How membrane currents interact to shape the integrative properties of motoneurones

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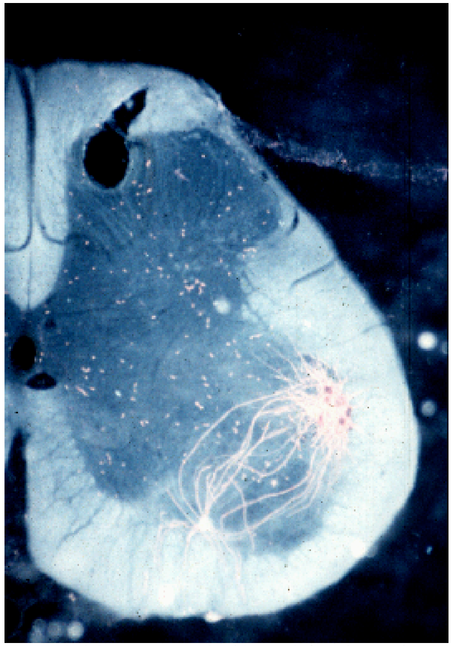
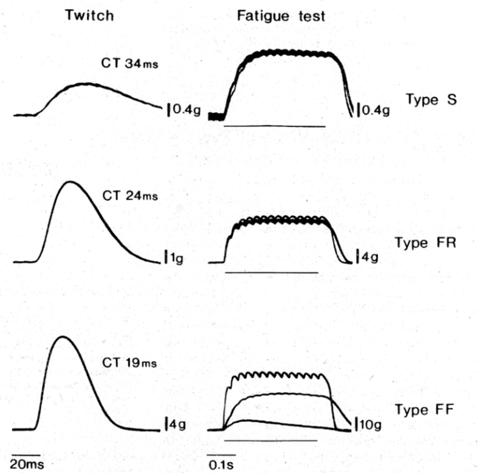
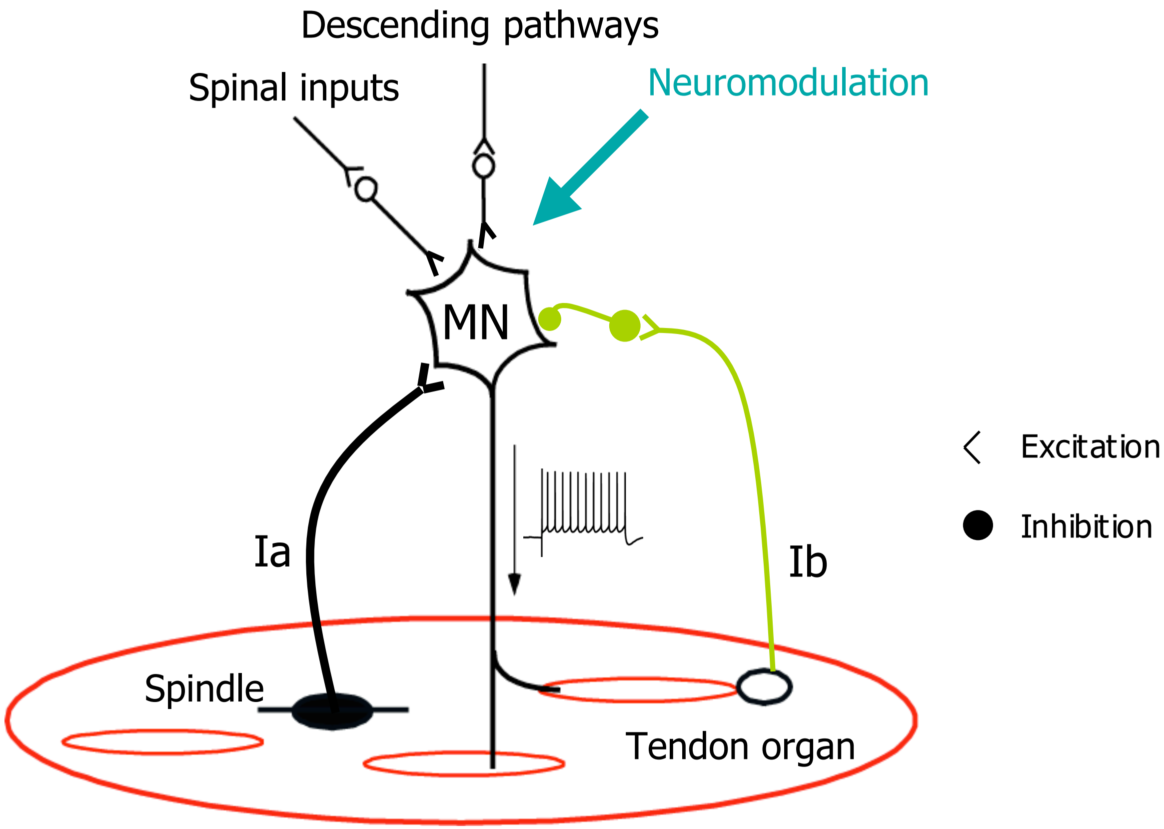
The final common pathway



