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ORIGINAL RESEARCH

Descriptive multiscale modeling in data-driven neuroscience

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Abstract
Multiscale modeling techniques have attracted increasing attention by philosophers of science, but the resulting discussions have almost exclusively focused on issues surrounding explanation (e.g., reduction and emergence). In this paper, I argue that besides explanation, multiscale techniques can serve important exploratory functions when scientists model systems whose organization at different scales is ill-understood. My account distinguishes explanatory and descriptive multiscale modeling based on which epistemic goal scientists aim to achieve when using multiscale techniques. In explanatory multiscale modeling, scientists use multiscale techniques to select information that is relevant to explain a particular type of behavior of the target system. In descriptive multiscale modeling scientists use multiscale techniques to explore lower-scale features which could be explanatorily relevant to many different types of behavior, and to determine which features of a target system an upper-scale data pattern could refer to. Using multiscale models from data-driven neuroscience as a case study, I argue that descriptive multiscale models have an exploratory function because they are a sources of potential explanations and serve as tools to reassess our conception of the target system.

Keywords Multiscale modeling · Explanation · Descriptive modeling · Neuroscience · Exploratory models

1 Introduction

In recent years, multiscale modeling techniques have attracted increasing attention by philosophers of the physical and the life sciences. Multiscale models tackle the

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so-called *tyranny of scales* (Batterman, 2013). Inactive materials like steel, but also active materials in biological systems display drastically different behaviors at different spatial, temporal or kinetic scales. These scale-dependent behaviors are governed by different physical principles (e.g., behaving liquid or solid-like) whose description requires mathematical models tailored to each scale. The scale-dependent behaviors also depend on each other, which is why researchers need a multiscale modeling schema to link scale-specific models together via top-down boundary conditions and bottom-up homogenization techniques. The goal of using these multiscale techniques is to select information from multiple scales that is relevant to explain a particular overall behavior of the system (e.g., the cracking of steel under macroscopic stress, Wilson 2017, ch. 5).

Multiscale models gain their explanatory power by referring to processes at non-fundamental scales. Hence philosophers of physics have largely discussed them with regard to issues of *explanation*, such as reduction and emergence (Batterman, 2013; Morrison, 2018). In biology, the success of multiscale models "offer[s] resistance to the idea that multi-scale systems can be modeled and explained "bottom up"" (Green & Batterman, 2017, p. 21). So far, the philosophical discussion of multiscale modeling focuses on its role in explaining the behavior of multiscale systems.

Although the explanatory role of models is widely acknowledged, several philosophers of science emphasize that models serve important roles besides explanation. Gelfert (2014, 2018) argues that *exploration* should stand alongside explanation (and prediction) as a genuine epistemic function of models. Like experiments, models serve exploratory functions when the target system is poorly understood, e.g., because no well-articulated theory is available to describe it. In these situations, exploratory models can serve as (i) a starting point for future inquiry (ii) a proof of principle, (iii) a source of potential explanations or (iv) a tool for reassessing the target system. In a similar vein, Ankeny (2000) has introduced the notion of a *descriptive model* to emphasize that biologists often generate descriptions of model organisms in a pre-explanatory context, but later use these descriptions in several different explanations of the behavior of these organisms. Because the literatures on exploratory/descriptive models and on multiscale models have not intersected so far, it is an open question if the latter also have exploratory and descriptive roles, alongside their role in explanation and prediction.

In this paper, I argue that besides explanation, researchers also use multiscale modeling to explore systems whose organization at different scales is ill-understood, and to describe the relationship between those scales. I distinguish between *explanatory* and *descriptive* multiscale modeling based on which epistemic goal scientists aim to achieve. In explanatory multiscale modeling, the overall behavior and the lower-scale behaviors of the system are sufficiently well-understood to explain the former in terms of the latter. Thus, researchers use multiscale modeling techniques to select scale-specific information that is relevant to the macroscale behavior being explained. In descriptive multiscale modeling, however, both the descriptive adequacy of upper-scale data patterns and the explanatory relevance of lower-scale information is partially or completely unknown. Researchers thus use multiscale techniques to (a) explore lower-scale features which could be explanatorily relevant

to many types of behavior of the target system, and to (b) determine which feature of a system the upper-scale data pattern could refer to.

