



HAL
open science

Conductance-Based Phenomenological Nonspiking Model: A Dimensionless and Simple Model That Reliably Predicts the Effects of Conductance Variations on Nonspiking Neuronal Dynamics

Loïs Naudin, Laetitia Raison-Aubry, Laure Buhry

► **To cite this version:**

Loïs Naudin, Laetitia Raison-Aubry, Laure Buhry. Conductance-Based Phenomenological Nonspiking Model: A Dimensionless and Simple Model That Reliably Predicts the Effects of Conductance Variations on Nonspiking Neuronal Dynamics. *Neural Computation*, 2023, 35 (7), pp.1209-1233. 10.1162/neco_a_01589 . hal-04242759

HAL Id: hal-04242759

<https://cnrs.hal.science/hal-04242759>

Submitted on 15 Oct 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 Conductance-based phenomenological non-spiking
2 model: a dimensionless and simple model that reliably
3 predicts the effects of conductance variations on
4 non-spiking neuronal dynamics

5 Loïs Naudin^{1**}, Laetitia Raison-Aubry¹⁺, and Laure Buhry¹

6 ¹Laboratoire Lorrain de Recherche en Informatique et ses Applications,
7 CNRS, Université de Lorraine, Nancy, France

8 *Corresponding author: lois.naudin@gmail.com

9 ⁺These authors contributed equally (joint first author)

10 October 15, 2023

11 **Abstract**

12 The modeling of single neurons has proven to be an indispensable tool in decipher-
13 ing the mechanisms underlying neural dynamics and signal processing. In that sense,
14 two types of single-neuron models are extensively used: the conductance-based mod-
15 els (CBMs) and the so-called ‘phenomenological’ models, which are often opposed in
16 their objectives and their use. Indeed, the first type aims to describe the biophysical
17 properties of the neuron cell membrane that underlie the evolution of its potential,
18 while the second one describes the macroscopic behavior of the neuron without taking
19 into account all its underlying physiological processes. Therefore, CBMs are often
20 used to study ‘low-level’ functions of neural systems, while phenomenological models
21 are limited to the description of ‘high-level’ functions. In this paper, we develop a
22 numerical procedure to endow a dimensionless and simple phenomenological non-
23 spiking model with the capability to describe the effect of conductance variations on
24 non-spiking neuronal dynamics with high accuracy. The procedure allows to deter-
25 mine a relationship between the dimensionless parameters of the phenomenological

26 model and the maximal conductances of CBMs. In this way, the simple model com-
27 bines the biological plausibility of CBMs with the high computational efficiency of
28 phenomenological models, and thus may serve as a building block for studying both
29 ‘high-level’ and ‘low-level’ functions of non-spiking neural networks. We also demon-
30 strate this capability in an abstract neural network inspired by the retina and *C.*
31 *elegans* networks, two important non-spiking nervous tissues.

32
33 **Keywords:** Simple neuron model; non-spiking neurons; conductance variations;
34 bifurcation; *Caenorhabditis elegans*; retina.

35 1 Introduction

36 To better understand how neuronal circuits control behavior and brain functions, neuron
37 modeling is a widely-used tool. Two types of models characterizing the dynamics of sin-
38 gular neurons can be used. The first one is the conductance-based model (CBM), which
39 inherits the Hodgkin-Huxley formalism (Hodgkin and Huxley, 1952) and aims to describe
40 the biophysical properties of the neuron cell membrane that underlie the evolution of its
41 potential. In this model, every individual parameter and state variable has an established
42 electrophysiological meaning. Therefore, CBMs are broadly used to understand ‘low-level’
43 functions of neural systems (Eliasmith and Trujillo, 2014; O’Leary et al., 2015), such as
44 monitoring the effects of specific conductance variations on neuronal dynamics (Giovan-
45 nini et al., 2017; Poirazi and Papoutsis, 2020; Naudin et al., 2022c), or modeling gain- or
46 loss-of-function mutations in genes encoding ion channels (Lemaire et al., 2021).

47 The second type of model is often qualified by the term ‘phenomenological’, although
48 some authors contradict it (Brette, 2015). This type of model was developed in part to
49 overcome the drawbacks of CBMs, which are twofold: (i) they have a very high computa-
50 tional cost due to their complexity so that only a handful of neurons can be simulated in
51 real time (Izhikevich, 2004), and (ii) the insights obtained from a mathematical analysis
52 are quite limited as these are high-dimensional systems (Ermentrout and Terman, 2010).
53 A phenomenological model therefore aims to be lightweight, simple, and to describe the
54 macroscopic behavior of the neuron without taking into account all its underlying physi-
55 ological processes. Some classical examples are the FitzHugh–Nagumo model (FitzHugh,
56 1961), Izhikevich model (Izhikevich, 2003), or many integrate-and-fire models (Latham
57 et al., 2000; Smith et al., 2000; Górski et al., 2021). The counterpart of phenomenological
58 models is that their parameters are dimensionless, thus limited to the study of ‘high-level’
59 functions of neural systems.

60 A simple phenomenological model of non-spiking neurons was recently developed in
61 Naudin et al. (2022b). This type of neuron is found in a wide variety of nervous tissues
62 (Davis and Stretton, 1989b; Goodman et al., 1998; Field and Chichilnisky, 2007), encodes
63 neuronal information in an analog manner through graded responses (Lockery et al., 2009),
64 and plays a crucial role in the functioning of many nervous systems (Roberts and Bush,
65 1981; Burrows et al., 1988; Laurent and Burrows, 1989; Davis and Stretton, 1989a; Bidaye
66 et al., 2018). Further, three phenotypes of non-spiking neurons can be distinguished (Fig-
67 ure S2), each with its own computational properties (Naudin et al., 2022c): (i) near-linear,
68 defined by smooth depolarizations or hyperpolarizations from the resting potential (pheno-
69 type 1), (ii) bistable, characterized by nonlinear transitions between the resting potential
70 and a depolarized potential, with one resting potential (phenotype 2), and (iii) bistable
71 with two resting potentials (phenotype 3). Naudin et al. (2022c) described a general pat-
72 tern of the phenotypic evolution of non-spiking neurons as a function of changes in calcium
73 and potassium conductances. As an example, Figure 1 illustrates the phenotypic transi-
74 tions of non-spiking neurons as calcium conductance (g_{Ca}) decreases through a well-posed
75 retinal cone non-spiking CBM (Kourennyi et al., 2004). To sum up, the wild-type CBM
76 endowed with a phenotype 3 switches to a phenotype 2 and then 1 as g_{Ca} decreases.

77 The aim of this paper is the development of a numerical procedure to determine a
78 relationship between the dimensionless parameters of the phenomenological non-spiking
79 model (Naudin et al., 2022b) and the calcium conductance of a non-spiking cell, in order
80 to reproduce its phenotypic transitions as g_{Ca} decreases (Figure 1). In other words, the
81 dimensionless parameters of the simple model are expressed as a function of g_{Ca} . In
82 this way, our resulting simple model, called ‘conductance-based phenomenological non-
83 spiking model’, combines the biological plausibility of CBMs with the high computational
84 efficiency of phenomenological models, and thus may serve as a building block for studying
85 both ‘high-level’ and ‘low-level’ functions of non-spiking neural networks. To illustrate
86 our method, the procedure is applied to a model of an intrinsically non-spiking cell type,
87 the retinal cone. Finally, as a proof of concept, we simulate an abstract neural network
88 inspired by the networks of the retina and *C. elegans*, two non-spiking nervous tissues, in
89 which we show that the simple model predicts the same changes in the network output as
90 the CBM for different values of g_{Ca} .

91 The remainder of the paper is organized as follows. Section 2 describes the evolution
92 of the computational characteristics of the retinal cone CBM as g_{Ca} decreases, that is
93 representative of an ubiquitous and general pattern in non-spiking neurons (Naudin et al.,
94 2022c). Section 3 proposes a numerical procedure to build a phenomenological model

95 that reproduces the computational characteristic evolution of the retinal cone CBM as g_{Ca}
 96 reduces, as described in Section 2. Then, we analyse in Section 4 the dynamics of the
 97 resulting model and show that it is well-suited to characterize the phenotypic evolution of
 98 the neuron as g_{Ca} decreases. As a proof of concept, we show in Section 5 that the simple
 99 model predicts the same effects of conductance variations as the CBM on the output of
 100 an abstract neural network inspired by both the retina and *C. elegans* networks. Finally,
 101 Section 6 discusses the implications on the modeling of the retina and *C. elegans* networks.

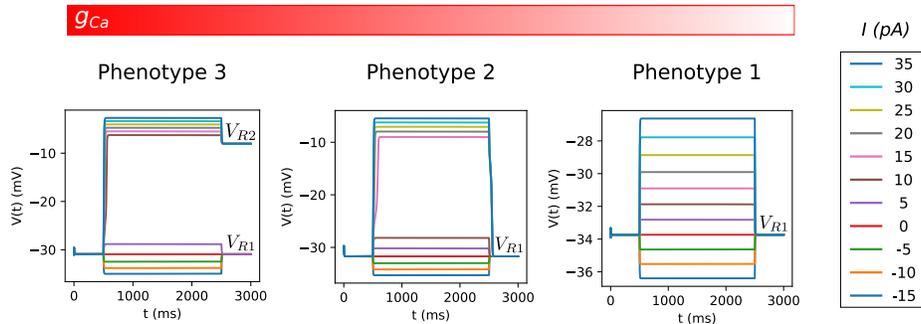


Figure 1: **Phenotypic transitions of the voltage dynamics as g_{Ca} decreases** (Naudin et al., 2022c). A well-posed retinal cone model, with a wild-type phenotype 3, was used as an illustration. A neuron with such a phenotype displays two resting potential values (V_{R1} and V_{R2}). Decreasing g_{Ca} changes the voltage dynamics of the neuron which becomes bistable with only one resting potential (phenotype 2). Finally, the even greater decrease of g_{Ca} leads to the loss of the bistability of the neuron which becomes near-linear (phenotype 1).

