

1 **Broadband aperiodic components of local field potentials reflect**  
2 **inherent differences between cortical and subcortical activity**

3 Abbreviated title: Cortical vs. subcortical aperiodic activity

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## 12 Abstract

13 Information flow in brain networks is reflected in intracerebral local field potential (LFP)  
14 measurements that have both periodic and aperiodic components. The  $1/f^\alpha$  broadband aperiodic  
15 component of the power spectra has been shown to track arousal level and to correlate with other  
16 physiological and pathophysiological states, with consistent patterns across cortical regions.  
17 Previous studies have focused almost exclusively on cortical neurophysiology. Here we explored  
18 the aperiodic activity of subcortical nuclei from the human thalamus and basal ganglia, in  
19 relation to simultaneously recorded cortical activity. We elaborated on the FOOOF (fitting of one  
20 over  $f$ ) method by creating a new parameterization of the aperiodic component with independent  
21 and more easily interpretable parameters, which allows seamlessly fitting spectra with and  
22 without an *aperiodic knee*, a component of the signal that reflects the dominant timescale of  
23 aperiodic fluctuations. First, we found that the aperiodic exponent from sensorimotor cortex in  
24 Parkinson's disease (PD) patients correlated with disease severity. Second, although the  
25 aperiodic knee frequency changed across cortical regions as previously reported, no aperiodic  
26 knee was detected from subcortical regions across movement disorders patients, including the  
27 ventral thalamus (VIM), globus pallidus internus (GPi) and subthalamic nucleus (STN). All  
28 subcortical region studied exhibited a relatively low aperiodic exponent ( $\chi^{STN}=1.3\pm0.2$ ,  
29  $\chi^{VIM}=1.4\pm0.1$ ,  $\chi^{GPi}=1.4\pm0.1$ ) that differed markedly from cortical values ( $\chi^{Cortex}=3.2\pm0.4$ ,  
30  $f_k^{Cortex}=17\pm5$  Hz). These differences were replicated in a second dataset from epilepsy patients  
31 undergoing intracranial monitoring that included thalamic recordings. The consistently lower  
32 aperiodic exponent and lack of an aperiodic knee from all subcortical recordings may reflect  
33 cytoarchitectonic and/or functional differences between subcortical nuclei and the cortex.

## 34 Significance Statement

35 The broadband aperiodic component of local field potentials is a useful and reproducible index  
36 of neural activity. Here we refined a widely used phenomenological model for extracting  
37 aperiodic parameters, with which we fit cortical, basal ganglia and thalamic intracranial local  
38 field potentials, recorded from unique cohorts of movement disorders and epilepsy patients. We  
39 found that the aperiodic exponent in motor cortex is higher in Parkinson's disease patients with  
40 more severe motor symptoms, suggesting that aperiodic features may have potential as  
41 electrophysiological biomarkers for movement disorders symptoms. Remarkably, we found  
42 conspicuous differences in the broadband aperiodic components of basal ganglia and thalamic  
43 signals compared to those from neocortex, suggesting that the aperiodic neural timescale of  
44 subcortical LFPs is slower than that in cortex.

## 45 Introduction

46 From the inception of EEG, understanding the neurophysiology of the oscillatory electrical  
47 activity—periodic activity of defined frequencies which is sustained for more than one period—

48 has been a paramount goal (Berger, 1929). These neural oscillations have been found to be  
49 widespread, spanning all brain regions and frequency bands, and correlate with many aspects of  
50 brain function and dysfunction (Basar and Güntekin, 2013; Engel et al., 2001). The study of  
51 neural oscillations has also been facilitated by commonly used methods like Fourier or wavelet  
52 transforms, which can decompose any signal into a sum of oscillatory components. However, the  
53 existence and mathematical validity of these decompositions does not imply that all brain  
54 activity arises from neural oscillations. Indeed, processes that create fluctuations in the signal  
55 with no underlying oscillatory component give rise to characteristic power spectra when  
56 analyzed by these same methods.

57 Local field potentials (LFPs) reflect the ensemble activity of ionic currents of populations of  
58 cells in the vicinity of the electrode (Lindén et al., 2010; Nunez and Srinivasan, 2006). The most  
59 salient feature of the frequency power spectral density (PSD) of LFPs is the decline of power  
60 with frequency, a feature termed the 1-over-f ( $1/f^\chi$ ) “background noise” of the spectra. Studies  
61 using LFPs commonly remove the  $1/f^\chi$  broadband component by normalization and focus on  
62 modulation of power at specific frequency bands. To contrast the periodic nature of neural  
63 oscillations, the 1-over-f component is referred to as *broadband aperiodic activity*.

64 Until recently, aperiodic activity has been largely ignored or regarded as noise, perhaps due to  
65 inadequate computational tools and theoretical framework. In pioneering work, Miller et al.  
66 fitted a parametric description of the broadband aperiodic component to human  
67 electrocorticography (ECoG) PSD (Miller et al., 2009). The extraction of the aperiodic exponent  
68  $\chi$  has been greatly facilitated by the development of methods like the irregular-resampling auto-  
69 spectral analysis (IRASA) (Wen and Liu, 2016) and fitting of one-over-f (FOOOF) (Donoghue et  
70 al., 2020; Haller et al., 2018). The latter fits the periodic component of the spectrum as a  
71 superpositions of gaussians and parameterizes the aperiodic component as  $P_{aper} = A/(k + f^\chi)$ ,  
72 with an offset **A**, an aperiodic exponent  $\chi$ , and an optional knee parameter **k** (Donoghue et al.,  
73 2020; Haller et al., 2018) (see also Supplementary Materials). Note that this method requires an *a*  
74 *priori* decision of whether to use the knee parameter or not.

75 Using these methods, a recent body of work explored correlations of aperiodic parameters with  
76 different behavioral, physiological, and pathophysiological states, and anatomical regions. The  
77 cortical aperiodic exponent  $\chi$  decreases with age (Dave et al., 2018; Voytek et al., 2015),

78 increases under anesthesia and during sleep (Colombo et al., 2019; Lendner et al., 2020;  
79 Miskovic et al., 2019; Muthukumaraswamy and Liley, 2018), and differs across cortical regions  
80 (Chaoul and Siegel, 2021; Muthukumaraswamy and Liley, 2018). Likewise, the knee **k** of the  
81 spectra (i.e., the frequency at which the  $1/f^{\alpha}$  decline of power with frequency begins) also has a  
82 spatial structure in the cortex (Gao et al., 2020a). Thus, aperiodic parameters are useful  
83 population-average measures of neural activity.

