SUPPLEMENTAL INFORMATION FOR

Focal Changes to Human Electrocorticography with Drowsiness

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Signal decimation and digital filtering in EEG frequency bands

To examine the instantaneous amplitude and frequency, in wake and sleep states, across EEG frequency bands defined as: δ: 0-4; θ: 4-8; α: 8-14; $\theta\alpha$: 4-14; β: 14-30, and Υ: 30-80 Hz, we filtered the recorded ECoG signal with digital recursive elliptical filters (Oppenheim et al., 1999) (see Supplementary Figure 1). To increase filtering efficiency, we decreased the sampling rate of the recorded raw signal from 1 kHz to 20 Hz for filtering in δ band, to 50 Hz for θ and α band, to 100 Hz for β band, and to 200 Hz for Υ band. The decreasing of sampling rate (decimation) was done with the MATLAB (MathWorks, Natick MA) *decimate* function. First, the *decimate* passed the raw signal through a low-pass filter that limited the filtered signal bandwidth to $0.8*f_d/2$, where f_d was the decimation frequency f_d (e.g. 20 Hz for δ band). By using low-pass filtering prior to down-sampling, *decimate* ensured protection against aliasing that could occur if the bandwidth of signal to be decimated was higher than $f_d/2$ (Oppenheim et al., 1999). Then, the low-pass filtered signal was down-sampled by the function *decimate* to f_d. We selected the decimation frequencies such that the decimated signal had enough bandwidth prior to filtering in EEG bands (e.g. the decimated signal bandwidth computed as $0.8*f_d/2$ was 8 Hz for δ, 20 Hz for θ and α, 40 Hz for β, and 80 Hz for Υ band. To remove the 60 Hz noise, for the Υ band only, we passed the decimated signal through a notch filter centered at 60 Hz. The decimation allowed us to design efficient elliptical filters with low transition width between the pass- and stop band (1 Hz for low frequency bands and 2 Hz for the Υ band), low ripple in the bandpass band (1 dB) and high attenuation in the stop bands (40 dB) (Oppenheim et al., 1999). Digital filtering was done in both the forward and reversed directions with the MATLAB *filtfilt* function. Due to bi-directional processing, we doubled the stop-band attenuation of the filters, obtaining an attenuation of 80 dB in the stop bands.

Instantaneous amplitude and frequency

ECoG signals change with time both their amplitude and phase. They can be approximated with a signal of the general form $x(t) = a(t)cos[\varphi(t)]$. For such signals, one can define the instantaneous amplitude $a(t)$ and the instantaneous phase $\varphi(t)$ by associating to $x(t)$ the analytic signal $z(t) = x(t) +jy(t)$, where $y(t)$ represents the Hilbert transform of $x(t)$ (see below) (Picinbono 1997). The Hilbert transform of $\cos[\varphi(t)]$ is $\sin[\varphi(t)]$ (King 2009). Therefore, the analytic signal $z(t)$ can be written as:

$$z(t) = x(t) + jy(t) = a(t)\exp[j\varphi(t)] \quad (1)$$

where $a(t)$ is positive and the phase $\varphi(t)$ is defined modulo π.

Considering the above theory, the instantaneous amplitude (IA) $a(t)$ and the instantaneous phase $\varphi(t)$ of the signal $x(t)$ are given by:

$$a(t) = \sqrt{x(t)^2 + y(t)^2} \quad (2)$$

$$\varphi(t) = arctan\left[\frac{y(t)}{x(t)}\right] \quad (3)$$

where $y(t)$ is the Hilbert transform of $x(t)$ (Goswami and Hoefel 2004):

$$y(t) = \frac{1}{\pi}\int_{-\infty}^{\infty}\frac{x(\tau)}{t-\tau}d\tau \quad (4)$$