By grounding the difference between explanatory and descriptive modeling in the goal-oriented use of multiscale techniques, my distinction is ecumenical with regard to different philosophical accounts of explanation. Here I only assume that explanatory models aim to identify information which is relevant to a particular type of behavior of the target system. This assumption should be acceptable regardless of whether multiscale models are explanatory because they identify multilevel mechanisms (Craver, 2007), dynamic principles (Chemero and Silberstein 2013) or universality classes (Batterman, 2019). As it happens, I do think that the multiscale models in neuroscience discussed in this paper fit a mechanistic account of explanation, but defending this point is not necessary to justify my account of descriptive multiscale modeling.[1] Rather I restrict my comments to the relation between my account and mechanistic accounts of *discovery* when discussing the exploratory role of descriptive multiscale models.

I support the distinction between explanatory and descriptive multiscale modeling by discussing models from the data-driven field of neuroscience called *connectomics*. Such models describe anatomical and functional brain organization based on connection patterns between neural entities and their activities at different spatial and temporal scales. Recently, connectomics researchers developed multiscale models to explore the relation between *cortical gradients*—systematic progressions of scale-specific features across the brain—and hierarchical information processing (Haueis, 2021). I argue that multiscale models of cortical gradients are descriptive because (a) they use multiscale techniques to explore which micro- and mesoscale features are relevant to hierarchical information processing and because (b) they use this lower-scale information to determine what features of brain organization macroscale data patterns could refer to. These descriptive models have exploratory functions because they are resources for potential explanations of many types of brain function, and because they help neuroscientists to reassess hierarchical organization at different scales.[2]

The paper proceeds as follows. In Sect. 2, I introduce explanatory multiscale modeling using the case of explaining cracking behavior in steel (Sect. 2.1). I then analyze an influential multiscale model in connectomics to argue that the goal of using multiscale techniques in connectomics is not explanatory (Sect. 2.2). This motivates the need for an account of descriptive multiscale modeling, which I develop in Sect. 3. I introduce the main characteristics of descriptive models, extend them to multiscale models (Sect. 3.1), and then analyse two descriptive multiscale models of cortical gradients (Sect. 3.2). I finally show why multiscale gradient models are sources for

[1] A mechanistic view of explanatory multiscale models in connectomics would emphasize the importance of network organization (Zednik, 2018) and use a notion of decomposition that accounts for context-sensitivity and dynamic interaction (Burnston, 2019).

[2] Serban (2020) equally argues for the exploratory function of network models in biology. My discussion complements Serban's analysis since she focuses on the exploratory function of providing novel concepts and proofs of principle, whereas I focus on descriptive models being sources of potential explanation and tools for reassessing the target system.

potential explanations and tools for reassessing the target system (Sect. 4). Section 5 concludes.

2 Explanatory multiscale modeling

2.1 Explanatory multiscale modeling: the case of steel cracking behavior

Many physical and biological systems are organized at multiple length scales. "Scale" can refer to spatial sizes, temporal rates or amounts of energy. Although scale dimensions are continuous, a multiscale model describes a system with a discrete number of scales because entities in the system exhibit different behaviors at characteristic length scales (Batterman, 2013; Bursten, 2016; Wilson, 2017). What is missing in the philosophical literature, however, is a principled answer as to when a change in spatial size, temporal rate or amounts of energy leads to a change in scale. I propose the following working definition which I think is implicit in the literature:

> *Different Scales*: Two entities e_1 and e_2 and their behaviors b_1 and b_2 of system S are at different scales s_1 and s_2 if and only if (1) e_1 and e_2 differ in spatial size, or b_1 and b_2 occur at different temporal rates or require different amounts of energy and (2) there are nonredundant and recognizable regularities about b_1 and b_2, respectively.

Condition (1) captures that spatial, temporal or kinetic differences are necessary for entities to show different scale-dependent behaviors b_1 and b_2. Condition (2) says that such differences suffice for scale changes when b_1 and b_2 display regular patterns that are epistemically recognizable and provide scientists with nonredundant information about the organization of the system (Kästner & Haueis, 2021).[3]

This minimal explication of the scale concept captures well how scientists model systems at multiple scales. Consider first the standard example of steel displaying different scale-dependent behaviors. Figure 1 shows that at the *macroscale* above 0.1mm, steel consists of homogenous hunks (e_1) which respond elastically to stress. Regularities about elastic behavior (b_1) are discernable via a Hookean continuum model describing resistance to change in volume (Young's modulus of elasticity) and amount of deformation under stress (shear modulus). At the intermediate *mesoscales* between 0.1mm and 0.001 μm, steel consists of inhomogeneous structures like dislocations (0.5 μm). Dislocations (e_2) differ from continuous steel hunks in spatial size, and regularities about dislocation line shifts (b_2) are discernable via laminate models which provide nonredundant information about steel stress responses. Finally, at spatial sizes below 0.001 μm, steel consists of a rigid lattice structure of carbon and

[3] The conditions can be strengthened by demanding that s_1 and s_2 differ by an order of magnitude (scale-separation, cf. Hillebrand 2015, p. 75), and that higher-scale regularities cannot be derived from lower-scale ones (a version of emergence). I do not rely on these assumptions here because it is unclear if scale separation holds for living systems (Batterman & Green, 2021) and because multiscale modeling does not imply that the modeled system displays emergent behavior (Morrison, 2018).