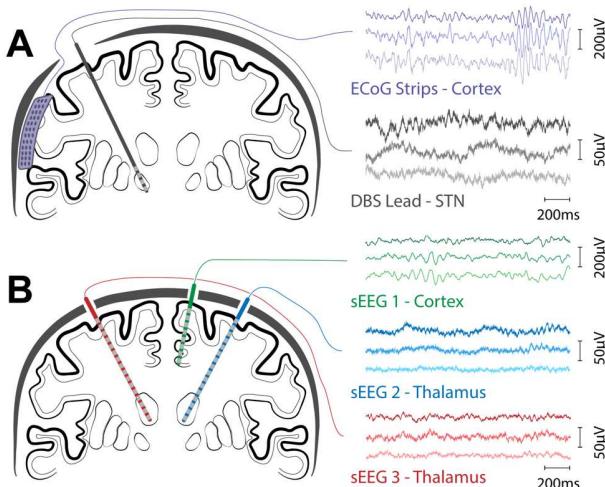
84 Given the importance of understanding the cortical-subcortical neural dynamics that underly  
85 normal human behavior and symptoms of brain diseases, we explored differences in the  
86 parameters of the aperiodic component of LFPs recorded from unique cohorts of neurosurgical  
87 patients. We elaborated on the parameterization of the broadband aperiodic component  
88 developed by (Donoghue et al., 2020; Haller et al., 2018) to obtain a model with better defined  
89 aperiodic parameters that avoids *a priori* assumptions on the presence of an aperiodic knee. We  
90 used this model to explore (across patients) the relation of cortical aperiodic activity with  
91 movement disorder pathophysiology and cortical anatomy, in movement disorders patients  
92 undergoing deep brain stimulation (DBS) surgery. We then performed within subject  
93 comparisons of aperiodic parameters in thalamic and basal ganglia nuclei to those in cortex,  
94 including a second cohort of patients with drug-resistant epilepsy undergoing intracranial  
95 monitoring.

## 96 **Methods:**

97 **Participants.** Movement disorder patients undergoing intracranial electrode implantation for  
98 deep brain stimulation therapy participated in a speech production task (Bush et al., 2021), for  
99 which the baseline periods were analyzed in this study. One or two high-density subdural  
100 electrocorticography (ECoG) strips were temporary placed through the standard burr hole,  
101 targeting the left superior temporal gyrus (covering also the ventral sensorimotor cortex) and left  
102 inferior frontal gyrus. ECoG electrodes were removed at the end of the surgery. Dopaminergic  
103 medication was withdrawn the night before surgery. All procedures were approved by the  
104 University of Pittsburgh Institutional Review Board (IRB Protocol #PRO13110420) and all  
105 patients provided informed consent to participate in the study. The following cohorts of  
106 movement disorder patients participated in the study: 29 Parkinson's disease patients (21M/8F,  
107  $65.6 \pm 7.1$  years) undergoing awake subthalamic (STN) DBS surgery, all of which had ECoG

108 recordings and 14 of which had simultaneous ECoG and DBS lead recordings; 5 Parkinson's  
109 disease patients (5M/0F,  $69.1 \pm 5.7$  years) undergoing awake pallidal (GPi) DBS surgery, of  
110 which 4 had ECoG recordings and 3 had simultaneous ECoG and DBS lead recordings; 22  
111 essential tremor patients (11M/11F,  $65.3 \pm 9.7$  years) undergoing awake thalamic (Vim) DBS  
112 surgery, of which 20 had ECoG recordings and 11 had simultaneous ECoG and DBS lead  
113 recordings.

114 Additionally, we analyzed awake restfulness data from 8 epilepsy patients (5M/3F, age:  $18 \pm 11$   
115 years) undergoing stereo-EEG (sEEG) intracranial monitoring for epilepsy with additional  
116 electrodes implanted in the thalamus. This study was approved by the Massachusetts General  
117 Hospital (Boston, MA) Institutional Review Board (IRB Protocol #2020P000281).



118 **Figure 1. Schematic representation of coronal view of electrode montages.** A) Movement disorder  
119 patients undergoing DBS implantation surgery with simultaneous multichannel recordings from DBS  
120 leads and ECoG strips. B) Epilepsy patients undergoing intracranial monitoring with multichannel sEEG  
121 electrodes, some of which target thalamic nuclei.  
122

123 **Neural recordings.** Figure 1 and Table S1 describe the electrodes used in this study. Signals  
124 from ECoG electrodes and DBS leads were acquired at 30kHz (filtered between 1 Hz and 7.5  
125 kHz) with a Grapevine Neural Interface Processor equipped with Micro2 Front Ends (Ripple  
126 LLC, Salt Lake City, UT, USA). ECoG and DBS lead recordings were referenced to a subdermal  
127 scalp needle electrode positioned approximately on Cz. The sEEG signals were recorded at 1  
128 kHz sampling rate using a 128-channel Xltek digital video-EEG system (Natus Medical  
129 Incorporated, Pleasanton, CA). sEEG recordings were referenced to an EEG electrode placed  
130 extracranially (C2 vertebra or Cz).

131 **Electrode localization.** DBS electrodes were localized using the Lead-DBS localization pipeline  
132 (Horn et al., 2019). Briefly, a pre-operative anatomical T1 weighted MRI scan was co-registered  
133 with a post-operative CT scan. Position of individual contacts were manually identified based on  
134 the CT artifact and constrained by the geometry of the DBS lead used. This process rendered the  
135 coordinates for the leads in each subject's native space. The position of the ECoG strips were  
136 calculated from intra-operative fluoroscopy as described in (Randazzo et al., 2016). Briefly, the  
137 cortical surface was reconstructed from the pre-operative MRI using FreeSurfer (Fischl et al.,  
138 2002) and a model of the skull and stereotactic frame was reconstructed from the intra-operative  
139 CT scan using OsiriX ([osirix-viewer.com](http://osirix-viewer.com)). The position of the frame's tips on the skull and the  
140 implanted DBS leads were used as fiducial markers. The models of the pial surface, skull and  
141 fiducial markers were co-registered, manually rotated and scaled to align with the projection  
142 observed in the fluoroscopy. Once aligned, the position of the electrodes in the ECoG strip were  
143 manually marked on the fluoroscopy image and the projection of those position to the convex  
144 hull of the cortical surface was defined as the electrode location in native space. The coordinates  
145 were then regularized based on the known layout of the contacts in the ECoG strip  
146 ([github.com/Brain-Modulation-Lab/ECoG\\_localization](https://github.com/Brain-Modulation-Lab/ECoG_localization)). All coordinates were then transformed  
147 to the ICBM MNI152 Non-Linear Asymmetric 2009b space (Fonov et al., 2011) using the  
148 Symmetric Diffeomorphism algorithm implemented in the Advanced Normalization Tools  
149 (Avants et al., 2008).

150 Epilepsy patients were implanted with commercially available 8 – 16 contact electrodes (PMT  
151 Corporation, MN, USA; AdTech Medical Instrument Corporation, WI, USA). Electrode  
152 trajectories were tailored for each patient according to the surgical hypothesis and contact  
153 locations were determined by either post-implantation MRI, co-registration of the pre-operative  
154 T1 MRI with the post-implantation CT using Brainstorm (Tadel et al., 2011).

155 Anatomical labels were assigned to each electrode based on the HCP-MMP1 atlas (Glasser et al.,  
156 2016) for cortical electrodes, and the Morel (Morel, 2007) and DISTAL (Ewert et al., 2018)  
157 atlases for subcortical electrodes.

158 **Electrophysiological data preprocessing and power spectrum estimation.** Data recorded  
159 during DBS surgeries was processed using custom code based on the FieldTrip (Oostenveld et  
160 al., 2011) toolbox implemented in MATLAB, available at ([github.com/Brain-Modulation-Lab/bml](https://github.com/Brain-Modulation-Lab/bml)). Data was low pass filtered at 250Hz using a 4<sup>th</sup> order non-causal Butterworth filter,

162 down-sampled to 1 kHz and stored as continuous recordings in FieldTrip datatype-raw. No notch  
163 filter was applied. Electrodes were common average referenced per head-stage connector and  
164 electrode type. Power spectral density (PSD) was estimated using the Welch method (Welch,  
165 1967), using 1 s time windows over the inter-trial baseline periods of the speech task with a  
166 500ms overlap. The median PSD across all baseline periods was calculated for subsequent  
167 analysis. sEEG data recorded for epilepsy monitoring, was processed using the MNE toolbox in  
168 python. Recordings were bipolar referenced and PSDs were estimated using the Welch method  
169 by calculating periodograms for a sliding window of two seconds and overlap of 100 ms.