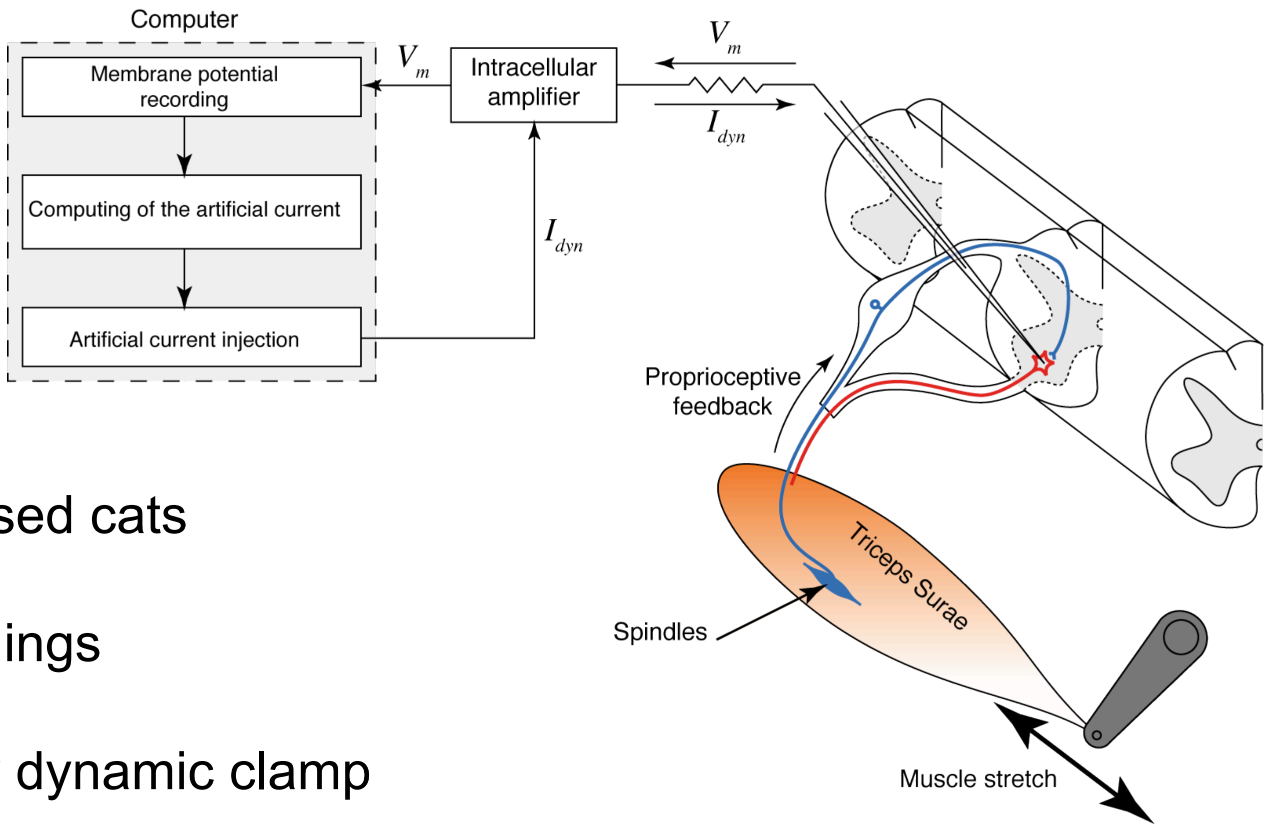


Jami et al., 1982



Slow and Fast-type motoneurones

Role of subthreshold currents in synaptic integration and firing



Deeply anaesthetised cats

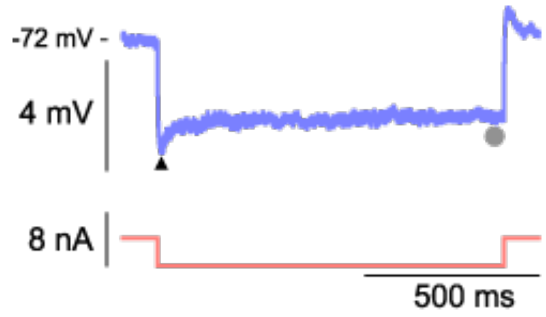
Intracellular recordings

Currents added by dynamic clamp

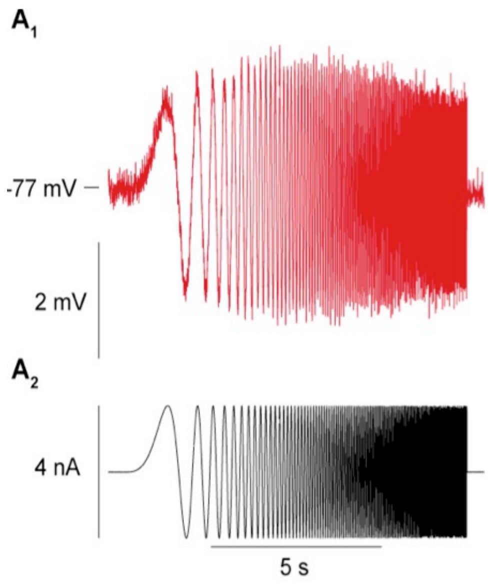
Experiments combined with simple models

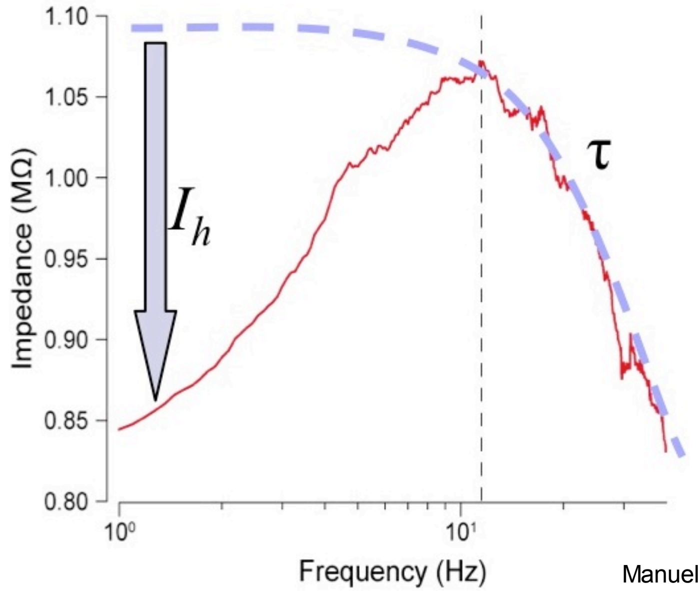
A physiological role for I_h

Little I_h in Slow-type motoneurones



F-type motoneurones display a subthreshold resonance

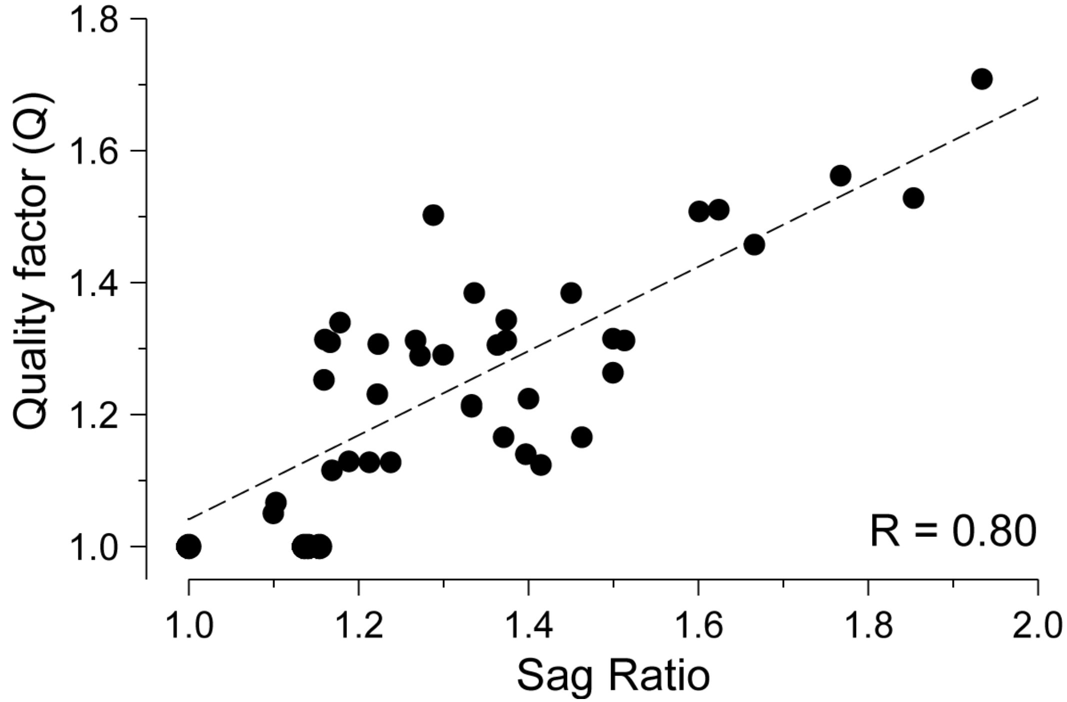




Manuel et al., 2007

$f_R = 11 \pm 3$ Hz

Resonance is caused by I_h



