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# 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

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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<sup>1\*\*</sup>, Laetitia Raison-Aubry<sup>1+</sup>, and Laure Buhry<sup>1</sup>

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

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

9 <sup>+</sup>These authors contributed equally (joint first author)

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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.

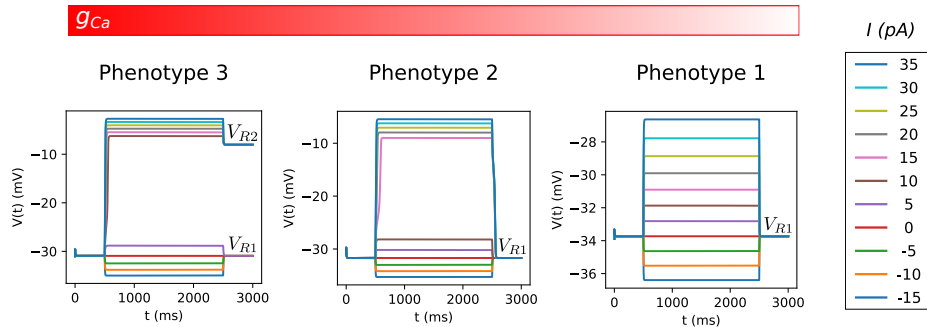


Figure 1: **Phenotypic transitions of the voltage dynamics as  $g_{Ca}$  decreases** (Naudin et al., 2022c). A well-posed retinal cone model, with a wild-type phenotype 3, was used as an illustration. A neuron with such a phenotype displays two resting potential values ( $V_{R1}$  and  $V_{R2}$ ). Decreasing  $g_{Ca}$  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.

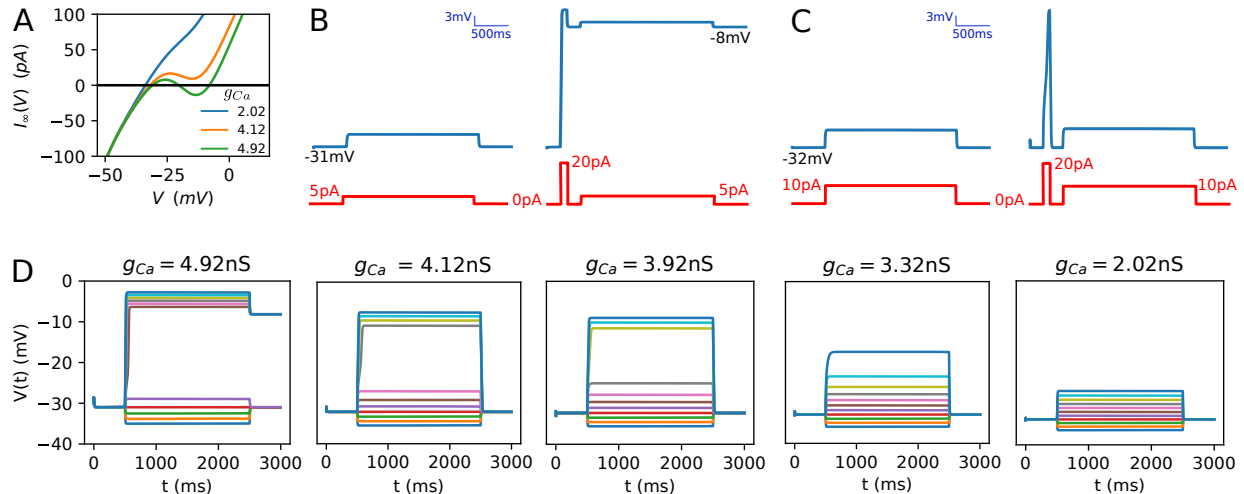


Figure 2: **Evolution of the computational characteristics of the retinal cone CBM as  $g_{Ca}$  decreases.** (A) SSC curve for three different values of  $g_{Ca}$  (4.92 (WT), 4.12, 2.02). (B) Short-term memory capacity of the WT phenotype of the CBM (phenotype 3). (Left) A depolarizing current step (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