170 **Spectral parameterization.** We elaborated upon the spectral parameterization introduced by  
171 (Donoghue et al., 2020; Haller et al., 2018) to capture the frequency domain characteristics of  
172 electrophysiological data. This parameterization decomposes the log-power spectra **log(P(f))**  
173 into a broadband aperiodic component **log(L(f))** and the summation of **N** narrowband periodic  
174 components which are each modelled as a Gaussian.

$$\log(P(f)) = \log(L(f)) + \sum_{n=0}^N a_n e^{-\frac{(f-f_{c,n})^2}{2w_n^2}} \quad (1)$$

175 where **f** is the frequency, **a<sub>n</sub>** is the power, **f<sub>c,n</sub>** the center frequency and **w<sub>n</sub>** is the width of the  
176 Gaussian **n** (i.e., the standard deviation). Gaussians were used to model physiological oscillations  
177 and spectral artifacts like line noise. This approach was preferred over using notch filters as  
178 spectra with notches were not adequately fitted by the proposed model. In this work we propose  
179 a new parameterization of the aperiodic component defined as

$$L(f) = A \frac{f_k^\chi + f_{\min}^\chi}{f_k^\chi + f^\chi} \quad (2)$$

180 where **A** is the broadband offset and can be interpreted as the power fitted at the minimal  
181 frequency of interest **f<sub>min</sub>**, that is, the smallest positive frequency for which power can be reliably  
182 estimated based on acquisition, preprocessing, and PSD estimation method and parameters. For  
183 the current work, it was determined as **f<sub>min</sub> = max{f<sub>HP</sub>, f<sub>s</sub>/m}**, the largest between **f<sub>HP</sub>**, the  
184 cutoff frequency of the high-pass filter applied at acquisition (or preprocessing), and the smallest  
185 positive frequency calculated by the Welch method **f<sub>s</sub>/m**, where **f<sub>s</sub>** is the sampling rate and **m**  
186 the number of samples in the Welch window. The parameter **f<sub>k</sub>** is the knee frequency which (for  
187 **f<sub>k</sub> > f<sub>min</sub>**) can be interpreted as the frequency at which the power decays to approximately A/2.

188 The rate at which the power decreases for frequencies above  $f_k$  is defined by the aperiodic slope  
189  $\chi$ . We also modified the original algorithm proposed by (Haller et al., 2018) to scan  $f_k$   
190 logarithmically, therefore ensuring positive values. This change also allows the full model to  
191 adequately fit cases in which there is no knee in the PSD by converging to  $f_k \ll f_{min}$ . For  
192 computational reasons we restricted the range of  $f_k$  from  $f_{min}/10$  to  $f_{Nyquist}$ . See the  
193 supplementary materials for a discussion on the advantages of using this parameterization over  
194 the original one proposed by (Donoghue et al., 2020; Haller et al., 2018).  
195 Additionally, we modified the cost function ( $J$ ) of the fitting procedure by adding to the mean  
196 squared error term a regularization term that penalizes the integral of the gaussians over negative  
197 frequencies (Equation 3),

$$J = \frac{1}{M} \sum_{i=1}^M (Y_i - \hat{Y}_i)^2 + \lambda \sum_{n=0}^N \int_{-\infty}^{f_{min}} G_n(F) dF \quad (3)$$

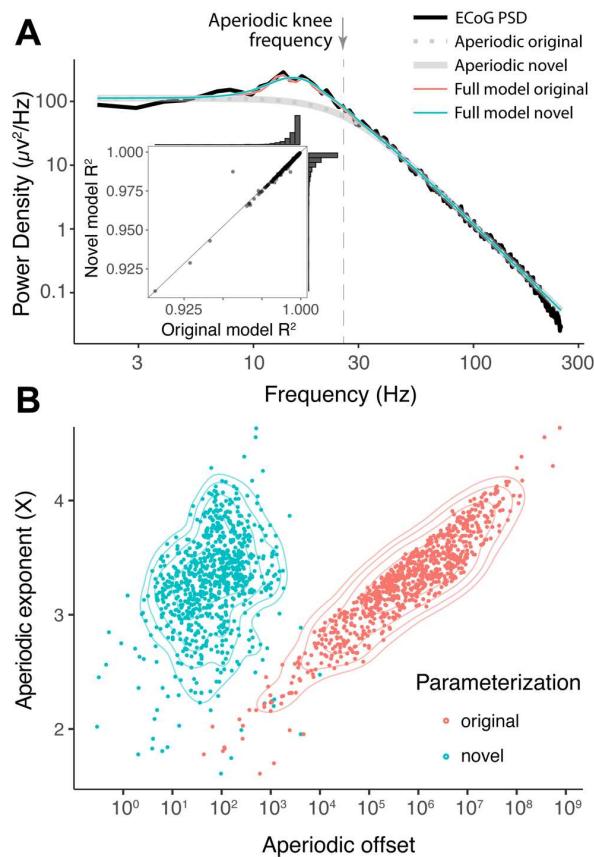
198 where  $Y_i$  is the log-power estimated by the Welch method at frequency  $f_i$ , and  $\hat{Y}_i$  is the value  
199 fitted by the model. The second term was added to prevent Gaussian peaks to extend beyond the  
200 fitting range, which can affect the estimation of aperiodic component (Gerster et al., 2022). The  
201 regularization parameter  $\lambda$  was empirically adjusted for each dataset. Algorithm development  
202 and analyses for this work were done in Python. Scripts and packages are available at  
203 [github.com/Brain-Modulation-Lab/foof/tree/lorentzian](https://github.com/Brain-Modulation-Lab/foof/tree/lorentzian).

204 **Statistical analysis.** We performed statistical analyses in R. Base functions were used for  
205 correlation tests, paired t-tests, linear models, and Fisher exact test for count data. The *coin*  
206 package was used for permutation tests (Hothorn et al., 2008), *lmerTest* for linear mixed effects  
207 models (Kuznetsova et al., 2017) and *multcomp* for multiple comparisons (Bretz et al., 2011).

## 208 Results

209 To explore differences between the aperiodic components of cortical and basal ganglia or  
210 thalamic LFPs, we elaborated upon the FOOOF method (Donoghue et al., 2020; Haller et al.,  
211 2018) by incorporating a new Lorentzian-like parameterization of the broadband aperiodic  
212 component, changing the way parameters are scanned and adding a regularization term (see  
213 methods and supplementary materials for details). These changes result in more easily  
214 interpretable parameters, with well-defined units and better parameter identifiability (Cedersund

215 and Roll, 2009) (Figure S1). These modifications also allow fitting of the same model to power  
216 spectra with qualitatively different profiles. In the original description, parameterization required  
217 an *a priori* selection of one of two possible models (with or without a “knee” parameter); our  
218 modifications allow seamless fitting of either case with the same model.