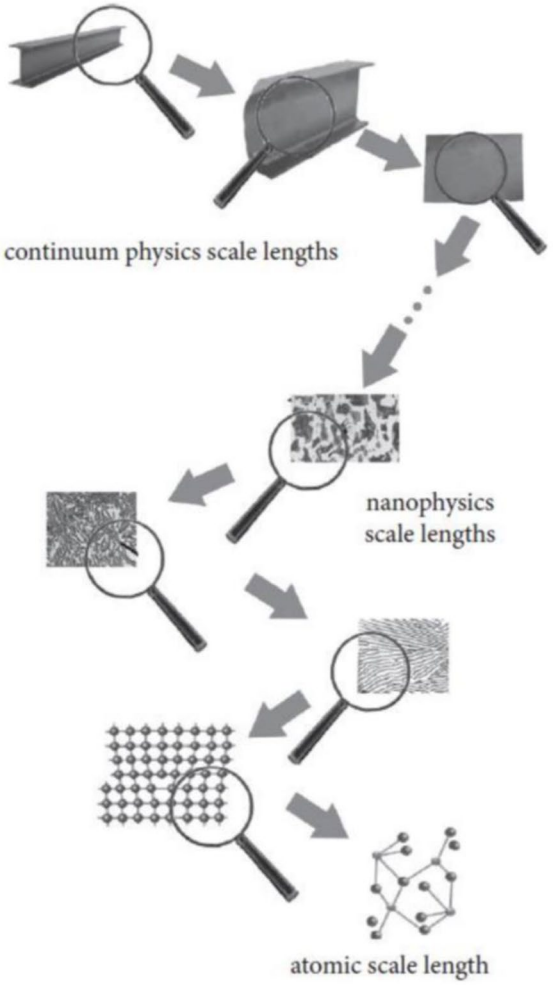

Fig. 1 The structure of steel at different spatial scales. Adapted from Batterman (2013)

iron atoms (e_3). Atoms exhibit regularities about ionic bonding strength (b_3) that are included in molecular models to determine when continuous stress turns steel brittle.

In explanatory multiscale modeling, scientists choose regular behaviors $b_1, \ldots b_n$ to delineate scales $s_1, \ldots s_n$ depending on the phenomenon they want to explain. In the steel case, regularities about elasticity, dislocation line shifts and ionic bonding strength affect how steel bars respond to stress, such as when a train moves across a railroad. Engineers need to know why railroad steel cracks under repeated stress. Answering this question allows them to predict under which circumstances cracking behavior occurs.[4] When steel cracks, it loses its capacity to respond elastically at

[4] Note that explanation and prediction can come apart. A model can be explanatory but lack predictive power, which happens when the phenomenon to be explained occurs stochastically and depends on background conditions not included in the model (Craver, 2007, p. 68). Conversely, a model can be highly

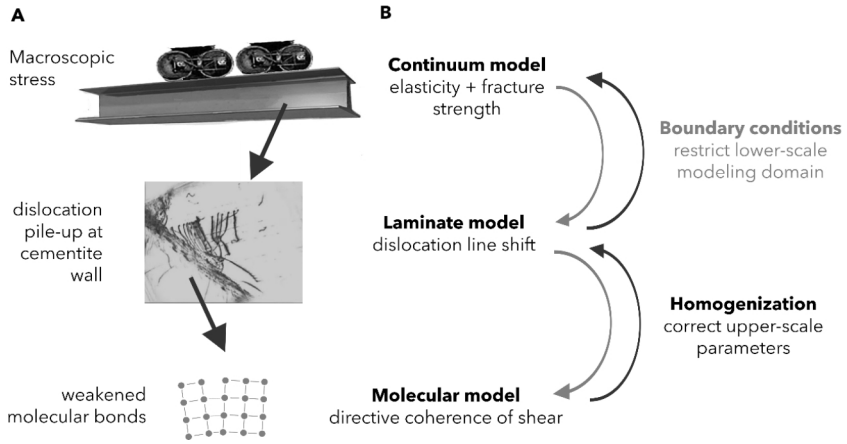

Fig. 2 **A.** Cracking behavior of steel multiple spatial scales. **B.** Multiscale modeling schema of cracking behavior. Based on Wilson (2017, pp. 222, 224)

the macroscale of homogenous continua. The capacity is lost because mesoscopic dislocations stop moving around freely and start piling up along larger cementite walls. When dislocation pile-up occurs, the molecular bonds are exposed directly to macroscale stress, which turns the steel bar brittle and eventually induces a crack. The cascade of effects is shown in Fig. 2a.