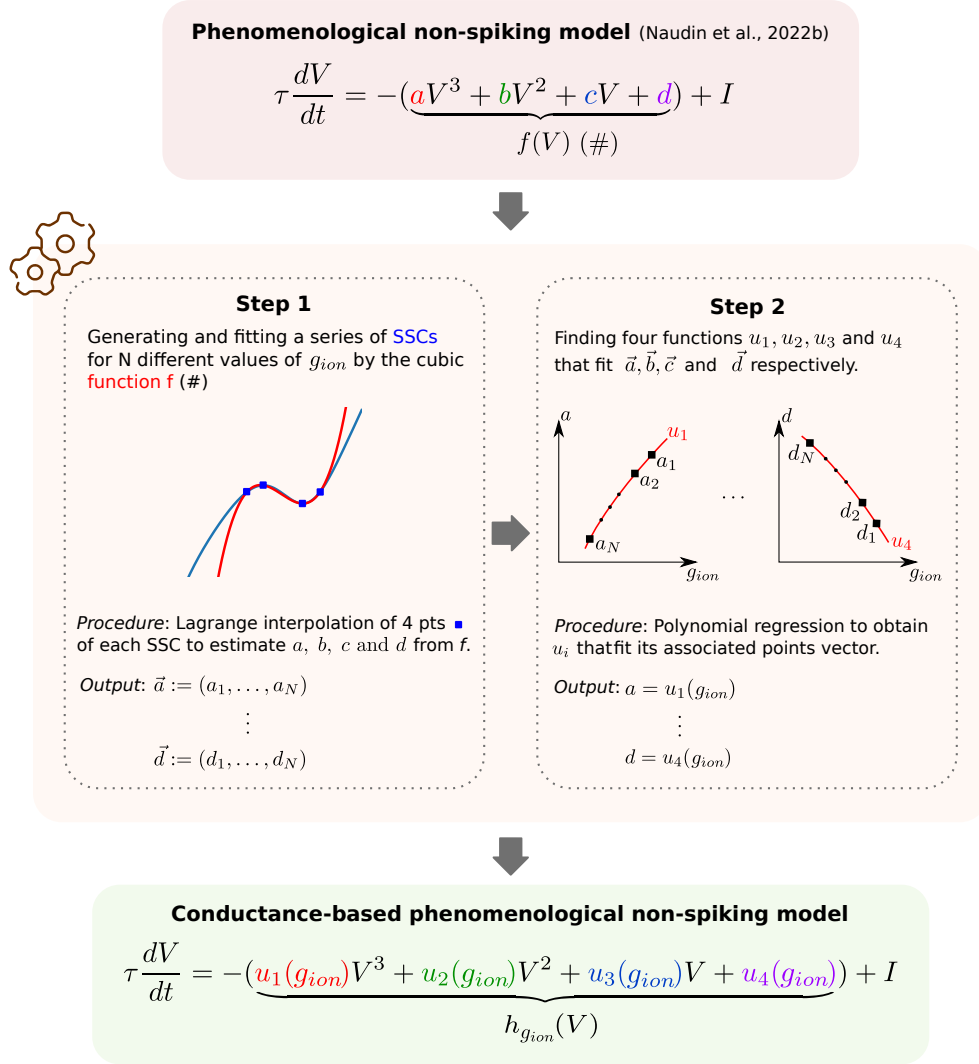


Figure 3: **Overview of the model design procedure.** **(Top)** The phenomenological non-spiking model (Naudin et al., 2022b) comprises 4 dimensionless parameters  $a$ ,  $b$ ,  $c$  and  $d$ . **(Middle)** The two-stage procedure aims to find a relationship between these parameters and maximal conductances  $g_{ion}$  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