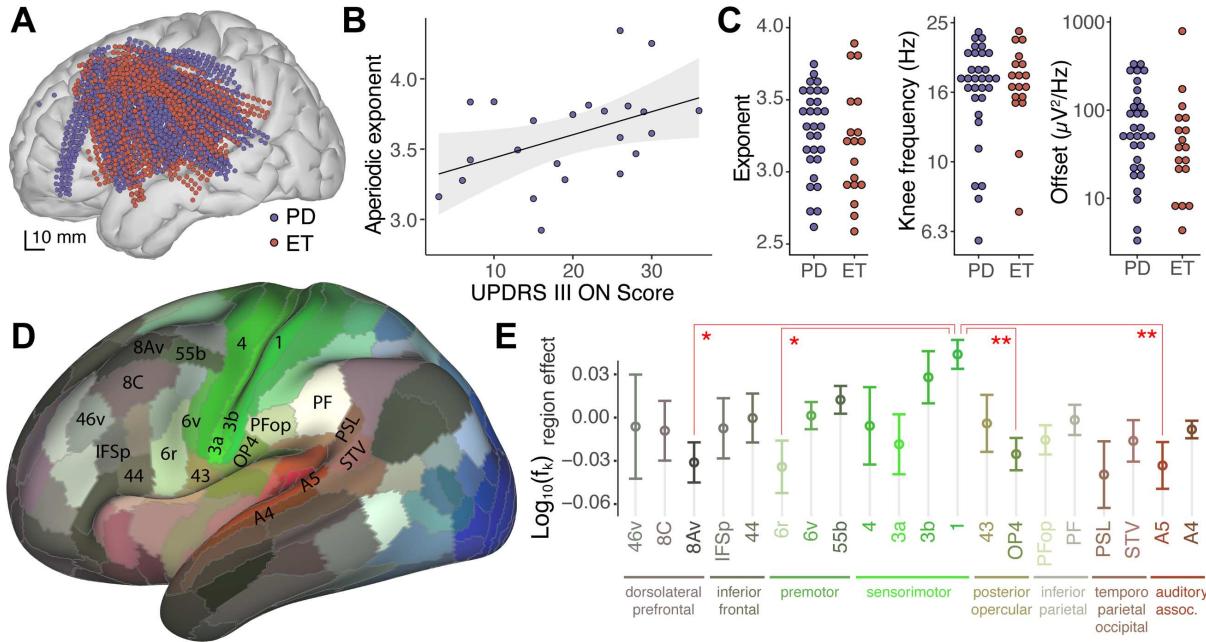


**Figure 2. The novel parameterization of the aperiodic component avoids collinearity between parameters.** A) Representative example of cortical power spectra with fits from original and novel models. The inset shows the correlation between  $R^2$  values for both models, and their univariate distribution in data from PD participants. B) Aperiodic exponent vs. offset parameters for ECoG recordings from PD patients, for the original (red) and novel (blue) parameterizations. Contour lines represent the 5%, 10%, 20%, 40% and 80% percentiles of 2D kernel density estimation.

219  
220 First, to assess the performance of the novel parameterization, we fitted the power spectra of  
221 ECoG recordings acquired from movement disorder patients undergoing awake DBS  
222 implantation surgery. Baseline epochs recorded during rest periods in a speech production task  
223 were used for this analysis. The novel parameterization fits the data as well as the original  
224 implementation (Figure 2a);  $R^2$  values of both models are virtually identical and tightly cluster at  
225 values above 0.975 (Figure 2a inset). However, the aperiodic parameters for the novel  
226 formulation do not show the strong collinearity observed for the parameters of the original model  
227 (Figure 2b and S2). In this context, collinearity is indicative of poor parameter identifiability,  
228 leading to larger uncertainties of the parameters (Cedersund and Roll, 2009). (Note however that  
229 there is a residual correlation between the aperiodic knee and the exponent of the spectra, Figure  
230 S2b). Our novel formulation also better constrains the range of values of the parameters, for

231 example the aperiodic offset spans 6 orders of magnitudes for the original model but only 2 in  
232 the novel formulation (Figure 2b).

233



234

235 **Figure 3. Cortical aperiodic parameters correlate with PD severity and anatomical regions.** A)  
236 Anatomical localization of ECoG electrodes used to record cortical activity from Parkinson's disease (PD,  
237 blue) and essential tremor (ET, red) patients undergoing DBS surgery. B) Median cortical aperiodic  
238 exponent from Rolandic and premotor ECoG recordings in PD patients undergoing STN-DBS surgery vs.  
239 preoperative UPDRS-III ON score. Shaded region represents CI<sub>95</sub>. C) Median values of cortical aperiodic  
240 exponent (left), knee frequency (center) and offset (right) for each subject, color coded by diagnosis. D)  
241 Lateral view of cortical parcellation defined by MMP1 on an inflated brain, colored according to fMRI  
242 response to visual (blue), auditory (red) or somatosensory (green) tasks (Glasser et al., 2016). E)  
243 Aperiodic knee frequency cortical region effect (after accounting for subject effect) vs. anatomical  
244 regions, as defined in the MMP1 atlas, for regions recorded by electrodes from 10 or more subjects. To  
245 avoid effects from differences in sampling density, statistics were done on the average per region per  
246 subject. Error bars indicate the SEM across subjects. Colors as in D.

247

248 Using this new parameterization, we explored cortical aperiodic activity from ECoG recordings  
249 in PD patients undergoing STN-DBS implantation. Across participants, electrodes covered the  
250 left inferior frontal cortex, precentral and postcentral gyrus, superior and middle temporal gyrus  
251 (blue dots in Figure 3a). Interestingly, we found a significant positive correlation between the  
252 pre-operative UPDRS-III ON score and the aperiodic exponent from Rolandic and premotor  
253 cortical areas ( $r=0.4$ ,  $p=0.036$ , Pearson correlation, Figure 3b), but not from other cortical  
254 regions. However, no significant correlation was found with the UPDRS-III OFF score ( $r=0.25$ ,