A multiscale modeling schema of cracking behavior (Fig. 2B) mimicks the cascade of effects when a steel bar is exposed to macroscale stress.[5] At the macroscale, we use a continuum model to calculate how locomotive weight affects Young's modulus of elasticity, shear modulus and the fracture strength of the entire steel bar. The calculation allows us to select steel regions where the applied weight causes the highest stress levels. We then switch to a laminate model of the preselected regions and calculate dislocation line shifts at the highest stress levels. In the next step we select all regions where dislocations pile-up at a cementite wall, and switch to a molecular model. At this scale, we calculate where shear stress is coherent enough to weaken or break molecular bonds in the lattice structure.

Each of these modeling steps is then repeated. The iteration is necessary in part because cracking behavior results from hysteresis, i.e. the loss of elastic responses depends the history of prior stresses. By iteratively correcting the results of each scale-specific submodel, "the computational architecture of a multiscalar modeling scheme can successfully ape the physical manner in which hysteresis effects slowly corrupt the properties of a macroscopic body" (Wilson, 2017, p. 224). In other words, the multiscale modeling schema can be used to explain why the steel bar cracks when

predictive but of little explanatory value because it does not quote factors on which the occurrence of the phenomenon depends (Craver, 2006, p. 358). By contrast, the multiscale model of steel predicts cracking behavior from factors without which cracking does not occur.

[5] I simplified the schema to illustrate core features of explanatory multiscale modeling (Wilson, 2017, p. 223 discusses further details).

it does because it reflects the causal processes at different scales which occur when the steel bar responds to stress imposed by a macroscopic object.

To explain why cracking occurs, scale-specific models must be linked together by the multiscale techniques of *boundary conditions* and *homogenization*. The techniques exploit physical information about how regular behaviors of entities at different scales affect each other. For example: dislocation pile-up only occurs under high stress levels. The laminate model incorporates this physical constraint in the form of a boundary condition, i.e. by "imposing limits on the domain of the model" (Green & Batterman, 2017, p. 21). The laminate model only calculates dislocation line shifts for those regions where dislocation pile-up most likely occurs. Similarly, molecular modeling only calculates directional coherence of shear in regions where pile-up occurs. Thus, in explanatory multiscale modeling, boundary conditions have the function to *restrict* the lower-scale modeling domain to regions where information relevant to the overall behavior most likely occurs.

To incorporate the lower-scale information during the iterative modeling process, researchers use the technique of homogenization. For example: researchers cannot incorporate information about dislocation pile-up into the continuum model directly because that model describes steel as a homogeneous continuum without dislocations. Homogenization overcomes this problem because it takes an asymptotic limit to describe the heterogenous mesoscale structure of steel as a fictitious homogenous material which exhibits the same behavior (Batterman & Green, 2021, p. 1169). The homogenized description allows researchers to correct the macroscale elasticity and fracture strength parameters in regions where dislocation pile-up occurs (Wilson, 2017, p. 224). Thus, the function of homogenization in explanatory multiscale models is to *correct* the upper-scale parameters using explanatorily relevant information from lower scales. The success of homogenization depends on achieving moment closure, i.e. finding a finite number of parameters which reasonably approximate the lower-scale behaviors which are homogenized. Although various mathematical approaches to closure have proved practically successful, their utility is limited to certain system configurations (Kuehn, 2016, p. 264).[6]

The steel case shows that in explanatory modeling contexts, the use of multiscale techniques is tailored to the particular behavior or phenomenon one tries to explain. Change the phenomenon and you change which length scales should be delineated, which behavioral regularities are relevant, how to restrict lower-scale models via boundary conditions, and how to correct upper-scale models via homogenized descriptions of lower-scale processes. These core features of explanatory multiscale modeling are equally found in the life sciences. Multiscale models of embryo development use boundary conditions to restrict the number of possible movements of embryonic tissue that need to be modeled (Green & Batterman, 2017, p. 24). Multiscale models of bone use homogenization to correct upper-scale parameters with lower-scale information that is relevant to explain bone fracture (Batterman & Green, 2021, p. 1179). Yet, not all uses of multiscale techniques have such an explanatory function.

