

1 **The timescale and magnitude of 1/f aperiodic activity decrease with cortical**
2 **depth in humans, macaques, and mice**

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28 **Abstract**

29 Cortical dynamics obey a $1/f$ power law, exhibiting an exponential decay of spectral power with
30 increasing frequency. The slope and offset of this $1/f$ decay reflect the timescale and magnitude of
31 aperiodic neural activity, respectively. These properties are tightly linked to cellular and circuit
32 mechanisms (e.g. excitation:inhibition balance and firing rates) as well as cognitive processes (e.g.
33 perception, memory, and state). However, the physiology underlying the $1/f$ power law in cortical
34 dynamics is not well understood. Here, we compared laminar recordings from human, macaque
35 and mouse cortex to evaluate how $1/f$ aperiodic dynamics vary across cortical layers and species.
36 We report that $1/f$ slope is steepest in superficial layers and flattest in deep layers in each species.
37 Additionally, the magnitude of this $1/f$ decay is greatest in superficial cortex and decreases with
38 depth. We could account for both of these findings with a simple model in which superficial
39 cortical transmembrane currents had longer time constants and greater densities than those in
40 deeper layers. Together, our results provide novel insight into the organization of cortical
41 dynamics, suggesting that the amplitude and time constant of local currents control circuit
42 processing as a function of laminar depth. This may represent a general mechanism to facilitate
43 appropriate integration of fast sensory inputs (infragranular) with slow feedback-type inputs
44 (supragranular) across cortical areas and species.

45

46 Introduction

47 Local field potentials (LFPs) in cortex exhibit pronounced oscillations of various
48 frequencies (Buzsáki and Draguhn, 2004). Across the power-spectral-density (PSD) relationship,
49 narrow-band oscillations such as alpha or gamma manifest as increases ('bumps') superimposed
50 on a ramp of gradually decreasing power with increasing frequency (**Fig. 1c**). Across spatial scales,
51 behavioral states and animals, this ramp is accurately modeled by an exponential function. This
52 ramp of decreasing power, known as "1/f activity", is aperiodic and conceptually distinct from
53 rhythms like alpha or gamma, which are superimposed on it (**Fig. 1c**) (Gao, 2016).

54 1/f activity was previously disregarded as noise, but recent studies have shown that its
55 slope and offset are correlated with cognition and behavior (Bódizs et al., 2021; Colombo et al.,
56 2019; Freeman and Zhai, 2009; Gao et al., 2020; Lendner et al., 2020; Miller et al., 2009b; Ouyang
57 et al., 2020; Podvalny et al., 2015; Waschke et al., 2021), age (Dave et al., 2018; Schaworonkow
58 and Voytek, 2021; Voytek et al., 2015), pharmacological manipulation (Stock et al., 2019;
59 Timmermann et al., 2019), and disease (Robertson et al., 2019; Veerakumar et al., 2019). Despite
60 tracking such a broad range of biological and cognitive phenomena, the neural substrate(s) of 1/f
61 activity remain unknown. Physiologically, 1/f may be a result of self-organized-criticality (Beggs
62 and Plenz, 2003; V. Stewart and Plenz, 2006), population dynamics (Chaudhuri et al., 2018;
63 Podvalny et al., 2015) or E-I balance (Gao et al., 2017).

64 1/f aperiodic dynamics can be quantified by a $P \propto b * f^{-\alpha}$ power law, where P is power,
65 f is frequency, b is a constant, and α is a positive exponent between .5 and 4 (He, 2014).
66 Arithmetically, $\log P \propto \log b + \log f^{-\alpha}$, is the same as $\log P \propto -\alpha * \log f + \log b$. Therefore,
67 log power is linearly related to log-frequency (**Fig. 1c**). In this formulation, α is the slope of (log)
68 power as a function of (log) frequency, and $\log b$ is its offset (though the PSD's slope is negative,
69 we refer to the slope α as positive by convention). The offset of this 1/f decay, or the power at
70 which it intercepts the y-axis at $f = 0 \text{ Hz}$, is proportional to the broadband amplitude of the LFP.
71 Physiologically, this offset may correspond to mean firing rates or cortical activation (Manning et
72 al., 2009; Miller et al., 2009a). The slope of this 1/f decay indicates a characteristic timescale, or
73 memory, of the underlying signal (Milotti, 2002; Podvalny et al., 2015) (for the LFP,
74 transmembrane currents (Buzsáki et al., 2012)). A slope of zero (flat 1/f) is the spectral
75 representation of Poisson noise, and indicates no history-dependence; conversely, a large-

76 magnitude slope (steep $1/f$) indicates strong history dependence, or a long characteristic timescale
77 (**Supplementary Fig. 1**). This timescale reflects the degree of integrative processing in different
78 areas: sensory cortex has a short timescale, while association cortex exhibits a long one. Certain
79 behavioral tasks also exhibit different characteristic timescales (Gao et al., 2020).

80 Though previous studies have demonstrated that cortical LFPs obey a $1/f$ power law
81 (Freeman and Zhai, 2009; He et al., 2010; Miller et al., 2009a; Voytek et al., 2015), none have
82 measured whether $1/f$ dynamics change across cortical layers. This is important for understanding
83 the generation of $1/f$ dynamics, as different cortical layers have distinct functional and anatomical
84 properties and could be differentially responsible for generating aperiodic activity (He et al., 2010).
85 Characterizing $1/f$ activity across layers could also tell us which laminae drive $1/f$ dynamics in
86 scalp EEG and MEG. Insofar as the slope of the $1/f$ indicates a characteristic timescale of local
87 processing (**Supplementary Fig. 1**) (Milotti, 2002), it may also indicate whether different cortical
88 layers are specialized for integration over long periods versus fast non-integrative processing. To
89 address this, we used microelectrode recordings made from humans, macaques and mice to
90 measure the slope and offset of $1/f$ activity across cortical layers. We find that $1/f$ activity decreases
91 in slope and offset with increasing cortical depth. Intriguingly, this relationship held across three
92 mammalian species and multiple cortical areas.

93

94 **Results**

95 To measure human cortical PSDs from different layers simultaneously, we made laminar
96 microelectrode recordings in 16 patients with medically intractable epilepsy (Halgren et al., 2018;
97 István Ulbert et al., 2001) (**Fig. 1a-b**). During the implantation of clinical macroelectrodes, laminar
98 microelectrode arrays were inserted into cortex expected to be resected. Each probe had 24
99 channels with $150\ \mu\text{m}$ spacing, allowing us to record local field potentials throughout the cortical
100 depth. To attenuate volume conduction, we referenced each contact to its neighbor, yielding the
101 local-field-potential-gradient (LFPg) at 2000 Hz (filtered 0.2 – 500 Hz) (Halgren et al., 2018;
102 Kajikawa and Schoeder, 2012; István Ulbert et al., 2001) (**Fig. 2a-b**). The LFPg yields a more
103 focal measure of neural activity than the monopolar LFP without being as sensitive to noise as
104 current-source-density (Trongnetrpunya et al., 2016). We analyzed data from epochs of quiet
105 wakefulness, sleep, or when the state was unknown. When recordings from multiple states were