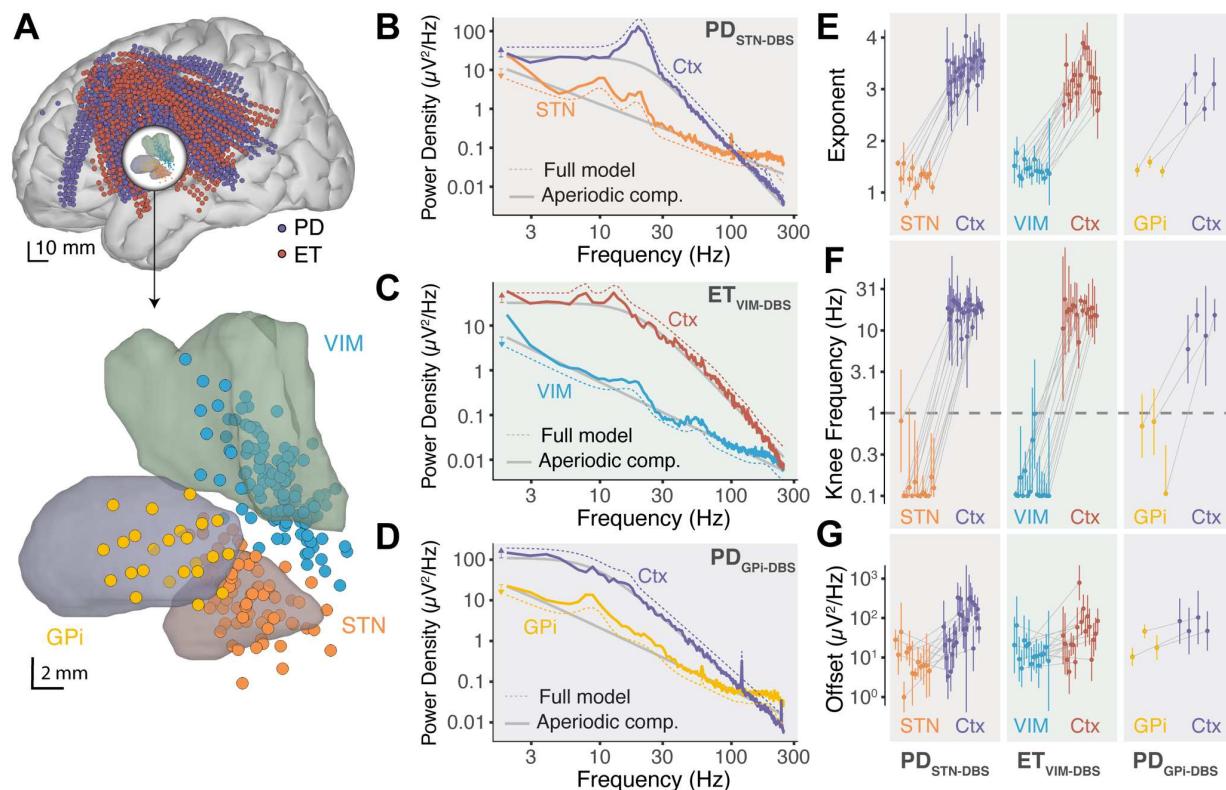
255 p=0.22), nor the UPDRS-III ON/OFF percent change ( $r=0.33$ ,  $p=0.13$ , Figure S3). There was no  
256 significant difference in cortical aperiodic parameters extracted from ECoG of PD and essential  
257 tremor (ET) patients for the exponent ( $p=0.28$ , permutation test), knee frequency ( $p=0.68$ ) or  
258 offset ( $p=0.28$ , Figure 3c). Therefore, we pooled data across these two cohorts for subsequent  
259 analyses. There was no significant correlation of the aperiodic components with age ( $p=0.44$ ,  
260 Pearson correlation). Note that the age range of this cohort (43-79 yrs) does not include the  
261 younger adult group (18-30 yrs) from previous studies (Dave et al., 2018; Voytek et al., 2015).  
262 We grouped electrodes according to the multimodal parcellation 1 atlas (HCP-MMP1, (Glasser  
263 et al., 2016), Figure 3d), and used a mixed effects model to account for subject-to-subject  
264 variability. In line with recent reports (Chaoul and Siegel, 2021; Gao et al., 2020a;  
265 Muthukumaraswamy and Liley, 2018) we found significant differences in aperiodic parameters  
266 across cortical regions (Figure 3e, Table S2). We observed that the aperiodic knee frequency in  
267 primary sensory cortex “1” was significantly greater than that observed in frontal regions “8Av”  
268 ( $p=0.014$ ) and “6r” ( $p=0.017$ ), opercula area 4 “OP4” ( $p<0.01$ ) and secondary auditory cortex  
269 “A5” ( $p<0.01$ , Tukey’s Contrast for region effect).

270 Next, we explored the aperiodic potentials from subcortical recordings acquired through the DBS  
271 leads. For PD patients, DBS leads targeted the dorsal-posterior-lateral portion of the subthalamic  
272 nucleus (STN) or the inferior-posterior-lateral globus pallidus internus (GPi), whereas for ET  
273 patients leads targeted the ventral intermedius (VIM) nucleus of the thalamus (Figure 4a). In  
274 contrast to what was observed for cortical recordings, no obvious ‘knee’ was apparent in power  
275 spectra from the STN, VIM or GPi (Figure 4b, 4c and 4d); the aperiodic component of  
276 extracellular potentials for these subcortical structures decreases with frequency starting from the  
277 minimal frequency acquired. These qualitative differences with ECoG PSDs could be due to the  
278 different electrode types (see Table S1 for details), reflect underlying electrophysiology, or a  
279 combination of both effects (see discussion). To quantify these differences, we fit subcortical  
280 power spectra using the same model as for cortical data (Figure 4b, 4c and 4d).

281 The distribution of aperiodic parameters in STN recordings is remarkably different to that in  
282 cortical ECoG signals from the same subjects (Figure 4e, 4f and 4g, left panels). The aperiodic  
283 exponent for the STN has a median of  $1.30\pm0.21$  (median  $\pm$  standard deviation across subjects),  
284 almost 3-fold smaller than that of ECoG recordings  $3.41\pm0.30$  for the same subjects ( $p<10^{-5}$ ,  
285 paired t-test, Table 1, Figure 4e). This difference in the aperiodic exponent between cortical and

286 STN recordings reaches significance for all individual subjects analyzed (Figure 4e). Contrary to  
 287 what we observed for cortical recordings, there was no correlation between the aperiodic slope  
 288 from the STN and preoperative UPDRS-III ON or OFF scores ( $p=0.9$  and  $p=0.7$  respectively,  
 289 Pearson correlation). The aperiodic exponent from DBS lead recordings in VIM and GPi were  
 290 also significantly different from the simultaneous cortical recordings in each patient ( $p<10^{-5}$  for  
 291 VIM,  $p=0.03$  for GPi, paired t-test, Figure 4e).

292



293

294 **Figure 4. Power spectra of extracellular potentials from STN, VIM and GPi show no knee and**  
 295 **lower aperiodic exponent than cortical recordings.** A) Anatomical localizations of cortical and  
 296 subcortical electrodes from the DBS lead, relative to the STN, GPi and VIM (Distal and Morel atlases,  
 297 respectively). B) Representative example of power spectra, aperiodic component (gray lines) and model  
 298 fit (dashed lines) for a STN and a cortical contact from the same subject. Note that for visual clarity the  
 299 full-model fits were displaced vertically as indicated by the colored arrows on the left of the plot. C)  
 300 Same as B for VIM. D) Same as B for GPi. E) Distribution of fitted aperiodic exponents for STN, VIM  
 301 and GPi compared to cortex in individual subjects. Each dot corresponds to the median and error-bars to  
 302 the standard deviation of all electrodes within the corresponding brain region. Gray lines join subcortical  
 303 and cortical values for individual subjects. F) Same as E for the aperiodic knee frequency. Note that the y  
 304 axis is in log-scale. The dashed horizontal line represents the smallest positive frequency acquired  $f_{\min}$ .  
 305 Fits with knee frequencies smaller than  $f_{\min}$  indicate spectra without observable knee. G) Same as E for  
 306 the aperiodic offset.