102 2 Preliminaries: evolution of the non-spiking neuron 103 computational characteristics as g_{Ca} decreases

104 A previous work (Naudin et al., 2022c) determined an ubiquitous and general pattern of
 105 non-spiking neuron dynamics as g_{Ca} decreases, illustrated through a well-posed retinal
 106 cone CBM (described in Supplementary materials) in Figure 1. It consists in a transition
 107 from phenotype 3 to 2 and then to 1 as g_{Ca} decreases. This section aims at describing
 108 the computational implications of this phenotypic evolution on the dynamics of the CBM
 109 under study.

110 The evolution of the computational characteristics of a non-spiking CBM can be inferred
 111 from the evolution of its steady-state current (SSC). Indeed, the SSC is the underlying data

112 that confers *all* the qualitative neuro-computational characteristics to non-spiking neurons
113 (Naudin et al., 2022a). Thus, we show in Figure 2.A the evolution of the SSC of the CBM
114 under study as g_{Ca} decreases. The wild-type (WT) SSC ($g_{Ca} = 4.92$ nS) exhibits a region
115 with negative slope that becomes less and less steep and then disappears as g_{Ca} decreases.
116 This evolution is due to a counterbalanced flow of I_{Ca} and I_K that underlies the negative
117 slope in the SSC of the neuron (Naudin et al., 2022c). This specific voltage-dependence of
118 membrane current is a common mechanism across the animal phyla, including *C. elegans*
119 neurons (Goodman et al., 1998; Mellem et al., 2008; Nicoletti et al., 2019), vertebrate
120 retina cells (Kourennyi et al., 2004; Aoyama et al., 2000; Usui et al., 1996), vertebrate hair
121 cells (Art and Goodman, 1996; Fettilplace, 1987) and thalamocortical neurons (Hughes
122 et al., 1999; Williams et al., 1997). Therefore, the evolution of the SSC under the effect of
123 decreasing g_{Ca} shown in Figure 2.A is representative of a general pattern. This evolution
124 implies a qualitative change in the computational characteristics of non-spiking neurons
125 that we discuss now.

126 The wild-type SSC ($g_{Ca} = 4.92$ nS) is N-shaped with two stable zeros (phenotype 3).
127 This provides the neuron with two resting potentials, which gives it a short-term memory
128 capacity: the response of the cell depends on its recent history of activity by storing
129 information about its last input (Figure 2.B). For detailed explanations from a dynamical
130 system viewpoint about the mechanism underlying this phenomenon, we refer to Figure S3
131 and Naudin et al. (2022c). Then, the negative slope of the SSC becomes less and less steep
132 as g_{Ca} decreases (Figure 2.A), until its local minima becomes positive (*e.g.*, $g_{Ca} = 4.22$
133 nS). Therefore, the neuron is still bistable but with only one resting potential (phenotype
134 2). This implies that the neuron has lost its short-term memory capacity, so the cell's
135 response no longer reflects the history of its inputs and of its activity (Figure 2.C). Finally,
136 an even more decreased value of g_{Ca} (*e.g.*, $g_{Ca} = 2.02$ nS) gives a monotonic SSC: the
137 neuron becomes near-linear. To sum up, the wild-type neuron with phenotype 3 switches
138 to a phenotype 2, and then from 2 to 1 as g_{Ca} decreases. In other words, the neuron
139 first loses its short-term memory capacity (transition from phenotype 3 to 2), then loses
140 its bistable behavior to a near-linear one (transition from phenotype 2 to 1). One last
141 important evolution of the computational characteristics of the neuron as g_{Ca} reduces is
142 the decrease of the voltage amplitude (Figure 2.D).

143 The aim of the following section is to propose a procedure that endows a recent and
144 novel non-spiking phenomenological model with the capability to reproduce the evolution
145 of these computational characteristics of the retinal cone CBM as g_{Ca} varies.

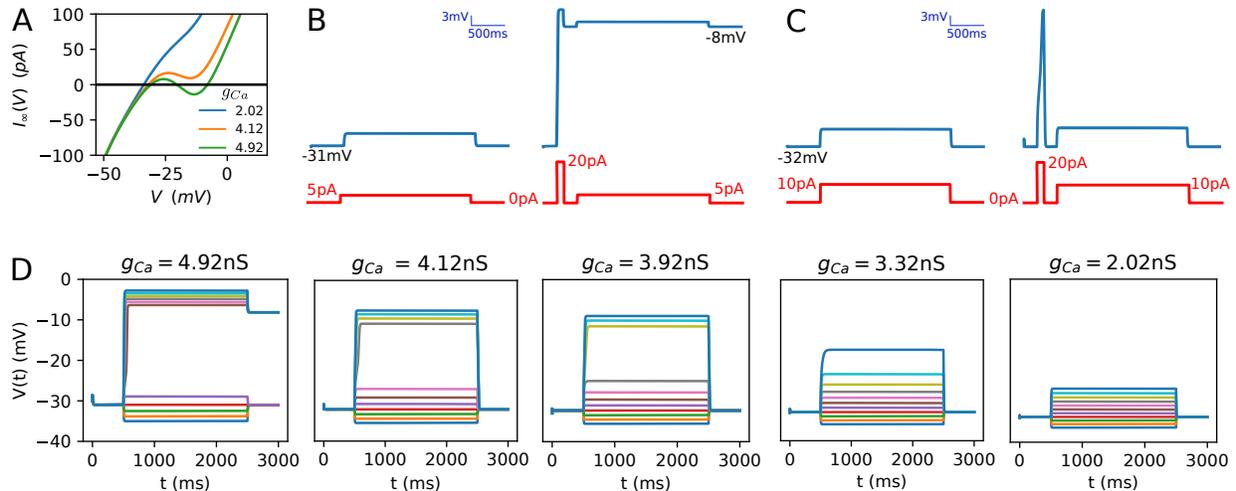


Figure 2: **Evolution of the computational characteristics of the retinal cone CBM as g_{Ca} decreases.** (A) SSC curve for three different values of g_{Ca} (4.92 (WT), 4.12, 2.02). (B) Short-term memory capacity of the WT phenotype of the CBM (phenotype 3). (Left) A depolarizing current step (5 pA) of 2000 ms duration into the neuron is applied. On cessation of the current step, the voltage stabilizes at its lower resting potential (about -31 mV). (Right) A high transient pulse (20 pA) of 100 ms duration is first injected into the neuron. Its membrane potential then relaxes to its highest resting potential value (approximately -8 mV), and finally stabilizes at about -6 mV in response to the same current injection protocol as before (current injection step at 5 pA under 2000 ms). (C) Response of the neuron with a reduced value of g_{Ca} ($g_{Ca} = 4.22$ nS). Whatever the stimulation protocol used, the neuron stabilizes at a steady-state value of about -29 mV: the response of the neuron no longer reflects the history of its inputs. (D) Decrease of the voltage amplitude as g_{Ca} decreases, for a series of current injections starting from -15 pA and increasing to 35 pA by 5 pA increments.

3 Design procedure of the conductance-based phenomenological non-spiking model

This section aims at proposing a methodology to build a simple and lightweight model that reproduces the qualitative evolution of non-spiking neuron dynamics as g_{Ca} decreases, as described in the previous section. The simple model, described in Materials and methods, has the advantage of having a very low computational cost so that one can simulate large-scale neuronal networks in real time (Naudin et al., 2022b), which is more difficult with CBMs due to their complexity (Izhikevich, 2004). Moreover, the simplicity of this model allows a theoretical mathematical analysis to gain insight into neuronal dynamics (Naudin,

2022). Thus, this section proposes a methodology to build such a simple model that reliably predicts the effects of calcium conductance variations on the neuron dynamics. In this way, the model would combine a high computational efficiency and simplicity of mathematical analysis, with the biological plausibility of CBMs.

The methodology is based on the fitting of the evolution of the SSC as g_{Ca} decreases since it determines the neuro-computational features of a non-spiking neuron, as explained above. The fitting of the SSCs by the cubic function

$$f(V) = aV^3 + bV^2 + cV + d \quad (1)$$

of the simple model is based on the Lagrange interpolation theorem. This theorem gives unique combinations of parameters (a, b, c, d) for which the third-degree polynomial f passes through any four given points. Therefore, the aim is to consider four specific points of the SSC to be interpolated by f . Figure 3 shows the two general steps of the procedure, that we apply to the CBM under study in the case of g_{Ca} . The detail of the procedure is given below.

- **Step 1a.** Reproducing the wild-type SSC of the neuron by the cubic function f (1):
Procedure: To fit the wild-type SSC of the neuron ($g_{Ca} = 4.92$ nS in our case), we need to consider four points to be interpolated by the cubic function f . Based on the previous section, the four points of the SSC that play a paramount role in the dynamics of the neuron of phenotype 3 are the following:

- *Resting potentials:* The two stable zeros of the SSC curve, *i.e.* the resting potentials (red points in Figure 4.A).
- *Local minima and maxima of the SSC:* The local minima and maxima of the SSC curve (blue points in Figure 4.A) because they determine the current injection thresholds at which the voltage jumps to a new plateau.

Therefore, the parameters (a, b, c, d) of the function f are determined through Lagrange interpolation so that f passes through these four points.