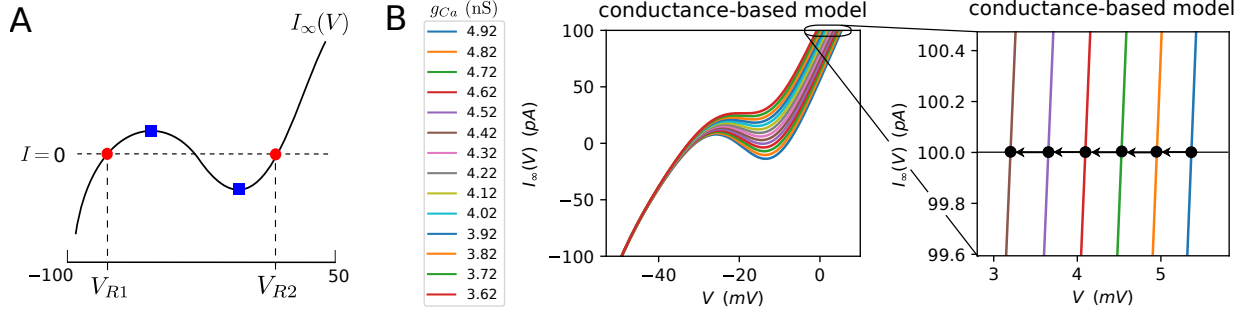


Figure 4: **(A)** The four points of the wild-type SSC to be interpolated by the cubic function of the simple model. Blue squares denote the local minima and maxima of the SSC, representing the current injection thresholds at which the neuron jumps to a new voltage plateau. Red points denote the two 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.

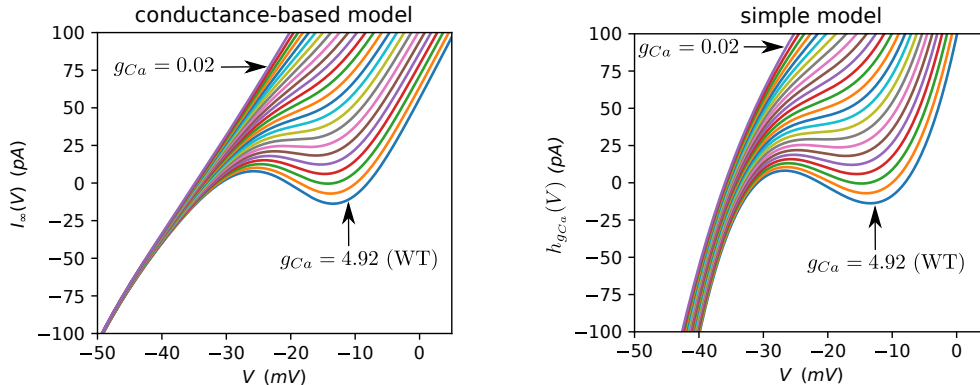


Figure 5: Comparison between the SSC of the CBM and the function  $h$  defined in (3) for a series of calcium conductance values  $g_{Ca}$  starting from 4.92 nS (WT) and decreasing to 0.02 nS by 0.2 nS decrements.

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).

