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Computational models in neurosciences between mechanistic and phenomenological characterizations

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Abstract (162 words)

Objective: Computational neuroscience combines mathematics, computer science models, and neurosciences for theorizing, investigating, and simulating neural systems involved in the development, structure, physiology, and cognitive abilities of the brain. Computational models constitute a major stake in translational neuroscience: the analytical understanding of these models seems fundamental to consider a translation towards clinical applications.

Method: We propose a minimal typology of computational models, which allows distinguishing between more realistic models (e.g., mechanistic models) and pragmatic models (e.g., phenomenological models).

Result: Understanding the translational aspects of computational models goes far beyond the intrinsic characteristics of models. First, we assume that a computational model is rarely uniquely mechanistic or phenomenological. Idealization seems necessary because of i) the researcher's perspectives on the phenomena and the purposes of the study (i.e., by the relativity of the model); ii) The complexity of reality across different levels and therefore the nature and number of dimensions required to consider a phenomenon. Especially, the use of models goes far beyond their function, and requires considering external characteristics rooted in path dependence, interdisciplinarity, and pluralism in neurosciences.

Conclusion: The unreasonable use of computational models, which are highly complex and subject to a shift in their initial function, could be limited by bringing to light such factors.

Keywords: Computing Methodologies; Computer Simulation; Models, Biological; Models, Theoretical.

Summations

- A detailed understanding of computational models seems fundamental to consider a translation towards clinical applications: a typology of computational models distinguishing their realistic part from their pragmatic part can be fruitful.
- The realistic part involves understanding the biological plausibility, the notion of validity of models, and the necessary internal and external approximations of computational models.
- The pragmatic part involves understanding the need to simplify computational models in order to reproduce behaviors, and to enable prediction and generalizability.
- The use of computational models brings at least three challenges that go beyond the internal understanding of the models themselves: i) concerning the historical anchoring inseparable from the models and the notion of path dependence; ii) concerning the necessary idealization of models when translating to practice; iii) concerning the necessary challenge of pluralism and sociological factors which lobbied during the translation of computational models.

Perspectives

- A simplistic conception of this typology (pragmatic / realistic) could lead to a naive view of computational neuroscience; conversely, qualifying these differences enable to support the inherent complexity of computational models.
- Highlighting external factors (path dependence, sociological factors, interdisciplinarity, etc.) influencing computational models does not necessarily improve their use and translational aspect – such findings should not undermine the inherent prudence and humility of this highly complex neuroscientific field.
- The knowledge of the various factors isolated in this article would need to be considered by the modelers as by the users of the computational models — programmatic horizon necessary to avoid a drift of uses, at the base of the theoretical stakes of translational neuroscience.

1 Introduction

2

3 Computational neuroscience is a relatively new but already extremely complex and dynamic field.
4 Through its methodologies and applications mixed between dynamical systems, machine and deep
5 learning analyzes, biological simulations, Bayesian statistics, the creation and use of computational
6 models is one of its main challenges. Indeed, computational neuroscience developed models that can
7 be reused for clinical applications (Varenne *et al.* 2018), and various other uses, e.g., for their
8 descriptive power (Kording *et al.* 2020). Likewise, computational theories, for the most part resulting
9 from the relevance of these models (Borsboom *et al.* 2020), are exported between different fields and
10 applied in research programs that diverge in their foundations as in their objectives (Kuhn 1971).
11 Thereby, neuroscience models are exported within ambitious projects such as the Blue Brain Project
12 (BBP), initiatives that seek to develop infrastructure research projects exploring the human brain
13 (Markram 2012). Despite minimum output, this project has been followed in Europe by the Human
14 Brain Project (1.19 billion euros over ten years) (HBP now gives birth to a platform, EBRAINS,
15 which includes a very important part of simulations, through tools such as The Virtual Brain) and in
16 the USA by the BRAIN Initiative (\$ 300 million per year for 10 years).

17 For methodological and ethical reasons, it seems essential to clarify the different concepts underlying
18 these models involved in various areas of computational neuroscience, in order to increase their
19 transparency, analyze whether they can be used with robustness outside their initial context of
20 development, or explore their potential in terms of explanation, realism or pragmatism.
21 Neuroscientists seem keenly aware of the social, ethical, and regulatory challenges of computational
22 neuroscience, from potential threats to privacy until an understanding of the awareness and meaning
23 of human and personal identity (Evers 2017). But it seems important that clarification of experiments,
24 models, theories, and the whole scope of computational neuroscience comes from the researchers
25 themselves involved in this scientific field – and such theoretical work has already been started in
26 other biological fields (Blohm *et al.* 2020; Brette 2015, 2019; Haefner 2005; Pradeu *et al.* 2021).

