

# Conductance-Based Models of Nonlinear Dynamics in Vertebrate Motoneurons

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## Definition

The term “conductance-based models of nonlinear dynamics in vertebrate motoneurons” refers to conductance-based motoneuron models that capture the complex nonlinear membrane properties (e.g., bistability) of vertebrate motoneurons observed both *in vivo* and *in vitro* under certain conditions. Numerous conductance-based motoneuron models with widely varying morphological complexities and different ionic current composition exist that reproduce the experimentally observed nonlinear membrane properties. This article focuses on models that assume minimally required morphological complexity (e.g., two compartments) and ionic conductances. The resulting reduced set of equations and parameters describing such models have enabled detailed analyses of model behavior using geometric dynamical systems methods to provide insight into the basis of nonlinear membrane properties in vertebrate motoneurons.

## Detailed Description

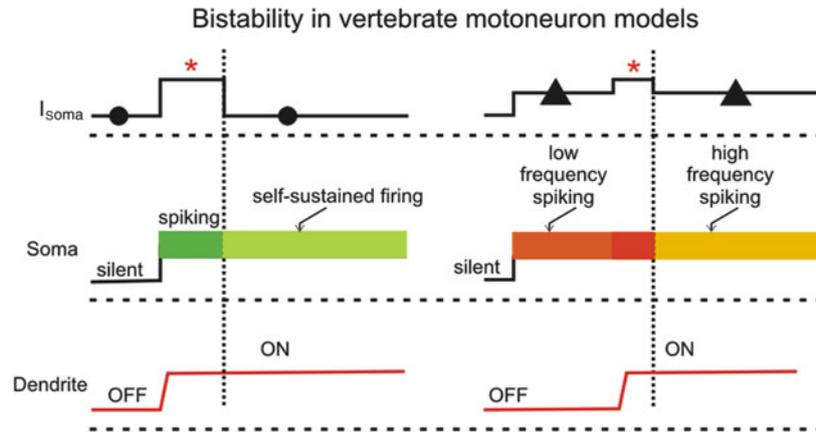
Dynamics of vertebrate motoneurons are phylogenetically conserved sharing common phenomenology from turtles to humans (Hornby et al. 2002). Under certain experimental conditions, these neurons display nonlinear membrane properties such as bistability (Bennett et al. 2001; Hounsgaard and Kiehn 1985; Schwindt and Crill 1977; Sigvardt et al. 1985; Lee and Heckman 1998a). Physiologically, bistability arises due to plateau potentials that develop and persist on a slower timescale (order of seconds to minutes) relative to the millisecond timescale action potential events. In most adult vertebrates, plateau potentials are generated by noninactivating “persistent inward currents” (Lee and Heckman 1998b) predominantly composed of low-voltage-activated L-type calcium and to a lesser extent by persistent sodium currents (Lee and Heckman 1996; Li and Bennett 2003). It is generally accepted that such currents are of dendritic origin (Carlin et al. 2000). When activated, they produce a persistent plateau in the somatic membrane voltage that can be sufficient to sustain action potentials even after the removal of plateau producing depolarizing input – also known as “self-sustained firing” (see Fig. 1). Additionally, activation of plateau potentials can induce higher-frequency firing for the same depolarizing current injection that produced a low-frequency firing before plateau activation (see Fig. 1).

## Models of Motoneuron Bistability

Models of motoneuron bistability have faithfully captured the nonlinear dynamics arising at the soma in experimental settings.

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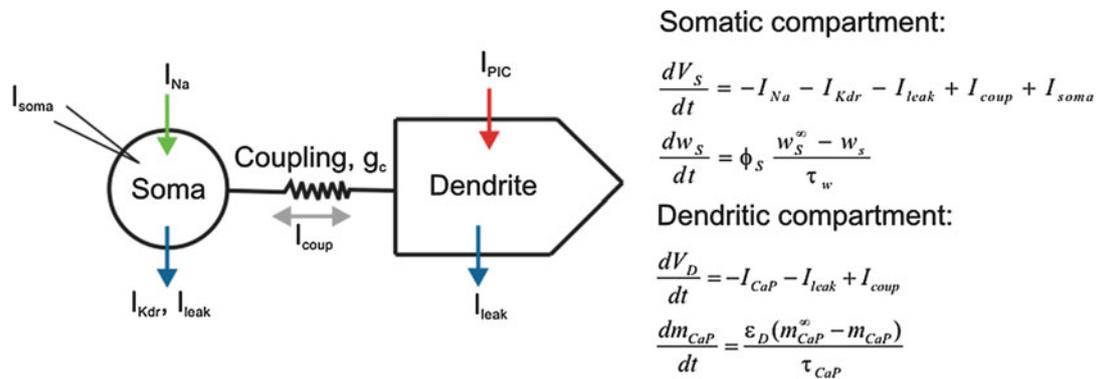
**Fig. 1 Bistable membrane behavior in vertebrate motoneurons.** *Left:* Somatic current injection ( $I_{\text{soma}}$ ) marked by red asterisk induced somatic spikes (dark green) that in turn also activates dendritic plateau (dendrite switches from OFF to ON state). This dendritic plateau persists even after the somatic current returns to its initial level (demarcated by vertical dotted line) at which the soma was silent. This sustained plateau now drives somatic spikes resulting in self-sustained firing (light green). Black circles indicate zero  $I_{\text{soma}}$ . *Right:* Figure shows the two levels of  $I_{\text{soma}}$ , low current (black triangle) that initially induces a low-frequency firing in the soma (orange) but does not activate the dendrite followed by a brief high  $I_{\text{soma}}$  (red asterisk) that turns on the plateau. Subsequent return of  $I_{\text{soma}}$  to its initial value (black triangle) results in a higher-frequency firing (yellow) due to the additional persistent depolarization by the dendritic plateau