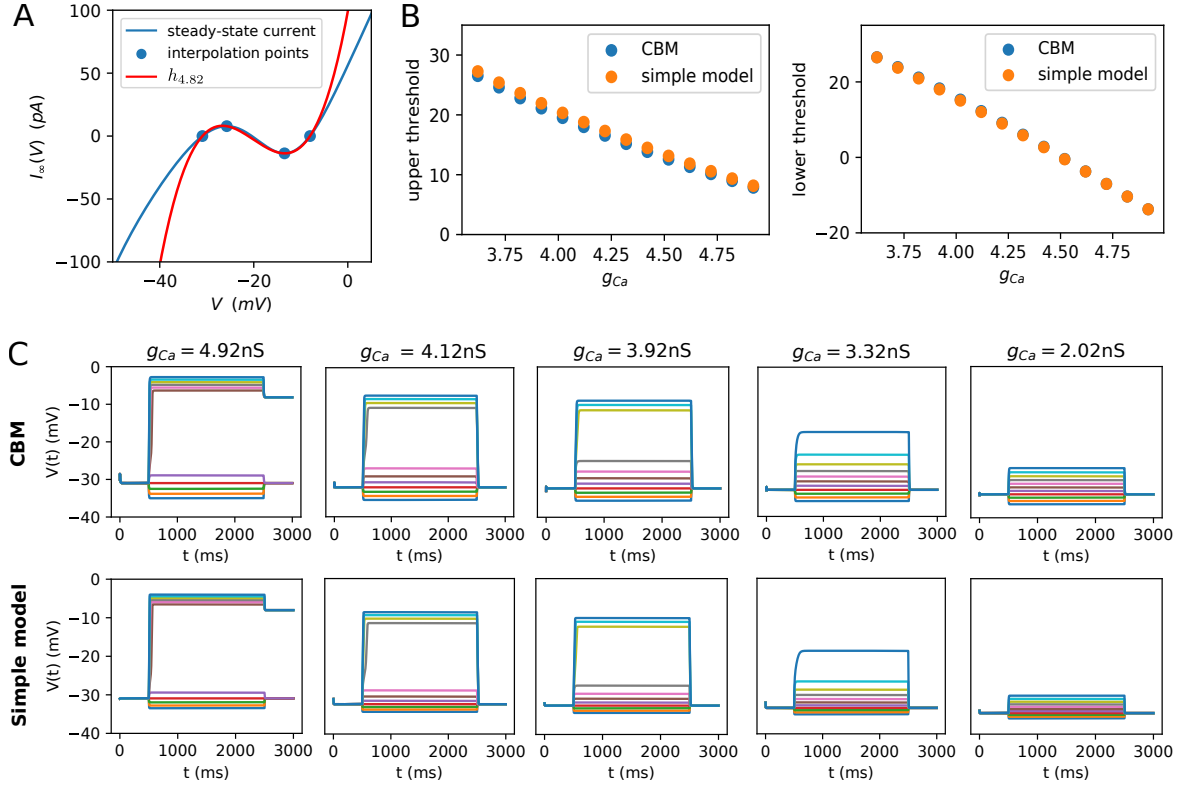


Figure 6: **(A)** Example of SSC ( $g_{Ca} = 4.82$  nS) of the CBM (in blue) against the function  $h_{4.82}$  of the simple model (in red) defined in (3). **(B)** Upper and lower threshold of injection currents between the down- and up-states in the CBM and in the simple model. **(C)** Comparison of 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.