The instantaneous phase φ computed with (3) is limited between $-\pi$ and π. To compute the instantaneous frequency (IF) one needs to unwrap the phase $\varphi(t)$, which means to transform the phase φ into a monotonous increasing function φ_u by adding 2π every time when the phase φ drops from π to $-\pi$. Then, the instantaneous frequency $f(t)$ is computed as the derivative of the unwrapped instantaneous phase $\varphi_u(t)$:

$$f(t) = \frac{1}{2\pi}\frac{d\varphi_u(t)}{dt} \quad (5)$$

For a discrete time-sampled signal $x(n)$, the IA and IF are computed as:

$$IA(n) = |z(n)|; z(n) = x(n) + j\{DHT[x(n)]\} \quad (6)$$

$$IF(n) = f_s\,[\varphi_u(n) - \varphi_u(n-1)]/2\pi \quad (7)$$

where n is the time moment, |.| is the modulus function, DHT is the Discrete Hilbert Transform, f_s is the sampling frequency and $\varphi_u(n)$ is the unwrapped phase of the analytical signal $z(n)$. We used the MATLAB function *hilbert* as *DHT*. The function *hilbert* implements *DHT* by multiplying the discrete Fourier spectrum $X(\omega)$ of $x(n)$ with $H(\omega)$, where $H(\omega) = 2$ for $\omega > 0$ and 0 for $\omega < 0$. Then, *hilbert* makes use of the inverse discrete Fourier transform of $X(\omega)H(\omega)$ to obtain the *DHT* of $x(n)$, $y(n) = hilbert[x(n)]$.

Equation (7) gives the exact value of *IF* only for *intrinsic mode functions* (*IMF*). According to Huang et al. 1998 an *IMF* "*is a function that satisfies two conditions:* (1) *in the whole data set, the number of extrema and the number of zero crossings must either equal or differ at most by one; and* (2) *at any point, the mean value of the envelope defined by the local maxima and the envelope defined by the local minima is zero*". Huang et al. showed that for any signal $x(n)$ one can find K intrinsic mode functions $c_i(n)$ such as:

$$x(n) = \sum_{i=1}^{K} c_i(n) + r_K(n) \quad (8)$$

where $r_K(t)$ is a residue that can be either the mean trend or a constant. Thus, the filtered ECoG signal for which we estimate *IF* is not an *IMF*, but a sum of *IMFs*. For this reason, the *IF* is only approximated by using equation (7) (see Supplementary Figure 2). Even if the *IF*s were approximately computed, we preferred to use EEG filtered signals instead of *IMFs*, due to the possible biological connections that could be made between the local sleep phenomenon and the frequency changes in different EEG bands. We reduced the noise introduced by the *IA* and *IF* estimation by smoothing with median and moving average filtering.

Smoothing the instantaneous amplitude and frequency

To improve the detection of the channels' active/inactive state, we had to smooth the noisy *IA* in δ band and noisy *IF* in $\theta\alpha$ band. For records lasting hours (referred as short records in the text), we computed the medians of both *IA* and *IF* in moving windows of 10s, overlapping for 2s. A moving window of 10s contains enough δ band oscillations to compute a statistically representative median value of the δ instantaneous amplitude. Then, we smoothed the medians by using the moving average filtering in windows of 20s length, overlapping for 2s. Thus, for records on the order of hours, the smoothed *IA* and *IF* were sampled every 2s (see Supplementary Figure 3). For whole day (24 h) records, we used windows of 20 s for the median filtering and windows of 40 s for the subsequent moving average. For both median and average filtering, the moving windows overlapped by 10s. Thus, for 24 h records, the smoothed *IA* and *IF* were sampled every 10s. For

24h long records we changed the moving window length and its overlapping interval to increase the signal processing efficiency, without losing essential information.

Due to the differences in electrode impedance, the magnitude of *IA* was very different (up to even one order of magnitude) between channels. To compensate for each channel, we normalized the smoothed *IA* by dividing it by its standard deviation. As a result, each channel contributed equally to the averaged *IA* across channels (see below). The normalized, smoothed *IA* in δ band was denoted as δA in the text, while the smoothed *IF* in $\theta\alpha$ band was denoted as $\theta\alpha F$ (see Figure 3B, Figure 6A-B, Supplementary Figure 3).

Average of the smoothed amplitude and frequency across channels

We denoted by $m\delta A$ the average of δA across channels:

$$m\delta A(n) = \sum_{k=1}^{M} \delta A_k(n)/M \qquad (9)$$

where $\delta A_k(n)$ was the δA in the channel k at the moment n, and M was the number of channels recorded in the subject.