27 Models are one of the main tools of computational neuroscience. A model is a material or formal
28 construction used to represent a real-world object. It is an object of facilitating mediation that allows
29 to transform reality or to anticipate it (Morgan & Morrison 1999; Varenne 2007). Minsky defines a
30 model as an object A^* , which is a model of an object A , inasmuch as an observer B can use A^* to
31 answer questions that interest her/him about A (Minsky 1965). Such a minimal definition enables to
32 understand computational models as (mathematical) functions acting as mediators between the
33 modeled object and a user or a modeler. Such mathematical models aim to reproduce a certain number
34 of brain observable phenomena, functions, or dynamics. However, they cannot reproduce all the
35 aspects of a brain function or a structure, unless being the considered brain itself. Given the significant

36 complexity of the objects studied in computational neuroscience, this mediator value represented by
37 the model depends on the question asked by the researcher. Indeed, as we will detail later, the choice
38 of the model should be clearly conceived according to the question which must be solved –
39 influencing the number of dimensions introduced in a specific model. For instance, single neuron
40 models (*neudels*) like Izhikevich’s models cannot fully account for a biological neuron (Izhikevich
41 2003). Indeed, they do not have a whole biophysical representation, but show apparent realistic
42 dynamics (Izhikevich & FitzHugh 2006) by modeling behaviors similar to the time evolution of the
43 membrane potential of a biological neuron. In other words, some of these models enable the
44 prediction of neuronal behavior without seeking to exactly reproduce the biological parameters of the
45 (human) brain. These examples are from a specific type of model, dynamical systems, based on
46 differential equations. In the first section of this work, we mainly consider and refer to this category
47 of model and open to a broader definition in the remaining sections.

48

49 *Aims of the Study.* A typology of models might be useful to discuss the relationship between the
50 idealization of the model and its different applications. In this article, we will see that such a typology
51 could explain the use, generalization and appropriation of a model by a scientific community.

52

53 Material and methods

54

55 In this perspective, we aim to propose a minimal typology of computational models. For this purpose,
56 we use a set of inclusion criteria according to the SANRA guidelines (Scale for the Assessment of
57 Narrative Review Articles) (Baethge et al. 2019):

- 58 • identify articles discussing the translational aspect and the use of computational models, and
59 more particularly models of biological neurons;
- 60 • English or French language studies published in peer-review journals are used, especially by
61 using MEDLINE (– 2021) and Cochrane (– 2021) databases;
- 62 • for all identified articles published, reference lists were also scanned to see whether we had
63 missed any articles suitable for inclusion. These steps allowed us to reduce the possibility of
64 non-indexed studies being missed. Single case studies, commentary, opinion articles,
65 unpublished studies, conference posters and reviews and meta-analyzes were allowed.

66 Finally, the full text of the chosen literature was manually reviewed to determine inclusion into this
67 perspective.

68

69 Results

70

71 This perspective allows to distinguish between realistic models (e.g., mechanistic models) and
72 pragmatic models (e.g., phenomenological models).

73

74

75 **1. A framework for computational models**

76

77 Three essential characteristics of a computational model can be distinguished: a level of idealization
78 (“modeling involves a selection of characteristic features of the modeled target”), a level of relativity
79 (“the representation is oriented by tools and objectives”), and reversibility (“such models serve both
80 as a representation of reality and as a support for its future modification”) (Potochnik 2017). Indeed,
81 all computational models have a level of idealization. Their relativity to technical tools can be
82 variable, but it remains low compared to many other scientific fields (e.g., in medicine). They are
83 highly reversible because they support research in the present time while serving as a support for its
84 future modifications.

85 In accordance with the classical theorization of models (Hempel 1965), computational models have
86 at least two main components: a realistic component and a pragmatic component. Indeed, it could be
87 useful to distinguish the realistic part of models, used in order to facilitate mechanistic designs of a
88 scientific object (e.g., the wooden model of an airplane) or facilitate its intelligible presentation (e.g.,
89 the double helix of DNA presented by Watson and Crick) (Varenne *et al.* 2018). On the other hand,
90 the pragmatic part of computational models could be used to determine what type of response is
91 expected in terms of action and behavior (e.g., the paper plane or an interdisciplinary model of
92 pandemic management). The pragmatic part of the models aims to reproduce the target behavior for
93 which the model was designed. Thereafter, we will detail these two components of the models,
94 classically called the realistic and pragmatic components.