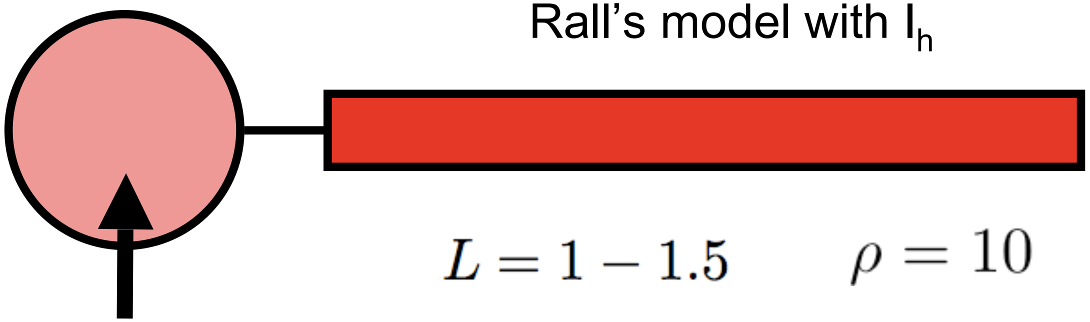
Manuel et al., 2007

Suppressed by depolarisation and enhanced by hyperpolarisation

Blocked by ZD-7288

which is located in dendrites

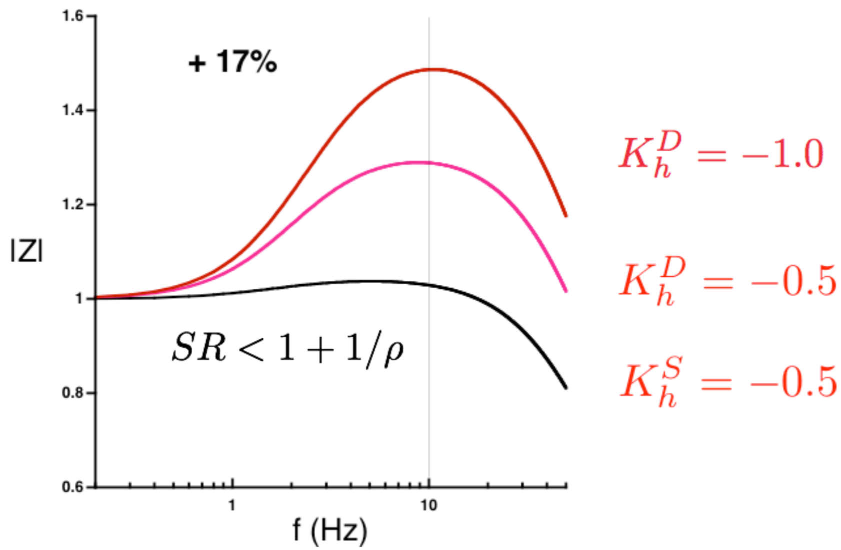
Rall's model with I_h



$$L = 1 - 1.5 \qquad \rho = 10$$

$$Y^S(\omega) + Y^D(\omega) = G_{soma}\left(1 + i\omega\tau_m - \frac{K_h S}{1 + \omega\tau_h}\right) + G_\infty q(\omega) tanh(\sqrt{1 + i\omega\tau_m - K_h^D/(1 + i\omega\tau_h)L})$$

$$K_h = \frac{G_h}{G_r}(V_h - V_r)\frac{dz_h^{ss}}{dV}(V_r) < 0$$

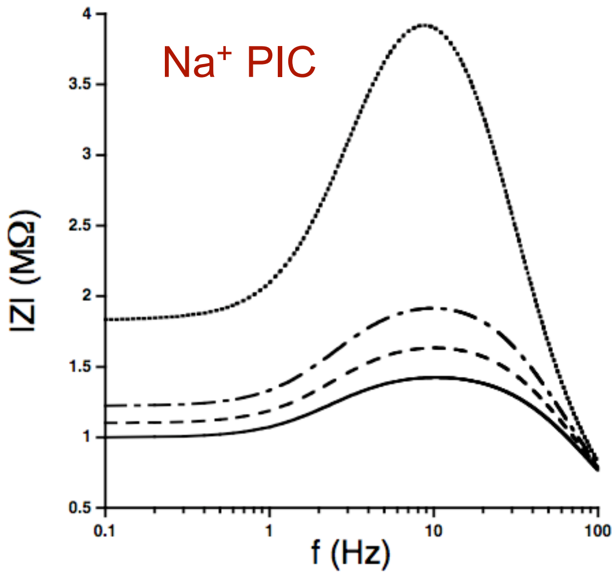


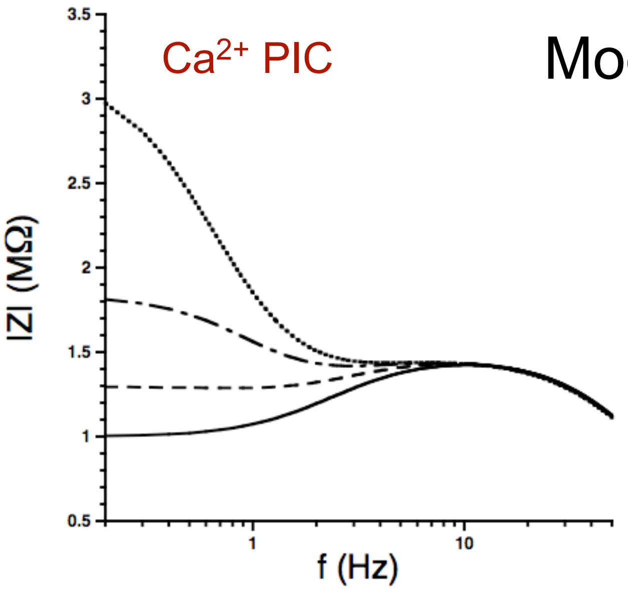
More than 90% of I_h in dendrites
(to be confirmed)