We denoted by $m\theta\alpha F$ as the average of $\theta\alpha F$ across channels:

$$m\theta\alpha F(n) = \sum_{k=1}^{M} \theta\alpha F_k(n)/M \qquad (10)$$

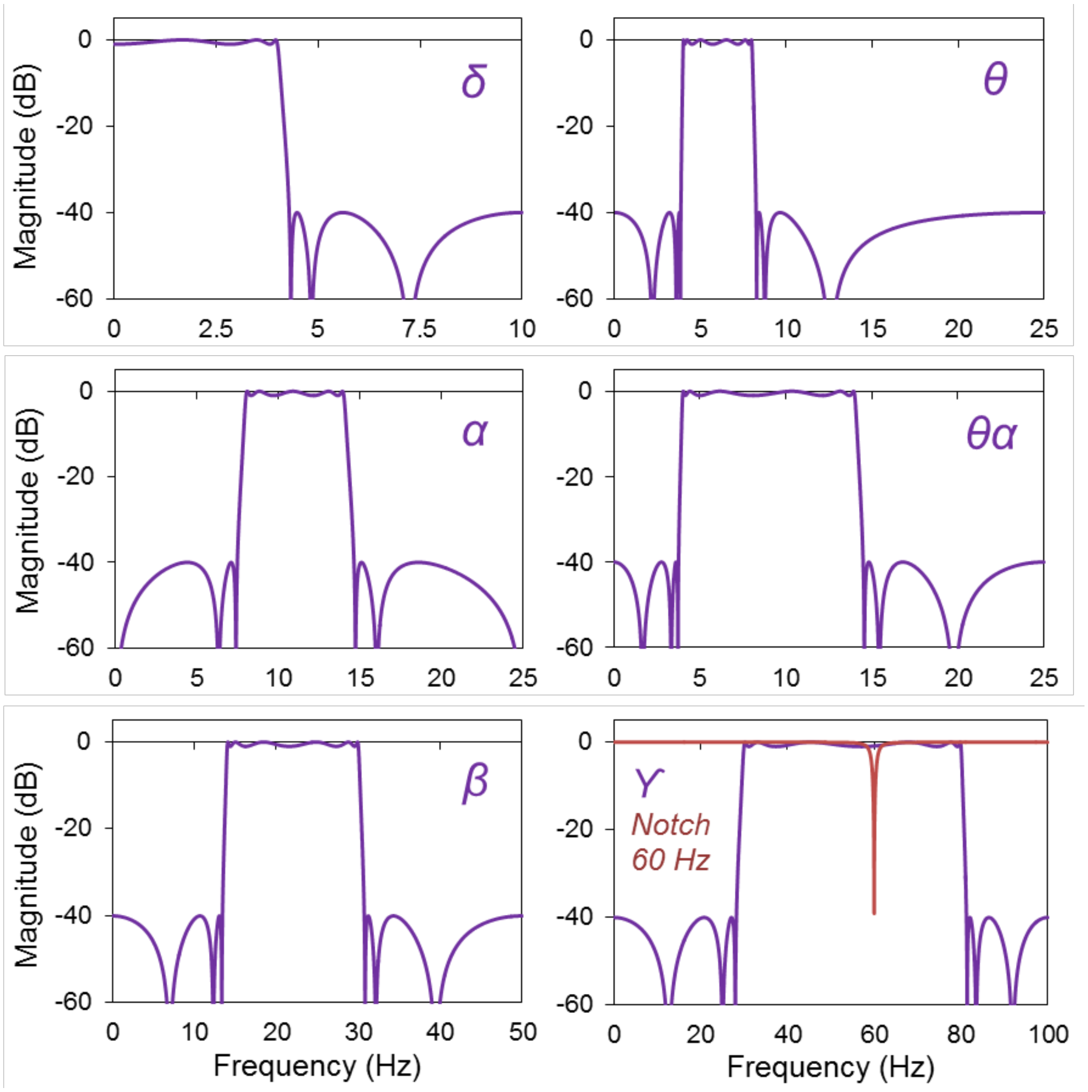
where $\theta\alpha F_k(n)$ was the $\theta\alpha F$ in the channel k at the moment n (Figure 4B, Supplementary Figure 4A, 4C). We used $m\delta A$ and $m\theta\alpha F$ to predict the number of inactive channels, ΣIC, with a linear regression model (see Equation 1 in Methods).