There are two basic features of these models that are critical for reproducing the experimentally observed bistable membrane properties in motoneurons. They include (1) the presence of at least two *weak moderately* coupled compartments and (2) sufficiently disparate membrane properties between the compartments (e.g., dendritic localization of persistent inward currents). A classic two-compartment conductance-based model that first explored the phenomenology of vertebrate motoneuron bistability is the Booth-Rinzel model (Booth and Rinzel 1995) that included dimensionless equations. Similar two-compartment models incorporated more realistic biophysically based ionic conductances to generate physiologically realistic membrane voltage responses and firing behavior in the specific motoneurons being modeled (e.g., Booth et al. 1997; Kurian et al. 2011; Venugopal et al. 2011, 2012).

### A Minimal Motoneuron Model for Understanding Bistable Membrane Behavior

Figure 2 shows the model schematic of a minimal two-compartment vertebrate motoneuron. The equations guiding this minimal model are given below:

Shown here are minimal set of ionic currents that include fast sodium ( $I_{\text{Na}}$ ) and delayed rectifier potassium ( $I_{\text{Kdr}}$ ) in the soma for action potential generation, a voltage-dependent persistent inward current in the dendrite ( $I_{\text{PIC}}$ ) that mediates dendritic plateau, a leak current ( $I_{\text{leak}}$ ) in both the compartments to maintain the resting potential, a coupling current ( $I_{\text{coup}}$ ) that arises due to the electrotonic coupling of the compartments whose magnitude depends on the coupling conductance ( $g_c$ ), and the proportion of area ( $p$ ) suggested to be occupied by the soma. The term  $I_{\text{soma}}$  refers to somatic current injection. The somatic and dendritic voltages are given by  $V_S$  and  $V_D$ , respectively. For a detailed description of the model, see (Booth and Rinzel 1995). Note that these form a general set of equations and conductances guiding the somatic and dendritic compartments and one can easily incorporate additional terms for ionic currents as well as increase the morphological complexity as relevant. Alternatively, such minimal models could guide the development of artificial motoneurons that may act as bistable switches in neuromorphic circuits.

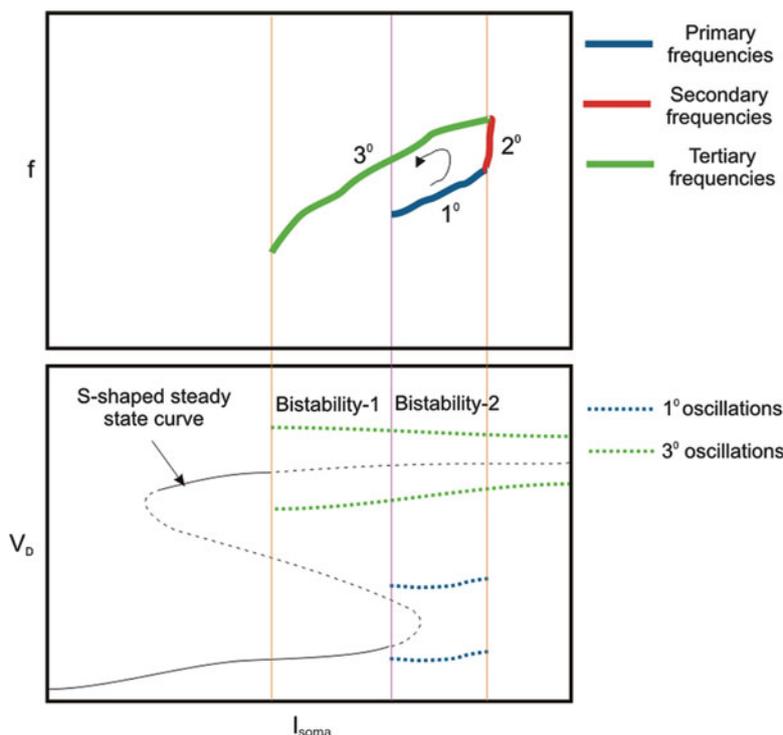


**Fig. 2 Minimal motoneuron model of bistability.** *Left:* A schematic showing the morphological and electrophysiological components of the model consisting of two electrotonically coupled compartments, namely, soma and dendrite. *Arrows* show the directions of inward and outward currents (see text for description of currents). *Right:* Equations guiding the membrane voltage dynamics in somatic and dendritic compartments