Manuel et al., 2007

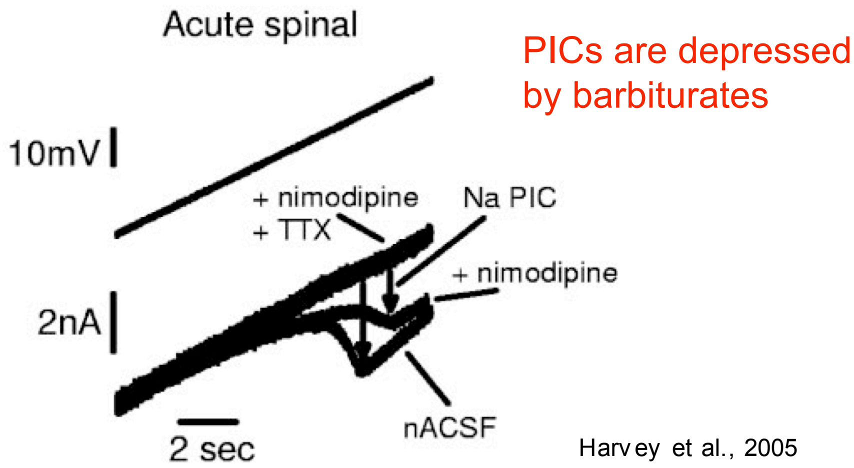
PICs enhance or suppress the resonance

Model

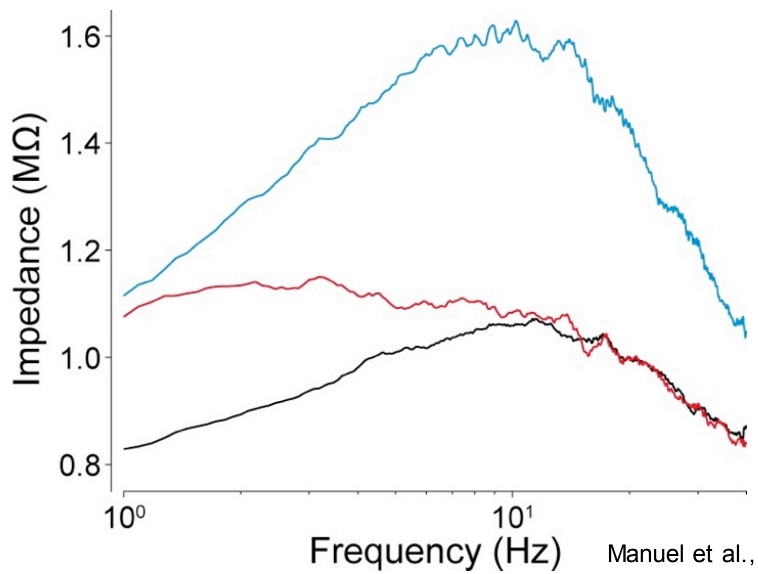




Experiments



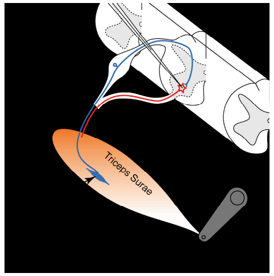
Harvey et al., 2005



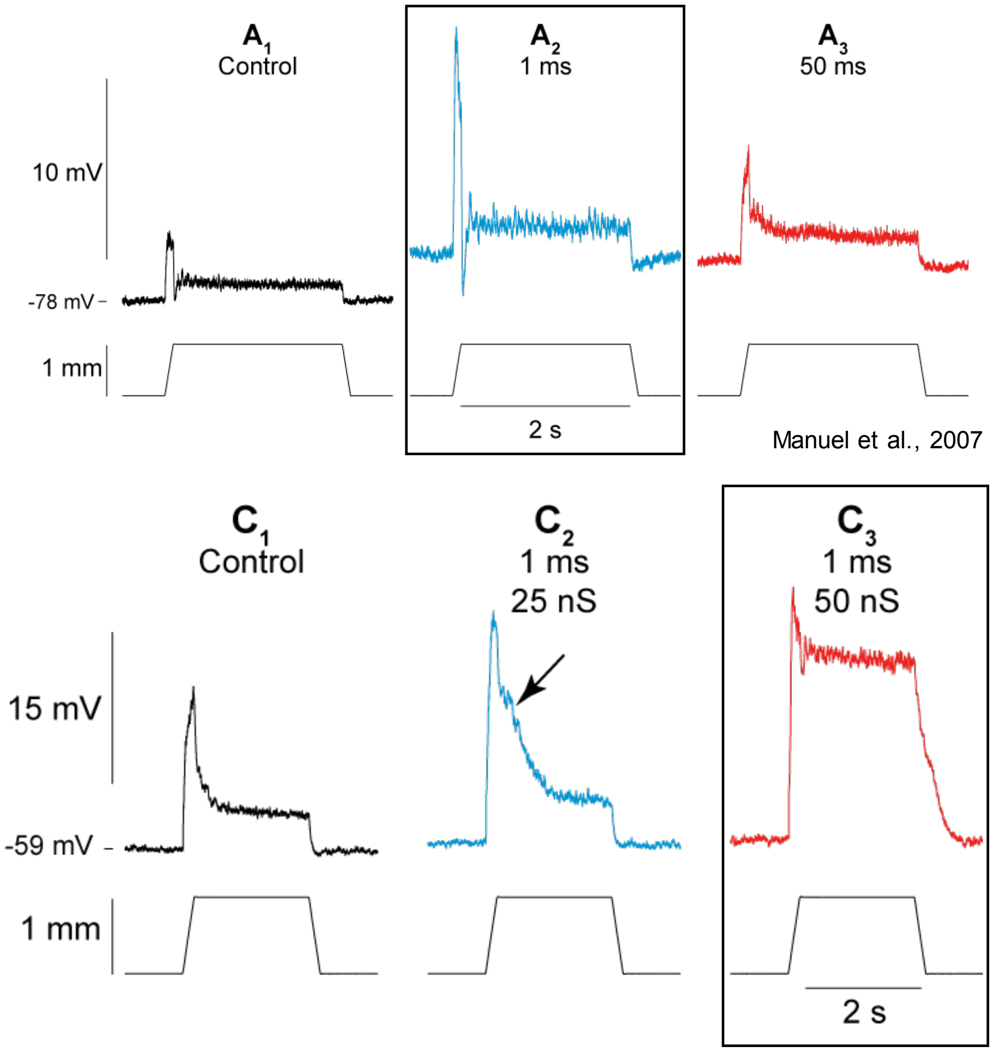
Manuel et al., 2007

Recruitment of motoneurones by proprioceptive input

Resonant (F-type)
Recovering balance

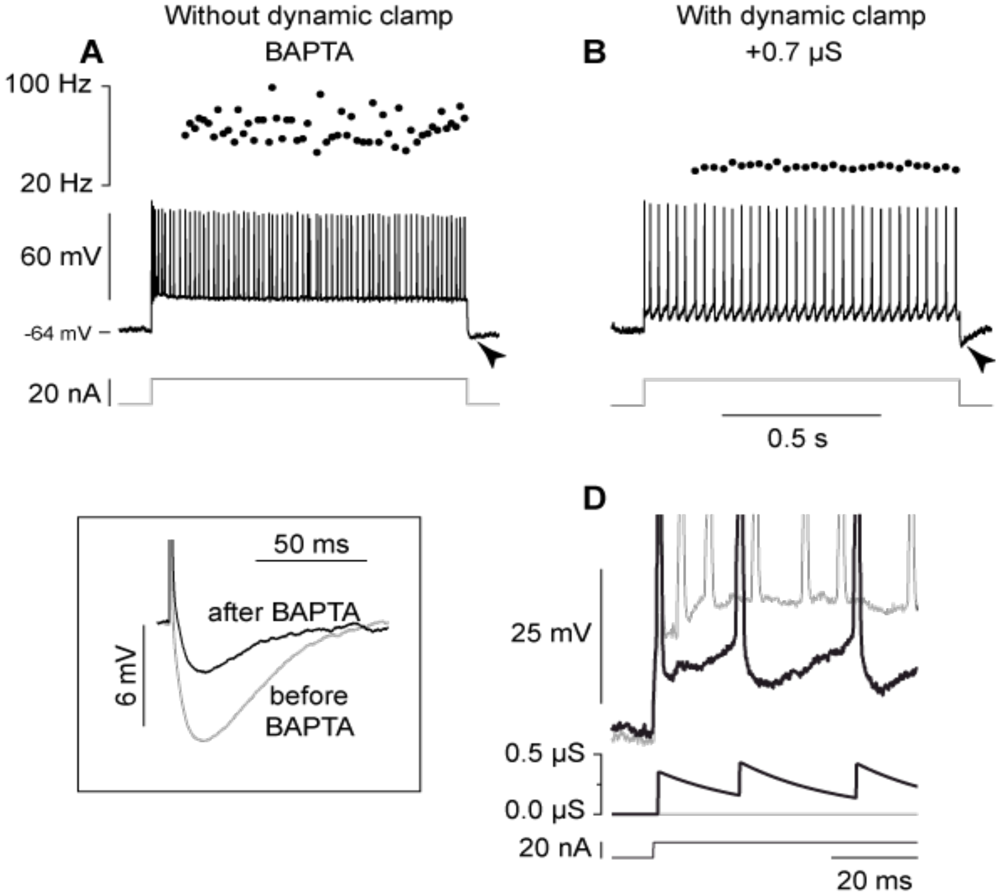


Non-resonant (S-type)
Maintaining posture



The AHP enters the picture

The AHP current regulates the discharge



Anaesthetised cats

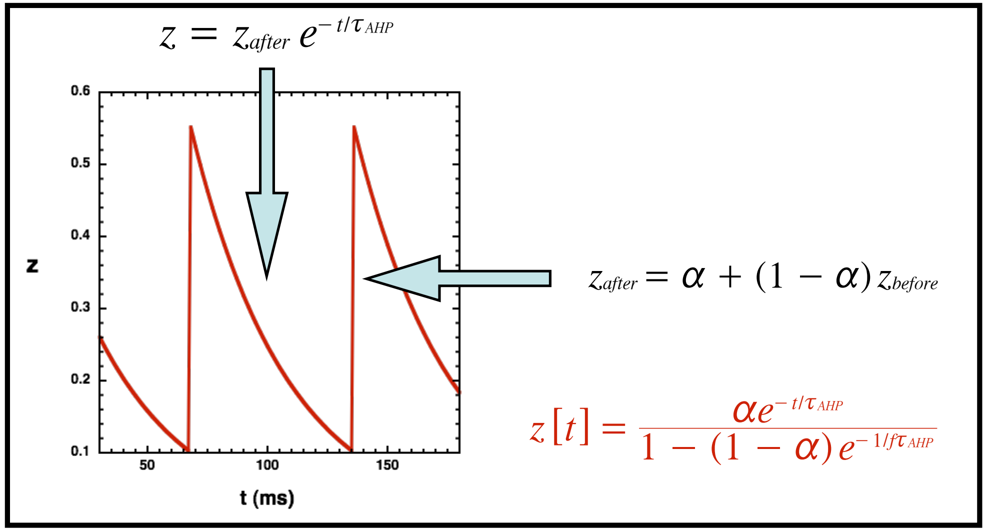
Manuel et al., 2006

A solvable model

Integrate-and-fire model with AHP conductance

$$C_m \frac{dV}{dt} = -G_{in} V - G_{AHP}^{max} z[t] \left(V - V_K\right) + I$$

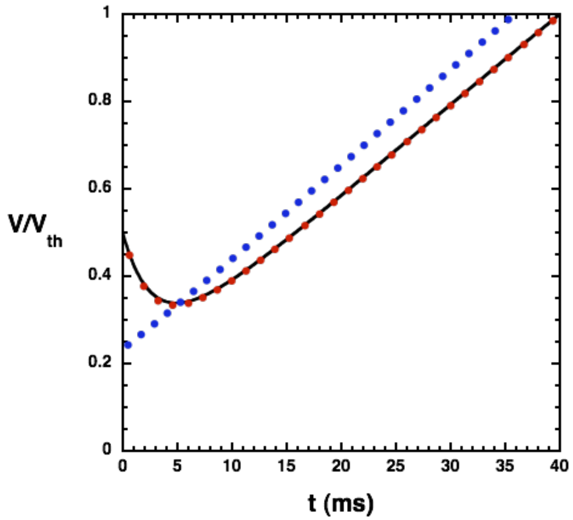
Effective voltage dependence $\tau_z[V] \frac{dz}{dt} = z_\infty[V] - z$