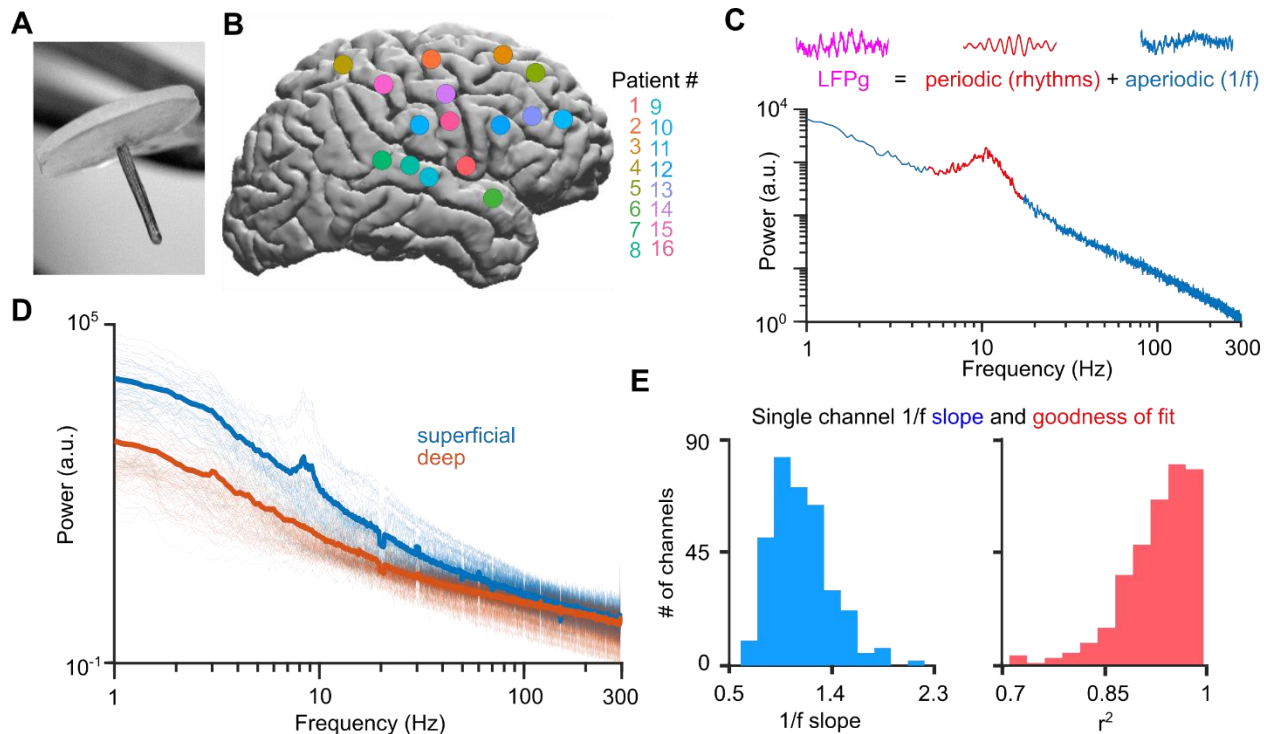


Figure 1: Laminar electrodes and aperiodic dynamics in humans. **(a)** Photomicrograph of a laminar array. Note the circular silastic sheet on top (adapted with permission from Ulbert et al., 2001). **(b)** Approximate locations of laminar implantations. We recorded from association cortex likely to be removed in prefrontal, temporal and parietal lobes. **(c)** Example wideband LFPg recording (purple trace) and power spectra (with 1/f fit) from Pt. 6, decomposed into periodic (red peak above 1/f line, red trace LFP bandpassed from 5-17 Hz) and aperiodic (blue power spectral density, blue time series bandstopped from 5-17 Hz) components. All LFPg traces are 1s. **(d)** All power spectra (light shade) and their means (dark) in superficial (blue, estimated layers I/II) and deep (orange, estimated layers V/VI) laminae. Superficial power spectra are both steeper and have greater offsets than deep ones. **(e)** Distribution of 1/f slopes and model fits to the 1/f.

106 available in a patient, we pooled data across states before further analysis, but patients in whom
 107 only sleep (Pts. 4, 5, 10) or wakefulness (Pt. 7) was recorded showed qualitatively similar effects.
 108 We then used Welch’s method to measure the Fourier Transform averaged across these epochs (10
 109 second windows, single Hanning taper), giving us the PSD at each cortical depth (Halgren et al.,
 110 2018) (**Fig. 2c**). Though laminar probes span the cortical depth, the exact cortical layer can only
 111 be estimated based on previous measurements of laminar width(Hutsler et al., 2005).

112 Averaged PSDs from superficial layers (150 - 750 μm , layers I/II) exhibited both steeper
 113 slope and greater offset than deeper layers (2400-3450 μm , layers V/VI) (**Fig. 1d**). To quantify
 114 this, we fit slopes to the PSD for each channel using the spectral parameterization package
 115 (Donoghue et al., 2020). Briefly, the algorithm fits the aperiodic 1/f after removing Gaussian-fitted

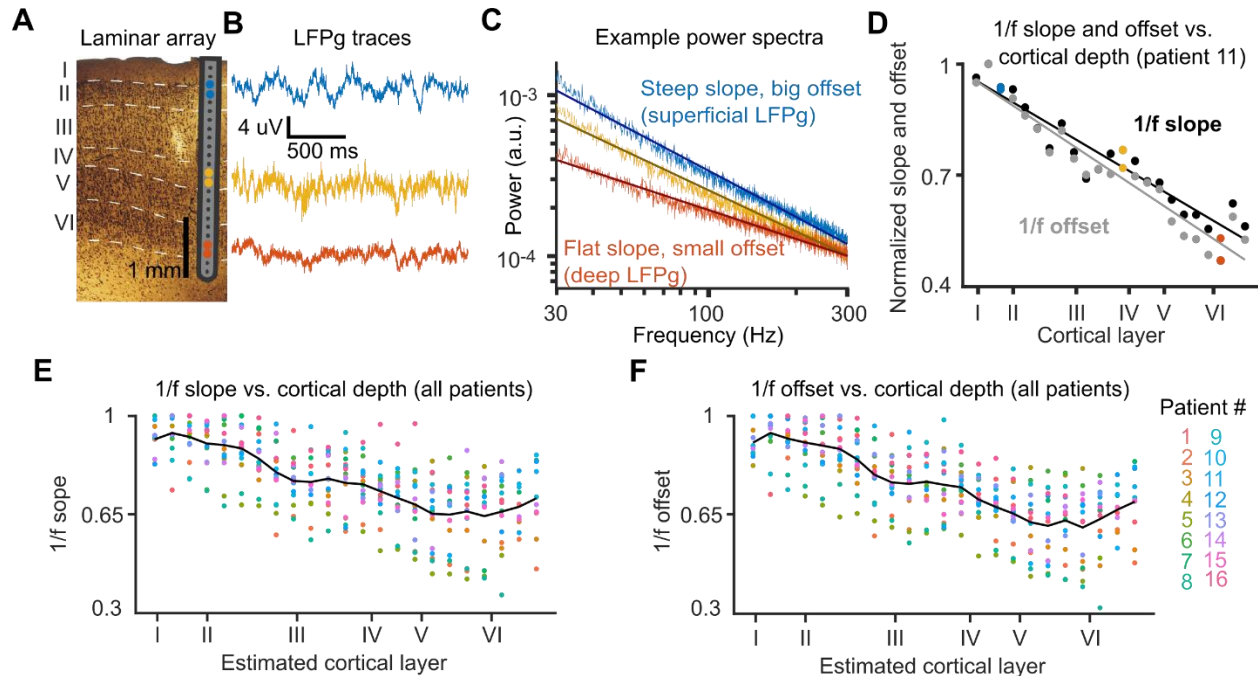


Figure 2: 1/f slope fitting analysis in an example human patient. **(a)** Pt. 11’s laminar microelectrode array overlaid on a histological section of the tissue surrounding the probe; note that the array spans the gray matter. **(b)** Sample traces of the local-field-potential-gradient (i.e. the voltage difference between adjacent contacts) in superficial, middle and deep cortical layers. **(c)** 1/f power spectra (on a log-log scale) with fitted slopes from the spectral parameterization algorithm. Note that power spectra are well fit by a straight line, and that superficial channels (blue) have steeper slopes, whereas deep channels (orange) have flatter slopes. To emphasize this effect, we show these spectra from 30 – 290 Hz (though we fit on 1– 290 Hz). **(d)** The slope and offset of each channel’s power spectrum versus cortical depth in this participant. The slope flattens (i.e. becomes less negative) and offset decreases with increased depth – the colored dots come from the same sites as the colored traces and power spectra in **(b)** and **(c)**. **(e)** 1/f slope and **(f)** offsets across all patients and contacts, normalized within patients.

116 narrowband-oscillations which manifest as peaks on top of the 1/f. We fit the slope of each PSD
 117 from 1-290 Hz to capture spectral slope over a broad range. The spectral parameterization
 118 algorithm was effective at fitting our slopes, with an r^2 across all channels of $.93 \pm .003$ (**Fig. 1e**).
 119 Observed slopes were in the range of 0.60-2.21 (**Fig. 1e**), similar to previously reported values in
 120 human intracranial recordings (He et al., 2010; Lendner et al., 2020; Miller et al., 2009a; Voytek
 121 et al., 2015). However, comparing absolute slope and offset values across different recordings is
 122 problematic: differences in hardware and ambient noise can affect these measurements. Therefore,
 123 the most meaningful comparisons are of 1/f slope and offset within a recording (i.e. within patients)
 124 across channels. To implement this, we normalized all 1/f slopes and offsets within patients before

125 visualization, such that the steepest (most negative) slope and largest offset had a value of 1 (**Fig.**
 126 **2d**).

127 We first examined the relationship between 1/f slope and cortical depth within single
 128 patients. All 16 patients had a significant correlation ($p < .05$, uncorrected Pearson's R) between
 129 cortical depth and 1/f slope; in all of these 16 recordings, 1/f slopes became flatter (less negative)
 130 in deeper layers, significantly more than expected by chance ($p < .001$, binomial test)
 131 (**Supplementary Fig. 2a**). The strength of this association varied, with r values ranging from $-.95$
 132 to $-.56$ across patients, but on average (across patients) cortical depth explained nearly two-thirds
 133 of the variance of 1/f slope ($r = -.78 \pm .03$, $r^2 = .62 \pm .05$, $\text{mean} \pm \text{standard error of the mean (SEM)}$)
 134 across patients). This can also be seen clearly by pooling data across patients (**Fig. 2e**). 1/f offset
 135 was also clearly related to cortical depth (**Fig. 2f**). Offset significantly decreased with cortical