[6] I thank an anonymous reviewer for drawing my attention to the limits of homogenization techniques.

2.2 Multiscale modeling in connectomics is not explanatory

To analyse multiscale models in connectomics, I use *Different Scales* to distinguish three scales of cortical organization. At the macroscale, the brain is organized into cortical areas which form networks via large-scale fiber pathways and via stable, recurring patterns of functional activity. These regular patterns of *structural connectivity* and *functional connectivity* (b_1) are discernable with different parameters of structural and functional magnetic resonance imaging—MRI and fMRI—respectively.

At the mesoscale, the brain is organized into *cortical circuits* (e_2) which consist of different inhibitory and excitatory *cell types*. Cell types occur in different layers of the cortex and are connected by stereotypic anatomical patterns. Cortical circuits are modeled in units of $1mm^3$ volume (Potjans and Diesmann 2014, Schmidt et al., 2018). At this scale, circuits exhibit regular, layer-specific oscillations (b_2) that provide nonredundant information about neural function and which are discernable via electrophysiological recordings and computational models (Bastos et al., 2015; Deco et al., 2013).

At the *microscale*, the brain consists of cellular and subcellular components. At this scale, the cortex differs in density of neuronal cells, their dendritic spines (parts where neurons receive excitatory and inhibitory inputs) and myelin (the insulating

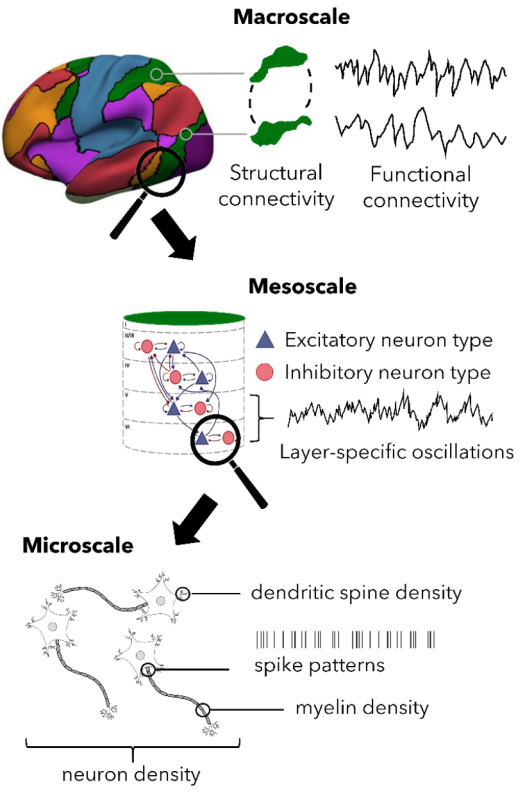

Fig. 3 Scales of brain organization in multiscale connectomic modeling. *Top*: parcellation of the brain into seven networks (visual, somatomotor, dorsal attention, salience, limbic, control and default mode network, adapted from Wang et al., 2019). *Middle*: canonical microcircuit model. (adapted from Beul & Hilgetag, 2015). *Bottom*: schematic drawing of neurons, Creative Commons CC0 1.0

layer around the axon). These properties determine regular spike patterns (b_3) of individual neurons which are discernable via singe-unit recording methods (Fellous et al., 2004). Figure 3 displays neural entities and their regular behaviors at each scale.

A multiscale modeling schema in connectomics attempts to describe the relationship between these different scale-dependent features of brain organization. In particular, multiscale models of cortical *gradients* describe how systematic progressions of network connectivity, circuit architecture and cellular/subcellular densities relate to each other (Sect. 3.2). These gradient models build on an influential multiscale model by Deco et al. (2013). I analyze this model now to show that multiscale techniques in connectomics do not serve an explanatory function.

A common assumption in connectomics is that structural connectivity patterns constrain the functional connectivity patterns observed with fMRI, but it is largely unknown how these macroscale patterns are related to mesoscale circuit dynamics and microscale spiking patterns. To investigate these relationships, Deco et al. developed the multiscale modeling schema shown in Fig. 4.

