

## **Supplementary Note**

### **Ionic currents underlying the dynamical model**

The dynamical model of **Fig. 8** relies on two voltage-gated ionic currents: an instantaneous, non-inactivating inward current, responsible for the N-shaped  $\dot{V}=0$  nullcline and a slow h-like current, which generates the rebound response underlying the bidirectional transitions. Two types of persistent inward currents, persistent sodium and persistent calcium, have been characterized in Purkinje cells<sup>1,2</sup>. Somatic Purkinje cell bistability has been associated with persistent sodium<sup>1</sup> whereas dendritic bistability has been shown to result from persistent calcium conductance<sup>2</sup>. We used persistent sodium in our simplified model but it is likely that in Purkinje cells it is the combination of these two currents that enables the bistability.

The rebound response requires a slow current, either a slowly inactivating inward current or a slowly activating outward current. Essential to the model is the assumption that this rebound current is not saturated in both the up and the down states of the cell. A possible candidate for the slowly inactivating inward current is the h-current. The potassium m-current could be the slowly activating outward current. Both of these currents have been reported to be active in Purkinje cells<sup>3-5</sup>. Purkinje cells in our *in vivo* recordings exhibit the classical characteristics of the activation of h-current (**Supplementary Fig. 1**), i.e. a time-dependent inward rectification (or “sag”) which has been studied extensively in slice preparations and shown to be caused by  $I_h$  activation<sup>3,4,6</sup>. Thus, these results indicate that the h-current is expressed at a significant level in Purkinje cells *in vivo*, and that this current generates the rebound response required for the bidirectional transitions between the states. However, it is possible that the potassium m-current participates in enabling these transitions, especially in the up state of the cell.

### **Incorporating slow oscillatory dynamics into the model**

Climbing fiber activation can account for most of the state transitions observed in our *in vivo* Purkinje cell recordings ( $73 \pm 4\%$ , see **Fig. 6c** and corresponding text). The remaining transitions appear to be spontaneous, as they are not preceded by any detectable postsynaptic potentials (see for example **Fig. 6a**), suggesting that they are triggered by intrinsic processes and not by external input. Similarly, Purkinje cells *in vitro* often exhibit regular transitions between depolarized and hyperpolarized states with a period of seconds<sup>1,3,7,8</sup>. The properties of the ionic conductances involved in this oscillatory activity have yet to be fully determined, but the mechanism is known to involve calcium-dependent potassium channels and voltage-dependent calcium channels<sup>8</sup>. To study the effect of these slow intrinsic dynamics on climbing fiber-induced transitions, we replaced some of the voltage-independent conductance with a slowly activating potassium current (see Model Parameters below). Spending an extended period of time in the depolarized state results in an increase of the potassium conductance (for example, as a result of calcium influx) and consequently an up-shift of the  $\dot{V} = 0$  nullcline. If the nullcline is sufficiently up-shifted, the depolarized fixed point disappears and the dynamics converge to the hyperpolarized fixed point. Similarly, a prolonged hyperpolarization generates a down-shift of the nullcline that will eliminate the hyperpolarized fixed point. Hence, the slow kinetics of the potassium current are able to generate periodic spontaneous up-to-down and down-to-up transitions in the model (**Supplementary Fig. 2a**). Furthermore, the immediate effect of substantial h-current down-regulation is hyperpolarization and the disappearance of the depolarized fixed point. However, the resultant slow increase in the potassium conductance will down-shift the  $\dot{V} = 0$  nullcline sufficiently to restore bistability (not shown).

The ability of a simulated climbing fiber input to induce state transitions depends on the level of the potassium conductance (**Fig. 8c,d**). If this conductance is insufficiently activated, climbing fiber input will induce a transition to the up state but not the opposite transition (**Fig. 8c**). Conversely, if this conductance is excessively activated climbing fiber input will only trigger transitions to the down state (**Fig. 8d**). Only over an intermediate range of

