## Supplementary Materials for: Action potentials in vitro: theory and experiment

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## I. ADDITIONAL FIGURES

Additional figures relating to the phase diagram in Section II B of the main text are shown here, namely different slices through the parameter space discussed in the main text. In all the figures shown,  $N_0 = 250$ ,  $V_N = 42$  mV, C = 330 pF, and  $\chi = 167$  pS ( $\chi$  being the conductance per unit channel).

Fig. S1(a) shows a "heatmap" constructed with the frequency of oscillation for an Artificial Axon with the given  $k_r$  and  $k_i$  value, similar to Fig. 2(b) in the main text (same  $\chi_c$  and  $V_c$  values). The difference with the latter is that we used a different threshold value relating to the III  $\rightarrow$  IV transition, as we discuss below.

Fig. S1(b) is constructed using different measures for the different regions, the computer algorithm mimicking the "operator based" qualitative determination in Fig. 2(a) of the main text. Correspondingly, all four regions appear in this diagram. The protocol to assign the regions is as follows: for each  $(k_r, k_i)$  on the plane, the system is started at  $V_0 = V_c = -200$  mV, and fired at t = 1 s by setting  $V_c = -50$  mV. These firings are recorded for T = 100 s and iterated by fixing  $k_i$  first and steadily increasing  $k_r$  in increments of  $0.01 \text{ s}^{-1}$  (i.e. the map is generated horizontally). For a given  $k_i$ , the frequency of each firing is divided by the frequency of the previous firing, and if the ratio exceeds the threshold value 1.2, the system is determined to have transitioned from Region I to Region II. The peak amplitudes of each firing is also recorded, and if the amplitude has decreased more than 60% over the course of T then the system is determined to be in Region III. Finally, the total number of peaks is recorded, and if there is only one peak remaining, then the system is determined to be in Region IV. By tracking all these measurements for each firing, the protocol also accounts for cases where the system "skips" certain regions, such as when  $k_i$  or  $k_r$  are very small.

In comparison to Fig. 2(b) of the main text, the threshold for detecting peaks in Fig. S1(a) was made more strict, such that the system is recognized to be in Region IV much earlier than before. This leads to a Region III which is slightly smaller than that of Fig. 2(a) in the main text, whereas Fig. 2(b) of the main text has a slightly larger Region III. This discrepancy is not a surprise, as the determination of the various regions cannot be made with a single "order parameter" such as the frequency of oscillation or the eigenvalues of a stability matrix. We emphasize that the our focus is on the nature of the transitions between the different regions, rather than the exact location of the boundaries.



FIG. 1. (a) A heat map representation of the parameter space of Fig. 2(a) of the main text, with the color indicating the frequency of oscillation (mHz) for each particular combination of  $k_i$  and  $k_r$ . Similar to Fig. 2(b) of the main text, the central region with high frequency oscillations indicate Regions II and III, while the darker regions on the left and right are Regions I and IV, respectively. ( $V_c = -50 \, mV$ )

(b) The same diagram as (a), but using different measures for the different regions, the colors directly indicating the region. Region I is dark blue, Region II is light blue, Region III is yellow, and Region IV is brown. See text for details on how the regions are determined.

Figs. S2 and S3 show different slices of the  $(k_r, k_i)$ 

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plane, for different values of  $V_c$  and  $\chi_c$ , respectively. They are qualitatively comparable to Fig. 2(b) of the main text. Figs. S4 and S5 show different 2D cuts through the  $(k_r, k_i, V_c, \chi_c)$  parameter space. Fig. S4 shows a diagram in the  $(k_r, \chi_c)$  plane and Fig. S3 in the  $(V_c, \chi_c)$  plane; the latter corresponds to the actual control parameters in the experiments. Of note, all the regions described in the main text are preserved in the different cuts.



FIG. 2. (a) A heat map (showing the oscillation frequency) obtained with the same conditions as Fig. S1(a), except with  $V_c = -45$  mV at t = 1 s. (b) Same conditions as Fig. S1(a), except with  $V_c = -55$  mV at t = 1 s.



FIG. 3. (a) A heat map with the same conditions as Fig. S1(a), except with  $\chi_c = 667$  pS ( $R_c = 1.5$  G $\Omega$ ). (b) Same conditions as Fig. S1(a), except with  $\chi_c = 400$  pS ( $R_c = 2.5$  G $\Omega$ )





FIG. 4. A heat map of the frequency of oscillations for an AA with given values of  $k_r$  and  $(1/\chi_c)$ . The lighter blue region corresponds to Region I, the curved bright region corresponds to Regions II/III, and the dark blue region on the right corresponds to Region IV

FIG. 5. A heat map of the frequency of oscillations for an AA with given values of  $V_c$  and  $(1/\chi_c)$ . The dark blue region on the left is where no firing occurs due to the clamp being set below the firing threshold ( $\approx V_c = -55 \text{ mV}$ ). The lighter blue region corresponds to Region I, the bright region in the middle corresponds to Regions II/III, and the dark blue region on the right corresponds to Region IV.