95

96

97 ***1.1. Mechanistic models (with a strong realistic component)***

98

99 Models with a strong realistic component could be based on direct description of actual biological
100 components of the brain. Most of them seek to reproduce neural mechanisms. In this approach of
101 computational models, a behavior is prescribed by an equation through functional relations between
102 components. This equation aims at reproducing dynamics of neural correlates at different scales.

103 Although the definition of a mechanism has been extensively discussed, we retain the definition of a
104 mechanism as a network of interrelated parts, each performing its own functions, that are combined
105 in such a way that each contributes to producing a behavior (Bechtel & Richardson 2010). For
106 example, they can be useful in providing a causal explanation for a phenomenon. Such models are
107 therefore mechanistic because they can be decomposable and offer a functional definition of their
108 relations (Bechtel & Richardson 2010), allowing the model to have a biological correspondence, i.e.,
109 the relationship between variables is specified in terms of biological processes. In other words, they
110 have a strong biological plausibility in terms of biophysics. The plausibility of a mechanistic model
111 can be thus measured by the ability of the experimenter to identify in the physical system parts
112 organized in a manner analogous to or conforming to the model. This realistic component and
113 biological plausibility are intrinsically related to the notion of validity of a model, which can itself be
114 understood in terms of validity: i) apparent, corresponding to the overall resemblance of the model to
115 the manifest phenomenon; ii) predictive, corresponds to the power of the model to predict; iii)
116 discriminating, corresponding to the relevance and representativity of its content; iv) structural,
117 corresponding to the explanatory power of the model (Belzung & Lemoine 2011).

118 However, describing biology does not necessarily lead to good predictions, or may even limit them.
119 In addition, the number of parameters within a computational model could be very large and cannot
120 be modeled. And moreover, the more there are free parameters, the lower the confidence in the model
121 is. Thus, it is often necessary to identify what are the minimum “ingredients” (biophysical variables
122 and parameters) that are necessary to provide biological plausibility. Thus, in practice, purely
123 mechanistic models are not possible, given the necessary consideration of a phenomenological part.
124 Any model that seeks to faithfully reproduce reality should, by definition, make approximations of
125 two types. The first type of approximation is internal (Batterman & Rice 2014). For modeling,
126 computational, temporal and tractability reasons, a computational model (e.g., a neuron) cannot
127 model all the parameters of a real brain structure (e.g., a neuron), and therefore approximates some
128 parameters, i.e., performs an idealization (e.g., with some ion channels) (Elgin 2017). The second
129 type of approximation is external. Whenever a mechanistic model wishes to integrate part of the
130 environment, it must simplify it to its limits.

131 These two impediments of mechanistic models (limits to prediction and internal and external
132 approximations) lead in computational neurosciences to the development of models with a strong
133 pragmatic component, such as the phenomenological models that we will describe.

134

135

136 ***1.2. Phenomenological models (with a strong pragmatic component)***

137

138 Models with a strong pragmatic component describe simplified patterns of data, unlike mechanistic
139 models which rather aim to grasp causes or processes (and which therefore have a higher biological
140 plausibility due to the structural analogy with the biology of the target phenomenon). In this approach,
141 a scale of granularity of the nervous system (e.g., a neuron) enable to describe emerging properties at
142 the scale of physiology or behaviors.

143 For example, models with a strong pragmatic component can be useful for prediction (rather than
144 explanation, as is the case with mechanistic models). These phenomenological models do not
145 deliberately seek (or little) biological correspondence between their parameters and the biological
146 parameters (Hilborn & Mangel 1997). Instead, they serve to facilitate biological understanding by
147 seeking to reproduce a behavior.