The microscale model in this schema is the *full spiking model*, which describes brain dynamics in terms of individual spiking neurons with three receptor types at the

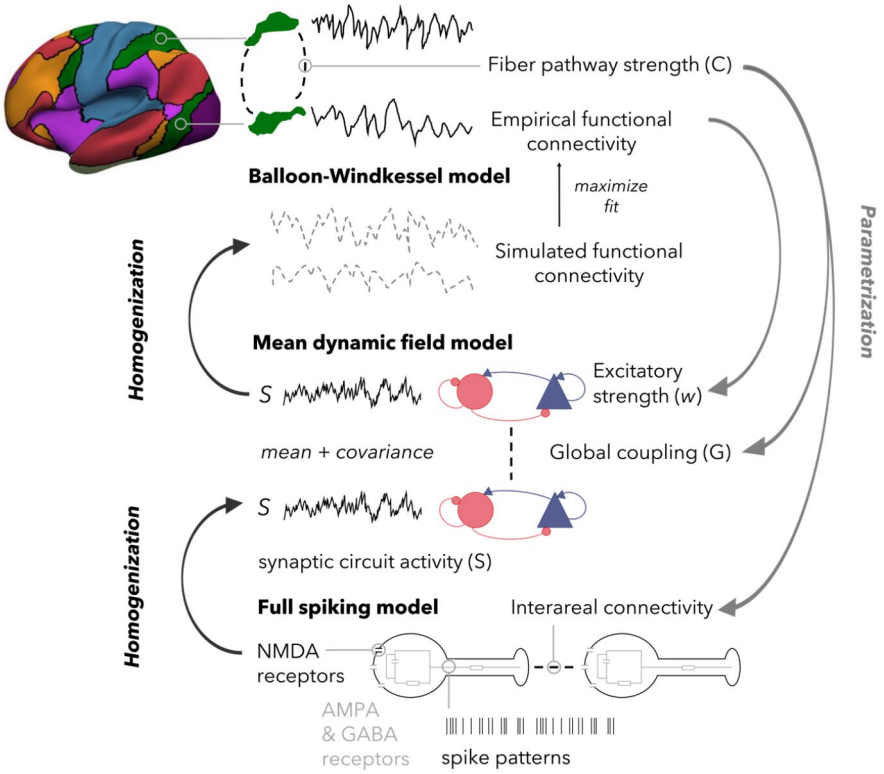

Fig. 4 Multiscale modeling schema developed by Deco et al. (2013). For explanation of model parameters, see text

synapse. The spiking model couples multiple integrate-and-fire model neurons (Fig. 4 bottom), which produce spiking patterns by integrating local excitatory (NMDA and AMPA) and inhibitory (GABA) synaptic inputs, long-range excitatory inputs and external inputs over time. Each cortical area is modeled as a network of recurrently connected integrate-and-fire neurons. To connect models of cortical areas together, the full spiking model uses values from the structural connectivity matrix *C*, which specifies strength of large-scale fibers between two areas derived from diffusion MRI measurements (Fig. 4 top, dotted lines). The *C* values thus provide macroscale constraints on microscale spiking behavior.

The full spiking model contains a large set of equations, which makes the use of macroscale constraints on neuronal spiking behavior across the entire brain computationally intractable. The *mean dynamic field model* overcomes this limitation (Fig. 4, middle). The model describes each cortical area in terms of mesoscale circuits with recurrently connected inhibitory and excitatory neuron populations (red circles and blue triangles in Fig. 4). Circuit activity is modeled by looking at two statistical moments: the *mean* of the synaptic gating variable *S* in each cortical area, and the *covariance* of *S* between two cortical areas.

By focusing on these statistical moments, Deco et al. homogenize full synaptic activity. Their homogenization assumes that circuit dynamics are dominated by the synaptic receptor with the longest timescale, which is the NMDA receptor in the full spiking model. This homogenization method achieves moment closure by considering first- and second-order moments only, which has previously been shown to reasonably approximate neuronal dynamics (Rodriguez and Tuckwell 1996). Such moment closure is only valid for certain system configurations—such as the resting state in the case of Deco et al.—and therefore cannot be assumed to hold equally in other system states such as task-induced activity patterns.

At the macroscale, Deco et al. constrain the mean dynamic field model by linking it to the *Balloon-Windkessel model*, which simulates macroscale functional connectivity patterns (Fig. 4, top). The main idea is that synaptic activity levels in each cortical area differ, causing different blood oxygenation levels that are observable as macroscale patterns in the fMRI signal. Deco et al. therefore use observed structural connectivity strengths (*C* values between 0 and 0.1) and functional connectivity patterns to *parametrize* two variables in the mean dynamic field model. The first is dimensionless parameter of recurrent excitatory strength *w* and the second is the global coupling factor *G*, which is a free control parameter. The connection strength between two areas is defined as the product of *C* and *G* values. The parametrized circuit model picks *w* and *G* values which maximize the statistical similarity between observed and simulated functional connectivity patterns across the brain. The multiscale modeling schema in Fig. 4 thus explicitly links microscale brain dynamics (via the homogenized *S* variable) to macroscale connectivity structure (via the parametrization of *w* and *G* with structural and functional connectivity patterns).