Pearson correlation

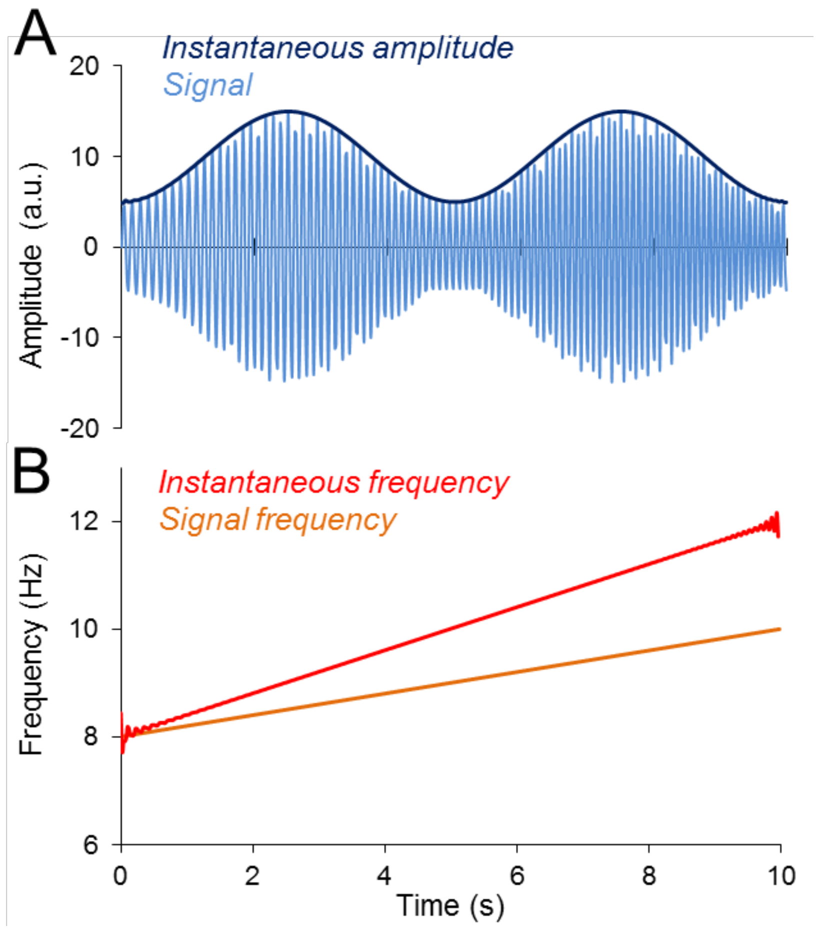
The Pearson correlation $R(x,y)$ of two discrete time series $x(n)$, $y(n)$, $n = 1,2,\ldots,N$ is given by:

$$R(x,y) = \frac{\sum_{n=1}^{N}[x(n)-\bar{x}](y(n)-\bar{y}]}{\sigma_x\sigma_y} \qquad (11)$$