## Hysteresis in the Frequency-Current Relationship and Mechanism Underlying Bistability

Motoneuron bistability described above can give rise to a counterclockwise hysteresis in the injected current firing frequency relationship (f-I) (see Fig. 3, *top*) although existence of f-I hysteresis itself is not sufficient for bistability.

Of importance in the f-I curve shown are the three ranges of firing frequencies, (1) primary, (2) secondary, and (3) tertiary ranges (see Kernell 1965; Schwindt 1973 for the first descriptions), that together lead to a counterclockwise hysteresis to the f-I relationship. Use of geometric dynamical systems methods has provided insight into the mechanism of bistability and the emergence of the three frequency ranges. Figure 3 (*bottom*) shows a typical bifurcation structure of the dendritic voltage  $V_D$  with  $I_{soma}$  as the parameter. In the class of two-compartment models described above, this corresponds to an S-shaped curve for a range of coupling conductances characterized as weak-moderate (e.g., see Booth and Rinzel 1995; Kurian et al. 2011). The lower branch (dendrite OFF) consists of stable fixed points (non-spiking steady states/resting) and a stable oscillatory regime. The upper branch (dendrite ON) also consists of stable fixed points (non-spiking plateau state) and a stable oscillatory regime. The height and width of the S shape as well as that of the regimes described are dependent on the properties of the ionic conductances considered (e.g., note differences among the various models Booth et al. 1997; Kurian et al. 2011; Venugopal et al. 2011). Superimposing the dendritic voltage changes during a somatic triangular ramp current injection in the model clarifies that (1) the primary firing frequencies correspond to the oscillatory frequencies emerging at the lower branch, (2) tertiary frequencies correspond to the oscillatory frequencies emerging at the upper branch, and (3) secondary frequencies would arise during plateau development and are transitory see (Venugopal et al. 2011). The same is illustrated using the steady-state bifurcation diagram (see Fig. 3) of dendritic voltage in response to  $I_{soma}$  clarifying that only 1° and 3° frequencies are stable oscillatory states, while the secondary range arising during plateau development is not evident as a stable steady state. This critical insight suggests the possible window of modulation of the plateau by synaptic inputs in turn regulating motoneuron firing frequencies and muscle output.



**Fig. 3 Bifurcation analyses of emergence of f-I hysteresis and bistability.** *Top:* Schematic of f-I relationship in response to a somatic triangular ramp current injection ( $I_{soma}$  trace not shown, but see *curved arrow* showing direction of  $I_{soma}$  changes). Spiking begins in the soma in the primary frequency range (*blue*) and continues into a steeper secondary range (*red*) as  $I_{soma}$  ramps up. On the descending  $I_{soma}$  ramp, tertiary frequencies (*green*) give rise to a counterclockwise hysteresis in the f-I relationship. *Bottom:* Bifurcation curve showing the various steady-state regimes. The *bold lines* in the steady-state *S-shaped curve* indicate stable fixed points and *broken lines* indicate unstable fixed points. *Blue dotted lines* demarcate the amplitude of dendritic oscillations due to soma firing in the primary range (only stable oscillations are shown here). *Red dotted lines* demarcate the amplitude of dendritic oscillations due to soma firing in the tertiary range. Note that there are no stable steady-state oscillations for the secondary range in this diagram suggesting that these frequencies are transitory. Bistability-1 (region between *left orange* and *magenta vertical lines*) marks the region where tertiary firing and (stable) non-spiking state can coexist underlying self-sustained firing described earlier. Bistability-2 (region between *magenta* and *right orange vertical lines*) marks the region where primary and tertiary firing can coexist as described earlier in Fig. 1 (*right*)

In summary, conductance-based mathematical models of vertebrate motoneurons have been useful platforms to examine nonlinear dynamics in these neurons and have provided important insights into the basis of experimentally observed membrane properties in this important class of cells in the nervous system.

## Cross-References

- ▶ [Bistability \(Neuron\)](#)
- ▶ [Compartmental Models of Spinal Motoneurons](#)
- ▶ [Morphologically Detailed Motoneuron Models](#)

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