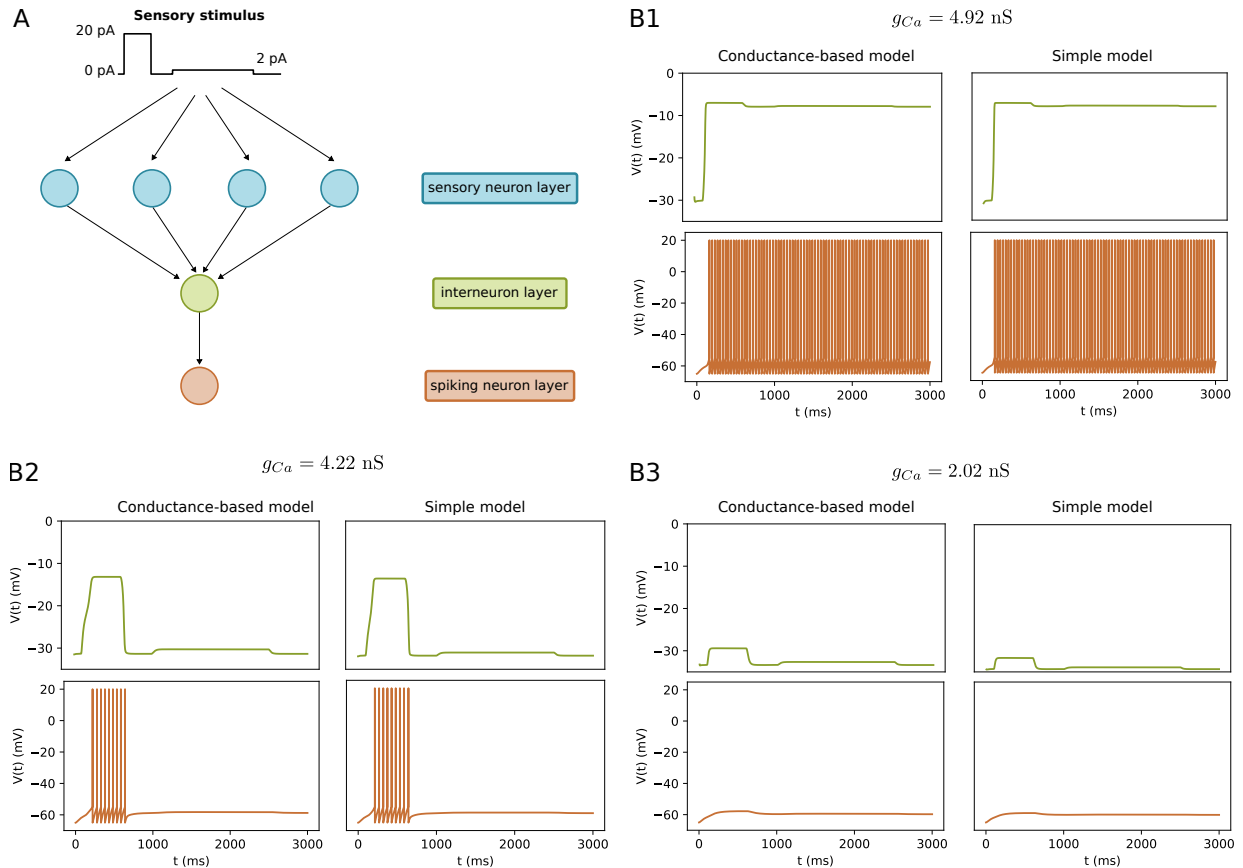


Figure 7: (A) Schematic of the neural network made up of three layers: four near-linear sensory neurons, one bistable interneuron, and one spiking output neuron. (B) Comparison of the neural network output (spiking activity) when coupled to the simple model or the CBM for three different values of  $g_{Ca}$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

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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  $I_{\infty}$  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  $I_\infty$  and  
 405 a horizontal line  $I = c$  where  $c$  is a constant. There are two standard steady-state  
 406 curves  $I_\infty$ , 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

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



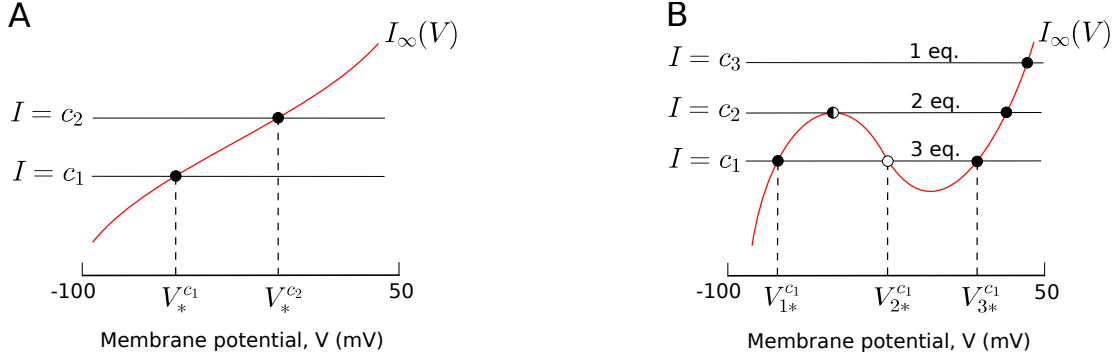


Figure S1: Two typical shapes of the SSC  $V \rightarrow I_\infty(V)$ , in red. Intersections of  $I_\infty$  and horizontal line  $I = c$  (with  $c$  constant) correspond to equilibria of the system. We denote stable equilibria as filled circles ●, unstable equilibria as open circles ○ and saddle-node 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  $I_\infty$  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  $\tau$  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 $E_{ion}$
$I_{Ca} = g_{Ca}m_{Ca}h_{Ca}(V - E_{Ca})$ $\frac{dm_{Ca}}{dt} = \alpha_{Ca}(1 - m_{Ca}) - \beta_{Ca}m_{Ca}$	$\alpha_{Ca}(V) = 3.1 e^{(V+16.6)/11.4}$ $\beta_{Ca}(V) = 3.1 e^{(-V-16.6)/11.4}$	$g_{Ca} = 4.92$ $E_{Ca} = 40$
$I_h = g_h(1 - (1 + 3m_h)(1 - m_h)^3)(V - E_h)$ $\frac{dm_h}{dt} = \alpha_{m_h}(1 - m_h) - \beta_{m_h}m_h$	$\alpha_{m_h}(V) = \frac{18}{(1 + e^{(V+88)/12})}$ $\beta_{m_h}(V) = \frac{18}{(1 + e^{-(V+18)/19})}$	$g_h = 3.5$ $E_h = -32.5$
$I_{Kv} = g_{Kv}m_{Kv}^3h_{Kv}(V - E_K)$ $\frac{dm_{Kv}}{dt} = \alpha_{m_{Kv}}(1 - m_{Kv}) - \beta_{m_{Kv}}m_{Kv}$ $\frac{dh_{Kv}}{dt} = \alpha_{h_{Kv}}(1 - h_{Kv}) - \beta_{h_{Kv}}h_{Kv}$	$\alpha_{m_{Kv}}(V) = \frac{5(V - 100)}{(1 - e^{-(V-100)/42})}$ $\beta_{m_{Kv}}(V) = 9e^{(20-V)/40}$ $\alpha_{h_{Kv}}(V) = 0.15 e^{-V/22}$ $\beta_{h_{Kv}}(V) = \frac{0.4125}{(1 + e^{(10-V)/7})}$	$g_{Kv} = 2$ $E_{Kv} = -80$