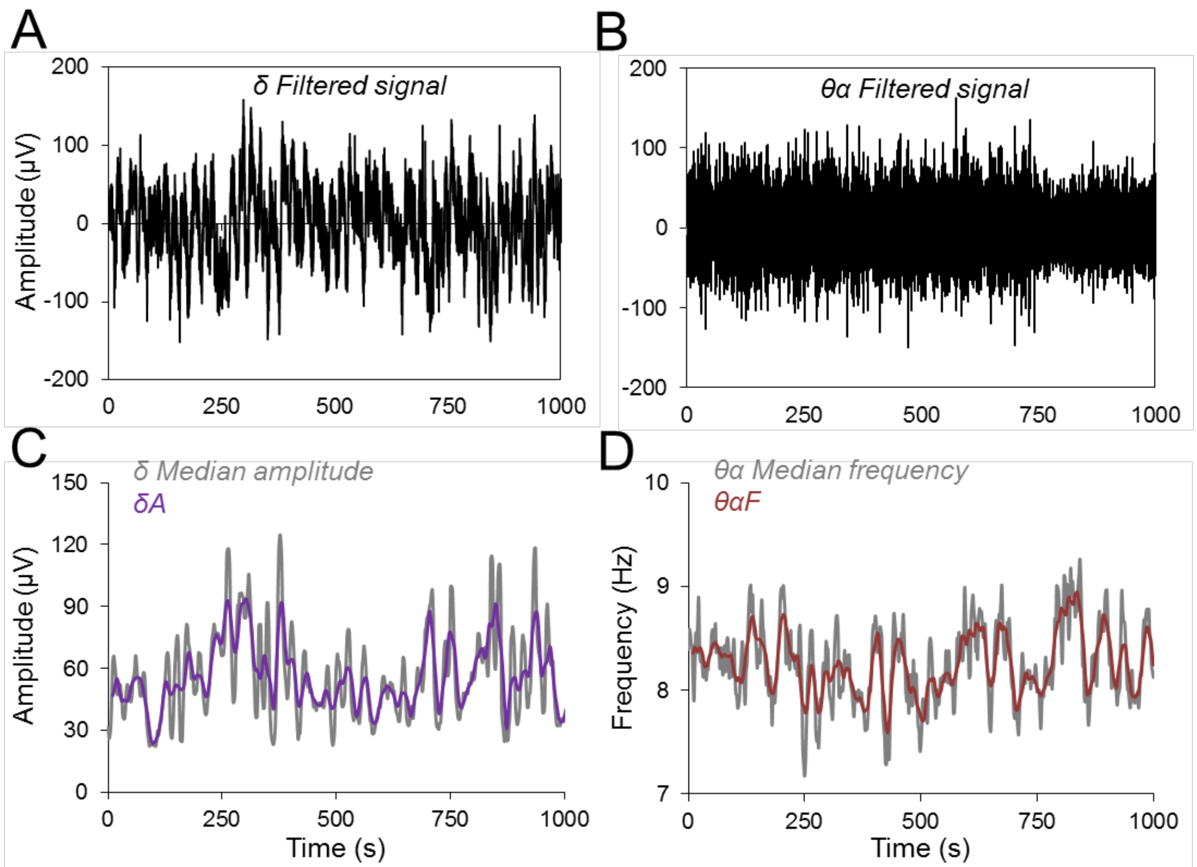
where $\bar{x}$ and $\bar{y}$ are the means of x and y, respectively, and σ_x and σ_y are the standard deviations of x and y, respectively (Rodgers and Nicewander 1988). We computed the Pearson correlation with the MATLAB function *corrcoef*.