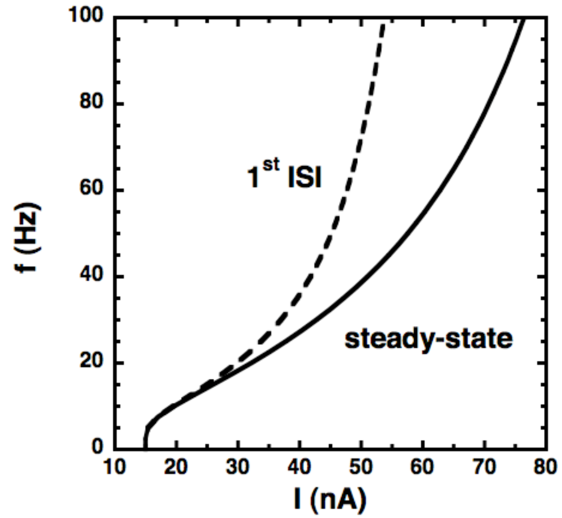
Meunier & Borejsza, 2005

Two time-scales analysis

$V_0\left[t/\tau_{AHP}\right] + \epsilon V_1\left[t/\tau_{AHP}, t/\tau_m\right] + \ldots \qquad \epsilon = \tau_m/\tau_{AHP}$



Meunier & Borejsza, 2005



$$\mathcal{G} = \frac{h(\alpha)}{G_{AHP}^{max}\tau_{AHP}\left(V_{th} - V_K\right)}\left(1 - \frac{\tau_m}{\tau_{AHP}}\left(\frac{G_{in}}{G_{in} + G_{AHP}(T)}\right)^2 + h.o.t.\right)$$

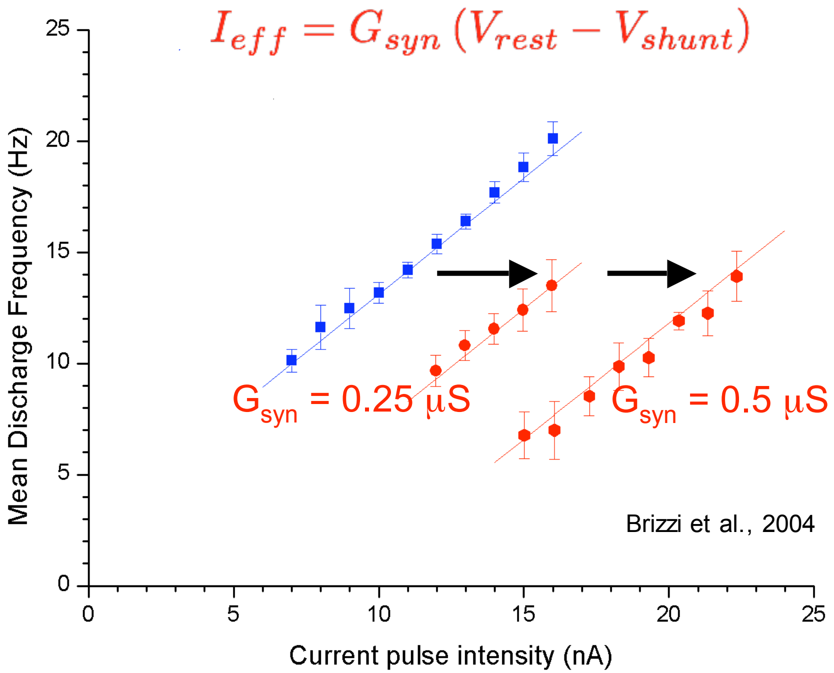
First interval: $h(\alpha) = e^2/4$

The gain is in inverse proportion to the charge transfered by the AHP current

Doubling the input conductance decreases the gain by less than 10%.

Experimental validation

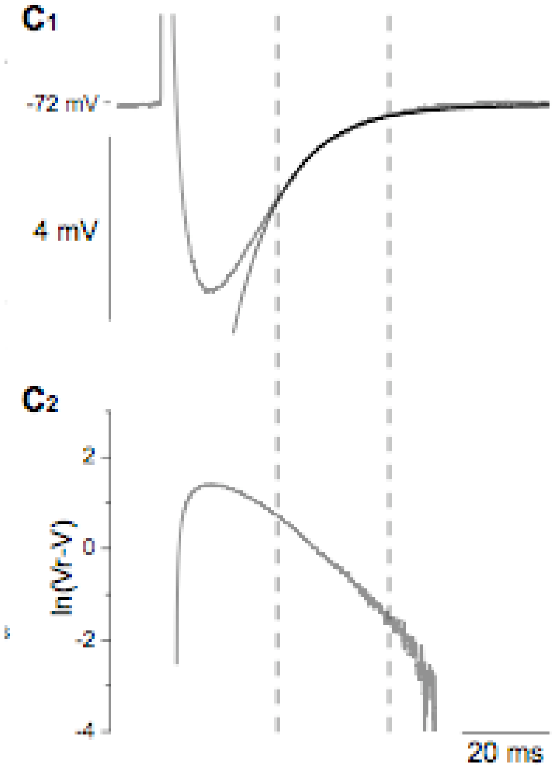
Shunting inhibition (Dynamic clamp)