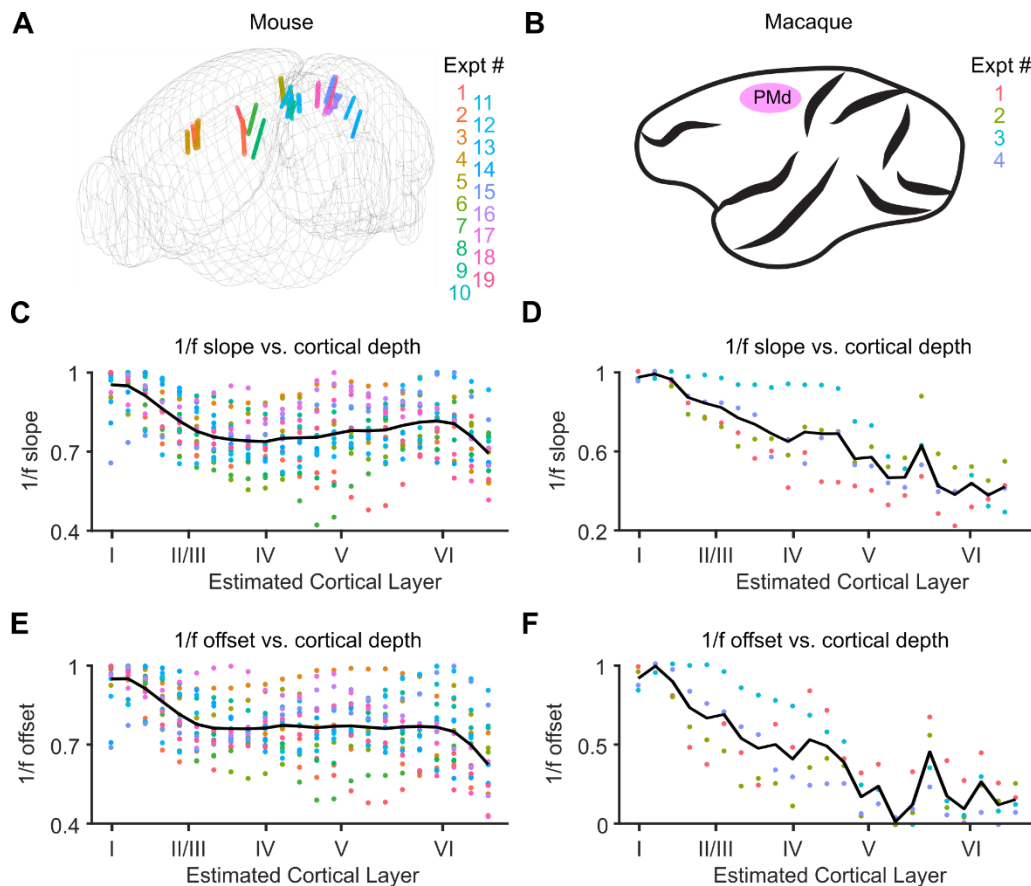


Figure 3: 1/f fitting in macaque and mouse laminar recordings. **(a)** Approximate locations of Neuropixel probes. When multiple recordings were made from the same cortical area within the same mouse, the probes share the same color. **(b)** All macaque recordings were made from dorsal premotor cortex (PMd). **(c)** 1/f slope in mice and **(d)** macaques versus cortical depth, normalized within sessions. **(e)** 1/f slope in mice and **(d)** macaques versus cortical depth, normalized within sessions. **(e)** 1/f offset in mice and **(f)** macaques versus cortical depth, normalized within sessions (**c-f** as in **Fig. 2e-f**).

136 depth in all 16 patients ($r = -.79 \pm .03$ across patients), similar to slope, indicating that broadband
137 aperiodic activity is smaller in deep cortical layers (**Supplementary Fig. 3a**).

138 Were our results specific to humans or did they represent a general principle for
139 mammalian cortical dynamics? To test this, we analyzed laminar recordings of spontaneous
140 cortical activity in mice (Steinmetz et al., 2019) and macaques using Neuropixel probes. Mouse
141 recordings were made from seven cortical areas, including visual, somatosensory, motor and
142 retrosplenial cortex (**Fig. 3a, Table 1**); all macaque recordings were made from dorsal premotor
143 cortex (PMd) (**Fig. 3b**). We selected experiments in which the probe was implanted approximately
144 normal to the brain's surface, and only analyzed contacts labeled as within the cortex. In order to
145 make these recordings as comparable as possible to our human data, we spatially interpolated
146 across channels to yield 23 bipolar LFPg series evenly spanning the cortical depth. Just as in
147 humans, we used the spectral parametrization algorithm to quantify aperiodic slope and offset from
148 1-290 Hz with a strong goodness-of-fit (mouse: $r^2 = .92$, macaque: $r^2 = .97$ across single channels)
149 and a plausible range of slopes (mouse: 0.81-2.55, macaque: 0.2-1.47). We found that 1/f slope
150 (mouse: $r = -.36 \pm .11$, macaque: $r = -.88 \pm .04$ across experiments) and offset (mouse: $r = -.47 \pm$
151 $.12$, macaque: $r = -.80 \pm .08$ across experiments) both decreased with cortical depth (**Fig. 3c-f,**
152 **Supplementary Fig. 2b, 3b**, $n=9$ mice, 1 macaque).

153 Slope and offset were strongly correlated in each species (human: $r^2 = .94$, $p < 10^{-10}$, mouse:
154 $r^2 = .89$, $p < 10^{-10}$, macaque: $r^2 = .85$, $p < 10^{-10}$), even when depth was controlled for (human: $r^2 =$
155 $.92$, $p < 10^{-10}$, mouse: $r^2 = .95$, $p < 10^{-10}$, macaque: $r^2 = .79$, $p < 10^{-10}$) (**Fig. 4b**). This strong
156 relationship between slope and offset is mathematically equivalent to the power spectra of adjacent
157 channels having a consistent x-intercept, and therefore “rotating” around a fixed frequency axis
158 (**Fig. 4a**). If two power spectra intersect, a difference in their slopes will necessarily be
159 accompanied by a proportional difference in their offsets (or vice-versa). Indeed, we found that
160 throughout our datasets, the power spectra of adjacent channels consistently intersected at a similar
161 median (human median: 106.77 Hz, mouse median: 115.41 Hz, macaque median: 28.68 Hz) (**Fig.**
162 **4c**).

163 What might account for these robust differences in aperiodic dynamics across laminae?
164 Several studies have shown that if the LFP is modelled by a Poisson spike train convolved with a
165 postsynaptic conductance (PSG), and this PSG takes the form of a double-exponential, a 1/f power

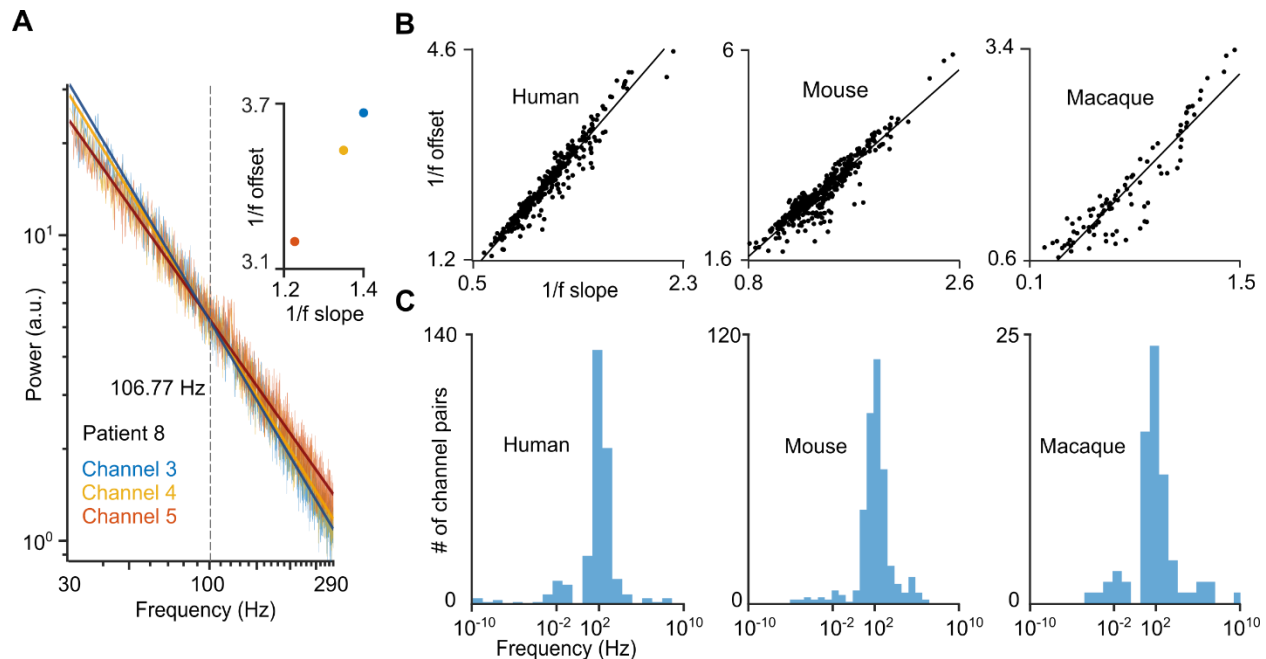


Figure 4: A common axis of rotation explains the correlation between 1/f slope and offset. **(a)** Three consecutive power spectra in an example patient; each of them intersect at approximately the same frequency of 106.77 Hz, the median intersection of all neighboring channels in humans. As seen in the inset, slope and offset are tightly correlated due to this common intersection. **(b)** 1/f slope versus offset for all single channels in each species. Note that 1/f slope and offset are highly correlated. **(c)** All intersection frequencies of neighboring power spectra across species; for visualization purposes, the 5th percentile of highest and lowest intersection points in humans and mice, and the 10th and 90th in macaques, were excluded.