potassium conductance can a climbing fiber input induce transitions in both directions (**Fig. 8a** right panel, **8b**). We simulated the dynamics of the model in the presence of random climbing fiber inputs at a rate of 1 Hz (comparable to the physiological frequency *in vivo*; **Supplementary Fig. 2b**). Similar to our experimental observations, the membrane potential histogram was bimodal (**Supplementary Fig. 2c**) and the model cell exhibited up and down states of variable duration. For a simulation of a one-hour period, the mean and standard deviation of the dwell times of the down and up states were  $1.08 \pm 0.66$  sec and  $1.30 \pm 0.59$  sec respectively. These values are comparable to the *in vivo* measurements (see **Fig. 1d** and corresponding text). We also found that the majority of transitions between states were induced by the simulated climbing fiber input and only a minority occurred spontaneously (**Supplementary Fig. 2b**, arrows). During the one-hour simulation, 69% (1042/1513 transitions) of the transitions from up-to-down and 88% (1327/1513) of the transitions from down-to-up were preceded by a climbing fiber input (**Supplementary Fig. 2d**). The efficiency of climbing fiber input to induce these transitions was 69% (2437/3551 complex spikes). We also assessed the state-dependence of complex spike efficiency. Complex spikes occurring during the down state were found to be effective in triggering down-to-up transitions in 87% (1327/1534) whereas complex spikes occurring during the up state were effective in 55% (1110/2017) of the cases (**Supplementary Fig. 2e**). These values are comparable with our experimental results (see **Fig. 6c,d** and corresponding text).

## Model parameters

The single-compartment model consists of the following ionic currents: an instantaneous, non-inactivating inward current ( $I_{Na}$ ), a slow h-like current ( $I_h$ ), an outward current ( $I_K$ ) and a leak current ( $I_l$ ). The current equation for the model is:

$$C \frac{dV}{dt} = -(I_{Na} + I_h + I_K + I_l), \quad \text{where} \quad I_{Na} = g_{Na} m_{\infty} (V - V_{Na}); \quad I_h = g_h h (V - V_h);$$

$$I_K = g_K n (V - V_K); \quad I_l = g_l (V - V_l); \quad m_{\infty} = (1 + e^{\frac{V - T_m}{\sigma_m}})^{-1}.$$

The dynamics of the inactivation term of the h-current is:

$$\frac{dh}{dt} = \frac{h_{\infty} - h}{\tau_h}, \text{ where } h_{\infty} = (1 + e^{\frac{V-T_h}{\sigma_h}})^{-1}; \tau_h = \frac{1}{\alpha + \beta}; \alpha = \frac{a_{\alpha} \cdot V + b_{\alpha}}{1 - e^{\frac{V+b_{\alpha}}{k_{\alpha}}}}; \beta = \frac{a_{\beta} \cdot V + b_{\beta}}{1 - e^{\frac{V+b_{\beta}}{k_{\beta}}}}.$$

The dynamics of the potassium current varied across simulations:

In **Fig. 8**,  $b=1$ . Note that in this case the potassium and leak currents can be considered as a single, voltage independent current.

In **Supplementary Fig. 2**,  $\frac{db}{dt} = \frac{b_{\infty} - b}{\tau_b}; b_{\infty} = (1 + e^{\frac{V-T_b}{\sigma_b}})^{-1}; \tau_b = \tau_b^0 \cdot \sec h\left(\frac{V-T_b}{4 \cdot \sigma_b}\right).$

The model parameters are:  $C = 1 \mu F \cdot cm^{-2}; g_{Na} = 60 \mu S \cdot cm^{-2}; V_{Na} = 55 mV; T_m = -53.8 mV; \sigma_m = 3 mV; g_h = 200 \mu S \cdot cm^{-2}; V_h = -30 mV; T_h = -76.4 mV$  (taken from measurements of the h-current in Purkinje cells<sup>3</sup>;  $\sigma_h = 20 mV; a_{\alpha} = -2.89 mV^{-1} sec^{-1}; b_{\alpha} = -445 sec^{-1}; k_{\alpha} = 24.02 mV; a_{\beta} = 27.1 mV^{-1} sec^{-1}; b_{\beta} = -1024 sec^{-1}; k_{\beta} = -17.4 mV$  (these parameters that determine the value of  $\tau_h$  were taken from measurements in entorhinal cortex layer II neurons<sup>9</sup>. There, two time scales were measured for the h-current that were associated with two conductances. We chose the time scale that was associated with the larger conductance). In **Fig 8a,b**  $g_K = 100 \mu S \cdot cm^{-2}$ ; in **Fig. 8c,d**, left,  $g_K = 90 \mu S \cdot cm^{-2}$ ; in **Fig. 8c,d**, right,  $g_K = 105 \mu S \cdot cm^{-2}$ ; in **Supplementary Fig. 2**,  $g_K = 165 \mu S \cdot cm^{-2}; V_K = -85 mV; T_b = -54 mV; \sigma_b = 5 mV; \tau_b^0 = 3 sec; g_l = 100 \mu S \cdot cm^{-2}; V_l = -70 mV$ . A complex spike was modeled as a 4 msec-long  $1200 \mu S \cdot cm^{-2}$  sodium conductance.

## References:

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