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**

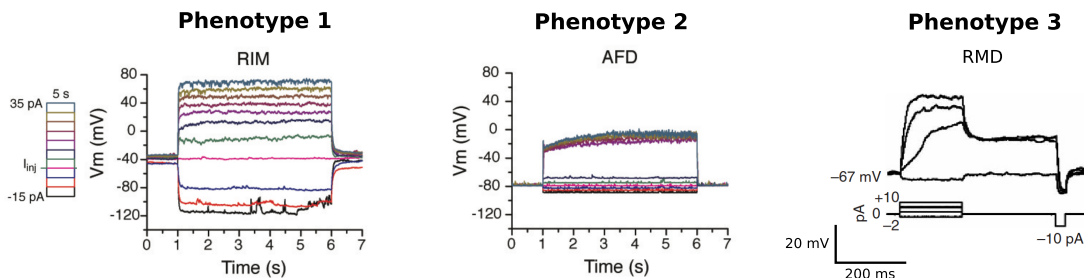


Figure S2: Experimental voltage examples from *C. elegans* of each phenotype for a series of current injections starting from  $-15\text{pA}$  and increasing to  $35\text{pA}$  by  $5\text{pA}$  increments for the RIM and AFD neurons, and starting from  $-2\text{pA}$  and increasing to  $10\text{pA}$  by  $3\text{pA}$  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.

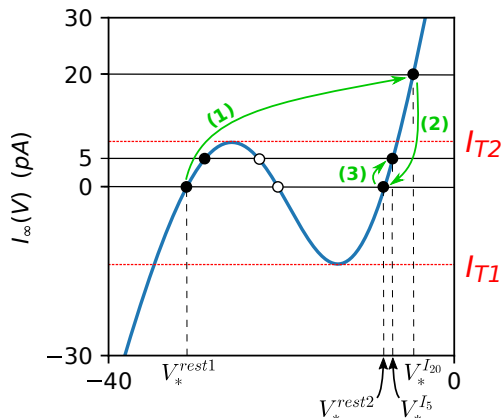


Figure S3: Diagram explaining the short-term memory capacity of a neuron with a phenotype 3.  $I_{T1}$  (resp.  $I_{T2}$ ) denotes the injection current thresholds at which the neuron jumps to its upper (resp. lower) voltage plateau. (1) A brief transient stimulus ( $20 > I_{T2}$  pA) is applied and 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 ( $5\text{pA}$ ) 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.