166 law emerges naturally (Freeman and Zhai, 2009; Gao et al., 2017; Miller et al., 2009a). This
 167 framework was used to show that a greater balance of inhibition over excitation (i.e. more GABA_A
 168 than AMPA PSGs) is associated with steeper 1/f slopes (Gao et al., 2017). Mathematically, this is
 169 due to the slower post-synaptic time constant of GABA_A compared to AMPA. Intuitively, a slower
 170 PSG will result in slower aperiodic dynamics, and therefore a steeper 1/f slope (as it has more low-
 171 frequency spectral power). A second discovery of these models is that the offset of 1/f power is
 172 directly related to the number of PSGs active; this has been previously used to argue that 1/f offset
 173 reflects mean firing rates (Miller et al., 2009a). Alternatively, differences in 1/f offset might reflect
 174 differences in postsynaptic receptor density (rather than differences in activation due to
 175 presynaptic firing). If each receptor is activated at an equal rate, an increase in receptor density
 176 should lead to an increase in postsynaptic currents and 1/f offset, or broadband LFP power.
 177 Accordingly, our results could be accounted for if: 1) aperiodic dynamics are affected by the time
 178 course of postsynaptic currents, 2) the ratio of postsynaptic channels activated with slow vs. fast
 179 time constants is largest in superficial layers, and 3) there is a greater receptor density in superficial

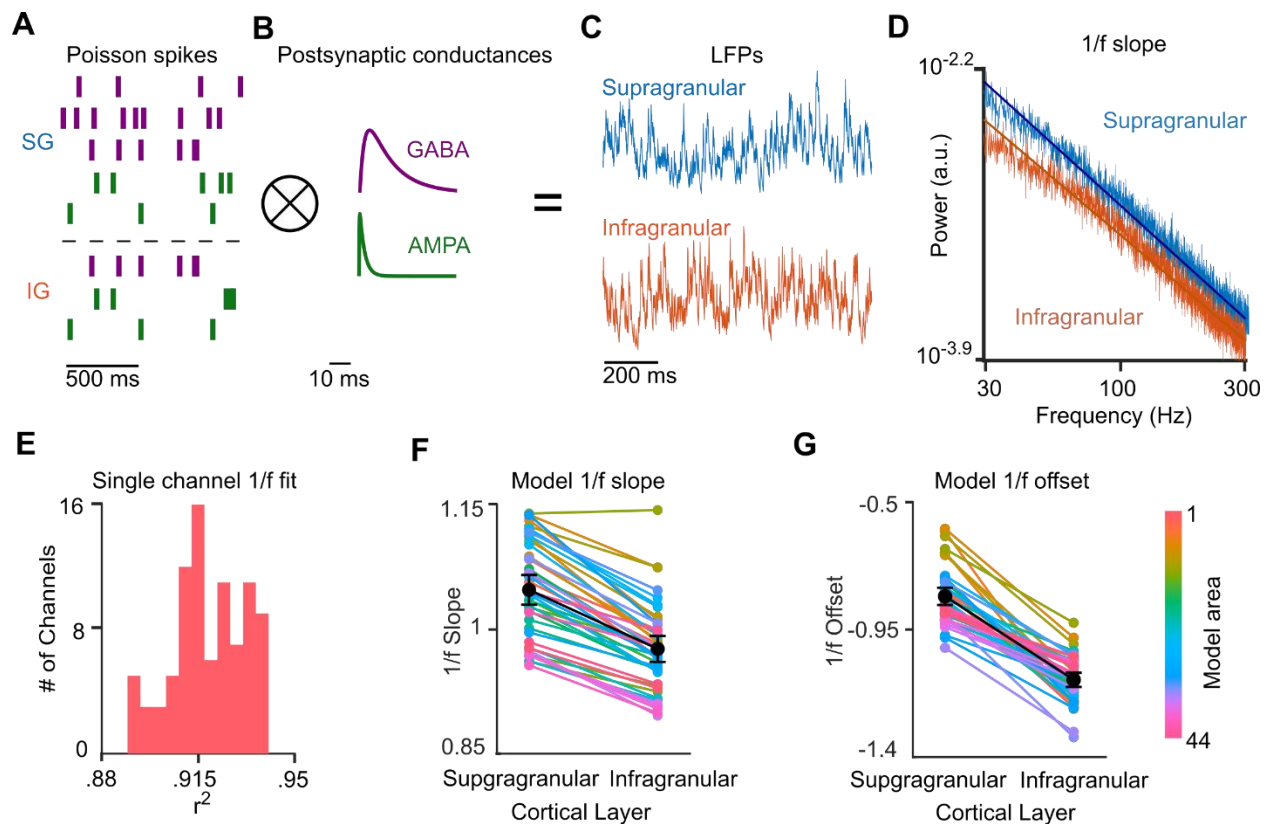


Figure 5: A simple model of 1/f dynamics across cortical layers based on AMPA and GABA_A receptor kinetics. (a) Poisson spikes corresponding to the fmol/mg density of GABA_A and AMPA in supragranular and infragranular layers are convolved with the (b) postsynaptic conductances (PSG) of these receptors. These yield LFPs (c) with log-linear power spectra (d), similar to our experimental recordings (see Fig. 2c). These spectra were then fit in log-log space with a straight line using the spectral parameterization algorithm (e). The slopes (f) and offsets (g) of these lines are higher in superficial than deep layers across areas.

180 than deep layers. We therefore hypothesized that a simple model which incorporates empirical
 181 receptor densities across layers in human cortex might reproduce the 1/f differences we observe
 182 with our laminar probes. Specifically, we utilized a database of receptor densities in 44 different
 183 cortical areas made from ex-vivo human tissue with autoradiography (Zilles and Palomero-
 184 Gallagher, 2017). Following previous work in modelling 1/f dynamics, we chose to model only
 185 the effects of ligand-gated AMPA and GABA_A receptors on the 1/f; these currents dominate
 186 excitatory and inhibitory postsynaptic currents in neocortex, respectively (Kandel et al., 1991). For
 187 each area, we generated two LFPs (and their PSDs) corresponding to supragranular and
 188 infragranular layers. Each LFP was generated by convolving Poisson spike trains (30 Hz) (Fig.
 189 5a) with AMPA and GABA_A PSGs drawn from aggregating previous studies (Fig. 5b) (CNRG
 190 Lab @ UWaterloo, *Neurotransmitter Time Constants*). The number of spike trains convolved with
 191 AMPA and GABA_A PSGs was equal to the density of each receptor in fmol/mg within that layer.

192 Summing across these Poisson spikes yielded model LFPs for each layer and area (**Fig. 5c**). When
193 we took the PSDs of these simulated LFPs (with the same window and taper we used on our actual
194 laminar recordings), they were linear in log-log space (**Fig. 5d-e**) (goodness of linear log-log fit:
195 $r^2 = .9980$ for supragranular, $r^2 = .9968$ for infragranular), and simulated 1/f slope was steeper in
196 supragranular than infragranular layers for 43/44 model cortical areas (**Fig. 5f**) ($p < 5.68 \cdot 10^{-14}$;
197 mean supragranular slope: -1.6243, mean infragranular slope: -1.4639, 7.29% difference in slope
198 on average). 1/f offset was also greater in superficial than deep layers of all 44 model cortical areas
199 (**Fig. 5g**) ($p < 2.56 \cdot 10^{-12}$; mean supragranular offset: -0.83, mean infragranular offset: -1.13,
200 25.92% difference in offset on average). These changes were comparable to our empirical changes
201 in slope and offset between supragranular and infragranular cortex (22.48% rotation in slope,
202 25.41% change in offset). Similar to our empirical data, model 1/f slopes were highly correlated
203 with offsets across simulated spectra ($r^2 = .49$, $p \leq 3.49 \cdot 10^{-14}$).

204

205 **Discussion**

206 We find that aperiodic activity flattens and decreases with cortical depth across several cortical
207 regions and three mammalian species. This suggests that the timescale and magnitude of aperiodic
208 currents decrease with cortical depth as a general principle of neocortical activity.

209 Our data is suggestive of potential interspecies differences in aperiodic dynamics; for
210 instance, the relationship between aperiodic dynamics and cortical depth was notable stronger in
211 macaques and humans than in mice (compare **Fig. 2c-d** and **Fig. 3c-f**). Unfortunately, differences
212 in experimental conditions preclude direct comparisons between species. Distinctions in aperiodic
213 dynamics across species could be due to different laminar probes (platinum-iridium vs. silicon),
214 noise levels, or angles of insertion with respect to the cortical surface rather than physiological
215 differences per se.

216 Using previously measured values of receptor density across human cortical layers in a
217 simple model, we showed that the lower ratio of AMPA to GABA_A receptors in superficial layers,
218 as well as the larger absolute number of receptors within superficial layers, could partially account
219 for differences in 1/f slope and offset across cortical laminae. Insofar as the LFP reflects the
220 activity of active postsynaptic channels, currents with slower timescales will lead to steeper slopes.