Cohort	Location	Electrode type	N <sub>s</sub>	Exponent	Offset (μV <sup>2</sup> /Hz)	f <sub>k</sub> (Hz)	P(f <sub>k</sub> < f <sub>min</sub> )	τ (ms)
PD <sub>STN-DBS</sub>	STN	DBS lead	13	1.30±0.21	7.6 [2.9; 20]	< 1	85±4%	> 159
	Cortex	ECoG	26	3.41±0.30	55 [15; 208]	17.6 [13.3; 23.3]	1.1±0.2%	9.0 [6.8; 12.7]
ET <sub>VIM-DBS</sub>	VIM	DBS lead	15	1.42±0.14	11.7 [6.0; 23]	< 1	87±3%	> 159
	Cortex	ECoG	18	3.20±0.36	38 [11; 133]	17.0 [12.9; 22.6]	0.9±0.2%	9.4 [7.0; 12.3]
PD <sub>GPI-DBS</sub>	GPI	DBS lead	3	1.43±0.10	17.8 [8.4; 38]	< 1	73±9%	> 159
	Cortex	ECoG	4	2.91±0.32	63 [42; 94]	11.4 [7.2; 18.2]	1.6±0.6%	13.9 [8.7; 22.1]
EP <sub>sEEG</sub>	Thalamus	sEEG	8	1.33±0.23	4.2 [1.0; 18.2]	< 1	79±4%	> 159
	Cortex	sEEG	8	2.96±0.36	96 [14; 664]	7.6 [3.1; 18.3]	3.7±1.6%	20.9 [8.7; 51.3]

**Table 1. Mean and dispersion of aperiodic parameters across patient cohorts and brain structures.**

Exponent: Mean ± Standard deviation across patients. Offset (μV<sup>2</sup>/Hz): Median [Q<sub>16</sub>; Q<sub>84</sub>], note the asymmetric distribution. f<sub>k</sub>: Knee frequency in Hz, Median [Q<sub>16</sub>; Q<sub>84</sub>]. P(f<sub>k</sub> < f<sub>min</sub>): percentage (± standard error) of electrodes with knee frequency lower than f<sub>min</sub>. τ = (2πf<sub>k</sub>)<sup>-1</sup>: aperiodic neural timescale in milliseconds. Abbreviations: PD, Parkinson's disease; ET, essential tremor; EP, epilepsy; STN, subthalamic nucleus; VIM, ventral intermedius nucleus of the thalamus; GPI, globus pallidus internus; N<sub>s</sub>, number of subjects.

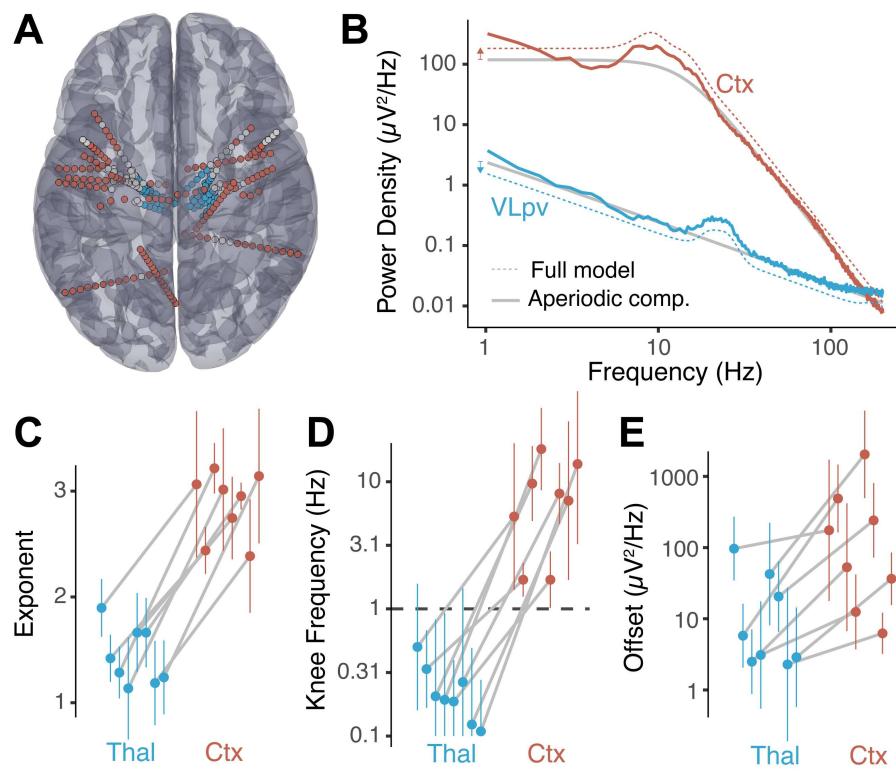
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314 The calculated aperiodic knee frequency also exhibited a strikingly different distribution for  
315 STN, VIM and GPI than for the cortex (Table 1, Figure 4f). While the cortical knee frequencies  
316 center at 17±5 Hz (median ± standard deviation across subjects), those for STN, GPI and VIM  
317 converge to values lower than the smallest positive frequency of the power spectra (f<sub>min</sub> = 1 Hz,  
318 dashed line in Figure 4f), in many cases reaching the lower boundary allowed for the fitting  
319 algorithm (0.1 Hz). It is important to note that knee frequency values smaller than f<sub>min</sub> should  
320 not be interpreted quantitatively, instead, they indicate the absence of a knee in the power spectra  
321 within the frequency range acquired. In other words, if there is a knee for the power spectra of  
322 STN, GPI and VIM, this value is lower than 1 Hz. Due to the high-pass frequency filters applied  
323 at acquisition it is not possible to explore lower frequencies in this dataset. The proportion of  
324 power spectra without a knee P(f<sub>k</sub> < f<sub>min</sub>) is significantly higher for STN, VIM and GPI  
325 recordings than for cortical recordings (Table 1, p<10<sup>-6</sup>, Fisher test).

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Given the large difference observed in aperiodic parameters for STN, GPI and VIM as compared  
to cortex, we asked if these differences are specific to the types of electrodes used to record from  
subcortical nuclei in movement disorder patients or, on the contrary, generalize to other electrode  
types, subcortical structures, and diagnoses. To this end, we explored baseline recordings from 8  
epilepsy patients undergoing intracranial monitoring with electrodes implanted in the thalamus

331 for the purpose of assessing thalamic participation in the hypothesized seizure network and  
332 potential for therapeutic neuromodulation (Richardson 2022) (Figure 5a). In these recordings, the  
333 same type of stereo-EEG electrode contacts, and in some cases contacts on the same electrode,  
334 were used for cortical and thalamic targets. Thalamic contacts covered several thalamic nuclei  
335 from the ventral division (VLpd, VPLp, VLpv, VLa, VPM) to intralaminar nuclei (CM, MDpc,  
336 Pf, CL) (Morel, 2007) (see Table S3), whereas selected cortical contacts covered parietal and  
337 frontal regions (Figure 5a). As before, we found that thalamic power spectra show no observable  
338 knee, whereas cortical spectra from the same patients show prominent aperiodic knees (Figure  
339 5b).



340

341 **Figure 5. Power spectra from thalamic sEEG recordings show no knee and lower aperiodic**  
342 **exponent than cortical sEEG signals. A)** Anatomical localizations of selected sEEG electrodes for  
343 epilepsy patients with thalamic implantations. **B)** Representative example of power spectra aperiodic  
344 component (gray line) and model fit (dashed lines) from a cortical sEEG contact (red) and thalamic sEEG  
345 (blue) recordings. For visual clarity, the full-model fits were displaced vertically as indicated by the  
346 colored arrows on the left. **C)** Distribution of fitted aperiodic exponents for thalamic bipolar pairs  
347 compared to cortex in individual subjects. Each dot corresponds to the median and the error-bars to the  
348 standard deviation of all bipolar pairs within the thalamus and cortex. The gray lines join parameters of  
349 the same subject. **D)** Same as C for the knee frequency. Note that the y axis is in log-scale. The dashed  
350 horizontal line represents  $f_{\min}$ . **E)** Same as C for the aperiodic offset.