I contend that the function of parametrization in multiscale connectomic modeling is not explanatory. In explanatory contexts, top-down boundary conditions restrict the scope of the lower-scale modeling domain to regions where explanatorily relevant information is expected to occur (Sect. 2.1). But Deco et al.'s parametrization does not restrict the scope of mesoscale model to a specific set of cortical areas.

Instead, their parametrization picks *w* and *G* values which fit simulated to empirical functional connectivity patterns across the *entire* brain (Fig. 4, grey arrows). The reason for this use is that these researchers want to fit the mesoscale model to functional connectivity patterns recorded *at rest*, i.e. in the absence of external stimuli or particular task demands. Therefore, no restriction to cortical areas where task demands change functional connectivity patterns is necessary.

The same goes for Deco et al.'s use of homogenization (black arrows, Fig. 4). Homogenization techniques often use mean and covariance to *upscale* a lower-scale model because they describe how interacting lower-scale entities behave collectively. In explanatory multiscale modeling, such homogenizations allow researchers to explain how a collection of heterogeneous lower-scale behaviors contribute to macroscale behavior (Batterman, 2013). Because of their explanatory relevance, upscaled values are used to correct the values of the upper-scale model that were initially estimated (Wilson, 2017, ch. 5). Deco et al. also use mean and covariance of the *S* variable to upscale the microscale spiking model. And they also upscale *S* values by using the Balloon-Windkessel model to generate simulated functional connectivity patterns. But these simulated patterns are not used to correct upper-scale parameters. They are instead fitted to the empirical functional connectivity patterns by parametrizing the mesoscale parameters *w* and *G*. Rather than correcting upper-scale parameters with explanatorily relevant information, the use of mean and covariance allows researchers to "*explore* the parameter space of the [mesoscale] model" (Deco et al., 2013, p. 11247, emphasis added).

Based on the homogenized *S* values, Deco et al. discovered that the parametrized *G* and *w* values lie close to a critical point. At this point the low activity state of the brain (the 'resting state' of spontaneous activity present independently of specific tasks) becomes unstable and switches to higher activity states to a high activity state (e.g., a network state responding to task demands). Like parametrization, Deco et al. use homogenization to discover previously unknown relations between different scale-dependent features of brain organization. I claim that this is an *exploratory* use of multiscale techniques, which should stand alongside their explanatory function in the philosophical analysis of multiscale modeling.

One may object that even though this multiscale model does not explain any particular type of brain function or behavior of the organism, it nonetheless explains the dynamics of the observed functional connectivity patterns themselves. The full spiking model describes how the dynamic behavior of each area arises from the interaction of inhibitory and excitatory synaptic activity. Deco et al. link this behavior to functional connectivity patterns via multiscale techniques. The fact that the parametrized *G* and *w* lie close to a critical point illuminates the functional relevance of functional connectivity patterns:

> [W]orking at the edge of a critical point allows the system to rapidly compute a specific brain function by representing it in an attractor. This may be a fundamental reason why [functional connectivity patterns] reflect cognitive functions and why [they] are so interesting for basic and clinical neuroscience (Deco et al., 2013, p. 11,250).

I agree that discovering information about critical brain dynamics can be important to explain brain function. But discovering such information is nonetheless different than using such information to explain a particular type of function or behavior. This difference is reflected in the difference between exploratory and explanatory uses of multiscale techniques.

Suppose that researchers aim to show that critical dynamics explain how the brain switches from low to high activity states, e.g., from resting state to task-related functional connectivity patterns. These switches do not occur uniformly across the brain. The default mode network, for example, has higher activity levels at rest than during self- or goal-oriented tasks (Margulies et al., 2016). Researchers can incorporate this prior knowledge into multiscale modeling. They can use boundary conditions to restrict the scope of the mesoscale model to regions outside the default mode network. This allows them to search for circuits whose G and w values lie near the critical point where the brain switches from low to high activity states. Calculating the values for NMDA, AMPA and GABA receptor activity in those pre-selected circuits would then reveal which subcellular activities underlie critical brain dynamics. This information can be fed back to the macroscale model. It would help researchers to distinguish between parts of the observed functional connectivity patterns that are relevant to switching from task to rest, and parts which reflect other aspects of brain function, such as metabolic activity or homeostatic maintenance mechanisms (McCaffrey & Danks, 2017; Haueis, 2018).