Output: One vector of parameters (a, b, c, d) for which the cubic function $f(V) = aV^3 + bV^2 + cV + d$ interpolates the four fundamental points of the SSC of the CBM (V_{R1} , V_{R2} and the local minima and maxima of the SSC curve)

- **Step 1b.** Generating four points of the SSC to be interpolated for a series of g_{Ca} associated with phenotypes 3 and 2 by 0.1 nS decrements:

Procedure: The SSC for phenotypes 3 and 2 is N-shaped (Figure 2.A). Then, the

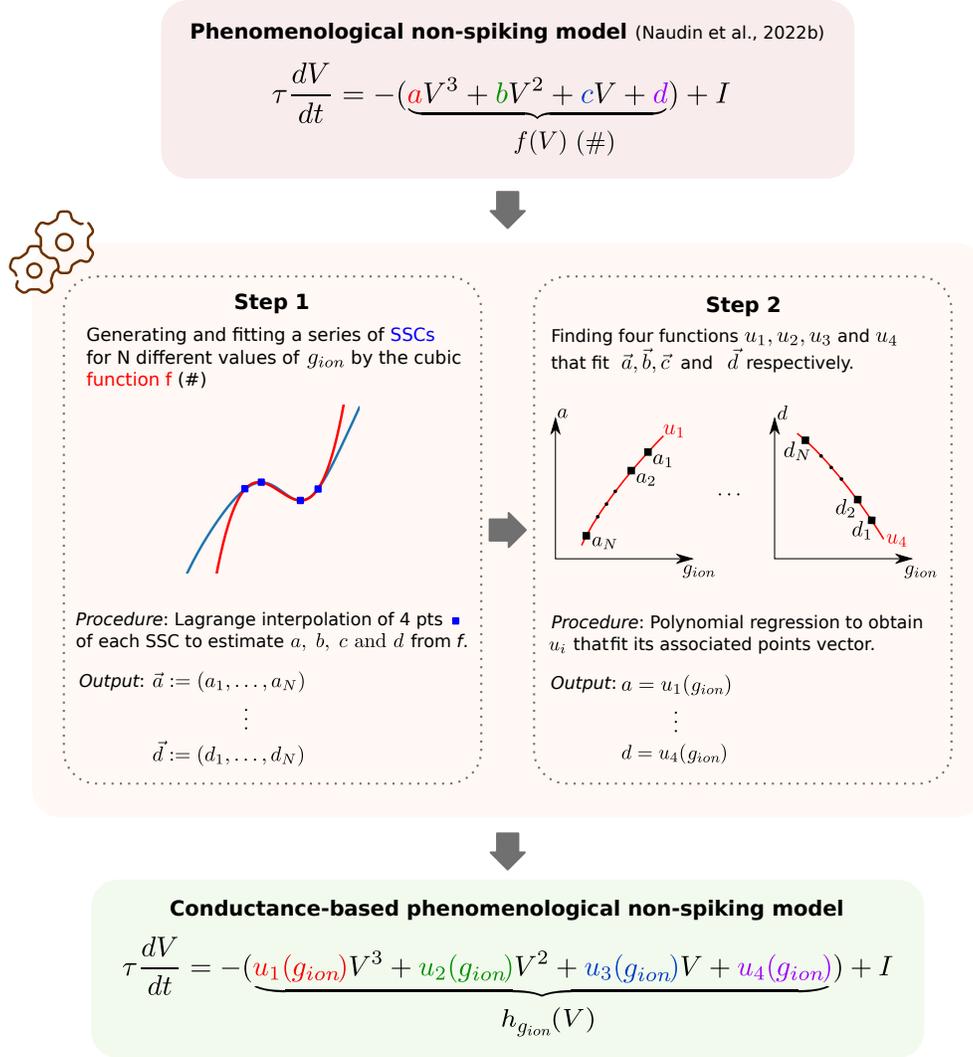


Figure 3: **Overview of the model design procedure.** **(Top)** The phenomenological non-spiking model (Naudin et al., 2022b) comprises 4 dimensionless parameters a , b , c and d . **(Middle)** The two-stage procedure aims to find a relationship between these parameters and maximal conductances g_{ion} of neurons or CBMs. **(Bottom)** After applying the procedure, the conductance-based phenomenological non-spiking model is obtained and depends only on the g_{ion} parameter.

186 four points for interpolation by the function f are the local minima and maxima of
 187 the SSC curve, and the two points of the lower and upper bounds (-100 pA and 100
 188 pA respectively in this paper):

- 189 – *Local minima and maxima of the SSC:* For each SSC of the CBM generated
- 190 with a new value of g_{Ca} associated with phenotypes 3 and 2, we compute its

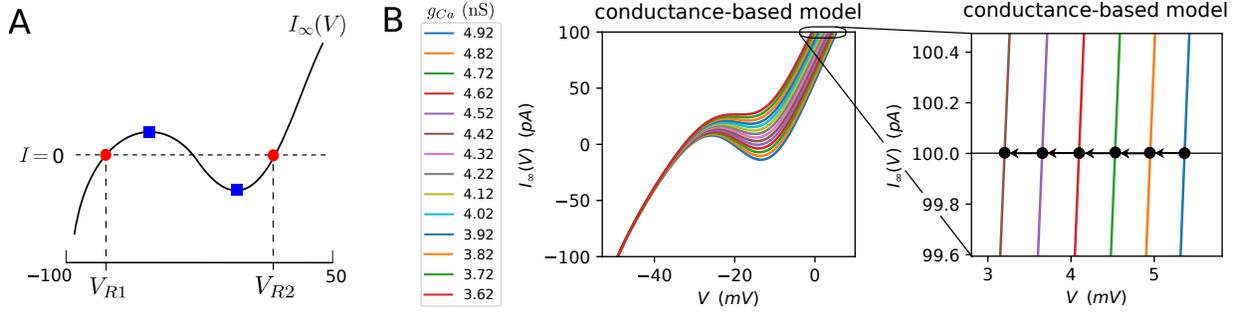


Figure 4: **(A)** The four points of the wild-type SSC to be interpolated by the cubic function of the simple model. Blue squares denote the local minima and maxima of the SSC, representing the current injection thresholds at which the neuron jumps to a new voltage plateau. Red points denote the two stable zeros of the SSC, representing the two resting potentials of the neuron. **(B)** The V -coordinate of the upper bound (100 pA) of the SSC of the CBM decreases more and more as g_{Ca} decreases, which implies a decrease of the voltage amplitude of the neuron as g_{Ca} decreases. The cubic function f of the simple model will then reproduce this pattern in its upper bound.

- 191 local minima and maxima, as in Step 1. For the CBM under study, we consider
 192 $g_{Ca} \in \{4.82, 4.72, \dots, 3.62\}$.
- 193 – *Upper bound of the SSC:* As can be seen in Figure 4.B, the V -coordinate of
 194 the upper bound of the SSC of the CBM decreases more and more as g_{Ca}
 195 decreases. This implies the decrease in voltage magnitude as g_{Ca} decreases, a
 196 paramount computational feature of the CBM shown in the previous section.
 197 To endow the simple model with this characteristic, we generate points in the
 198 upper bound that decrease in the V -coordinate in a recursive way from the cubic
 199 curve obtained in Step 1.
 - 200 – *Lower bound of the SSC:* As can be seen in Figure 4, the V -coordinate of the
 201 lower bound of the SSC of the CBM remains relatively constant. The cubic
 202 function f will seek to preserve such a characteristic.

203 **Output:** A series of vector points $\vec{a} := (a_{4.92}, a_{4.82}, \dots, a_{3.62})$, $\vec{b} := (b_{4.92}, b_{4.82}, \dots, b_{3.62})$,
 204 $\vec{c} := (c_{4.92}, c_{4.82}, \dots, c_{3.62})$, and $\vec{d} := (d_{4.92}, d_{4.82}, \dots, d_{3.62})$.

- 205 • **Step 2.** Fitting independently the points of \vec{a} , \vec{b} , \vec{c} , and \vec{d} obtained in Step 2:
 206 **Procedure:** Finding four functions u_1 , u_2 , u_3 and u_4 that verify $a = u_1(g_{Ca})$,
 207 $b = u_2(g_{Ca})$, $c = u_3(g_{Ca})$ and $d = u_4(g_{Ca})$. In this way, we establish a direct rela-
 208 tionship between the parameters a , b , c , and d of the simple model and the calcium

conductance g_{Ca} of the CBM. To that end, the functions u_1 , u_2 , u_3 and u_4 are considered as polynomials so that polynomial regressions are performed to fit the points of \vec{a} , \vec{b} , \vec{c} and \vec{d} , respectively. We stress the importance to choose polynomials that are not too complex, *i.e.* with degrees that are not too high. Indeed, the SSCs for the phenotype 1 are generated from these functions, *i.e.* for novel values of g_{Ca} not considered during the building of u_1 , u_2 , u_3 and u_4 through the polynomial regression processes. Therefore, the polynomials should not be too complex to avoid an overfitting of data points which would lead to an inability of the model to generate adequate SSCs for phenotypes 1. In our case, two-degree polynomials u_1 , u_2 , u_3 and u_4 will be sufficient to obtain good results (see next section).

Input: Vector points $\vec{a} = (a_{4.92}, a_{4.82}, \dots, a_{3.62})$, $\vec{b} = (b_{4.92}, b_{4.82}, \dots, b_{3.62})$, $\vec{c} = (c_{4.92}, c_{4.82}, \dots, c_{3.62})$, and $\vec{d} = (d_{4.92}, d_{4.82}, \dots, d_{3.62})$.

Output: Four functions u_1 , u_2 , u_3 , and u_4 that verify $a = u_1(g_{Ca})$, $b = u_2(g_{Ca})$, $c = u_3(g_{Ca})$ and $d = u_4(g_{Ca})$, such as we obtain the new model:

$$\tau \frac{dV}{dt} = -h_{g_{Ca}}(V) + I \quad (2)$$

with

$$h_{g_{Ca}}(V) := u_1(g_{Ca})V^3 + u_2(g_{Ca})V^2 + u_3(g_{Ca})V + u_4(g_{Ca}). \quad (3)$$

so that the simple model (2) depends only on the calcium conductance parameter.

In the next section, we show and discuss the results obtained from the procedure proposed in this section applied to the CBM under study.

4 Analysis of the model dynamics

A procedure to build a simple model that reproduces the qualitative evolution of non-spiking neuron dynamics as g_{Ca} evolves has been proposed in the previous section. Since the qualitative evolution of non-spiking neuron dynamics as g_{Ca} evolves is reflected by the evolution of the SSC, the procedure consists in reproducing this evolution of the SSC by the function $h_{g_{Ca}}$ of the model (2). The result of this procedure is shown in Figure 5 in which we compare the evolution of the SSC of the CBM with the function h (Eq. (3)) for different values of g_{Ca} , starting from 4.92 nS and decreasing to 0.02 nS by 0.2 nS decrements. The interpolation functions u_i , $i = 1, \dots, 4$, of the function h are shown in

236 Figure S4. In particular, we can observe in Figure 5 that the qualitative evolution of the
 237 SSC as g_{Ca} decreases is reproduced with a high fidelity by the cubic function. The purpose
 238 of this section is to discuss the implications on the resulting voltage dynamics.