148 For example, Leaky Integrate and Fire (LIF) models do not attempt to combine all the ion channels
149 of a neuron. Such a model captures a global aspect of the membrane by mimicking the sub-threshold
150 integration of the inputs, and the spiking phenomenology is a way to perform simulations by
151 circumventing the difficulty associated with the modelisation of a large number of biological
152 parameters. Moreover, the behavior of high-dimensional systems of nonlinear differential equations
153 is difficult to visualize or analyze beyond a two-dimensional system which can be more easily studied
154 by means of a phase plane analysis. Reducing the four-dimensional equation of Hodgkin Huxley
155 (HH) (Hodgkin & Huxley 1952) to two equations is possible without reducing the biological elements
156 considered (Depannemaecker *et al.* 2021b). This reduction leads to a loss in terms of dynamics (i.e.,
157 time evolution) but not in the number of elements considered. Another approach is to reduce it to its
158 core dynamics. In this case, the model will be the simplest equation that keeps the properties of the
159 phase-space to reproduce only the considered phenomenon, as the FitzHugh-Nagumo model does
160 (Gerstner *et al.* 2002; Izhikevich & FitzHugh 2006). In these examples, the HH model considers
161 biologically plausible underlying mechanisms to capture membrane excitability, while the FitzHugh-
162 Nagumo model only keeps the minimal elements necessary to exhibit excitable properties comparable
163 to neural excitability, but without giving any biophysical description. Thus, the interest of such
164 phenomenological models is to enable prediction and generalizability within simplified models, and
165 not to inherently imitate the physical parts of the mechanism of real biological neurons. This
166 prediction and this generalizability, referring to the pragmatic part of the model, are commonly called
167 the precision of the model (Massoud *et al.* 1998).

168

169

170 ***1.3. Interactions between mechanistic and phenomenological computational models***

171

172 A model of a wooden plane will seek to reproduce the features of the real airplane. A wooden airplane
173 model has a strong realistic component and is mechanistic due to the structural analogy with the shape
174 of the target phenomenon. However, such a model flies much worse than a paper plane model, which
175 however does not have the same shape as the real airplane, nor does it have a propeller or wheels
176 (Brette 2012). The paper plane is an illustration of a phenomenological model, which has a strong
177 pragmatic component. It mimics the functions and purposes for which the actual airplane was created
178 (fly). We recognized in this distinction Marr's levels applied to modeling: the phenomenological
179 model responds to the Level 3 (Computational), while the mechanistic model corresponds to the Level
180 2 (Algorithmic). Level 1 corresponds to the (organic) implementation (Bickle 2015).

181 In the same way, models such as LIF are very unrealistic while multicompartmental Hodgkin-Huxley
182 (HH) models have ion channels that reproduce the real biological neuron (Brette 2012; Nelson &
183 Rinzel 1995). However, as described in the HH model, the sodium activation variable has no
184 biophysical equivalent in the biological sodium channel: therefore, even though a biophysical
185 parameter is integrated into the model, there is a pragmatic dimension within the model. Various other
186 models in computational neuroscience have both the pragmatic component of phenomenological
187 models and the realistic component of mechanistic models. Some of them have even been designed
188 specifically to balance this distinction between realism and pragmatism, such as AdEx models
189 (Adaptive exponential integrate-and-fire models) which are phenomenological models whose
190 hybridization increases their predictability and generalizability (Touboul & Brette 2008).

191

192 To go further, we claim that any mechanistic model should embed a phenomenological aspect which
193 tie it to real life observations.

194 On the other hand, we also state that any phenomenological model is built on mechanistic relations
195 between entities, but these entities do not directly relate to observables. For example, an unrealistic
196 but very pragmatic biological neuron model, such as LIF (Brunel & van Rossum 2007), allows,
197 depending on the input current, to make predictions on the membrane potential and the temporality
198 of the spikes.

199 Indeed, in case of idealization of the model during its generalization, the comparison with the
200 biological components allows to revise the hypotheses by adding or deleting the composition of the
201 mechanism. The need for phenomenological models emanates from the difficulty to separate the
202 contributions of a large number of components and mechanisms. This said, it must be stressed that
203 commensurability between the level of description (scale and type) and the phenomenon to be
204 explained, is necessary to give a complete explanation at this level, i.e., a necessary and sufficient
205 relation between the elements considered and the observed phenomenon. This can be called a
206 stabilized level of description. However, it is rarely the case in neurosciences, as we are in the

207 presence of a very high-dimensional complex system, which makes it generally difficult to know
208 what levels of description (i.e., nature and number of components) should be chosen to explain a
209 given phenomenon. In other words, idealization seems necessary because: i) of the researcher's
210 perspectives on the phenomena and the purposes of the study (i.e., by the relativity of the model); ii)
211 of the messy nature of reality and ignorance of the number and nature of the dimensions of the
212 phenomenon to be considered.

213 To sum up, any model necessarily has a mechanistic part and a phenomenological part. However,
214 such a theoretical characterization depends on the triple relativity of the scientific field, of the
215 researcher's question and of the temporality in which computational models are used.