221 Furthermore, the high density of receptors in superficial layers lead to greater 1/f offset (i.e.
222 broadband power). Though several post-synaptic channels with long time constants such as
223 NMDA are predominantly located in superficial layers (Eickhoff et al., 2007; Zilles and Palomero-
224 Gallagher, 2017), we only modeled the effects of ligand-gated AMPA and GABA_A receptors on
225 the LFPg, similar to other recent models of 1/f activity The strong correlation of 1/f slope and
226 offset suggests a common physiological factor; our model indicates this could be due to a high
227 density of postsynaptic channels with long time-constants in superficial laminae. However, it is
228 important to note that other (non-exclusive) factors also likely contribute to laminar differences in
229 aperiodic dynamics. One other such factor includes voltage gated (active) channels. Specifically,
230 h-currents may contribute to the steep slopes / slow aperiodic dynamics observed in supragranular
231 laminae. Firstly, h-currents can strongly shape the extracellular LFP (Ness et al., 2018). Secondly,
232 the density of h-channels on the dendrites of layer 5 cortical pyramidal cells increases with distance
233 on the apical trunk from the soma (Harnett et al., 2015; Kole et al., 2006), mirroring the smooth
234 increase in 1/f slope from deep to superficial cortex. Additionally, human supragranular cells
235 exhibit higher densities of h-channels when compared to rodents (Beaulieu-Laroche et al., 2018;
236 Kalmbach et al., 2018); this may explain why the correlation between 1/f slope and depth was
237 stronger in primates than mice. Alternatively, our effects could be due to biophysical differences
238 across cortical layers. For instance, a gradual change in cortical impedance across layers could
239 lead to different 1/f slopes and offsets, though cortical impedance is isotropic in macaque cortex
240 (Logothetis et al., 2007). Similarly, gray matter may intrinsically filter extracellular currents in a
241 frequency-dependent manner (though this is highly contentious (Bédard et al., 2006; Bédard and
242 Destexhe, 2009)) in a way that changes between layers. These other factors may be incorporated
243 in future, more biophysically complete models.

244 We employed a bipolar referencing scheme to emphasize local activity (**Fig. 2a**).
245 Monopolar LFP recordings, made with a distant reference, may show an entirely different
246 relationship between 1/f dynamics and cortical depth (Shirhatti et al., 2016), likely due to
247 contamination by volume conduction (Kajikawa and Schoeder, 2012). Because infragranular LFPs
248 are particularly susceptible to volume conduction from superficial cortex (Kajikawa and
249 Schroeder, 2015), a monopolar reference might even find the opposite of our results (i.e. 1/f slope
250 and offset would increase with cortical depth), despite the neural generators of these aperiodic
251 dynamics residing in superficial layers.

252 Previous work has shown that currents in superficial layers underlie low-frequency
253 oscillations, which are distinct from the aperiodic dynamics reflected in $1/f$ slope (Cash et al.,
254 2009; Csercsa et al., 2010; Haegens et al., 2015; Halgren et al., 2015, 2019, 2018) (**Fig. 1c**).
255 Crucially, the spectral parameterization algorithm is able to remove the oscillatory peaks before
256 fitting the slope and offset of our power spectra. Furthermore, our results were robust even when
257 slopes were fit from 30-290 Hz, far outside the range of delta, theta, alpha or beta oscillations
258 (**Supplementary Fig. 5**). Therefore, both slow oscillatory activity and slow aperiodic dynamics
259 are concentrated in superficial layers. It's possible that channels with long time constants (such as
260 HCN or NMDA receptors) are responsible for sustaining both low-frequency oscillations and slow
261 aperiodic dynamics. Whether this implies a common physiological origin should be explored in
262 future work.

263 What do differences in $1/f$ slope between cortical layers imply about the functional role of
264 different laminae? $1/f$ represents the history-dependence, or “memory” of the LFPg
265 (**Supplementary Fig. 1**) (Milotti, 2002). For cognition, the brain must simultaneously represent
266 multiple timescales at different orders of magnitude (Kiebel et al., 2008). Indeed, it's been
267 previously shown that sensory cortex has the shortest processing timescales (presumably for
268 encoding veridical representations of fast-changing stimuli), and that association cortex has the
269 longest (Runyan et al., 2017). These timescales (as measured both by the LFPg and spiking)
270 smoothly increase from lower to higher order cortex (Gao et al., 2020; Murray et al., 2014; Siegle
271 et al., 2021; Spitmaan et al., 2020). Our work indicates that the gradation of neuronal timescales
272 across areas is mirrored by differences in timescales across layers: currents in superficial layers
273 have a longer timescale than currents in deep layers. This is anatomically expected, as superficial
274 layers are the primary recipients of feedback and modulatory inputs (thought to have long
275 timescales), whereas deeper layers receive more feedforward, driving inputs (thought to have a
276 short timescales) (Markov et al., 2014). The long timescale of supragranular currents could allow
277 them to have stronger integrative properties than infragranular currents, which may be specialized
278 for faster bottom-up inputs.

279

280 **Materials and Methods**

281 *Human Laminal Recordings*

282 Laminar microelectrode arrays were inserted on the basis of two criteria: first, the tissue must be
283 very likely to be resected (Istvan Ulbert et al., 2001). This could be because it was clearly within
284 the seizure onset zone, or because it was healthy tissue overlying the seizure onset zone which
285 would have to be removed during the resection. Secondly, the cortex in question must have had
286 no chance of being eloquent. A silicone sheet attached to the array's top was used to keep the
287 probe perpendicular to the cortical depth, with surface tension between the sheet and the pia, as
288 well as pressure from the overlying grid and dura, keeping the array in place. This sheet also
289 ensured that the laminar array was perpendicular to the cortex and that the first contact was
290 placed ~150 microns below the cortical surface. Electrode impedances and phases were
291 measured prior to implantation to ensure that recording properties were similar across contacts.
292 Each laminar probe spanned the cortical depth with a length of 3.5 mm and diameter of .35 mm.
293 Contacts had a 40-micron diameter spaced every 150 microns. Recordings were made during for
294 an average of 17.32 minutes of task-free activity in each patient.

295 In patients 9 and 11, co-histology was performed on the tissue surrounding the laminar
296 probe to confirm which layers each channel recorded from (**Fig. 2a**). In other patients, the
297 correspondence of channels to individual laminae was approximated from previous
298 measurements of laminar width. Channels 1, 4, 9, 14, 16 and 21 were the approximate centers of
299 layers I-VI, respectively.

300 *Human clinical implantation details*

301 All data were visually inspected for movement, pulsation and machine artifacts. The data was
302 also screened for epileptic activity such as interictal discharges and pathological delta by a board
303 certified electroencephalographer. Laminar arrays with significant amounts of artifactual or
304 epileptiform activity, and/or insufficient technical quality, were rejected prior to further analysis.
305 All epochs with artefactual or epileptiform activity from accepted arrays were also excluded
306 from analyses.

307

308 The effects of Anti-Epileptic Drugs (AED) on the LFP is a potential concern, as these
309 sometimes affect scalp EEG (Blume, 2006). While some patients in this study may have been
310 taking AEDs, most recordings were performed after the patient's medications had been tapered
311 to encourage spontaneous seizure occurrences during the monitoring period. Critically, the

312 results were highly consistent across all participants regardless of medication history, etiology,
313 electrode location, or degree of epileptic activity. Expert screening and consistency across
314 participants strongly suggest that our findings are generalizable to the non-epileptic population.

315 Because we did not systematically track behavioral state with EMG or sleep-scoring from
316 scalp EEG, we were not able to investigate the effect of state on 1/f dynamics. However, in a
317 subset of patients recordings were made only during definitive wakefulness (Pt. 7) or sleep (Pts.
318 4, 5, 10). The single-subject relationship between 1/f slope and offset with depth was highly
319 similar in all cases (**Supplementary Fig. 2a, 3a**), suggesting that our findings generalize across
320 states.

321 *Mouse laminar recordings*

322 Mouse recordings were used from “Distributed coding of choice, action, and engagement across
323 the mouse brain”(Steinmetz et al., 2019). Details on these experiments, as well as all of the data
324 we analyzed, can be found at
325 (https://figshare.com/articles/Dataset_from_Steinmetz_et_al_2019/9598406). Only implantations
326 which were approximately normal to the cortical surface were selected for further analysis, to
327 avoid confounding cortical depth with lateral or anterior/posterior position. This was done by
328 visual inspection of electrode trajectories on the Allen Institute common-coordinate-
329 framework(Wang et al., 2020). However, because these recordings were not made with this in
330 mind, these recordings were likely not as normal as our human recordings (**Fig. 3a**). Mice were
331 headfixed to perform a visual contrast detection task. We analyzed both periods of spontaneous
332 activity when the mouse was neither being presented stimuli nor actively performing a task
333 (spontaneous.intervals.npy). When multiple sessions from the same cortical area in the same
334 mouse were available, we averaged spectra across all available sessions.

335 Only channels labeled as being in cortex were analyzed. We first spatially averaged
336 Neuropixel LFPs between consecutive blocks of four adjacent channels (yielding 96
337 pseudochannels per probe) to reduce noise. Then, a spatial Gaussian filter with a standard
338 deviation of 68 μm was applied. To reject superficial contacts which were out of the brain, we
339 only analyzed pseudochannels below or the pseudochannel immediately above the
340 pseudochannel in which the most superficial unit was recorded. To make the spatial resolution of
341 our recordings similar to humans, we then spatially interpolated evenly across the

342 pseudochannels to get LFP timeseries spanning the cortical depth. Finally, we took the difference
343 between these adjacent channels to derive the 23 channel mouse LFPg.

344 *Macaque Laminar Recordings*

345 Rhesus Neuropixels recordings (4 sessions, 1 macaque) were performed in dorsal premotor
346 cortex (PMd) using Neuropixels NHP probes supplied by IMEC and Janelia. We analyzed an
347 average of 37.42 minutes of task-free, spontaneous activity per session. The Neuropixels probe
348 was inserted along the axis of the recording chamber with the intent to be orthogonal to the
349 surface of the cortex and spanning cortical lamina. Neuropixels probes were inserted using a
350 custom adapter to mount the probe on a microelectrode drive (Narishige). A blunt 23-gauge
351 stainless steel guide tube was mounted in a second tower and positioned in contact with the
352 surface of the dura. The granulation tissue and dura was perforated using a tungsten electrode,
353 then the Neuropixels probe was inserted through the same guide tube into the brain. Recordings
354 were performed using the 384 channels closest to the probe tip, spanning 3.84 mm of length
355 along the probe. The recording depth was selected so as to situate the most superficial observable
356 spiking neurons aligned with the top recording channel. LFP data were acquired using
357 SpikeGLX software and were digitized at 1kHz. Before fitting these LFPs, we applied the same
358 procedure to our macaque recordings that we applied to our mouse recordings (i.e. spatially
359 averaging adjacent channels, interpolating, and then taking the potential difference between these
360 pseudochannels).