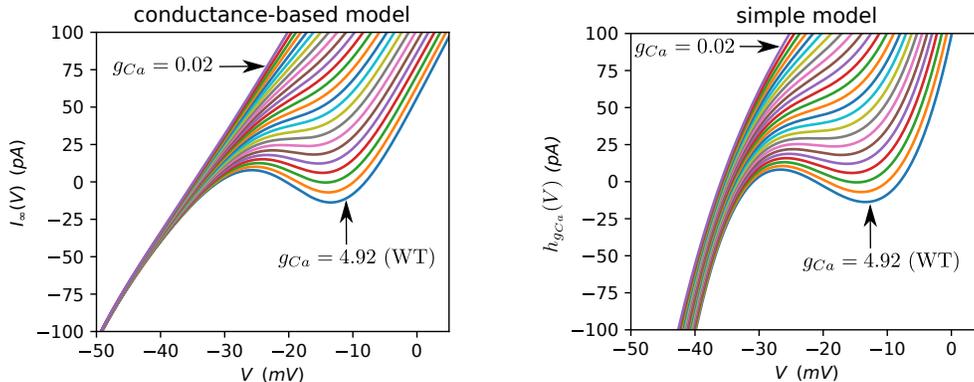


Figure 5: Comparison between the SSC of the CBM and the function h defined in (3) for a series of calcium conductance values g_{Ca} starting from 4.92 nS (WT) and decreasing to 0.02 nS by 0.2 nS decrements.

239 The first important implication is the occurrence of transitions between different phe-
 240 nototypes for the same g_{Ca} values in the CBM as in the simple model. Indeed, the transition
 241 between phenotype 3 and 2 occurs at $g_{Ca} = 4.50$ nS, both in the CBM and in the simple
 242 model. In other words, the CBM and the simple model lose their short-term memory ca-
 243 pacity at the same g_{Ca} value. Similarly, the transition between phenotype 2 and 1 occurs
 244 at $g_{Ca} = 3.59$ nS in the CBM, and at $g_{Ca} = 3.50$ nS in the simple model. Therefore, the loss
 245 of bistability in favor of a near-linear type behavior occurs at about the same g_{Ca} values
 246 in the CBM as in the simple model.

247 The second implication stems from the perfect fitting of the function $h_{g_{Ca}}$ with the
 248 intermediate values of its associated SSC for any value of g_{Ca} (see Figure 6.A that exem-
 249 plifies this for $g_{Ca} = 4.82$ nS). For phenotypes 2 and 3, this implies that the voltage jumps
 250 between the down- and up-states of the neuron occur for the same values in the CBM as in
 251 the simple model for any value of g_{Ca} (Figure 6.B). That is, the saddle-node bifurcations in
 252 the CBM and in the simple model appear for the same values of injection current. Figure
 253 S5 shows a representative example (for $g_{Ca} = 4.82$ nS) of the voltage jump to its up-state
 254 in the CBM and in the simple model. In the same way, the CBM and the simple model
 255 relax to the same resting values for any value of g_{Ca} (Figure S6).

256 Furthermore, both in the CBM and in the simple model, we observe a loss of the overall
 257 voltage amplitude as g_{Ca} decreases (Figure 6.D), which is a paramount characteristic of the
 258 behavior of non-spiking neurons under the effect of calcium conductance decrease. This

259 observation is partly due to the increase in voltage jump threshold values, as well as the
260 decrease in resting potential values (Figure S6), both resulting from the decrease of g_{Ca} .

261 Finally, a relative deterioration of the fitting of the SSC for higher and lower values can
262 be observed in Figure 6.A. Nonetheless, it should be noted that substantial noise in the
263 recording of SSCs of non-spiking *C. elegans* neurons can be observed for extreme values, as
264 in the bistable AFD neuron (Figure S7), which is similar to what we obtain (Figure 6.A).

265 Taken together, the aforementioned observations confirm that the main qualitative
266 features of the raw neuron dynamics are accurately preserved by the simple model. From
267 then on, it can be safely concluded that the simple model is adequate for the description
268 of the neuron behavior as g_{Ca} evolves. In the following section, we consider an abstract
269 neural network inspired by the retina and *C. elegans* non-spiking nervous tissues in which
270 we show, as well, that the simple model predicts the same neuronal changes as the CBM
271 at the network scale.

272 5 Implementation of a non-spiking neuronal network

273 In this section, we implement a non-spiking neuronal network inspired by the retina and
274 *C. elegans* networks which are two non-spiking nervous tissues. The neuronal network
275 is composed of three layers (Figure 7.A): (i) a first layer composed of 4 near-linear non-
276 spiking neurons that receive sensory stimuli, (ii) a second layer composed of one bistable
277 non-spiking neuron that could represent mammal bipolar retinal cells (Usui et al., 1996)
278 or the AIA *C. elegans* neuron (Dobosiewicz et al., 2019) for instance, and (iii) a third layer
279 composed of one spiking neuron. This neuron can represent muscles in *C. elegans* which
280 are known to elicit trains of action potentials (Liu et al., 2011), or the retinal ganglion cells
281 – the output neurons of the retina whose axons project to higher processing centers in the
282 brain (Fohlmeister et al., 1990). We use a leaky integrate-and-fire model for the spiking
283 neuron (Gerstner et al., 2014). The near-linear neurons of the first layer are modeled
284 using a near-linear CBM as in Naudin et al. (2022b). Finally, the neuron which composes
285 the second layer is modeled using the CBM or the simple model under study where the
286 parameters have been adjusted according to our procedure (see Section 3).

287 We consider that all neurons in the first layer receive an identical stimulus input,
288 namely a high transient depolarizing current (20 pA) of 500 ms duration followed by a
289 small depolarizing current step (2 pA) for 1000 ms (Figure 7.A). The resulting electrical
290 signals generated in these sensory neurons are then transmitted to the bistable neuron in
291 the second layer, which itself connects the spiking neuron in the third layer (Figure 7.A).

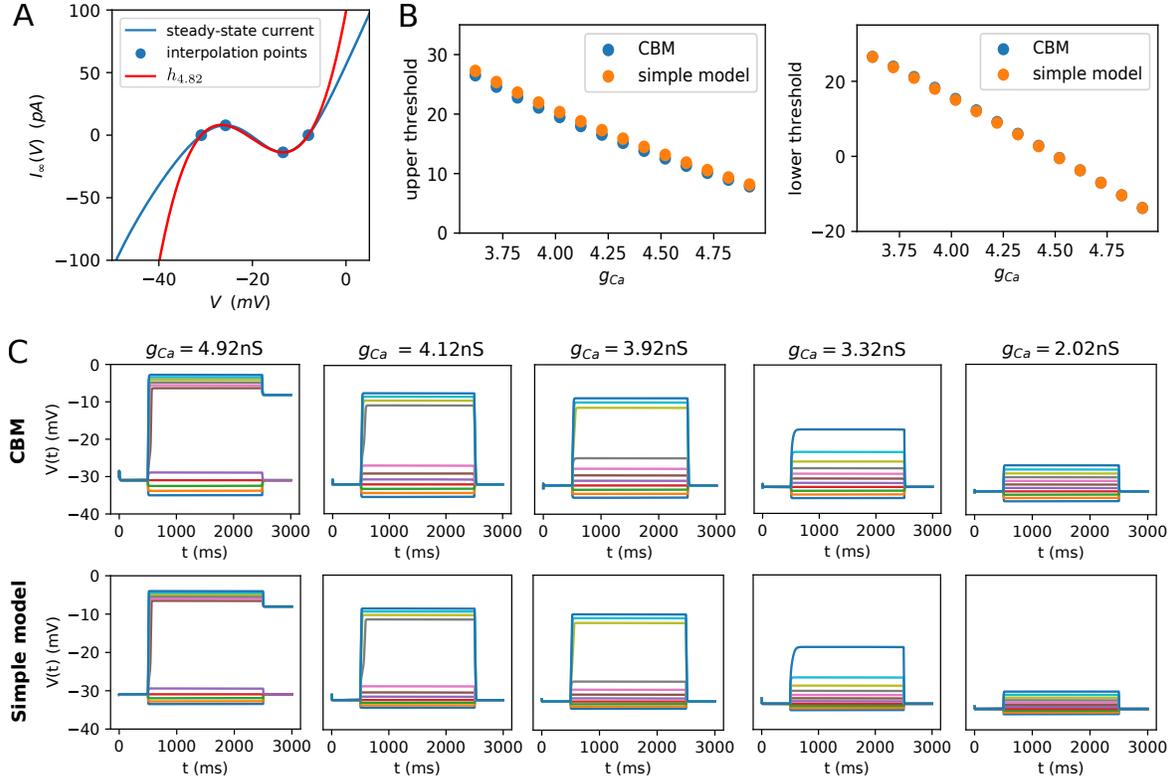


Figure 6: **(A)** Example of SSC ($g_{Ca} = 4.82$ nS) of the CBM (in blue) against the function $h_{4.82}$ of the simple model (in red) defined in (3). **(B)** Upper and lower threshold of injection currents between the down- and up-states in the CBM and in the simple model. **(C)** Comparison of the voltage amplitude decrease in CBM and in the simple model. For each calcium conductance value, we simulate the models through a series of injection currents starting from -15 pA to 35 pA by 5 pA increments.

292 The synapses between each layer are considered excitatory and graded, as in *C. elegans*
 293 (Lindsay et al., 2011) and in the retina (Dowling, 1987) (see Supplementary materials for
 294 the description of the equations). The aim is then to compare the impact of g_{Ca} reduction
 295 in the two models on the resulting dynamics of the spiking neuron, the output of the
 296 network.