$$V_{shunt} = \int_0^T V(t)Z(t)dt \Big/ \int_0^T Z(t)dt$$

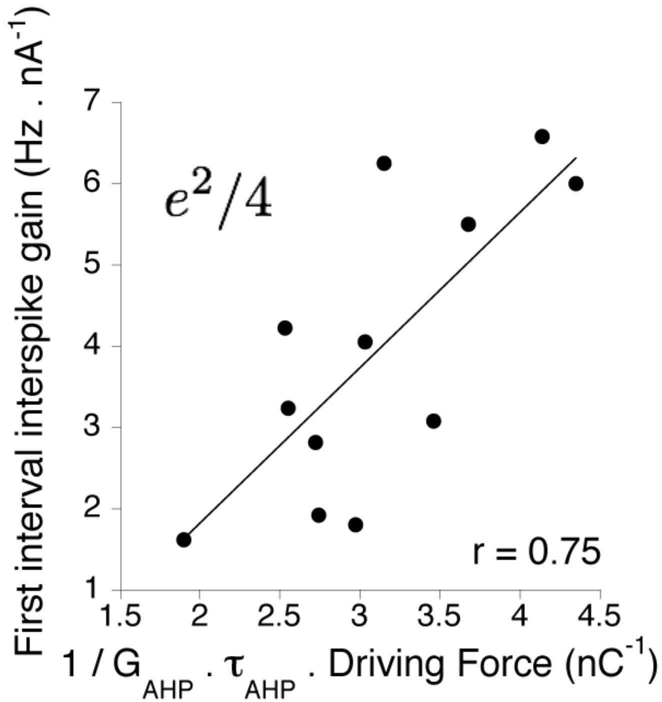
Z(t) is the phase response

T_{AHP}

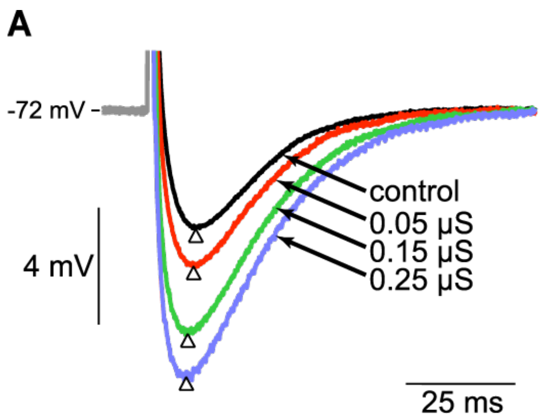


Uncontaminated by I_h

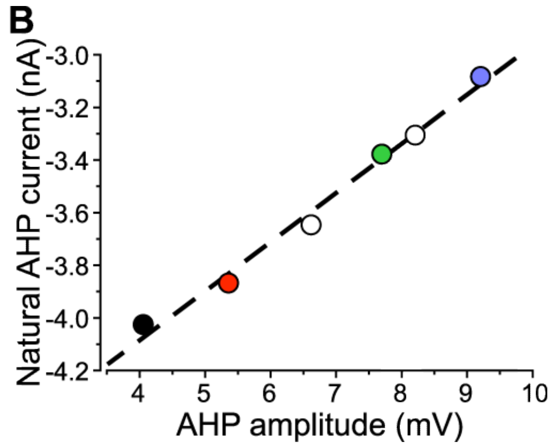
Manuel et al., 2005



Manuel et al., 2006

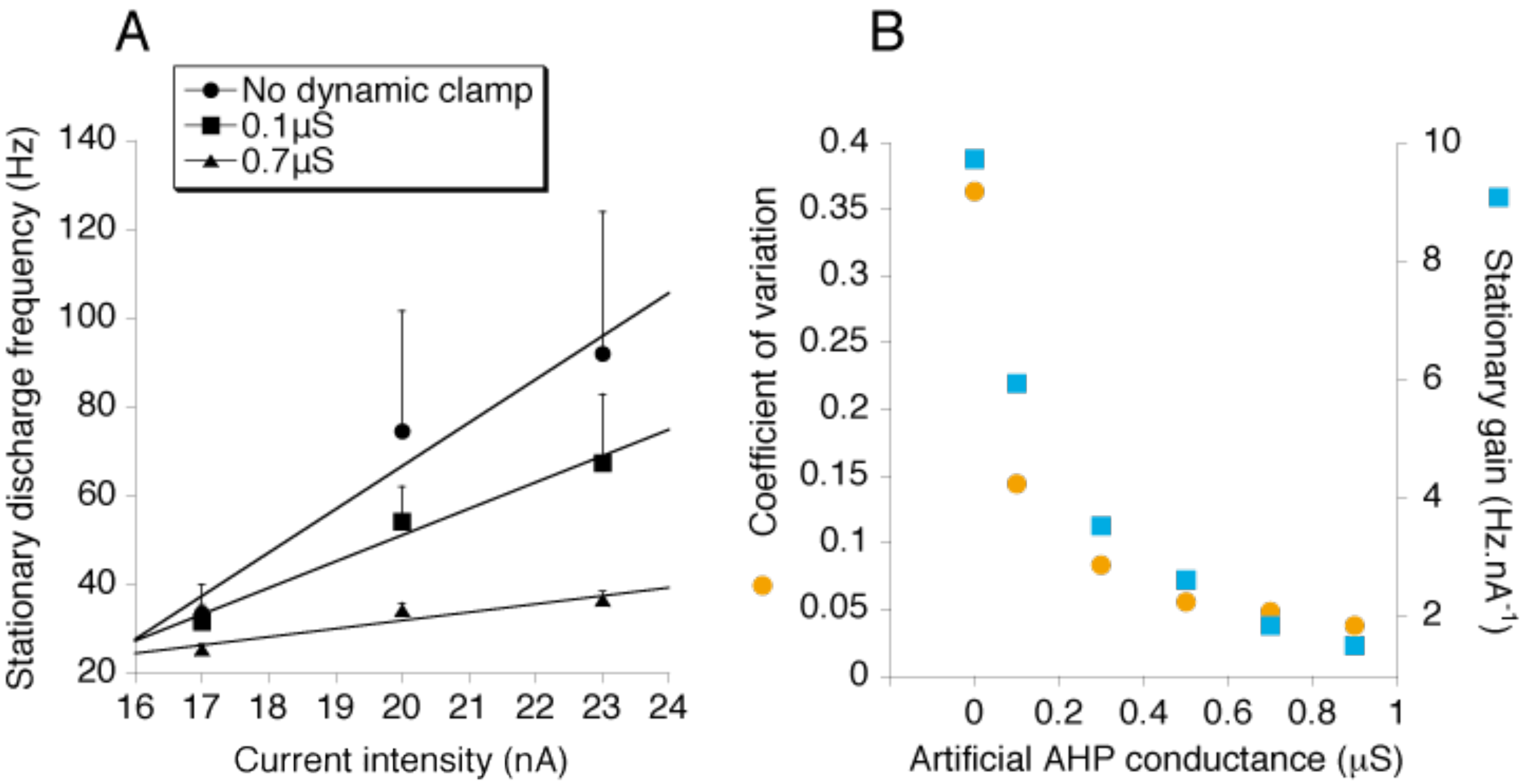


G_{AHP} and V_K



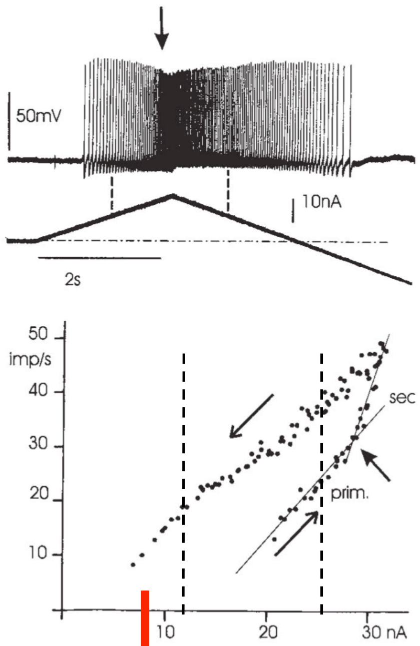
5 to 10% accuracy

AHP controls firing variability

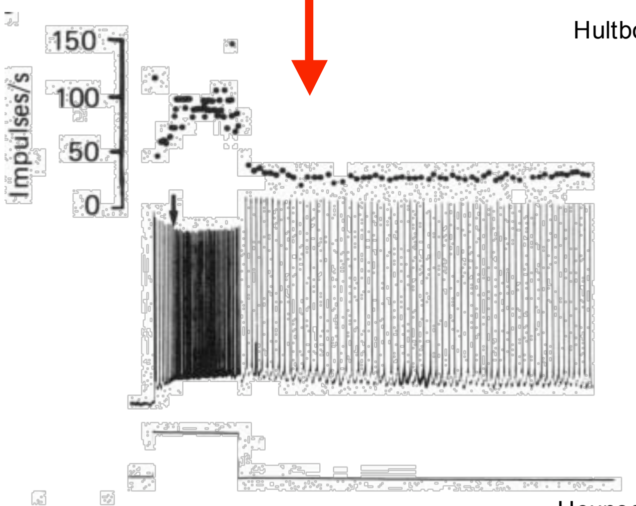


Manuel et al., 2006

Neuromodulation may induce bistability

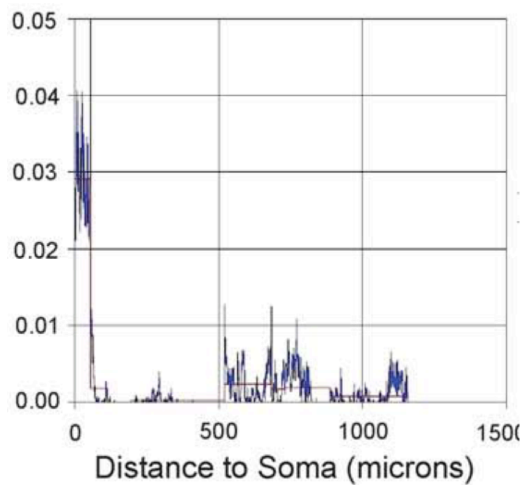


Hultborn et al., 2004



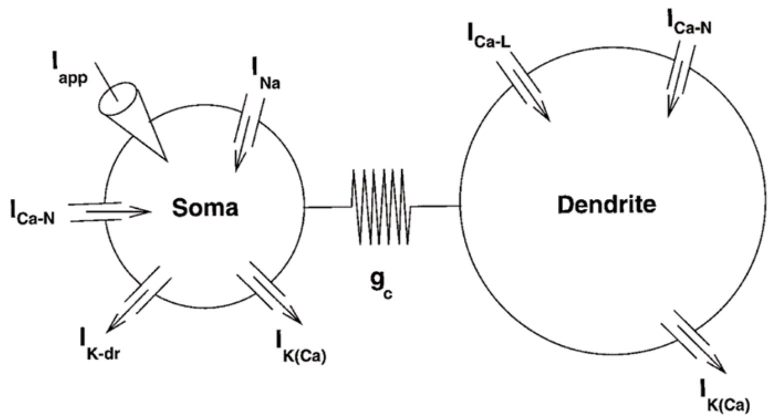
Hounsgaard et al., 1988

Persistent calcium current

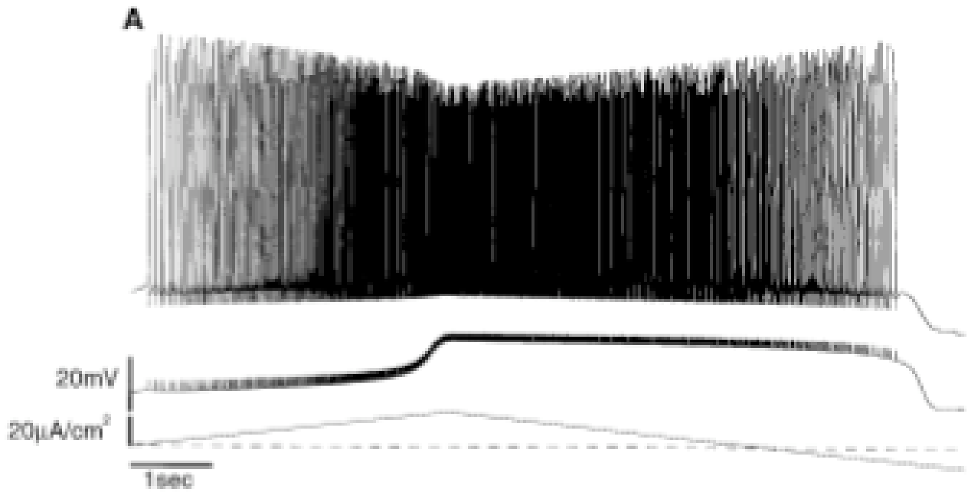


Ballou et al., 2006