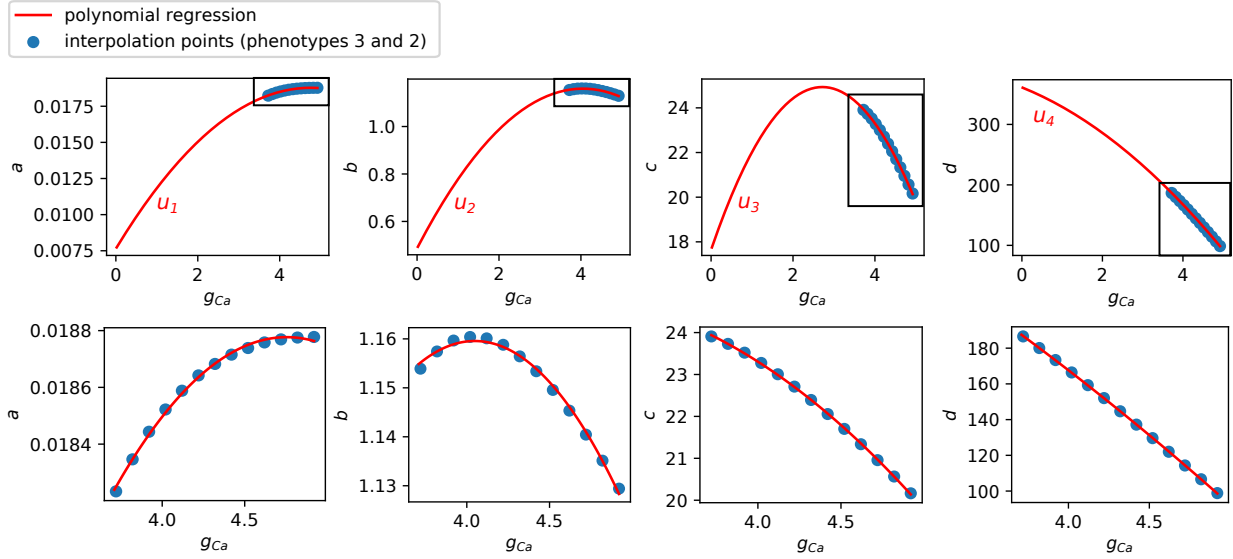


Figure S4: **(Top)** Two-degree polynomials  $u_i$ ,  $i = 1, \dots, 4$ , built from the polynomial regression of blue points. These points are generated following Step 1 and Step 2 of the procedure described in Section 3. **(Bottom)** Zoom of the rectangles in (Top).

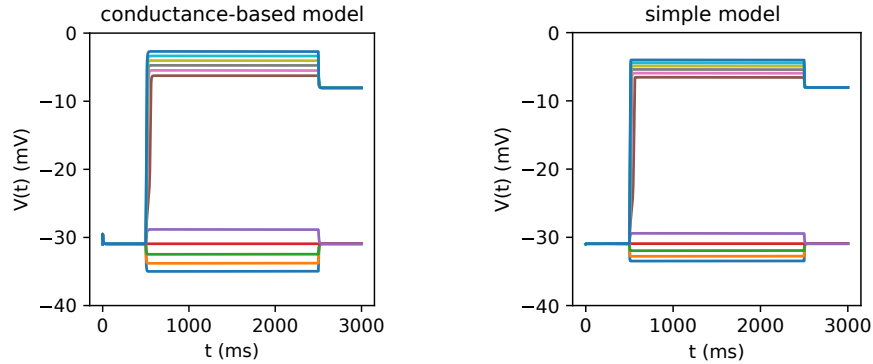


Figure S5: Comparison of voltage dynamics between CBM and the conductance-based phenomenological non-spiking model for  $g_{Ca} = 4.82\text{nS}$  for a series of injection currents starting from  $-15\text{pA}$  and increasing to  $35\text{pA}$  by  $5\text{pA}$  increments.

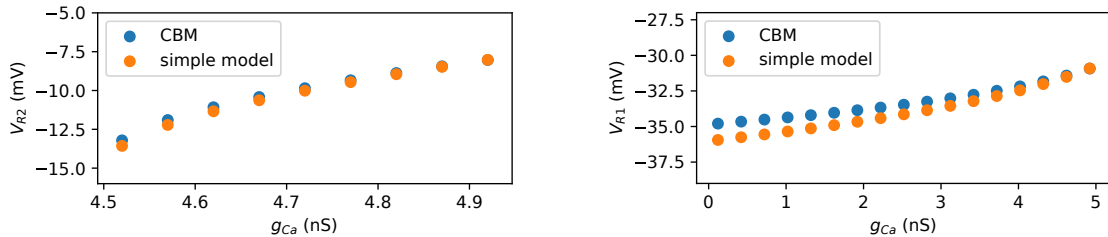


Figure S6: Comparison of the resting potential values ( $V_{R1}$  and  $V_{R2}$ ) for various values of  $g_{Ca}$  in the CBM and in the simple model.

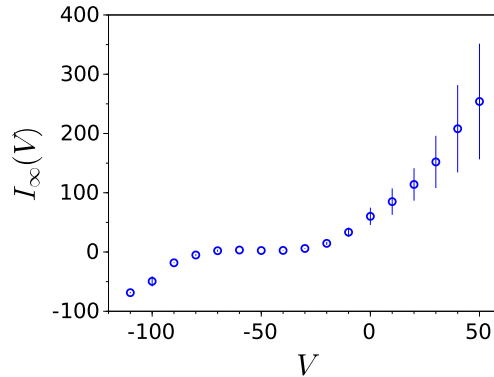


Figure S7: SSC of the AFD neuron obtained from averaged voltage-clamp recordings ( $n = 3$ ) (Liu et al., 2018).

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