361 *Analysis*

362 All analysis was performed in MATLAB (R2019b, Natick, MA) using custom and FieldTrip
363 functions (Oostenveld et al., 2011). In each participant, the Fourier Transform was calculated in
364 10 second epochs on the zero-meaned data after a single Hanning taper was applied. FFTs were
365 taken across all recordings made in each patient, even if recordings were made during multiple
366 behavioral states, yielding a single 1/f slope at each cortical depth per patient. The frequency
367 spectra of faulty channels (an average of 3 per probe) were linearly interpolated from the
368 normalized frequency spectra of good channels above and below on the laminar probe. For
369 instance, if channel 2 was defective, its power spectrum would be replaced by the average of
370 channels 1 and 3's power spectra. To ensure that interpolation wasn't yielding spurious results,

371 we examined the 1/f depth profiles of patients without any interpolated channels (2, 3, 7, 8, 9).
372 These patients displayed the same pattern as those with interpolated channels.

373 Power spectra were visually examined for noise peaks, such as 60 Hz line noise, and
374 power values at ± 5 Hz around these high-frequency noise artifacts were removed. After this, we
375 normalized the power spectra within each patient by the median power value across all channels
376 and frequencies from 1-290 Hz (within that patient). In both humans and mice, we fit on all
377 frequencies (excluding artifactual noise peaks) from 1 – 290 Hz. In humans, we used a peak
378 sensitivity rating of 7, and in mice we used a peak sensitivity rating of 4. Peak width limits of 3-
379 14 Hz were used in both species.

380 As a first control analysis, we replicated our results using a simple linear fit with a first-
381 degree polynomial (polyfit.m) after both power spectra and the frequency axis were log
382 transformed. This linear fit (in log-log space) found the same relationship between slope/offset
383 and cortical depth (**Supplementary Fig. 6**), demonstrating that our results are robust to different
384 fitting algorithms.

385 Another concern is that a correlation between the spectral parameterization algorithm's
386 goodness of fit (r^2) with cortical depth, offsets or slopes could yield spurious relationships
387 between depth and offset or slope and offset. To ensure that this was not the case, we measured
388 the Pearson correlation between goodness of fit and depth, slope and offset across all channels
389 within our mouse and human datasets (separately). All of these correlations in humans were
390 insignificant ($r^2 \leq .006$, $p \geq .14$), and were very weakly correlated (albeit significantly) in mice
391 ($r^2 \leq .06$, $p \geq 1.05 * 10^{-7}$). We there for re-measured the average correlation between
392 slope/offset and depth for only channels in a very narrow range of goodness of fits ($r^2 = .99-1$),
393 reducing the correlation between goodness of fit and depth, slope or offset. Even with this
394 restricted range of channels, we observed high correlations of slope and offset to cortical depth
395 ($r^2 = .31, .48$ for slope and offset respectively). This suggests that our results cannot be explained
396 by systematic variations in our fitting accuracy.

397 To make sure our slope-fitting wasn't contaminated by low-frequency oscillatory peaks
398 (though these should be removed by the spectral parameterization algorithm), we replicated our
399 results using a fitting band of 30 – 290 Hz. 30 Hz was chosen as a lower bound to exclude delta,
400 theta, alpha and beta oscillations (**Supplementary Fig. 5**).

401 As a last control, we re-ran our fitting across a wide range of frequency bands. 1/f
402 slope/offset and cortical depth were strongly correlated across almost all of these control bands
403 (**Supplementary Fig. 4**). That these correlations remained even when the upper frequency bound
404 was relatively low (<80 Hz) suggest that our results are not due to residual spiking contamination
405 of the LFPg.

406 A point of potential conceptual confusion is our use of the aperiodic 1/f exponent, as
407 opposed to the knee-frequency, to derive timescale. Though some previous papers have used the
408 knee-frequency to measure the timescale (Gao et al., 2020), we rarely found spectral knees in our
409 recordings. Furthermore, both the aperiodic exponent and spectral knee (usually not present in
410 our data) determine LFPg timescale (Gao et al., 2020; Milotti, 2002) (**Supplementary Fig. 1**).
411 This justifies our use of the aperiodic exponent instead of the knee-frequency for our analysis.

412 *Model*

413 Our model is similar to earlier studies of 1/f dynamics (Freeman and Zhai, 2009; Gao et
414 al., 2017; Miller et al., 2009a). We modelled LFPs as a convolution between Poisson spiking (30
415 Hz for 490 seconds) and post-synaptic conductance kernels for AMPA and GABA_A receptors.
416 The number of Poisson spikes convolved with each receptor-type was equal to the (rounded)
417 density in fmol/mg of that receptor. We then summed these convolutions within the
418 supragranular/infragranular layers of each cortical area, yielding 88 artificial LFPS (Zilles and
419 Palomero-Gallagher, 2017). The FFT was made using the same window and Hanning taper as
420 our laminar recordings, and plotted in log-log space. Slopes were fitted in the same way as our
421 empirical laminar recordings in humans (i.e. with the spectral parameterization algorithm from 1
422 – 290 Hz, peak sensitivity of 7 and peak width limits of 3-14 Hz).

423 *Code Accessibility*

424 Data and analysis scripts are freely available (<https://github.com/harnett/LaminarAperiodic>)

425

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439

440 **Declaration of interests**

441 The authors declare no competing interests.

442

443

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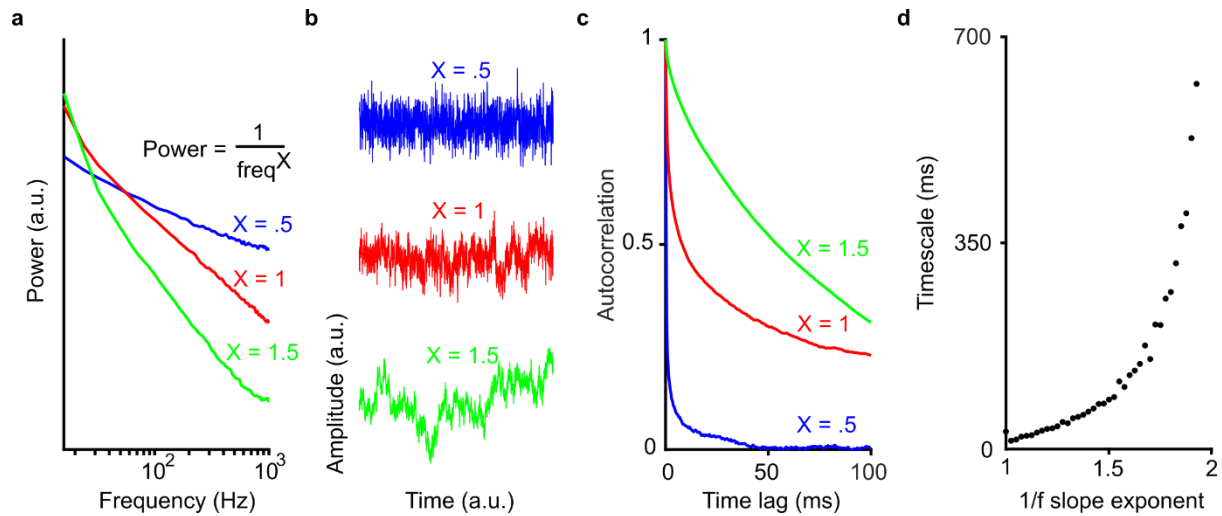
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- 637
- 638

639 **Table 1**

Expt #	Cortical Area	Mouse	Session Label(s)
1	Primary motor area	Moniz	Moniz_2017-05-18
2	Primary motor area	Radnitz	Radnitz_2017-01-12
3	Secondary motor area	Muller	Muller_2017-01-07
4	Secondary motor area	Radnitz	Radnitz_2017-01-08, Radnitz_2017-01-09, Radnitz_2017-01-10
5	Retrosplenial area	Lederberg	Lederberg_2017-12-07
6	Retrosplenial area	Radnitz	Radnitz_2017-01-11
7	Primary somatosensory area	Moniz	Moniz_2017-05-18
8	Primary somatosensory area	Radnitz	Radnitz_2017-01-12
9	Anterior visual area	Hench	Hench_2017-06-15
10	Anterior visual area	Moniz	Moniz_2017-05-16
11	Anterior visual area	Richards	Richards_2017-10-29
12	Anteromedial visual area	Moniz	Moniz_2017-05-15
13	Anteromedial visual area	Radnitz	Radnitz_2017-01-10
14	Primary visual area	Cori	Cori_2016-12-14, Cori_2016-12-18
15	Primary visual area	Forssmann	Forssmann_2017-11-01
16	Primary visual area	Hench	Hench_2017-06-15, Hench_2017-06-17
17	Primary visual area	Lederberg	Lederberg_2017-12-05
18	Primary visual area	Moniz	Moniz_2017-05-16
19	Primary visual area	Theiler	Theiler_2017-10-11