216

217

219

220

221 **1. Computational models and path dependence**

222

223 Based on the identification of the two types of models widely confused, we broaden the understanding
224 of these computational models to embed them in their research environment, in relation to their
225 historical path dependence. Path dependence explains the continued use of a model based on historical
226 preference or current use: a model may persist even if newer and more efficient alternatives are
227 available, for instance because it is easier or more cost-effective to continue along an already set path
228 than to create an entirely new one (Pierson 2000).

229 We propose to identify two possible path dependencies: the polysemy of the term “computation” and
230 a precocious occurrence of theoretical questions about computational neuroscience in the history of
231 cognitive sciences.

232

233 First, the term of computation has evolved over time. In the scientific literature of cognitive science,
234 we track down a confusion between the term “computational” and “computationalism”. The former
235 is applied to a particular science (such as brain science) and seems more restricted than the term of
236 computationalism. Indeed, the term “computational” refers only to the processing of information
237 allowing the performance of the function (hence its association with the term “functionalism”) (Marr
238 1982). However, there may be different mechanisms underlying this realization of a function (e.g.,
239 the flight of a bird depends on the flapping of wings, but the bird can also hover). For Marr
240 (1982/2010), the level of the computation is the level of the function, while the level of the mechanism
241 is both the level of the rules which allows this function (i.e., algorithm level) and the level of the
242 structural characterization of the system (i.e., implementation level), which are well separate.
243 However, computational sciences bear a slightly different sense of “computational”, by sitting in
244 between Marr’s levels, as they generally aim at explaining functions by algorithms.

245 In a completely different field, computationalism is a form of cognitivism: it refers to the processing
246 of information, via different methods, which can be especially connectionist. Such terminological
247 confusion has led to a hermeticity of the fields of study of computational neuroscience (Aizawa 2010).

248

249 Secondly, theoretical questions about computational aspects of neurosciences emerged very early in
250 the history of cognitive sciences. Computational neuroscience was born with models of biological
251 neurons, with a seminal article published in 1907 (Brunel & van Rossum 2007; Lapique & Lapique
252 1907), introducing dynamical systems theory within neurosciences, on the assumption that neuronal

253 spiking was the support of in the peripheral nervous system. We can trace back to the first Macy
254 Conference in 1941 the need to promote communication between scientific disciplines in an attempt
255 to “restore the unity of science”, a main objective of scientific positivism. This interest in so-called
256 cybernetics and the presentation by Turing of a model of cognition as an embedded mechanism of
257 treatment of information constrained by a hardware (Turing 1950) has led to limit the modeling of
258 complexity, whether at the neuronal or mechanical level (Hevern 2012; Nagel & Newman 2008).

259

260 The distinctions between the computational models currently used in different fields of neurosciences
261 must therefore be understood through their history, which itself influences the different fields
262 currently involved in the use of these models.

263

264

265

266 **2. Idealization and pluralisms in computational neuroscience**

267

268 Computational models derive their robustness from coherent interactions between the three fields of
269 physics, mathematics and biology. However, as in any science, there are limitations in the use of such
270 models which do not come from the intrinsic model, but from its use and extrapolation, and therefore
271 involve notions like those of idealization and abstraction (Bickle 2006; Sober 1999).

272

273 In many areas of the brain, neurons seem organized in populations of units which share some similar
274 properties. Prominent examples are columns in the somatosensory and visual cortex (Hubel & Wiesel
275 1962; Mountcastle 1957) and pools of motor neurons (Frotscher 1996). Given the large number of
276 neurons within such a column or pool, one possible approach is to describe the mean activity of the
277 neuronal population, rather than the spiking of each individual neurons (Abbott & van Vreeswijk
278 1993; Amit & Brunel 1997; Brunel & Hakim 1999; Gerstner *et al.* 1993). The population activity
279 equations allow study signal transmission, neural coding, oscillations and synchronization as well as
280 the formation of activity patterns in spatially structured populations (Kähne *et al.* 2017). Moreover,
281 density equations allow integration of different internal states (Knight 1972), with the stochastic spike
282 triggering (Abbott & van Vreeswijk 1993; Brunel & Hakim 1999) or the state of refractoriness
283 (Wilson & Cowan 1972). For instance, for the Wilson–Cowan model (describing the dynamics of
284 interactions between populations of simple excitatory and inhibitory neuron models), the validity of
285 these population equations relies on stringent assumptions such as homogeneous populations, absence
286 of finite size effects and adaptation. In this type of model, all the dynamical complexity that may exist
287 at the lower scale is eliminated. Of course, these limits can be smoothed. For example, the variability

288 of a parameter between one neuron and the next is often replaced by slow noise in the parameters. In
289 the same vein, adaptation could be phenomenologically corrected by introducing a slow variable that
290 integrates over the population activity in the past (Knight 1972). However, some deeper questions
291 resist any such correction.