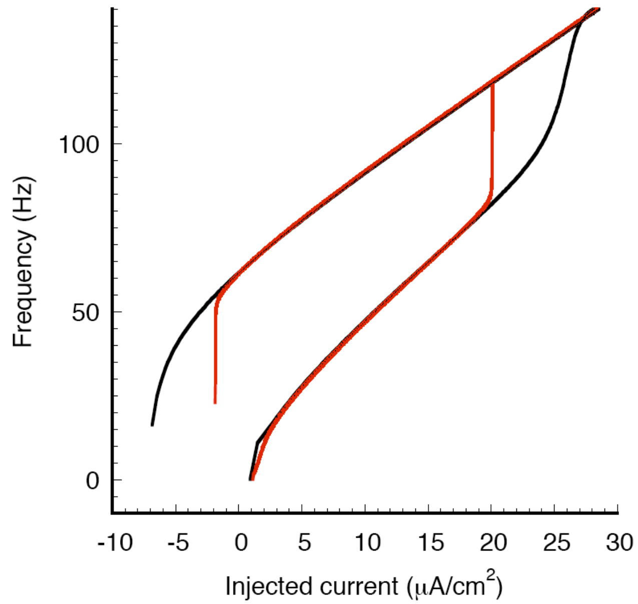
The BRK model



Weak coupling : $g_c = 0.1\ mS/cm^2$



Bistability of dendritic I-V curve



Studies with this model have supported the hypothesis that the bistable firing patterns require a nonuniform distribution of ionic conductances and, specifically, a ***segregation of plateau-generating currents from spike-generating currents****.*

Booth, Rinzel & Kiehn, 1997

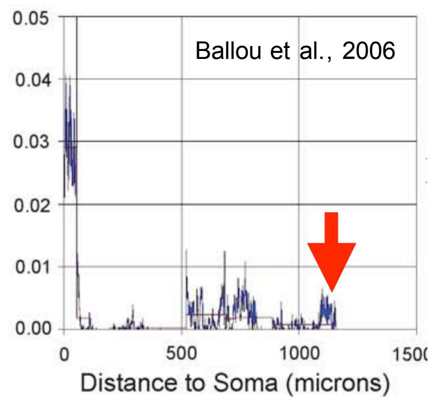
Is it relevant for motoneurones?

Parameters	Motoneurone	BRK model
ρ	10	2.7
τ_m	6 ms	2 ms
τ_{AHP}	15 ms	50 ms
G_{AHP}/G_{in}	0.3 (no neurodulation)	0.02

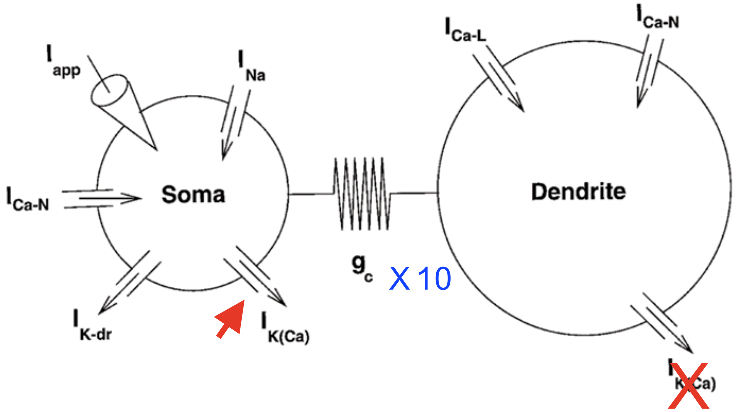
Weak coupling -> Dendritic voltage is attenuated and low-pass filtered

Stationary voltage : 70%
Spikes : 96%

Distal location of PIC: 1.2 λ (L = 1-1.5)