351 A large difference in aperiodic exponent between cortical and thalamic electrodes was observed  
352 ( $p < 0.001$ , paired t-test, Figure 5c, Table 1), consistent with the results obtained from movement  
353 disorder patients (Figure 4e). This difference holds at the single subject level, showing consistent  
354 changes across subjects (Figure 5c, gray lines). The aperiodic knee frequency also showed  
355 significant differences for thalamic and cortical contacts (Figure 5d), with thalamic values falling  
356 almost exclusively below  $f_{\min}$  (smallest positive frequency of the spectra) and cortical values  
357 above this threshold ( $p < 10^{-6}$ , Fisher exact test).

358 Note that the aperiodic exponent of thalamic sEEG recordings in epilepsy patients ( $1.33 \pm 0.23$ )  
359 was not significantly different than that of DBS lead recordings in movement disorder patients  
360 (Table 1,  $p > 0.05$  for all pairwise comparisons by FDR-corrected permutation test). Similarly, the  
361 knee frequency extracted was below the cut-off value of  $f_{\min} = 1\text{Hz}$ , as was the case for DBS  
362 recordings.

### 363 Discussion

364 Almost every cortical region projects to and receives projections from the thalamus and other  
365 subcortical structures (Caviness and Frost, 1980; Sherman, 2016). These interactions provide a  
366 substrate for communication between distant cortical regions, facilitating spatial integration of  
367 the brain (Grant et al., 2012) and creating circuits with massive convergence and divergence in  
368 cell number at different nodes, as in the cortico-basal ganglia-thalamo-cortical loop (Bergman,  
369 2021; Wilson, 2013). This organization involves regions whose cell types differ on many levels  
370 including channel and receptor expression, morphology, cytoarchitectures, and proportions of  
371 excitatory and inhibitory interactions, differences that allow for distinct dynamical behaviors and  
372 computational properties across brain structures.

373 In this study we performed systematic analysis of the broadband aperiodic component of brain  
374 recordings from multiple locations of the cortico-basal ganglia-thalamo-cortical loop, by fitting a  
375 phenomenological model to the power spectra of LFPs (Donoghue et al., 2020; Haller et al.,  
376 2018). We developed a novel parameterization of the broadband aperiodic component with the  
377 following advantages: 1) well-defined units for all parameters, 2) easily interpretable parameters,  
378 3) structurally uncorrelated parameters, 4) parameters with more constrained physiological  
379 ranges, and 5) ability to fit spectra with or without an aperiodic ‘knee’ using the same model (see  
380 Figure 2a-b and Supplementary Materials). Interestingly, even with the novel parameterization of

381 the aperiodic exponent, which removes structural correlations between parameters (Cedersund  
382 and Roll, 2009), residual positive correlation between the aperiodic knee and the exponent of the  
383 spectra (Figure S2b) was observed, suggesting that these parameters could be coupled.

384 Using this model to fit power spectra from baseline ECoG recordings from patients undergoing  
385 DBS implantation surgery, we found that the cortical aperiodic exponent correlates with  
386 Parkinson's disease severity as assessed by the pre-operative UPDRS III (on-medication, Figure  
387 3b). This novel result is in line with a MEG finding showing higher aperiodic exponents for PD  
388 patients compared to neuro-typical controls (Vinding et al., 2020). In our data, the correlation  
389 with the aperiodic exponent did not reach significance for the pre-operative UPDRS-OFF score,  
390 even though patients were in an OFF state during the intra-operative recordings. This could be  
391 due to less sensitivity or higher variability for the UPDRS-OFF score (as compared to the ON  
392 score) for the clinical population undergoing DBS treatment, which is biased to high symptom  
393 severity. There were no significant correlations of the STN LFP aperiodic exponent with  
394 UPDRS-III score (ON nor OFF levodopa), consistent with a recent report (Wiest et al., 2022).

395 Total beta power is known to correlate with PD disease severity in the basal ganglia (Brown et  
396 al., 2001; Cassidy et al., 2002; Kühn et al., 2004) and sensory-motor cortex (Pollok et al., 2012;  
397 Williams et al., 2002). FOOOF was designed to decouple oscillations from the underlying  
398 broadband aperiodic component, which reflects features of the entire spectrum, not just a specific  
399 band. However, estimations of aperiodic parameters can be affected by oscillatory components  
400 that extend beyond the fitting range (Gerster et al., 2022). This is not the case for our data since  
401 beta (12-30Hz) frequencies are above the lower frequency acquired ( $f_{\min}=1\text{Hz}$ ). Additionally, we  
402 included a regularization term penalizing peaks below  $f_{\min}$  to avoid this pitfall (see methods).  
403 Indeed, the fact that we obtained a significant correlation of the aperiodic exponent with UPDRS  
404 for motor cortex but not in the basal ganglia (which has prominent pathological beta  
405 oscillations), suggests that the method is correctly decoupling the aperiodic component from  
406 oscillatory features. Interestingly, changes in the aperiodic exponent could contribute to the  
407 known correlation of total beta power with UPDRS (Pollok et al., 2012; Williams et al., 2002)  
408 and to the ability of algorithms based on holistic spectral features to differentiate PD patients  
409 from controls (Anjum et al., 2020).

410 The main finding of this work is the conspicuous difference in the aperiodic component of the  
411 spectra between cortical recordings and those of basal ganglia and thalamic nuclei (Figure 4 and

412 5). Whereas cortical recordings showed an aperiodic knee with significant changes across  
413 cortical regions (Figure 3e, consistent with recent reports (Chaoul and Siegel, 2021; Gao et al.,  
414 2020b; Muthukumaraswamy and Liley, 2018)), spectra from basal ganglia and thalamic nuclei  
415 show no knee, an observation we could systematically evaluated thanks to the novel  
416 parameterization of the broadband aperiodic component. Spectra from subcortical regions  
417 showed an aperiodic exponent close to one ( $\chi = 1.3 \pm 0.2$ ), significantly smaller than in cortex  
418 ( $\chi = 3.2 \pm 0.3$ ). These results are reproducible across patients, two medical centers, electrode  
419 types, recording systems, referencing montages, diagnoses, and subcortical structures.  
420 Furthermore, the value for the aperiodic exponent in the STN we measured is consistent with  
421 recent studies that estimated this parameter (Huang et al., 2020; Wiest et al., 2022).

422 A limitation of this work is that ECoG electrodes lie over the pia mater, whereas the DBS leads  
423 penetrate the brain parenchyma. However, our data from epilepsy patients was recorded from the  
424 same type of sEEG electrodes for cortical and thalamic regions. Notably, these multi-contact  
425 electrodes are similar in size, shape, and impedance value to DBS lead contacts (Supplementary  
426 Table S1). We observed the same qualitative difference in aperiodic parameters between cortical  
427 and subcortical regions in both datasets, suggesting that these differences cannot be fully  
428 explained by electrode type and are due to structural and/or functional properties of the recorded  
429 brain areas. Another important limitation of our work is that different subcortical regions were  
430 recorded from different clinical populations. Therefore, we did not compare parameters across  
431 subcortical regions since the pathology would be an unavoidable confound; we limited our  
432 analysis of cortical vs. subcortical aperiodic activity to within-subject comparisons.