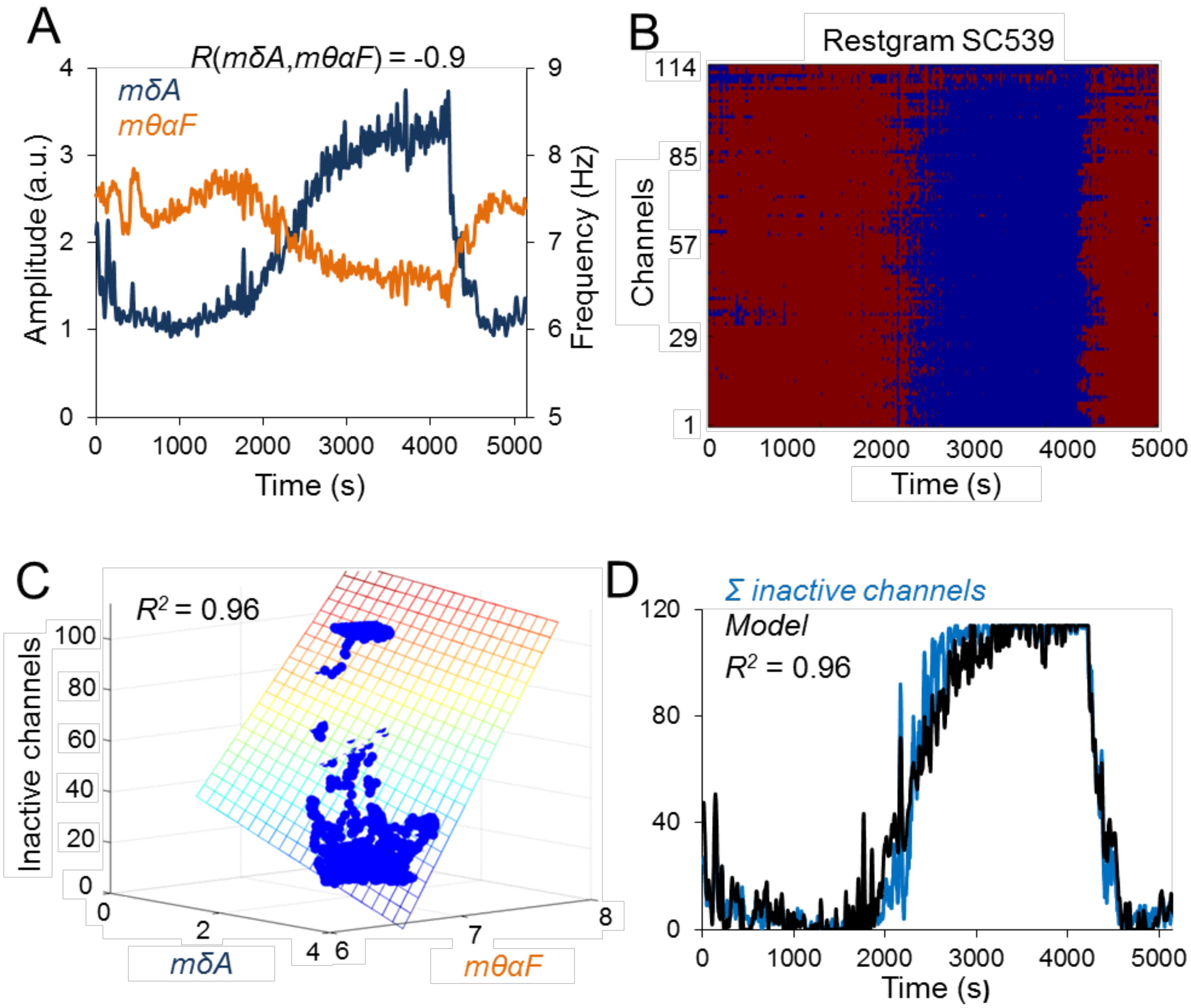
Supplementary Figure 1. Filtering of ECoG signal in EEG bands. We used elliptic, recursive digital filters in order to select the information specific to EEG bands. To design efficient, low order filters (e.g. of order 6 for the low-pass filter of δ band, and of order 12 for the band-pass filters of other bands) we had to use, for each filter, a sampling frequency having the same magnitude order as the filter cutoff frequency. Thus, we had to down-sample (decimate) the original ECoG signal to 20 Hz for δ band, 50 Hz for θ, α, and $\theta\alpha$ bands, 100 Hz for β band, and 200 Hz for Υ band. The decimation was done by low-pass filtering the signal to a cutoff frequency of 0.8**fs*/2, where *fs* was the decimation frequency, followed by discarding a fixed number of samples, imposed by the decimation factor. Thus, no band specific information was lost after the decimation process (e.g. the spectrum bandwidth limit after decimation was 8 Hz for δ, 20 Hz for θ and α, 40 Hz for β, and 80 Hz for Υ band. By filtering, in both forward and backward direction, we doubled the stop-band attenuation from -40 dB to -80dB.



Supplementary Figure 2. Example of estimating the instantaneous amplitude (*IA*) and instantaneous frequency (*IF*). **(A)** Amplitude and phase modulated signal (light blue line) $s(n) = A(n)\sin[2\pi f(n)nT_s]$, where $T_s = 0.02$s, together with corresponding *IA* (dark blue line). **(B)** The signal frequency $f(n)$ (orange line) and the corresponding *IF* (red line). The *IA* in (A) and the *IF* in (B) were computed with Equations (6) and (7), respectively, by using the MATALB *hilbert* function. While *IA* was a very good approximation of the amplitude modulation signal $A(n)$, *IF* was a modest approximation of the signal frequency $f(n)$ (e.g. 20% relative error at 10s). *IF* can be computed exactly only for intrinsic mode functions (see above). To improve the detection of local sleep, we decreased the variability of *IA* and *IF* by smoothing with median and moving average filtering (see Supplementary Figure 3).



