG. Note this is two epochs split down the middle. The first half shows an epoch of N1 that transitions into N2. A sleep spindle is obvious in the second epoch consistent with the transition to N2.



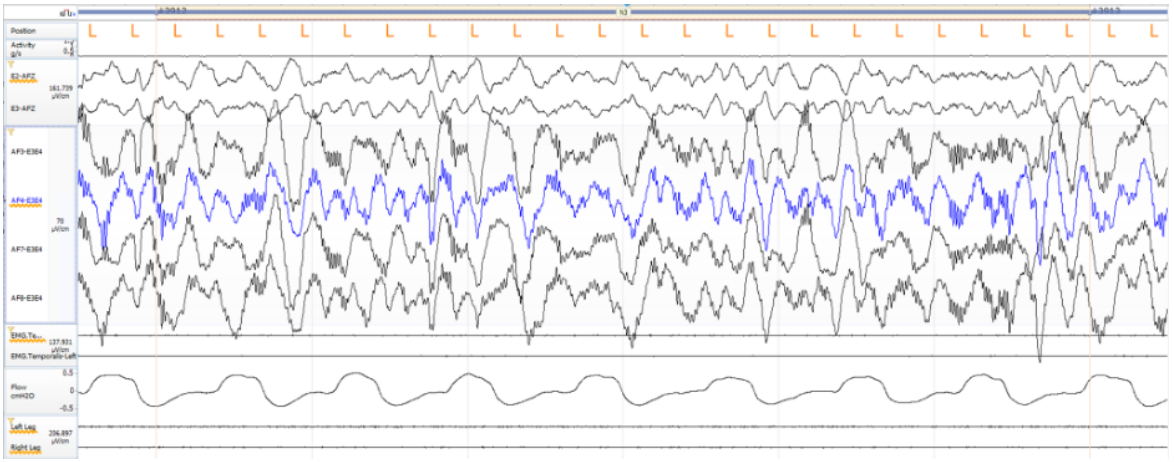
The two examples below show clear N2 waveforms with sleep spindles and K-complexes.





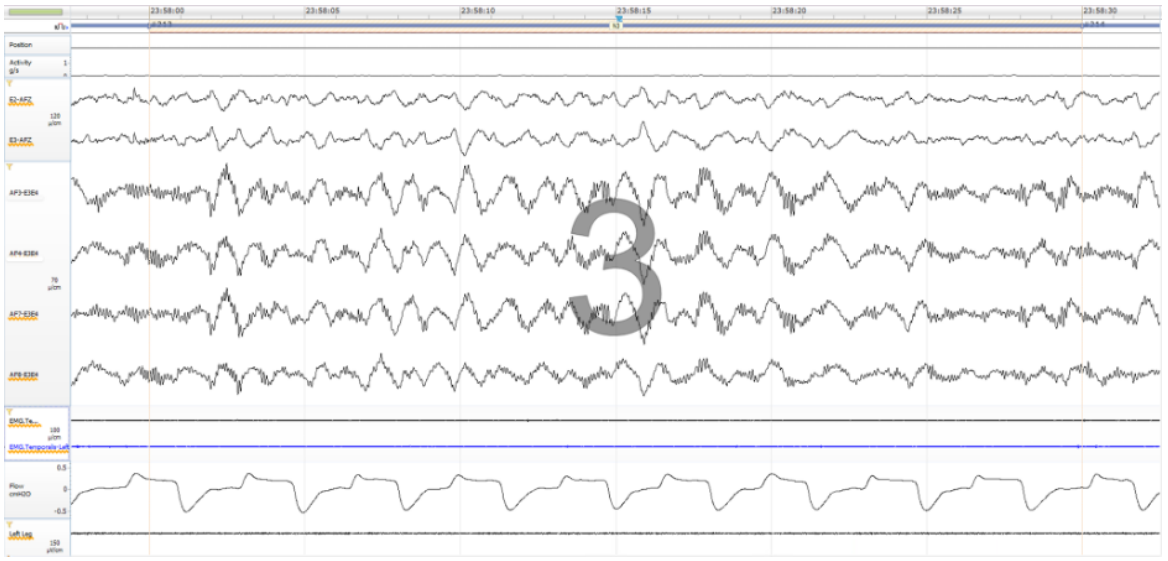
Stage N3

The example epoch below shows distinctive delta wave morphology for all EEG signals (frontal signal ON).