433 Neural morphology affects the shape and amplitude of extracellular potentials and could explain  
434 the differences in aperiodic activity observed between cortical and subcortical structures. Cells  
435 with large spatial separation between current sinks and return currents (like cortical pyramidal  
436 neurons) induce substantial extracellular ionic flows and large perturbations of the extracellular  
437 potential (Johnston and Wu, 1995). In contrast, neurons with roughly spherically symmetric  
438 dendritic arbors (like thalamocortical or STN neurons) do not produce strong current dipoles,  
439 with smaller contributions to recorded extracellular field potentials (Buzsáki et al., 2012;  
440 Johnston and Wu, 1995). However, synaptic inputs to subcortical structures may have  
441 asymmetric distributions which can produce measurable field potentials (Buzsáki et al., 2012;  
442 Lindén et al., 2010; Tanaka and Nakamura, 2019), for example having inhibitory synapses closer

443 to the soma and more distal excitatory inputs (Lempka and McIntyre, 2013; Mazzoni et al., 2015;  
444 Wilson, 2010).

445 Although neuronal densities are comparable between cortical gray matter, STN and VIM  
446 (Bergman, 2021; Lévesque and Parent, 2005), the spatial arrangement of neurons can also have a  
447 large effect on the recorded extracellular potential (Gold et al., 2006; Johnston and Wu, 1995;  
448 Pettersen et al., 2008). In neuronal populations organized in layers, such as the 6-layered  
449 neocortex, simultaneous contributions from multiple similarly oriented cells will add up to give  
450 large fluctuations of the extracellular potential. In contrast, in neurons that have spatially  
451 isotropic arrangements, as in subcortical nuclei, simultaneous contributions from different units  
452 in diverse orientation can cancel out to some extent, producing overall smaller extracellular  
453 potentials (Johnston and Wu, 1995). These structural differences can explain why the overall  
454 power of field potentials is lower in subcortical nuclei than in neocortex. However, they do not  
455 explain why the aperiodic exponent and knee are different across these structures.

456 Several mechanisms have been suggested as the origin of the  $1/f^\chi$  aperiodic component,  
457 including ionic diffusion and induction of electric fields in passive cells (Bédard et al., 2006a;  
458 Bédard and Destexhe, 2009). However, these effects are likely to be present in all brain regions.  
459 The shape and length of the dendrites, along with the location of the synaptic input can give rise  
460 to different frequency dependences of the intrinsic dendritic filtering (Lindén et al., 2010). Due  
461 to the different morphology of cortical versus thalamic and basal ganglia neurons, this could  
462 contribute to the difference in  $1/f^\chi$  slope observed. However, the aperiodic slope in the STN  
463 has been shown to change with Propofol anesthesia (Huang et al., 2020), dopaminergic  
464 medication and DBS treatment (Wiest et al., 2022), demonstrating that this parameter depends on  
465 dynamical aspects of neural activity and cannot be fully explained by morphology and  
466 cytoarchitecture.

467 Functional differences like the profile and characteristic duration of post-synaptic currents can  
468 affect the aperiodic slope. For example, sharp rise and exponential decays for post-synaptic  
469 currents give rise to a  $1/f^2$  decline of power (Bédard et al., 2006b; Miller et al., 2009; Milstein  
470 et al., 2009), and the ratio of excitatory to inhibitory inputs can affect the aperiodic knee  
471 frequency of the spectra (Gao et al., 2017). Transitions between UP and DOWN states (i.e., rapid  
472 trains of correlated synaptic inputs followed by quiescent periods), can give rise to power spectra

473 following  $1/f^2$  decline (Baranauskas et al., 2012; Milstein et al., 2009). In contrast, Poissonian  
474 inputs uncorrelated across cells do not contribute to the frequency dependency of the spectra  
475 (Bédard et al., 2006b; Miller et al., 2009; Milstein et al., 2009). Interestingly, there is a  
476 surprisingly low spike-timing correlation in the pallidum (Bar-Gad et al., 2003; Nini et al., 1995;  
477 Raz et al., 2000) and structures with strong pallidal input, including GPi, STN and several nuclei  
478 of the ventral thalamus will have low input correlation, which contribute to the low amplitude  
479 (Lindén et al., 2011) and slow decline with frequency of the power spectra in these regions.

480 There is currently no consensus on the physiological interpretation of the aperiodic knee and its  
481 change across brain structures. Miller et al. showed in ECoG recordings an aperiodic slope of  
482  $\chi=2$  for frequencies above 15 Hz up to a "knee" around 75 Hz, at which the aperiodic slope  
483 changed to  $\chi=4$ , implying the existence of a characteristic time scale  $\tau = (2\pi f_k)^{-1} = 2 - 4\text{ms}$   
484 (Miller et al., 2009). Using similar reasoning on the knee observed around 10 Hz, Gao et al.  
485 proposed the existence of an "aperiodic neural timescale" (of around 10 to 50 ms) that can be  
486 interpreted as the characteristic duration of an aperiodic fluctuation of the LFP (Gao et al.,  
487 2020b). In our data, this timescale is in the range of 10 to 20 ms (Table 1) and changes across  
488 cortical locations (Figure 3e), which is consistent with previous findings and suggests that this  
489 parameter might be reflecting an intrinsic feature of cortical micro-circuitry and computation  
490 (Gao et al., 2020b).

491 The lack of an observable aperiodic knee for thalamic and basal ganglia recordings (i.e., the  
492 fitted value is lower than the cut-off frequency  $f_{\min}$ ; Figure 4 and 5) can be interpreted as  
493 reflecting the absence of any characteristic duration of aperiodic fluctuations (strict  $1/f$  power  
494 law). However, the neural morphology and cytoarchitecture of these regions might prevent  
495 characteristic aperiodic fluctuations from being reflected in LFPs. Alternatively, the aperiodic  
496 neural timescale could be longer than what can be detected by our method due to technical  
497 limitations. The latter interpretation puts a lower bound of 129ms for the subcortical aperiodic  
498 neural timescale ( $\tau > (2\pi f_{\min})^{-1} = 129\text{ms}$  for  $f_{\min} = 1\text{Hz}$ ) and suggests that basal ganglia  
499 and ventral thalamic nuclei are slower than cortex in terms of their aperiodic fluctuations.  
500 Although speculative, this interpretation suggests that the basal ganglia-thalamo-cortical loop  
501 could be a site of temporal-integration, a notion that aligns well with the known role of this  
502 circuit in spatial-integration, action selection and motor control (Bergman, 2021; DeLong and  
503 Wichmann, 2010; Grant et al., 2012; Mink, 1996; Turner and Desmurget, 2010).

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508 <https://dabi.loni.usc.edu/dsi/1U01NS098969>) and is available upon request.

509 **Author Contributions:** W.J.L. and R.M.R. performed the intraoperative recordings. A.B.,  
510 W.J.L., and V.K. reconstructed the electrode localizations. A.B., W.J.L., V.K., and J.Z.  
511 preprocessed electrophysiological data. A.B. and J.Z. developed and implemented the model and  
512 analyzed data. A.B. and R.M.R. conceived the study and wrote the manuscript. All authors  
513 discussed the results and commented on the manuscript. The authors declare no competing  
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515  
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