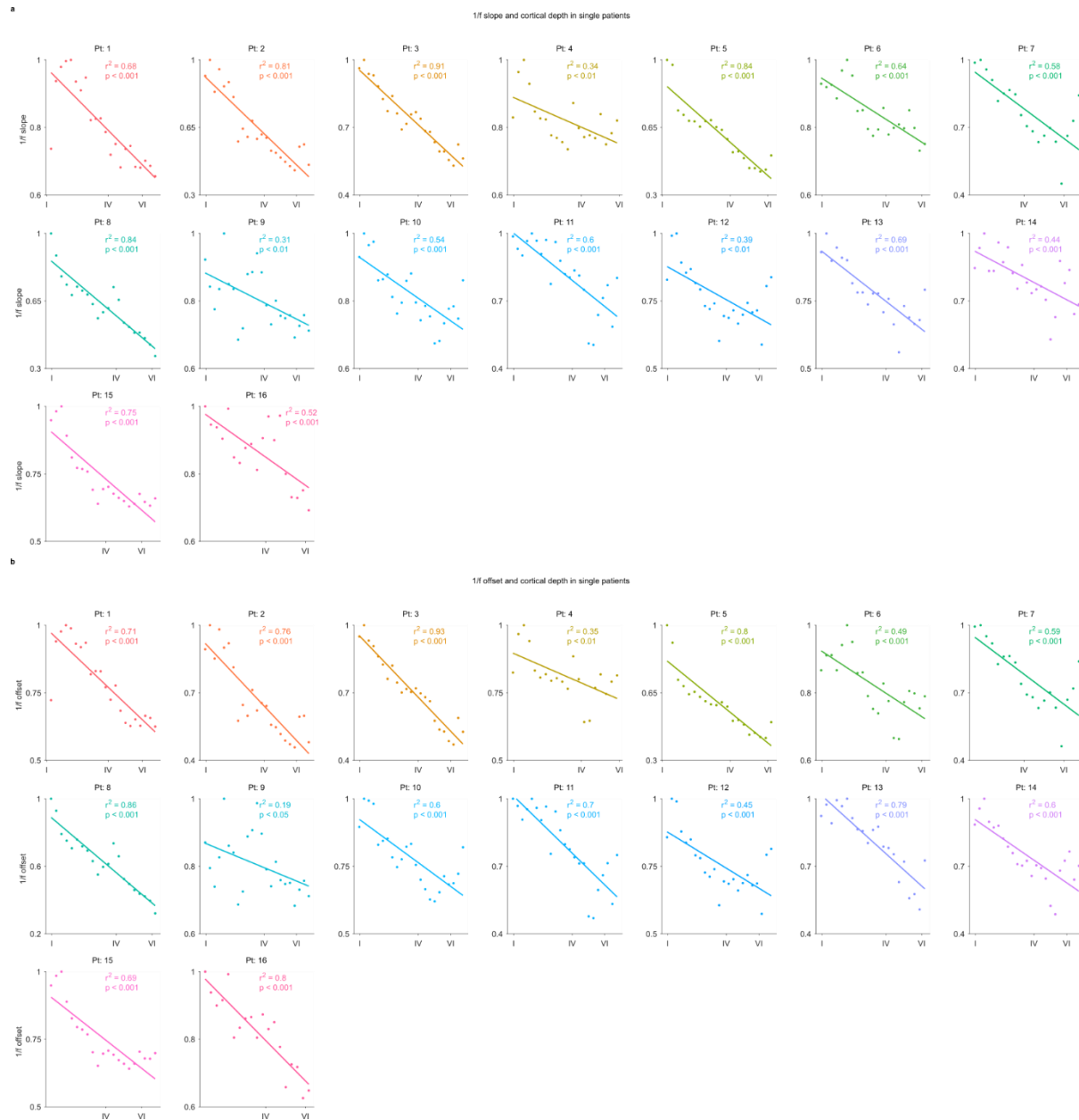
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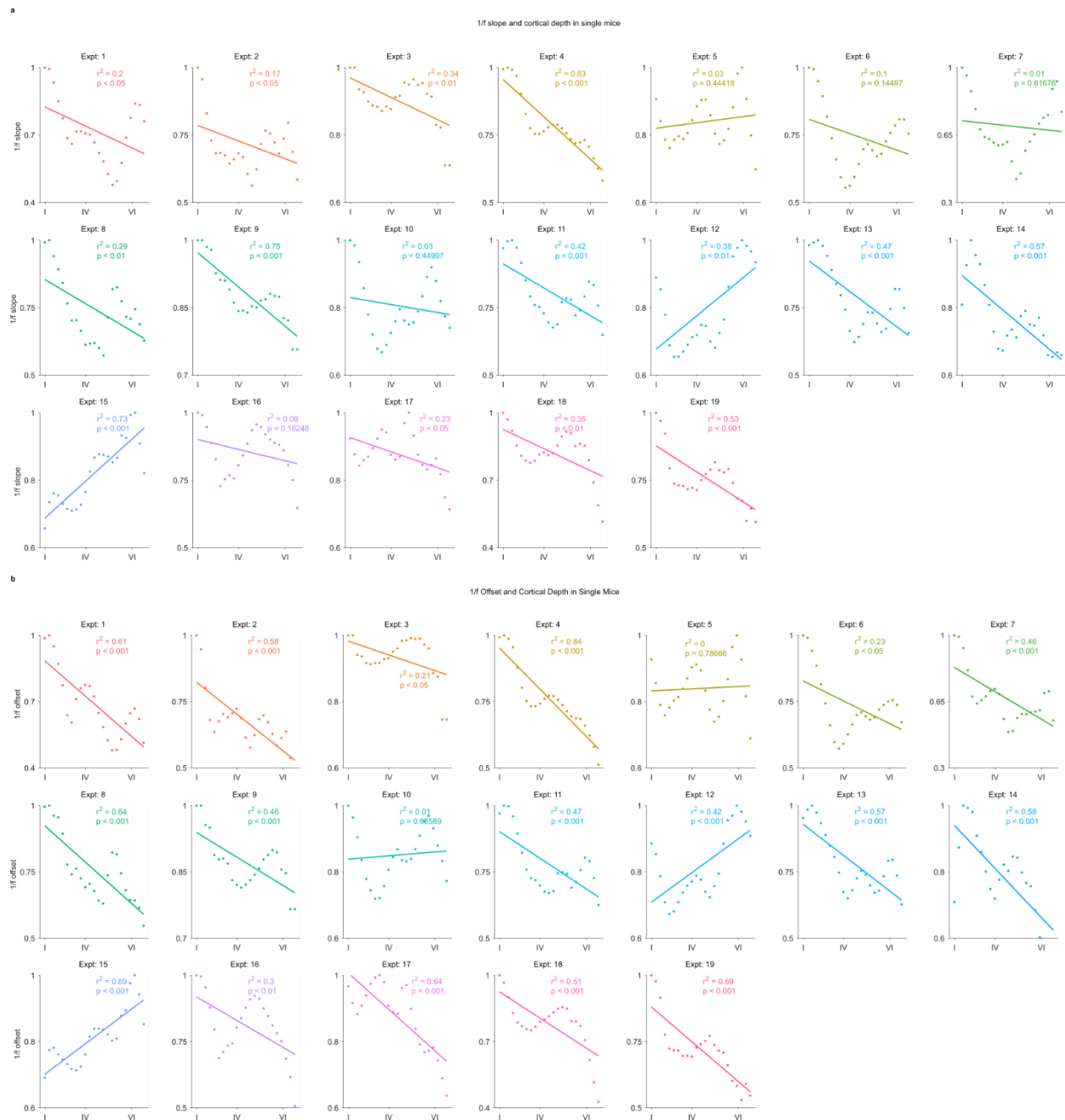
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643 **Supplementary Figure 1:** 1/f slope reflects timescale of activity in the time-domain. **a)** Three simulated
644 power spectra with different slope exponents (.5, 1, 1.5). **b)** 1 s of simulated time series corresponding to
645 the spectra in a. Note that the time series with the slowest fluctuations corresponds to the spectrum with
646 the steepest exponent. **c)** Autocorrelation functions for the three simulated timeseries in **b)**. The highest
647 autocorrelation function (i.e. most time dependence or memory) corresponds to the steepest power
648 spectrum ($X = 1.5$). **d)** Timescale as a function of slope exponent for 38 simulated time series (slopes
649 between 1 and 2). Timescale is defined as the lag at which the autocorrelation decays to $1/e$.



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651 **Supplementary Figure 2:** 1/f slope and offset decrease with cortical depth in single patients. 1/f slope (a)
652 and offset (b) vs. cortical depth in all human patients.