297 To this end, Figure 7.B compares the dynamics of the spiking neuron output for $g_{Ca} \in$
 298 $\{4.92, 4.22, 2.02\}$ in its presynaptic neuron (i.e. the non-spiking CBM or the conductance-
 299 based phenomenological non-spiking model). Whether the network is composed of the
 300 CBM or the simple model, the spiking activity of the network output neuron is qualitatively
 301 and quantitatively similar for the three different values of g_{Ca} . In particular, the short-
 302 term memory capacity of both models for $g_{Ca} = 4.92$ nS results in a sustained activity
 303 of the spiking neuron even after the stimulus ceases (Figure 7.B1). For $g_{Ca} = 4.22$ nS,

304 both models have lost their short-term memory capacity (Figure 7.B2), while no activity
 305 is observed when $g_{Ca} = 2.02$ nS (Figure 7.B3). Taken together, these observations suggest
 306 that the simple model reliably predicts the conductance changes at the network scale.

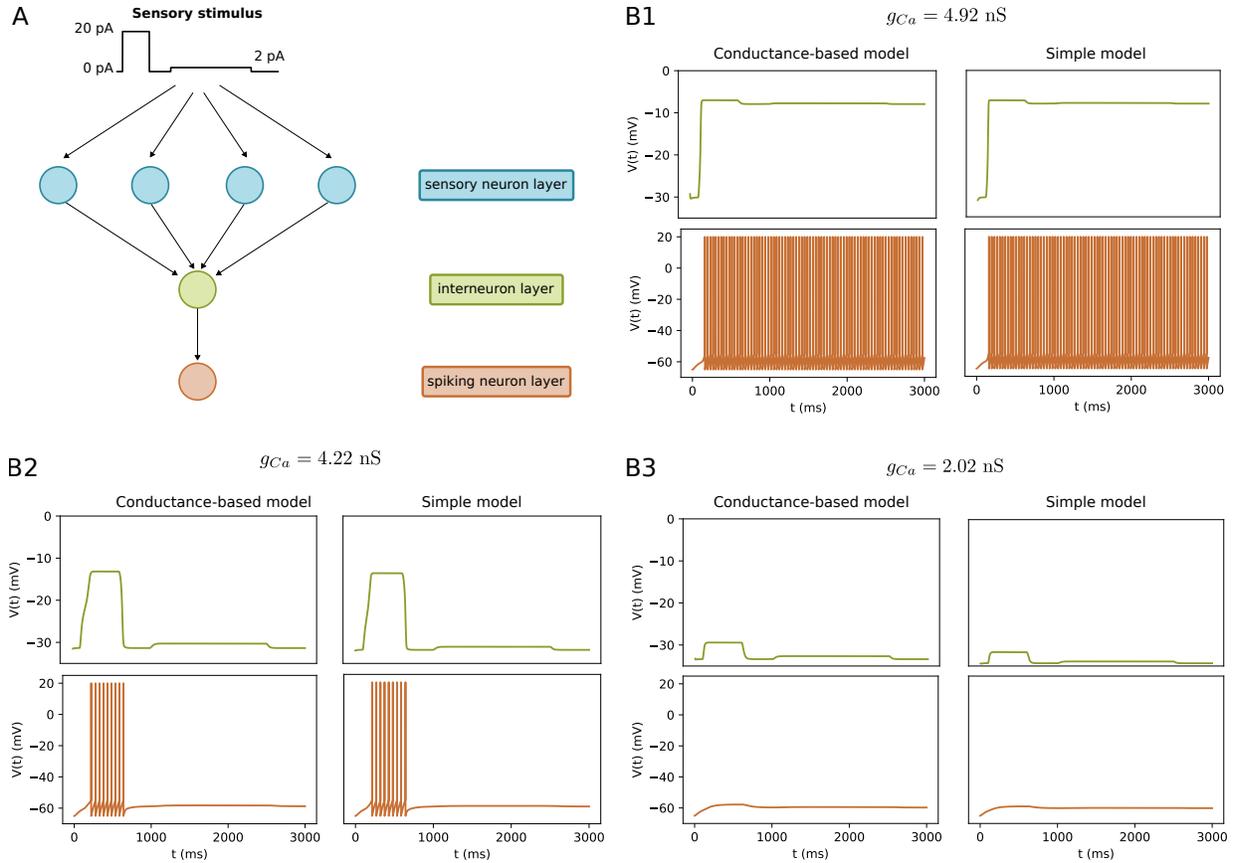


Figure 7: (A) Schematic of the neural network made up of three layers: four near-linear sensory neurons, one bistable interneuron, and one spiking output neuron. (B) Comparison of the neural network output (spiking activity) when coupled to the simple model or the CBM for three different values of g_{Ca} , each being associated with a distinct phenotype.

307 6 Discussion

308 **Summary.** CBMs and ‘phenomenological’ models are often used to deal with distinct
 309 issues. CBMs are well suited to study ‘low-level’ functions of nervous systems, depending
 310 on physiological microscopic parameters such as ion conductances. Indeed, a CBM is
 311 a biophysical representation of a neuron in which every individual parameter and state
 312 variable has an established electrophysiological meaning. Nevertheless, the simulation of
 313 this type of model is very time-consuming, so the size of neural networks composed of CBMs

314 that can be studied is inherently limited. In contrast, “phenomenological” models are very
315 lightweight and simple so that one can simulate large-scale networks in real time. But their
316 drawback is the lack of biophysical realism since it describes the macroscopic behavior of
317 neurons regardless the underlying microscopic physiological processes. As a consequence,
318 ‘phenomenological’ models exhibit dimensionless parameters and are therefore limited to
319 the study of ‘higher-level’ functions of neural systems. This paper aimed to propose a
320 model for non-spiking neuron dynamics that combines the strengths of the two types of
321 models: the biological plausibility of CBMs with the high computational efficiency of
322 phenomenological models. To do this, a numerical procedure was proposed to establish
323 a relationship between the dimensionless parameters of a non-spiking phenomenological
324 model (Naudin et al., 2022b) and the ion conductances of CBMs or neurons. We applied
325 it to a model of an intrinsically non-spiking cell type, the retinal cone, associated with
326 a decrease in g_{Ca} . We showed that the resulting ‘conductance-based phenomenological
327 non-spiking model’ was able to accurately depict the phenotypic transitions of non-spiking
328 neurons as g_{Ca} evolves, previously described with CBMs (Naudin et al., 2022c). These
329 cellular properties translated at the network level where the dynamics of our simple model
330 fits the one of the CBM as g_{Ca} varies, resulting in similar network outputs. Therefore, the
331 resulting model combined the biological plausibility of CBMs with the high computational
332 efficiency of phenomenological models, and thus may serve as a building block for studying
333 both ‘high-level’ and ‘low-level’ functions of non-spiking neural networks.

334 **Potential applications to the study of the effect of physiological and patho-**
335 **logical changes on non-spiking neural network dynamics.** Given the importance
336 of ion channels and ion flow for many physiological and pathological functions, both in
337 spiking and in non-spiking neurons, it could be valuable to have a direct relationship with
338 ion conductances when using phenomenological models. This would allow to study various
339 systems and nervous tissues, considering the physiological range of functioning, as well as
340 the pathological variations of their associated ion conductance. Our conductance-based
341 phenomenological non-spiking model was designed in this context, with a particular fo-
342 cus on the calcium conductance variations due to its crucial role in the electrical signal
343 generation in non-spiking neurons.

344 Indeed, non-spiking neurons, such as *C. elegans* neurons or retinal cells, exhibit a
345 variety of ion channels on their cell membrane, including many voltage-gated calcium and
346 calcium-gated potassium channels (Bargmann, 1998; Taylor et al., 2021; Van Hook et al.,
347 2019). The flow of ions in and out of the cells through these channels provides non-spiking
348 neurons with several crucial physiological properties, including their electrical activity.

349 In particular, voltage-gated calcium channels are essential in *C. elegans* which lacks the
350 voltage-gated Na^+ channels (Bargmann, 1998) that are usually involved in action potential
351 generation in vertebrates. Likewise, in many retinal cell classes including the cone, rod,
352 bipolar, horizontal and some amacrine cells, voltage-gated Na^+ channels are absent or
353 barely expressed, giving great importance to calcium channels in retinal electrical signal
354 generation (Van Hook et al., 2019). Therefore, it may be particularly relevant to have the
355 ability to assess the impact of calcium gradient variations on neuron behavior as well as
356 on network dynamics.

357 Furthermore, several mechanisms may alter the “normal” function of ion channels.
358 In particular, many studies show that mutations within genes encoding calcium channels
359 are often associated with various neurological and psychiatric diseases (Andrade et al.,
360 2019). Yet, these ion channels are ubiquitous in the retina cells, whose electrical activity is
361 disturbed as suggested by electrophysiological recordings (electroretinograms) conducted
362 in patients suffering from Parkinson’s, Alzheimer’s and Huntington’s diseases, epilepsy,
363 depression and schizophrenia (Silverstein et al., 2020). In this case, it would also be of
364 particular interest to gain insight into the levels of ion conductance that might lead to
365 pathological behavior.

366 Taken together, these information confirm that the use of the simple phenomenological
367 model, rather than CBMs, to address these issues is justified both by its minimal computa-
368 tional cost and by its biological plausibility. This original combination allows for the study
369 of precise physiological and pathological changes in a context of large-scale simulations of
370 the retina or *C. elegans* networks.

371 Acknowledgements

372 We thank Dr. Mellem and Dr. Liu for their consents to reproduce their experimental
373 data.

374 We thank the INS2I-CNRS and Loria for their financial support on the ModERN-Psy
375 project.

376 Code accessibility

377 The code used in this paper to build the conductance-based phenomenological non-spiking
378 model is available at:

379 <https://gitlab.com/lois76/article-procedure-cbm-phenomenological-model>.

380 **Declaration of competing interests**

381 The authors declare no competing interests.

Supplementary materials

Here we present the phenomenological model capable of reproducing the qualitative behaviors of non-spiking neurons, developed in Naudin et al. (2022b). In addition, we recall the role played by the steady-state current (SSC) in the dynamics of non-spiking neurons, since the numerical method developed in this paper fundamentally rely on it.