292 Thus, in the case of neural mass and neural field models, the various tools mentioned above, specific
293 to averages and populations of neurons (e.g., a transfer function which designates which output is
294 produced as a function of the input), are introduced in the computational model. But such an
295 introduction needs to question if the effects observed within the model are observed for the same
296 reasons as the effects observed within the real biological neuron.

297 The causes that govern the behavior of the model are not necessarily the causes that govern the
298 behavior of the biological neuron. In other words: is the causality introduced into the model similar
299 to the biological causality, similarity necessary for extrapolation? For instance, doesn't the airplane
300 metaphor raise strong doubts that the causes that make the paper plane fly have anything to do with
301 the causes that make the real plane fly?

302 This deep question calls the legitimacy of translating a concept to build a model: does the model
303 equation contain the same set of concepts as the object being studied? Moreover, in the case where
304 the validation of the models is performed through simulations, the observed effect looks similar to
305 the real effect – but it cannot be proven that the causes of these effects are similar. The same
306 phenomenon is reproduced, without any intuitive or mathematical argument allowing to claim that
307 the cause of this observed behavior is similar to the real cause. It is true that when a pure mechanistic
308 single biological neuron is studied, the equations provide causal transparency. When scaling up, i.e.,
309 during the passage from one scale of description to another, it is not clear that causality is maintained.

310

311 This observation of the same phenomenon related to multiple underlying causal mechanisms is called
312 “multirealizability” (or multiple realizability). This could be understood as a generalization to models
313 of “degeneracy” observed in biology. Multiple realizability concerns the difficulty in relating the
314 behavioral function of a model with structural or organizational properties (e.g., flying can be
315 achieved in multiple ways, by flapping its wings or by soaring) (Polger & Shapiro 2016).

316

317

318 *2.1. Multirealizability and scales of explanations*

319

320 Multiple realizability may appear in particular in the very specific case of scaling up. To continue
321 with the example of biological neuron models, multirealizability appears when the model is translated
322 from a scale (which was used to build the model) to another, e.g., from neurons to neural network. A

323 macroscopic phenomenon (e.g., epilepsy) can be explained by different causal mechanisms evolving
324 at several scales (from genetic to interconnectivity network) having separate temporal scales
325 (temporal dissection) (Depannemaecker *et al.* 2021a). Therefore, multirealizability requires exploring
326 (or even integrating) different scales (from microscopic to macroscopic scales). Thus,
327 multirealizability necessarily appears when biological neurons models are integrated in a process of
328 scaling. However, knowledge of the structure of a phenomenon is not necessary to highlight, because
329 proxies may be sufficient to draw relevant inferences (e.g., Newton did not need to know the structure
330 of water to describe the phenomenon of tides, but only its coefficient of viscosity and its density).

331

332 We said that the injection of phenomenology into a computational model (e.g., AdEx) allows to
333 compensate for what the model does not intrinsically consider. Likewise, the scaling process within
334 the framework of biological neural networks requires reintroducing an approximation, by the
335 necessary addition of a part of phenomenology in the model. Take the example of hyper-dissipation
336 in meteorology: because researchers do not have infinite precision, they do not have access to what
337 is happening under a minimum size scale. As such minimal scales cannot be resolved, it is necessary
338 to add a parameter to the equation. This phenomenological injection corresponds to the “edges” of
339 the model, defined as the impossibility of integrating realistic parameters during the complexification
340 of the model. Scaling up takes the model away from biological plausibility by increasing its
341 phenomenological part (i.e., scaling up necessarily increases the phenomenology part of the model
342 since there are more external parameters to consider). The risk of such a scaling up is therefore to
343 neglect this phenomenological injection, which could lead to interpretation bias.

344

345 In this context, we could however cite the existence of causal modeling, which seems to offer a way
346 out of the problems posed by multiple realizability. Such models provide probabilistic or
347 deterministic versions to overcome the effects of multiple realizability from an interventionist
348 perspective. In practice, such models lose in explanatory power what they gain in intervention
349 capacity (Pearl 2009, 2010).

