AP initiation dynamics is substantially more voltage sensitive when  $k_a$  is reduced from 6 mV (S Fig 2A) to 1 mV (C), then to 0.1 mV (E). For  $k_a = 6$  mV, axonal voltage derivatives increase for less than 2 mV/ms within 10 mV (A). While for  $k_a = 1$  mV, the axonal voltage derivatives increase for more than 10 mV/ms within 5 mV from their local minima (C). When  $k_a = 0.1$  mV, the AP initiation dynamics is like a step function for all three model variants (E). Fixing the firing rate at 5 Hz and CV of ISI at 0.85, the dynamic gain functions display higher bandwidth, and larger Brunel effect ( $\tau$  increased from 5 ms to 50 ms), when  $k_a$  is smaller (B, D, E).

Increasing  $x_{Na}$ , the spatial separation between AP initiation site and soma, the axonal voltage derivative increases slightly faster when  $k_a = 6$  mV. The dynamic gain in the high frequency region is also enhanced, reflecting the acceleration of AP initiation speed. In contrast, when the AP initiation dynamics is extremely voltage sensitive ( $k_a = 0.1 \text{ mV}$ ),  $x_{Na}$  has limited impact on AP initiation speed. And the corresponding difference in dynamic gain is mainly due to the electrotonic filtering (Fig 3 in main text). Compared to  $k_a = 6 \text{ mV}$  and 0.1 mV,  $k_a = 1 \text{ mV}$  is an intermediate stage where the impact of AP initiation site on dynamic gain functions changes with  $\tau$ . For  $\tau = 5$  ms, increasing  $x_{Na}$  reduces the dynamic gain in the high frequency region, similar to  $k_a = 0.1 \text{ mV}$  (F). While for  $\tau = 50$  ms, increasing  $x_{Na}$  enhances the dynamic gain between 20 to 100 Hz is similar to  $k_a = 6 \text{ mV}$  (B). At higher frequencies, the gain curve decays faster when  $x_{Na}$  is larger.



Supplementary Figure 2: Impact of AP initiation site on AP initiation dynamics and dynamic gain functions with various  $k_a$ . A, C, E For each  $k_a$ , axonal voltage derivatives of three model variants aligned at (0 mV, 0 mV/ms). B, D, F Dynamic gain functions calculated with the firing rate fixed at 5 Hz, CV of ISI fixed at 0.85.  $\tau$  is set to 5 and 50 ms for each model variant.