The phenomenological model

The phenomenological model, developed in Naudin et al. (2022b), is built on the basis of the bifurcation structure of conductance-based models of non-spiking neurons. For the convenience of reading the paper, we present it in this section.

Conductance-based models (CBMs). In CBMs, the dynamics of the membrane potential V is described by a general equation of the form

$$C \frac{dV}{dt} = - \sum_{ion} I_{ion} + I \quad (4)$$

where C is the membrane capacitance, $\sum_{ion} I_{ion}$ is the total current flowing across the cell membrane, and I is an applied current. The currents I_{ion} take the form

$$I_{ion} = g_{ion} m_{ion}^a h_{ion}^b (V - E_{ion})$$

where m (*resp.* h) denotes the probability for an activation (*resp.* inactivation) gate to be in the open state; a and b are the number of activation and inactivation gates, respectively; g_{ion} is the maximal conductance associated with ion ; and E_{ion} is the reversal potential.

Bifurcation dynamics of non-spiking CBMs. In non-spiking CBMs, the SSC curve I_{∞} determines the number of equilibria of the system and their values, as well as the bifurcations of the resting state along with the values to which they occur. It takes the general form

$$I_{\infty}(V) = \sum_{ion} I_{ion\infty}(V) \quad \text{where} \quad I_{ion\infty}(V) = g_{ion} m_{ion\infty}^a(V) h_{ion\infty}^b(V) (V - E_{ion}) \quad (5)$$

with

$$x_\infty(V) = \frac{1}{1 + \exp\left(\frac{V_{1/2}^x - V}{k_x}\right)}, \quad x \in \{m, h\}.$$

401 where $V_{1/2}^x$ and k_x are constant parameters.

402 Any stationary point of gating variables $x \in \{m, h\}$ must satisfy $x_* = x_\infty(V_*)$. Replacing
 403 this into the first equation on V , fixed points V_* of such models satisfy the equation

$$I_\infty(V_*) = I. \tag{6}$$

404 In other words, equilibria V_* correspond to the intersection between the SSC I_∞ and
 405 a horizontal line $I = c$ where c is a constant. There are two standard steady-state
 406 curves I_∞ , monotonic and cubic (Figure S1), each involving fundamentally different neuro-
 407 computational properties for non-spiking neurons:

- 408 • As shown in Figure S1.A, CBMs with a monotonic SSC only have one equilibrium
 409 for any value of I . Non-spiking neurons with such a SSC display a near-linear behav-
 410 ior characterized by smooth depolarizations or hyperpolarizations from the resting
 411 potential, such as the RIM neuron (Figure S2).
- 412 • As shown in Figure S1.B, a N-shaped curve leads to a saddle-node bifurcation. When
 413 $I = c_1$, there are 3 equilibria, noted $V_{1*}^{c_1}$, $V_{2*}^{c_1}$ and $V_{3*}^{c_1}$. Increasing I results in coa-
 414 lescence of two equilibria (the stable $V_{1*}^{c_1}$ with the unstable $V_{2*}^{c_1}$). The value $I = c_2$,
 415 at which the equilibria coalesce, is called the *bifurcation value*. For this value of I ,
 416 there exist 2 equilibria. For $I > c_2$, the system has only one equilibrium (*e.g.* $I = c_3$).
 417 In summary, when the parameter I increases, a stable and an unstable equilibrium
 418 approach, coalesce, and then annihilate each other. Non-spiking neurons with a N-
 419 shaped SSC display a bistable behavior characterized by a voltage jump between
 420 the resting potential and a depolarized potential of higher voltage, such as the AFD
 421 neuron (Figure S2).

422 Therefore, it can be stated that the SSC determines the bifurcation structure of non-
 423 spiking neurons and the equilibrium values of their graded responses to particular stimuli.

424 **The simple model.** Let V represent the membrane potential of a neuron. The simple
 425 model takes the general form

$$\tau \frac{dV}{dt} = -f(V) + I \tag{7}$$

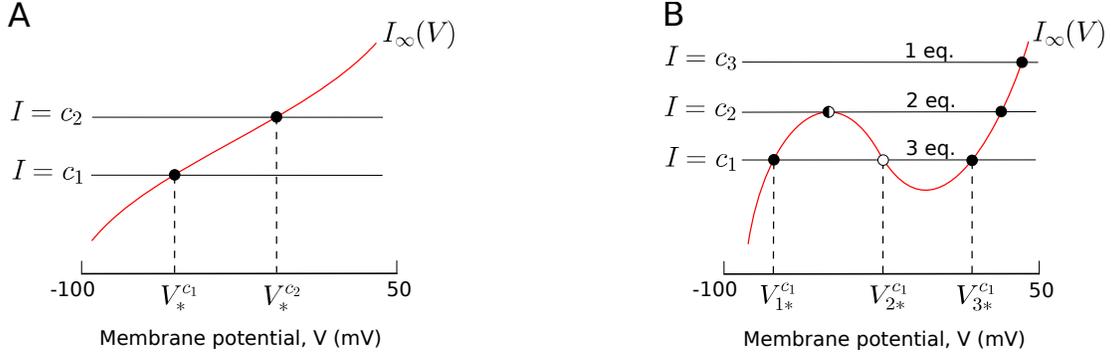


Figure S1: Two typical shapes of the SSC $V \rightarrow I_\infty(V)$, in red. Intersections of I_∞ and horizontal line $I = c$ (with c constant) correspond to equilibria of the system. We denote stable equilibria as filled circles ●, unstable equilibria as open circles ○ and saddle-node equilibria as ◐. **(A)** Monotonic SSC. $V_*^{c_1}$ and $V_*^{c_2}$ correspond to equilibria for a current injection $I = c_1$ and $I = c_2$ respectively. **(B)** N-shaped SSC. The number of equilibria of the system depends on the value of I . For the sake of readability, we highlight equilibria only for $I = c_1$, noted $V_{1*}^{c_1}$, $V_{2*}^{c_1}$ and $V_{3*}^{c_1}$.

426 with f a cubic function which reads as

$$f(V) = aV^3 + bV^2 + cV + d. \quad (8)$$

The function f plays the same role in the dynamics of the model (7) as the SSC I_∞ in CBMs (4). Indeed, fixed points V_* of model (7) satisfy

$$f(V_*) = I$$

427 so that the shape of f determines the neuro-computational features of the non-spiking
 428 model: a monotonic shape involves a near-linear behavior of the model, while a N-shape
 429 implies a bistable one with the occurrence of two saddle-node bifurcations. Therefore, the
 430 model proposes a simple cubic expression (8) that plays the same role as the complex SSC
 431 expression (5) of CBMs. Parameters a , b , c and d are dimensionless and are estimated in
 432 order to fit the experimental SSC. Parameter τ describes the *constant* time for which V
 433 reaches its equilibrium value V_* . This parameter can be either hand-tuned or estimated
 434 from experimental voltage.

435 Conductance-based model of the retinal cone

436 The conductance-based model of the canonical bistable cell is based on the retinal cone
 437 cell built in [Kourennyi et al. \(2004\)](#). It has four ion currents: a calcium current (I_{Ca}), a
 438 hyperpolarization-activated current (I_h), a delayed rectifying potassium current (I_{Kv}), and
 439 a leak current (I_L). The parameters are expressed in the following units: mV (voltage),
 440 pA (current), nS (conductance), and ms (time). The membrane capacitance (C) is set
 441 to 16 nF. We denote by g_{ion} the maximal conductance (namely the conductance of the
 442 channel when all the gates are open), and E_{ion} the reversal potential, that is, the potential
 443 at which the ion current reverses its direction. Leak current is classically described as
 444 $I_L = g_L(V - E_L)$ and the remaining currents are described in Table S1.

Ion current (I_{ion})	$\alpha_{ion}(V)$ and $\beta_{ion}(V)$ rates	g_{ion} and E_{ion}
$I_{Ca} = g_{Ca}m_{Ca}h_{Ca}(V - E_{Ca})$ $\frac{dm_{Ca}}{dt} = \alpha_{Ca}(1 - m_{Ca}) - \beta_{Ca}m_{Ca}$	$\alpha_{Ca}(V) = 3.1 e^{(V+16.6)/11.4}$ $\beta_{Ca}(V) = 3.1 e^{(-V-16.6)/11.4}$	$g_{Ca} = 4.92$ $E_{Ca} = 40$
$I_h = g_h(1 - (1 + 3m_h)(1 - m_h)^3)(V - E_h)$ $\frac{dm_h}{dt} = \alpha_{m_h}(1 - m_h) - \beta_{m_h}m_h$	$\alpha_{m_h}(V) = \frac{18}{(1 + e^{(V+88)/12})}$ $\beta_{m_h}(V) = \frac{18}{(1 + e^{-(V+18)/19})}$	$g_h = 3.5$ $E_h = -32.5$
$I_{Kv} = g_{Kv}m_{Kv}^3h_{Kv}(V - E_K)$ $\frac{dm_{Kv}}{dt} = \alpha_{m_{Kv}}(1 - m_{Kv}) - \beta_{m_{Kv}}m_{Kv}$ $\frac{dh_{Kv}}{dt} = \alpha_{h_{Kv}}(1 - h_{Kv}) - \beta_{h_{Kv}}h_{Kv}$	$\alpha_{m_{Kv}}(V) = \frac{5(V - 100)}{(1 - e^{-(V-100)/42})}$ $\beta_{m_{Kv}}(V) = 9e^{(20-V)/40}$ $\alpha_{h_{Kv}}(V) = 0.15e^{-V/22}$ $\beta_{h_{Kv}}(V) = \frac{0.4125}{(1 + e^{(10-V)/7})}$	$g_{Kv} = 2$ $E_{Kv} = -80$

Table S1: Summary of ion currents composing the generic bistable model.