350

351

352 ***2.2. Idealization and pluralism***

353

354 The multiplicity of physical and algorithmic implementations of a lower level at a higher level
355 challenges the connection and validity between levels. Epilepsy or depression, i.e., macroscopic
356 phenomena, could not be accurately modeled in the context of computational neuroscience: thus, even
357 if scientific progress is possible thanks to computational models, such models do not refer only to a

358 single higher level. However, the problem of multirealizability can be approached in a more fruitful
359 way for computational science than by raising the problem of reductionism.

360 Indeed, debates about levels of explanation in neurosciences demonstrate that the field is increasingly
361 departing from the classical hierarchical models in which a fundamental physical or algorithmic level
362 is deemed the only truly explanatory level, and which allows all higher levels of a complex system's
363 organization have to be reduced to it. Thereby, explanatory pluralism is the thesis according to which
364 the explanation of a phenomenon can especially refer to constructs or mechanisms belonging to
365 several different scales (Cartwright 1979; Hacking 2002; Suppes 1977). There are two forms of
366 explanatory pluralism: integrative pluralism (Mitchell 2009) and tolerant or non-integrative pluralism
367 (Kellert *et al.* 2006). By studying these two forms of pluralisms, we will see that the question of
368 integration between scales leads to the question of the necessary interdisciplinarity of neurosciences.

369

370

371

372 **3. Integrative and tolerant pluralism for computational neuroscience**

373

374 Integrative pluralism attempts to establish small local integrations between levels of analysis, without
375 seeking to build a large theoretical structure. In the case of biological neural networks modeling a
376 seizure disorder, there are many factors acting at different times and levels of the simulation of the
377 system (or pathology) – such as nonlinearity or noise. Neither the model itself, independently of these
378 factors, nor the environment external to the model are sufficient on their own to explain its behavior.
379 There is not a single composition of causes involving different levels that will do the job in all cases
380 (O'Malley *et al.* 2014).

381 In other words, certain factors and certain levels are more important than others. These factors at
382 certain levels are considered more important than others are called producers of differences (Kendler
383 2012). For example, epilepsy can be caused by several producers of differences on at least three
384 different levels: genetic (genetic variants influence the onset of epilepsy and / or the onset of a
385 seizure), neuronal (hyper-synchrony as it can be modeled by biological neural networks) and
386 environmental (trauma, dietary factors, disruption of circadian rhythms, etc.). All of these factors are
387 producers of differences because they are involved in the development and maintenance of an
388 epileptic disorder. But depending on the interindividual heterogeneity or different types of epilepsy,
389 causal signatures are different, i.e., differences makers seem to be more or less concentrated at certain
390 levels in some cases while in other cases they could be distributed on all levels (Woodward 2003).

391 Therefore, causal signatures designate certain sets of concentrated levels which best explain a
392 pathology. For example, a West syndrome or an epileptic encephalopathy would have more producers

393 of differences in the genetic domain, and therefore has a genetic causal signature. A generalized tonic-
394 clonic epilepsy would be better explained at the neuronal level and a temporal epilepsy has a causal
395 signature based on developmental mechanisms, where neuronal plasticity plays major roles in
396 creating a state of underlying hyperexcitability (Steinlein 2004). These findings are even more
397 pronounced in psychiatric disorders, where environmental factors, for example, represent an
398 important causal signature in depression while they are much less important in schizophrenia.
399 However, this kind of integrative pluralism does not seem relevant to understanding the interest of
400 models of biological neurons, an interest which would be restricted to certain macroscopic
401 phenomena. On the contrary, tolerant (or non-integrative) pluralism seems much more fruitful for
402 understanding biological neural networks.

403

404 The tolerant pluralism postulates that certain phenomena at different levels may be required to answer
405 different questions, without these levels necessarily being integrated into a coherent whole (Van
406 Bouwel 2011). The choice of a level of explanation depends on the epistemic and pragmatic interests
407 of the researcher (Kendler & Parnas 2017). Some levels are more important in terms of explanatory
408 strength, generalizability to several phenotypes, specificity or manipulability in terms of therapeutic
409 action. For example, biological neural networks are undoubtedly the best model in the current state
410 of science to represent neural synchronization in terms of strength, generalizability, specificity, even
411 manipulability, because despite all their approximations (necessary in any model), they allow to
412 obtain with confidence a representation of neurons behavior.