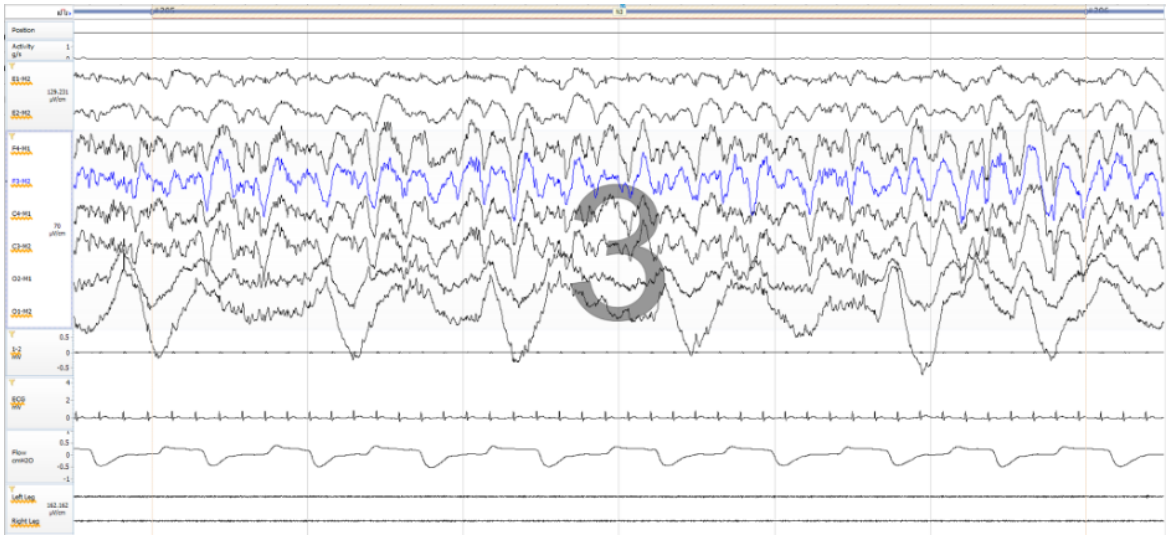


Below is a comparison of delta wave activity between SAS and conventional PSG. Both have clearly defined delta wave activity consistent with N3 staging. The amplitude of the Nox SAS waveforms can be seen to be slightly reduced, consistent with the findings of the Nox Medical team and feedback from the field. In both examples, the sleep stage is easily identifiable with the AASM staging rules.

Nox SAS:

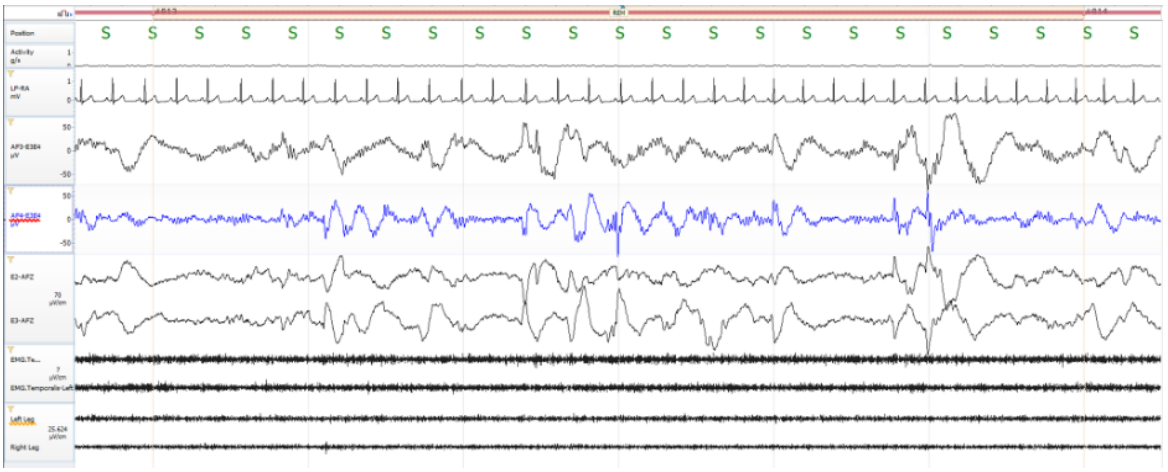


Conventional PSG:



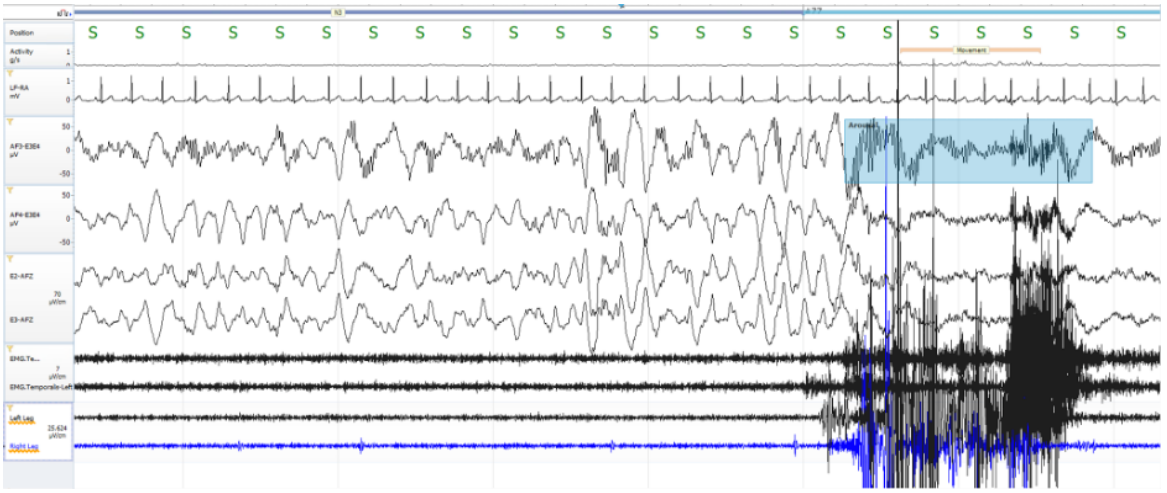
Stage R

The example epoch below shows clear REM waveforms and rapid eye movements with a flat EMG. Note the EOG bleed with REMs featuring in the EEG. It is important not to see this EOG bleed as a deviation from the low amplitude mixed-frequency (LAMF) waveform consistent with REM.

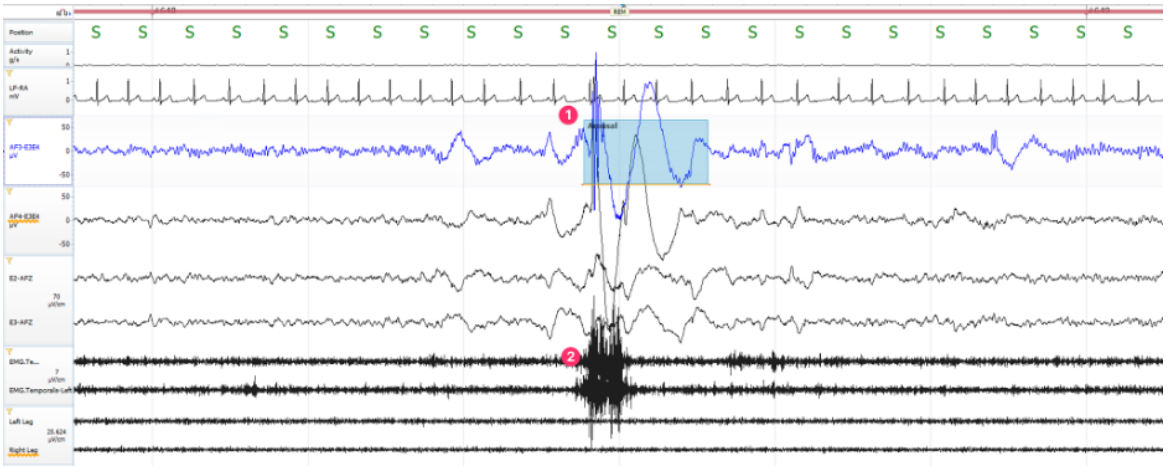


Nox SAS Arousals

Stage N3 arousal



The below example features an abrupt change in EEG frequency and amplitude and increased EMG (EOG) consistent with REM arousal.



References:

1. S. Kainulainen *et al.*, "Comparison of EEG Signal Characteristics Between Polysomnography and Self Applied Somnography Setup in a Pediatric Cohort," in *IEEE Access*, vol. 9, pp. 110916-110926, 2021, doi: 10.1109/ACCESS.2021.3099987.
2. Berry RB, Quan SF, Abreu AR, et al.; for the American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.6. Darien, IL: American Academy of Sleep Medicine; 2020.
3. Punjabi NM, Brown T, Aurora RN, et al. Methods for home-based self-applied polysomnography: the Multicenter AIDS Cohort Study. *Sleep Adv*. 2022;3(1):zpac011. Published 2022 Apr 29. doi:10.1093/sleepadvances/zpac011