445 Network models

The graded synaptic model used in this paper is described in [Wicks et al. \(1996\)](#), which is given by

$$I_{syn} = g_{syn}s(V_i - E_{syn})$$

where g_{syn} is the maximal synaptic conductance, and E_{syn} is the reversal potential for the synaptic current, set to 0 mV for excitatory synapses. The dynamics of the variable s is

given by

$$\frac{ds}{dt} = \frac{s_{\infty}(V_j) - s}{\tau_s}$$

where

$$s_{\infty}(V_j) = \frac{1}{1 + \exp\left(\frac{V_{1/2}^s - V_j}{V_{slope}}\right)}$$

446 We set the parameter values as follows: $g_{syn} = 0.2$ nS, $V_{1/2}^s = -10$ mV, $V_{slope} = 10$ mV,
447 and $\tau_s = 10$ ms.

448 **Supplementary figures**

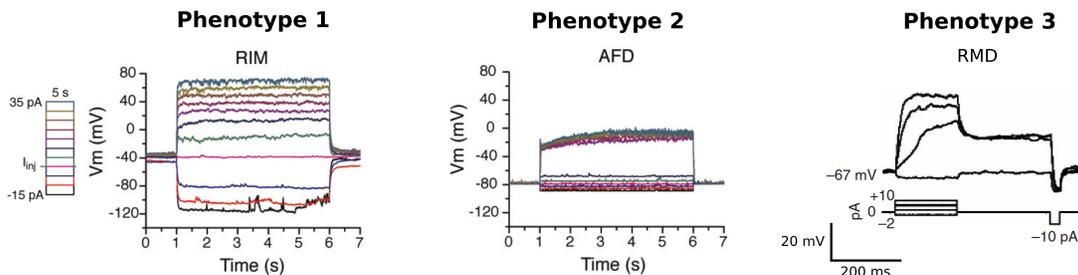


Figure S2: Experimental voltage examples from *C. elegans* of each phenotype for a series of current injections starting from -15pA and increasing to 35pA by 5pA increments for the RIM and AFD neurons, and starting from -2pA and increasing to 10pA by 3pA increments for the RMD neuron. Phenotype 1 refers to near-linear neurons, phenotype 2 to bistable neurons with one resting potential, and phenotype 3 to bistable neurons with two resting potentials. The experimental data of the RIM and AFD neurons have been reproduced from [Naudin et al. \(2022a\)](#), and from [Mellem et al. \(2008\)](#) for the RMD neuron with the consent of the authors.

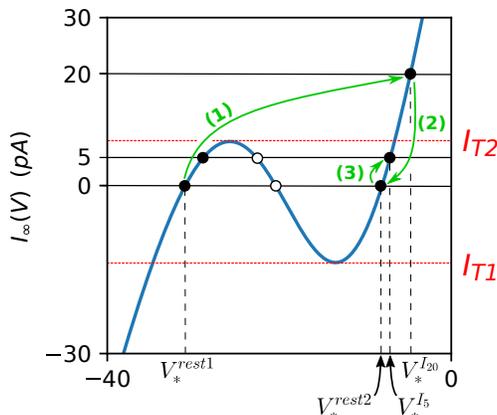


Figure S3: Diagram explaining the short-term memory capacity of a neuron with a phenotype 3. I_{T1} (resp. I_{T2}) denotes the injection current thresholds at which the neuron jumps to its upper (resp. lower) voltage plateau. (1) A brief transient stimulus ($20 > I_{T2}$ pA) is applied and the voltage converges to V_*^{I20} . (2) The stimulus ceases so that the voltage relaxes to V_*^{rest2} which is the new voltage initial condition. (3) A new depolarizing current step (5pA) is applied and the voltage goes to V_{2*}^{I5} and not V_{1*}^{I5} since V_*^{rest2} now belongs to the basin of attraction of V_{2*}^{I5} . This figure has been reproduced from [Naudin et al. \(2022c\)](#) with the consent of the authors.

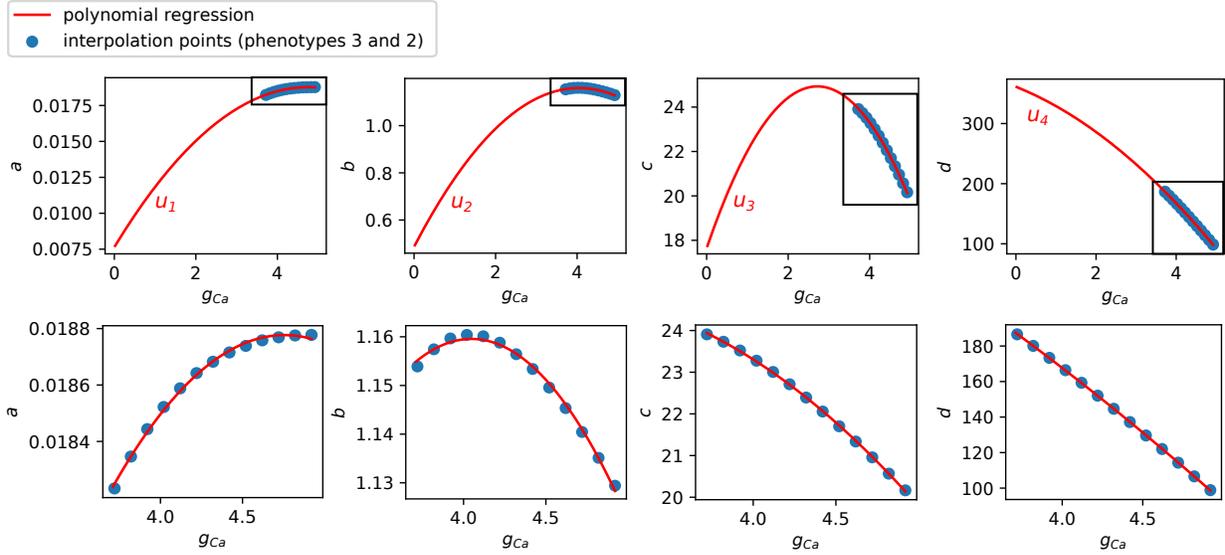


Figure S4: **(Top)** Two-degree polynomials u_i , $i = 1, \dots, 4$, built from the polynomial regression of blue points. These points are generated following Step 1 and Step 2 of the procedure described in Section 3. **(Bottom)** Zoom of the rectangles in (Top).

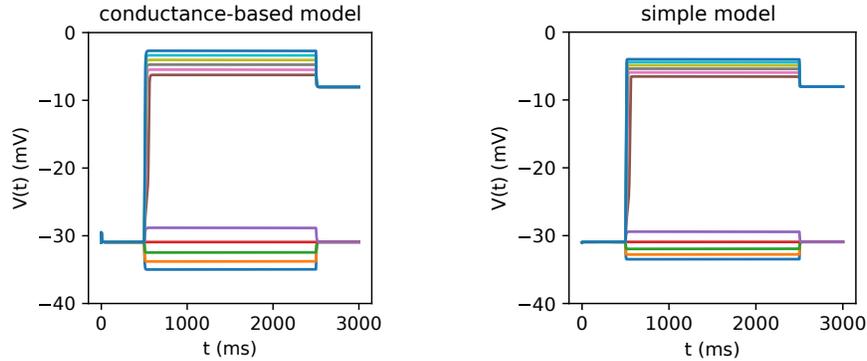


Figure S5: Comparison of voltage dynamics between CBM and the conductance-based phenomenological non-spiking model for $g_{Ca} = 4.82\text{nS}$ for a series of injection currents starting from -15pA and increasing to 35pA by 5pA increments.

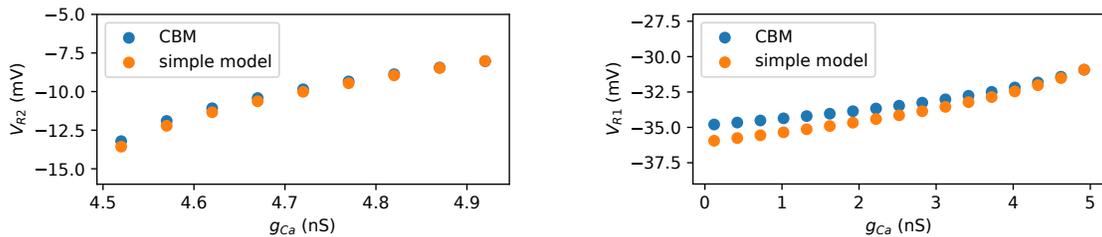


Figure S6: Comparison of the resting potential values (V_{R1} and V_{R2}) for various values of g_{Ca} in the CBM and in the simple model.

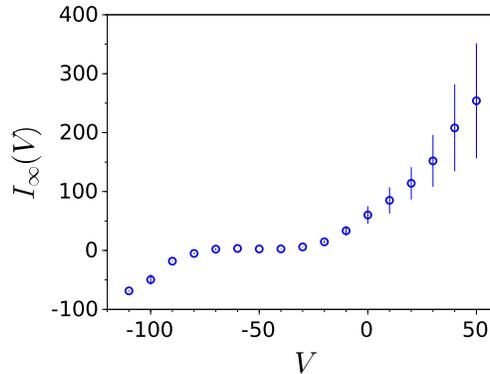


Figure S7: SSC of the AFD neuron obtained from averaged voltage-clamp recordings ($n = 3$) (Liu et al., 2018).

References

- 449
- 450 A. Andrade, A. Brennecke, S. Mallat, J. Brown, J. Gomez-Rivadeneira, N. Czepiel, and
 451 L. Londrigan. Genetic associations between voltage-gated calcium channels and psychi-
 452 atric disorders. *International journal of molecular sciences*, 20(14):3537, 2019.
- 453 T. Aoyama, Y. Kamiyama, S. Usui, R. Blanco, C. F. Vaquero, and P. de la Villa. Ionic
 454 current model of rabbit retinal horizontal cell. *Neuroscience Research*, 37(2):141–151,
 455 2000.
- 456 J. Art and M. Goodman. Ionic conductances and hair cell tuning in the turtle cochlea a.
 457 *Annals of the New York Academy of Sciences*, 781(1):103–122, 1996.
- 458 C. I. Bargmann. Neurobiology of the caenorhabditis elegans genome. *Science*, 282(5396):
 459 2028–2033, 1998.
- 460 S. S. Bidaye, T. Bockemühl, and A. Büschges. Six-legged walking in insects: how cpgs,
 461 peripheral feedback, and descending signals generate coordinated and adaptive motor
 462 rhythms. *Journal of neurophysiology*, 119(2):459–475, 2018.
- 463 R. Brette. What is the most realistic single-compartment model of spike initiation? *PLoS*
 464 *computational biology*, 11(4):e1004114, 2015.
- 465 M. Burrows, G. Laurent, and L. Field. Proprioceptive inputs to nonspiking local interneu-
 466 rons contribute to local reflexes of a locust hindleg. *Journal of Neuroscience*, 8(8):
 467 3085–3093, 1988.