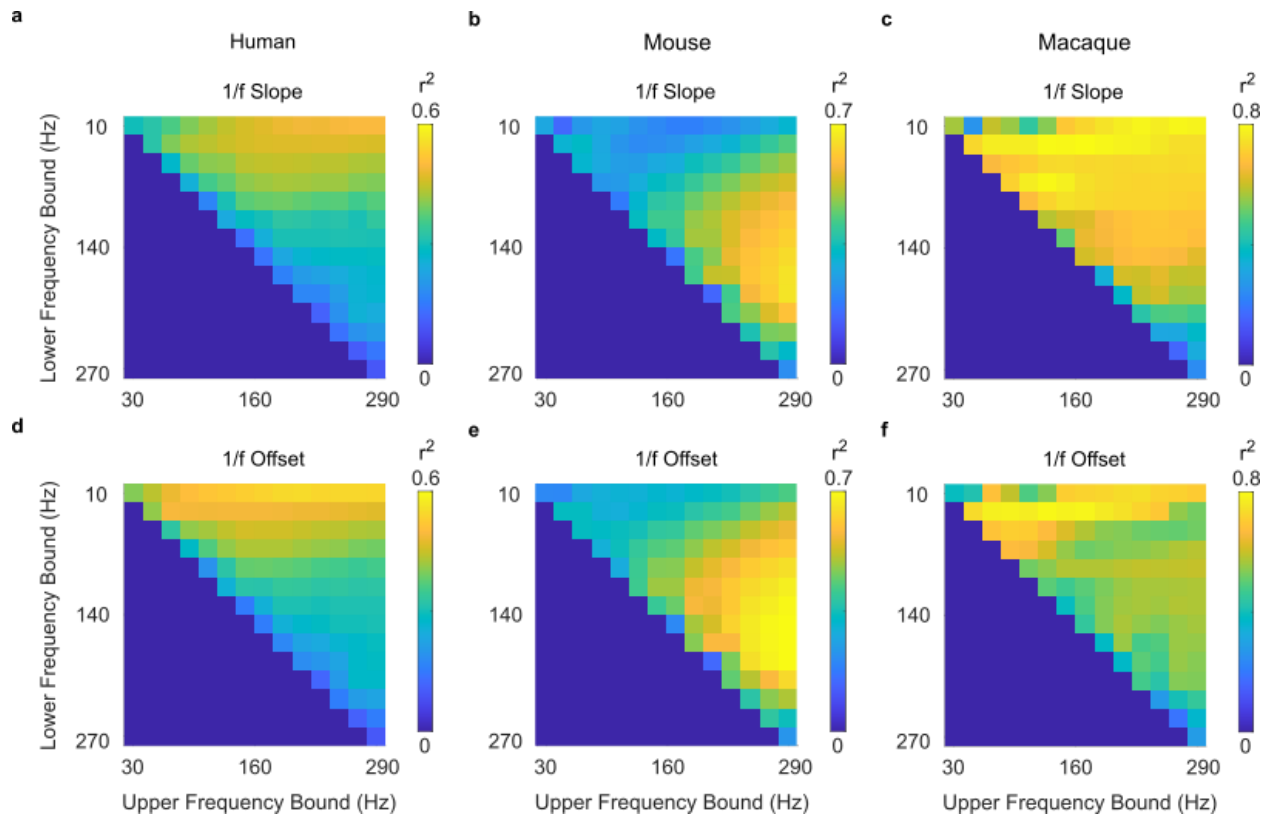


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654 **Supplementary Fig. 3** 1/f slope and offset decrease with cortical depth in individual mouse experiments.
655 1/f slope (a) and offset (b) vs. cortical depth (x-axis) in all mouse experiments.

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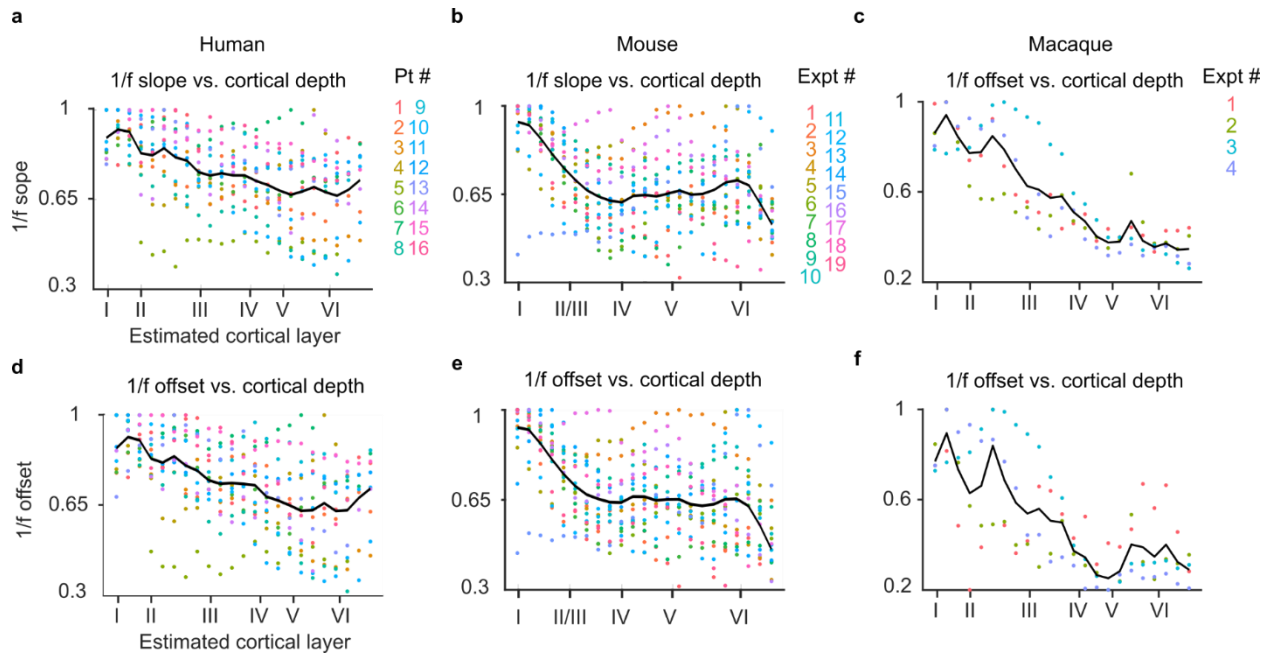
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659 **Supplementary Fig. 4** 1/f slope and cortical depth are highly correlated across a wide range of frequency
660 bands. For every frequency band between 10 and 270 Hz (20 Hz intervals), we found the correlation (r^2)
661 between 1/f slope or offset and depth within each patient (human) / experiment (mouse, macaque), and
662 then averaged this value across patients / sessions.

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665 **Supplementary Fig. 5** 1/f slope flattens and offset decreases with cortical depth from 30-290 Hz. 1/f slope
666 and offset vs. cortical depth in humans (**a, d**), mice (**b, e**) and macaques (**c, f**), fit using a frequency band
667 of 30-290 Hz (as opposed to 1-290 Hz in our main results).

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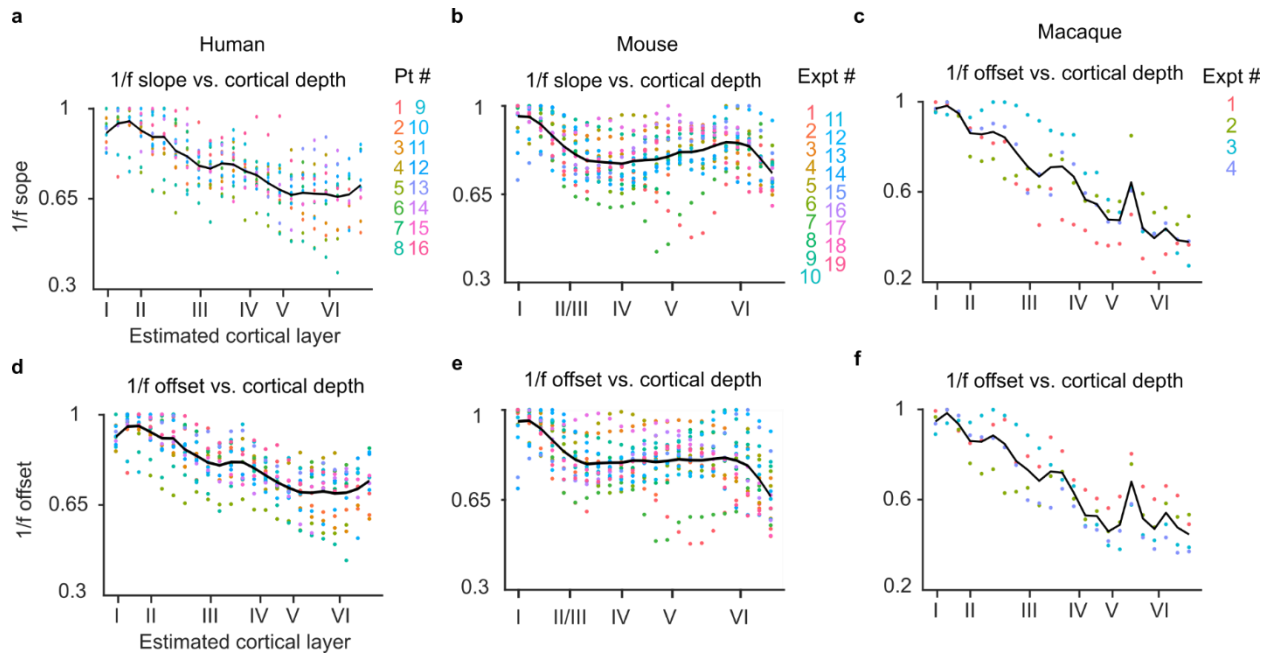
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682 **Supplementary Fig. 6** 1/f slope and offsets fit with simple linear regression (polyfit.m) instead of the
683 spectral parameterization algorithm yields similar results. 1/f slope and offsets across all humans (a, d),
684 mice (b, e), and macaques (c, f) normalized within each experiment.