Supplementary Figure 3 - Smoothing the instantaneous amplitude in the *δ* band (*δIA*) and instantaneous frequency in the *θα* band (*θαIF*). **(A)** Channel signal filtered in *δ* band (0-4 Hz) with a low-pass recursive digital filter working at 20 Hz sampling frequency. **(B)** Channel signal filtered in *θα* band (4-14 Hz) with a band-pass recursive digital filter working at 50 Hz (see Supplementary Figure 1). **(C)** *δ* Median amplitude (grey line) was obtained after the median filtering of *δIA*. Median filtering was done by computing the median of *δIA* in moving windows of 10s, overlapping by 2s. Then, the median amplitude was averaged in windows of 20s, overlapping by 2s. The resulting averaged amplitude (purple line) was subsequently used as a feature for the channel local sleep detection, being denoted as *δA* in text. **(D)** The smoothed instantaneous frequency (dark red line), denoted as *θαF* in the text, was computed every 2s by using the same moving median and average filtering as for the *δA*. First, we filtered *θαIF* with a median filter to get the *θα* Median frequency (grey line). Then, the median frequency was filtered with a moving average filter to obtain *θαF*. *δA* and *θαF* were used together, or separately, for the detection of the sleep/wake state. Since the smoothed *IA* (*δA*) and the smoothed *IF* (*θαF*) were computed every 2s from the raw ECoG signal sampled at 1Kz, the reduction in data sampling rate was 500 fold, without essential information loss. For 24-hour records the median filtering was done in moving windows of 40s, and average filtering in windows of 20s, both windows overlapping for 10s.



Supplementary Figure 4 - Modeling the sum of inactive channels. (**A**) The average across channels of normalized, smoothed δ instantaneous amplitude ($m\delta A$) and the average of the smoothed $\theta\alpha$ instantaneous frequency ($m\theta\alpha F$) for subject C539. For all the subjects, $m\delta A$ and $m\theta\alpha F$ were strongly, negatively correlated during sleep and for 24h records (see Figure 7C). (**B**) Restgram (see text) for subject C539: the number of active (red) and inactive (blue) channels was strongly correlated with $m\delta A$ and $m\theta\alpha F$. (**C**) Sum of inactive channels (ΣIC) was modeled with high accuracy by a regression model having $m\delta$A and $m\theta\alpha$F as predictors (see Equation 1 in Methods). Blue points indicate the sum of inactive channels and the mesh defines the regression surface. (**D**) Regression model explained a high percentage of the variability in ΣIC (blue line). Model output (black line) was limited between 0 and the number of recorded channel.

Table 1. The states (**Active**/**Inactive**) of the electrodes in a LTO grid implanted in subject C544 computed at three time moments. The subject was at sleep at 5am and awake at 9am and 11am (see also Figure 5 text).

Brain area	Electrode #	Sleep (5am)	Wake (9am)	Wake (11 am)
Inferior temporal gyrus	1	Active	Active	Active
	7	Inactive	Active	Inactive
	17	Inactive	Active	Active
Middle temporal gyrus	2	Active	Active	Active
	3	Inactive	Active	Active
	4	Inactive	Active	Active
	5	Active	Inactive	Inactive
	6	Inactive	Inactive	Inactive
	11	Inactive	Active	Active
	12	Inactive	Active	Active
	13	Inactive	Active	Active
	14	Inactive	Active	Active
	15	Inactive	Active	Active
	16	Inactive	Active	Active
	25	Inactive	Active	Active
	26	Inactive	Active	Inactive
	27	Inactive	Active	Inactive
	28	Active	Active	Active
	38	Inactive	Active	Active
	39	Active	Inactive	Inactive
Inferior occipital gyrus	8	Inactive	Active	Active
	9	Inactive	Active	Active
	10	Active	Active	Active
Middle occipital gyrus	18	Inactive	Active	Active
	19	Inactive	Active	Active
	20	Active	Inactive	Inactive
	29	Inactive	Active	Active
	30	Inactive	Active	Active
Superior temporal gyrus	21	Inactive	Active	Active
	22	Inactive	Active	Active
	23	Inactive	Active	Active
	24	Inactive	Active	Active
	32	Inactive	Active	Inactive
	33	Inactive	Active	Active
	34	Inactive	Inactive	Inactive
	35	Inactive	Inactive	Inactive
	36	Inactive	Inactive	Inactive
	37	Inactive	Active	Inactive
Traverse temporal gyrus	31	Inactive	Active	Active
Cuneus	40	Active	Active	Active

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