- 468 R. Davis and A. Stretton. Passive membrane properties of motorneurons and their role in
469 long-distance signaling in the nematode ascaris. *Journal of Neuroscience*, 9(2):403–414,
470 1989a.
- 471 R. E. Davis and A. Stretton. Signaling properties of ascaris motorneurons: graded ac-
472 tive responses, graded synaptic transmission, and tonic transmitter release. *Journal of*
473 *Neuroscience*, 9(2):415–425, 1989b.
- 474 M. Dobosiewicz, Q. Liu, and C. I. Bargmann. Reliability of an interneuron response
475 depends on an integrated sensory state. *Elife*, 8:e50566, 2019.
- 476 J. E. Dowling. *The retina: an approachable part of the brain*. Harvard University Press,
477 1987.
- 478 C. Eliasmith and O. Trujillo. The use and abuse of large-scale brain models. *Current*
479 *opinion in neurobiology*, 25:1–6, 2014.
- 480 G. B. Ermentrout and D. H. Terman. *Mathematical foundations of neuroscience*, volume 35.
481 Springer Science & Business Media, 2010.
- 482 R. Fettilplace. Electrical tuning of hair cells in the inner ear. *Trends in Neurosciences*, 10
483 (10):421–425, 1987.
- 484 G. D. Field and E. Chichilnisky. Information processing in the primate retina: circuitry
485 and coding. *Annu. Rev. Neurosci.*, 30:1–30, 2007.
- 486 R. FitzHugh. Impulses and physiological states in theoretical models of nerve membrane.
487 *Biophysical journal*, 1(6):445–466, 1961.
- 488 J. Fohlmeister, P. Coleman, and R. F. Miller. Modeling the repetitive firing of retinal
489 ganglion cells. *Brain research*, 510(2):343–345, 1990.
- 490 W. Gerstner, W. M. Kistler, R. Naud, and L. Paninski. *Neuronal dynamics: From single*
491 *neurons to networks and models of cognition*. Cambridge University Press, 2014.
- 492 F. Giovannini, B. Knauer, M. Yoshida, and L. Buhry. The can-in network: A biologi-
493 cally inspired model for self-sustained theta oscillations and memory maintenance in the
494 hippocampus. *Hippocampus*, 27(4):450–463, 2017.
- 495 M. B. Goodman, D. H. Hall, L. Avery, and S. R. Lockery. Active currents regulate sensi-
496 tivity and dynamic range in *c. elegans* neurons. *Neuron*, 20(4):763–772, 1998.

- 497 T. Górski, D. Depannemaecker, and A. Destexhe. Conductance-based adaptive exponential
498 integrate-and-fire model. *Neural Computation*, 33(1):41–66, 2021.
- 499 A. L. Hodgkin and A. F. Huxley. A quantitative description of membrane current and its
500 application to conduction and excitation in nerve. *The Journal of physiology*, 117(4):
501 500–544, 1952.
- 502 S. W. Hughes, D. W. Cope, T. I. Tóth, S. R. Williams, and V. Crunelli. All thalamo-
503 cortical neurones possess a t-type ca^{2+} ‘window’ current that enables the expression of
504 bistability-mediated activities. *The Journal of physiology*, 517(3):805–815, 1999.
- 505 E. M. Izhikevich. Simple model of spiking neurons. *IEEE Transactions on neural networks*,
506 14(6):1569–1572, 2003.
- 507 E. M. Izhikevich. Which model to use for cortical spiking neurons? *IEEE transactions on*
508 *neural networks*, 15(5):1063–1070, 2004.
- 509 D. E. Kourennyi, X.-d. Liu, J. Hart, F. Mahmud, W. H. Baldrige, and S. Barnes. Recip-
510 rocal modulation of calcium dynamics at rod and cone photoreceptor synapses by nitric
511 oxide. *Journal of neurophysiology*, 92(1):477–483, 2004.
- 512 P. E. Latham, B. Richmond, P. Nelson, and S. Nirenberg. Intrinsic dynamics in neuronal
513 networks. i. theory. *Journal of neurophysiology*, 83(2):808–827, 2000.
- 514 G. Laurent and M. Burrows. Intersegmental interneurons can control the gain of reflexes in
515 adjacent segments of the locust by their action on nonspiking local interneurons. *Journal*
516 *of Neuroscience*, 9(9):3030–3039, 1989.
- 517 L. Lemaire, M. Desroches, M. Krupa, L. Pizzamiglio, P. Scalmani, and M. Mantegazza.
518 Modeling *nav1.1/scn1a* sodium channel mutations in a microcircuit with realistic ion
519 concentration dynamics suggests differential gabaergic mechanisms leading to hyper-
520 excitability in epilepsy and hemiplegic migraine. *PLoS Computational Biology*, 17(7):
521 e1009239, 2021.
- 522 T. H. Lindsay, T. R. Thiele, and S. R. Lockery. Optogenetic analysis of synaptic trans-
523 mission in the central nervous system of the nematode *caenorhabditis elegans*. *Nature*
524 *communications*, 2(1):1–9, 2011.
- 525 P. Liu, Q. Ge, B. Chen, L. Salkoff, M. I. Kotlikoff, and Z.-W. Wang. Genetic dissection
526 of ion currents underlying all-or-none action potentials in *c. elegans* body-wall muscle
527 cells. *The Journal of physiology*, 589(1):101–117, 2011.

- 528 Q. Liu, P. B. Kidd, M. Dobosiewicz, and C. I. Bargmann. C. elegans awa olfactory neurons
529 fire calcium-mediated all-or-none action potentials. *Cell*, 175(1):57–70, 2018.
- 530 S. R. Lockery, M. B. Goodman, and S. Faumont. First report of action potentials in a c.
531 elegans neuron is premature. *Nature neuroscience*, 12(4):365–366, 2009.
- 532 J. E. Mellem, P. J. Brockie, D. M. Madsen, and A. V. Maricq. Action potentials contribute
533 to neuronal signaling in c. elegans. *Nature neuroscience*, 11(8):865–867, 2008.
- 534 L. Naudin. Biological emergent properties in non-spiking neural networks. *AIMS Mathe-*
535 *matics*, 7(10):19415–19439, 2022.
- 536 L. Naudin, J. L. Jiménez Laredo, Q. Liu, and N. Corson. Systematic generation of bio-
537 physically detailed models with generalization capability for non-spiking neurons. *PloS*
538 *one*, 17(5):e0268380, 2022a.
- 539 L. Naudin, J. L. J. Laredo, and N. Corson. A simple model of nonspiking neurons. *Neural*
540 *Computation*, 34(10):2075–2101, 2022b.
- 541 L. Naudin, L. Raison-Aubry, and L. Buhry. A general pattern of non-spiking neuron
542 dynamics under the effect of potassium and calcium channel modifications. *Journal of*
543 *Computational Neuroscience*, pages 1–14, 2022c.
- 544 M. Nicoletti, A. Loppini, L. Chiodo, V. Folli, G. Ruocco, and S. Filippi. Biophysical
545 modeling of c. elegans neurons: Single ion currents and whole-cell dynamics of awcon
546 and rmd. *PloS one*, 14(7):e0218738, 2019.
- 547 T. O’Leary, A. C. Sutton, and E. Marder. Computational models in the age of large
548 datasets. *Current opinion in neurobiology*, 32:87–94, 2015.
- 549 P. Poirazi and A. Papoutsis. Illuminating dendritic function with computational models.
550 *Nature Reviews Neuroscience*, pages 1–19, 2020.
- 551 A. Roberts and B. M. Bush. *Neurons without impulses: their significance for vertebrate*
552 *and invertebrate nervous systems*, volume 6. Cambridge University Press, 1981.
- 553 S. M. Silverstein, D. L. Demmin, J. B. Schallek, and S. I. Fradkin. Measures of reti-
554 nal structure and function as biomarkers in neurology and psychiatry. *Biomarkers in*
555 *Neuropsychiatry*, 2:100018, 2020.

- 556 G. D. Smith, C. L. Cox, S. M. Sherman, and J. Rinzel. Fourier analysis of sinusoidally
557 driven thalamocortical relay neurons and a minimal integrate-and-fire-or-burst model.
558 *Journal of neurophysiology*, 83(1):588–610, 2000.
- 559 S. R. Taylor, G. Santpere, A. Weinreb, A. Barrett, M. B. Reilly, C. Xu, E. Varol,
560 P. Oikonomou, L. Glenwinkel, R. McWhirter, et al. Molecular topography of an en-
561 tire nervous system. *Cell*, 184(16):4329–4347, 2021.
- 562 S. Usui, A. Ishihaiza, Y. Kamiyama, and H. Ishii. Ionic current model of bipolar cells in
563 the lower vertebrate retina. *Vision research*, 36(24):4069–4076, 1996.
- 564 M. J. Van Hook, S. Nawy, and W. B. Thoreson. Voltage-and calcium-gated ion channels of
565 neurons in the vertebrate retina. *Progress in retinal and eye research*, 72:100760, 2019.
- 566 S. R. Wicks, C. J. Roehrig, and C. H. Rankin. A dynamic network simulation of the nema-
567 tode tap withdrawal circuit: predictions concerning synaptic function using behavioral
568 criteria. *Journal of Neuroscience*, 16(12):4017–4031, 1996.
- 569 S. R. Williams, T. I. Toth, J. P. Turner, S. W. Hughes, and V. Crunelli. The ‘win-
570 dow’component of the low threshold ca^{2+} current produces input signal amplification
571 and bistability in cat and rat thalamocortical neurones. *The Journal of physiology*, 505
572 (3):689–705, 1997.