413 With a view to translational research and according to the logic of tolerant pluralism, the transfer of
414 these models to clinical practice (i.e., diagnosis based on semiology and therapeutic management)
415 should be carried out carefully. The best level of explanation for epilepsy (or any other neurological
416 or psychiatric pathology) will depend on the question of the researcher (or the research and medical
417 community), and there is no evidence to intuitively say that the questions answered by biological
418 neural networks (including hyper-synchrony) will be relevant, for example, to the clinician. At least,
419 it will be up to the researcher building models of biological neurons to convince other research
420 communities of the relevance and applicability of his/her findings to the fields of application to which
421 she/he is addressing.

422

423

424

425 **4. Sociological factors**

426

427 Finally, the adoption of a tolerant pluralism, which accepts to conceive of multiple explanatory levels
428 but retains only the most relevant for a given research question, leads to the question of
429 interdisciplinarity. Often, a scientific result (e.g., biological neural networks) in a given context have
430 to be translated to another level (e.g., to a pathology or to a larger integrative project such as the
431 Human Brain Project).

432 It seems important to consider sociological constraints that follow these scientific results. Each result
433 engages the conviction of a researcher that his/her hypothesis, which has been proven by
434 experimentation, can become a hypothesis transferable to another discipline or another project
435 (Callon 1986). In this way, science studies and social epistemology has developed frameworks, e.g.,
436 theories of translation and regimes of promise (Joly 2015). For instance, for a result to be accepted
437 by the research community and reach a larger audience, it is not so much the proof of its effectiveness
438 for new discoveries in this field that is important (necessary, but not sufficient), but its credibility and
439 legitimacy. Three types of legitimacy are described: charismatic, tradition-based, and rational (Kim
440 2020). Credibility depends on factors such as the plausibility of the model in the scientific landscape,
441 the verification procedures or its pragmatic aspect (Blok & Jensen 2011). Note that this transferability
442 hypothesis can also be misused, as it is not impossible that a researcher, relying on his/her legitimacy
443 and credibility, extrapolates non-transferable results in other disciplines or projects.

444 Computational neuroscience could be thus analyzed as a network of social and political relationships.
445 Scientific controversy constitutes an important stage in the validation of a scientific object (Pestre
446 2006): a model will not necessarily prevail because it is close to reality, but because it is embedded
447 in a context and a scientific community (Latour 2005). Obtaining an experimental result would not
448 be enough to end scientific debates. On the contrary, such a result will be developed in a scientific
449 community during an acculturation to practices and a concrete use of this result, through the exchange
450 of arguments in the midst of controversies (Raynaud 2017). Consensus on a result would therefore
451 be more the result of controversy than of a formal explanation isolated from any context. Therefore,
452 in the scientific landscape, the contingency of discoveries depends on the acceptance of a
453 computational model in a given context, at a given time and for a given community.

454

455

456 **5. Conclusion**

457

458 Computational neurosciences are concerned with analyzing models, providing a hierarchy of
459 scientific concepts embedded in a scientific dynamic. A minimal typology of computational models
460 allows distinguishing between more realistic models (i.e., mechanistic models) and pragmatic models
461 (i.e., phenomenological models). A model is rarely (if ever) uniquely mechanistic or

462 phenomenological but has a part of each. When designing the model, or when using it, the cursor
463 should be placed to best answer a particular question. More precisely, the model must be optimized
464 for a specific function towards addressing this question.

465 Questions about idealization and scientific pluralism are related hot topics. Indeed, the passage from
466 one scale of description to another for a computational model requires discussing the interaction
467 between scales, a discussion that can be conducted through scientific pluralism. Pluralism proposes
468 to consider interdisciplinarity in computational neuroscience. Adopting a tolerant version of pluralism
469 leads to conceiving a hierarchy of the epistemic relevance of a discovery. This prioritization
470 necessarily involves unscientific factors, leads to a discussion of interdisciplinarity and involves
471 sociological aspects which condition the success of some computational models among many others.
472 Computational neurosciences, based on mathematics, seem to offer a common language to different
473 sciences and thus facilitate their empirical, conceptual and sociological interactions. However, the
474 presence of a theoretical framework guiding the construction of the models entails a path dependence
475 of these models, at the risk of biasing the statement necessarily oriented by this framework.

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477 GAULD Christophe: Writing, Original draft preparation, Conceptualization.

478 BRUN Cédric: Conceptualization, Methodology, Supervision.

479 BORAUD Thomas: Supervision, Reviewing, Validation.

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489 **Abbreviations**

490 AdEx: Adaptive Exponential integrate-and-fire

491 HH: Hodgkin-Huxley

492 LIF: Leaky Integrate and Fire

493 BBP: Blue Brain Project

494 TVB: The Virtual Brain

495 HBP: Human Brain Project

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