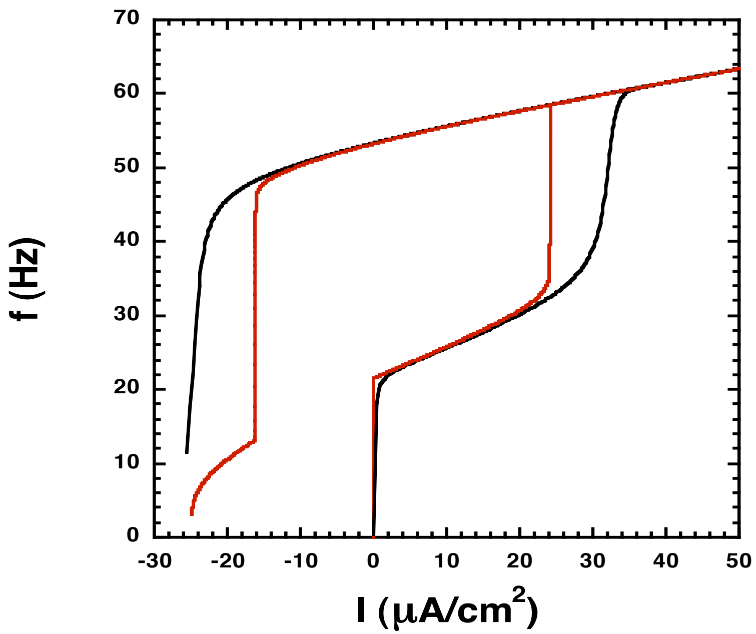


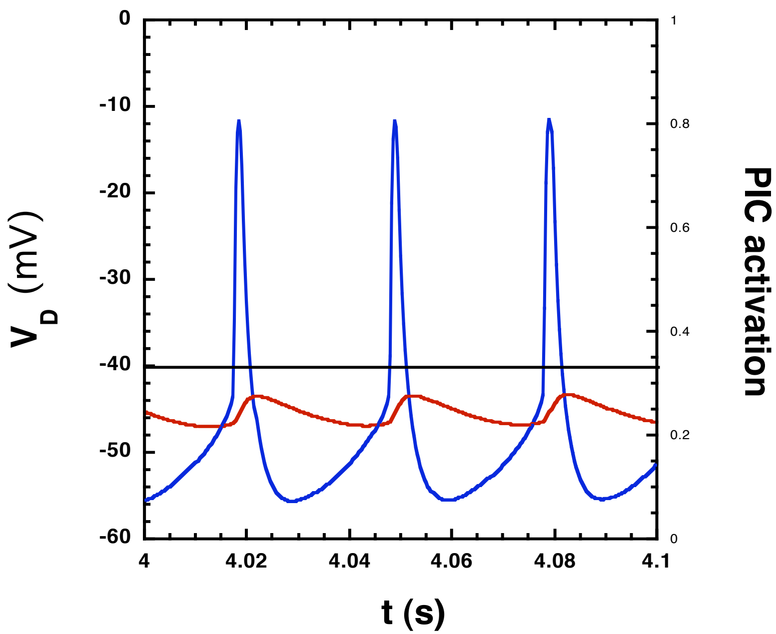
An alternative model



More realistic parameters:
ρ, G_{in}, G_{AHP} , τ_m, $\tau_{AHP,}$ PIC location

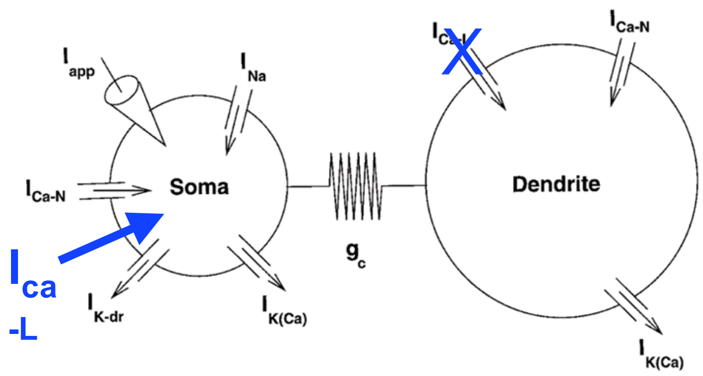
Bistability stems from the competition between the dendritic PIC and the somatic AHP current

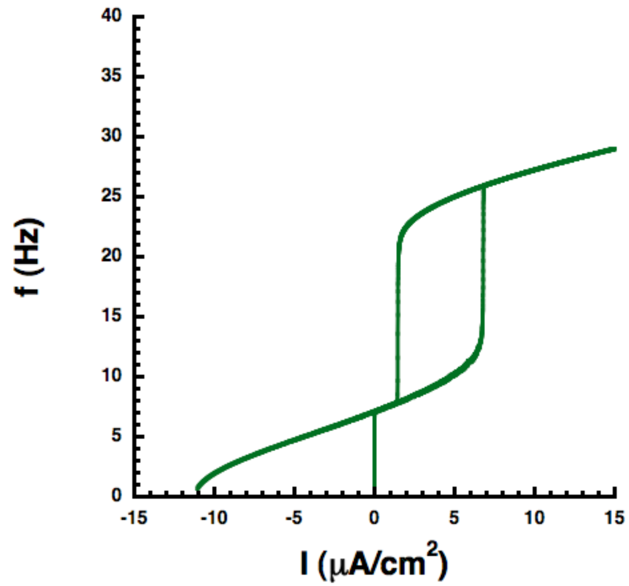




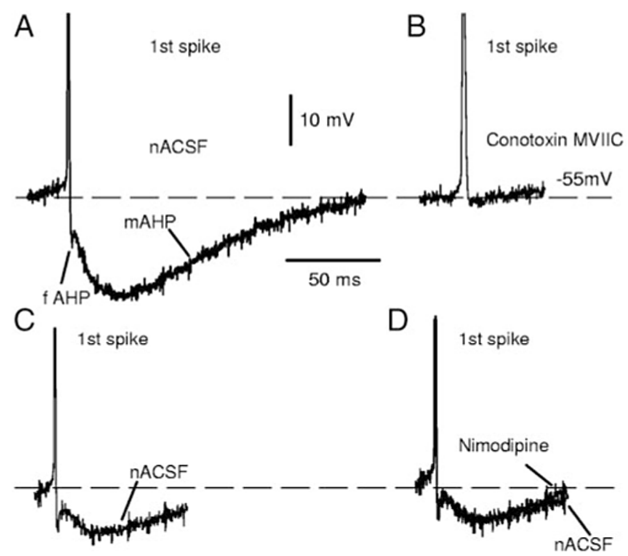
Somatic bistability: Model

Calcium PIC at the soma only





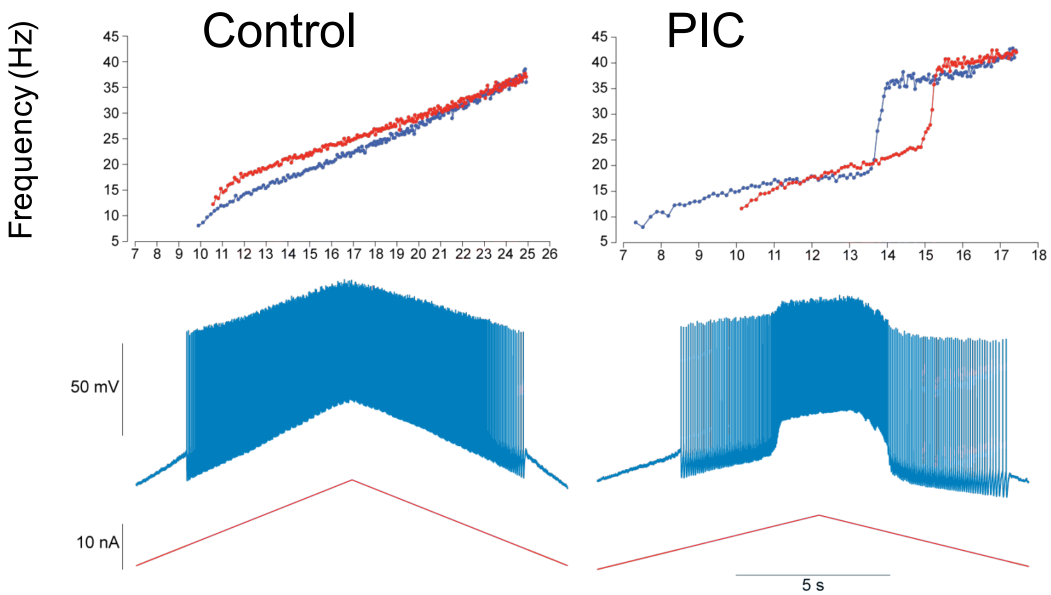
Calcium decoupling between PIC and AHP current is required



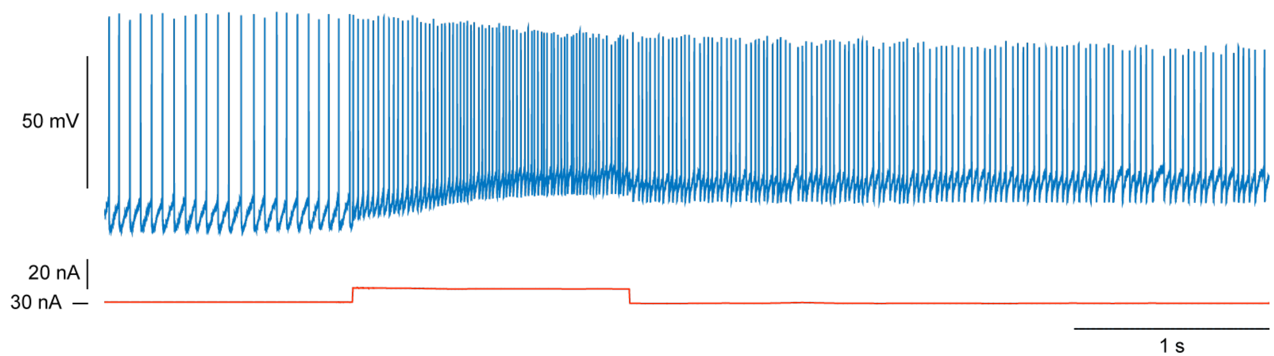
Li and Bennett 2007

and experiments

Counterclockwise hysteresis



Firing bistability



Conclusions

Subthreshold currents shape the integrative properties of motoneurones

A major role is played by the *competition between stabilizing and destabilizing currents*:

I_h and PICs below threshold
-> selective amplification of synaptic input and recruitment of motoneurones

AHP current and Calcium PIC above threshold
-> control of the firing states

Neuromodulation controls the balance between these currents according to the physiological requirements

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