The biophysical characteristics of the fMRI signal at rest are still too poorly understood, however, to determine exactly to which lower-scale behaviors functional connectivity patterns are related to, and what their exact functional relevance is. Thus Deco et al. use multiscale techniques to explore which lower-scale features of brain organization the upper-scale data patterns could be related to. This exploratory use of multiscale techniques is consistent with the discovery of explanatorily relevant information since exploratory models can function as sources for potential explanations (Sect. 4.1).

3 Descriptive multiscale modeling

3.1 From descriptive models to descriptive multiscale models in connectomics

The nonexplanatory function of multiscale techniques in connectomics is congenial to philosophical accounts which analyse *descriptive models* of brain organization (Ankeny, 2000, Haueis and Slaby 2017). Descriptive models are not constructed to test a particular theory or hypothesis of how the target system functions. Rather, they identify patterns (i.e. discernable regularities) that "can serve as the basis for further development of explanations and ultimately theories" (Ankeny, 2000, S269). Unlike explanatory models, which only include information that is relevant to a particular type of behavior, descriptive models describe patterns of system organization that are relevant to multiple types of behavior of the target system. I now extend this notion of descriptive models from mono- to multiscale models in connectomics.

To gather information relevant to many types of behavior, descriptive models formulate a *fundamental presupposition* about the overall organization of the target system. In connectomics, a fundamental presupposition specifies the relation between neural structure and function in a nervous system or a class of nervous systems. Information about the overall organization of a system will be relevant to any behavior whose explanation refers to this organization. For example: the fundamental presupposition of the descriptive model analyzed by Ankeny—the wiring diagram of the nematode worm *c.elegans*—is that the function of individual neurons is directly determined by their morphology (e.g. receptor density) and their synaptic structural connectivity. This presupposition us sometimes abbreviated as *structure determines function* (cf. Ankeny, 2000, S266). Information about synaptic structural connectivity patterns is relevant to explain multiple types of worm behaviors—e.g. how one set of neurons is active during egg-laying behavior, and how another set of neurons is active during touch-avoidance response. The wiring diagram thus describes patterns which researchers can use to explain different types of behavior of the target system. Note that fundamental presuppositions are revisable by further research. For example: further research showed that one cannot derive the derive inhibitory and excitatory nature of connections from the *c.elegans* wiring diagram, which let to the revised presupposition that that synaptic structural connectivity is necessary but insufficient to determine neuron function (Haueis and Slaby 2017, p. 155).

The explanatory pluripotency of descriptive models can be found both in anatomical and physiological models. Consider the mesoscale model of the *canonical microcircuit* in the mammalian neocortex (Fig. 3 middle). The model selects information about the physiology and connectivity of neuron types based on the fundamental presupposition that *form follows function* (Douglas & Martin, 1992). This presupposition emphasizes basic commonalities in the circuit mechanisms found across brain areas. Consequently, researchers can use the model to explain how circuit activity in particular areas contributes to specific types of cortical function. Each explanation typically adds further area-specific details to the model, e.g. temporal information about subcortical inputs to explain direction-selective processing in primary visual cortex (Haueis, 2018, Fig. 5) or structural connectivity information to explain eye-saccade behavior in the frontal eye field (Heinzle et al., 2007). These examples show how a fundamental presupposition helps descriptive modelers to select information about the overall organization that is relevant to many types of behavior of that system. Just as in the case of explanatory modeling, this type of modeling is used by researchers from various fields to explore the systems they study.[7]

In multiscale systems, many different features can realize the overall organization specified by a fundamental presupposition. Researchers thus use *scale-specific modeling assumptions* to link data types to scale-specific features that realize the overall organization specified by the fundamental presupposition (Haueis and Slaby 2017). For example: in the *c.elegans* wiring diagram, a scale-specific assumption is that electron microscope images reveal connection patterns that are invariant between individuals, and that occur between neuron types (Ankeny, 2000, S264). In

[7] An example from physics would be descriptive models of the hydrogen emission spectrum such as Balmer's formula, see Wilholt (2005), pp. 156–160 and Craver (2006), p. 358 for discussion.

the canonical microcircuit model, a scale-specific assumption is Peters' rule, which allows researchers to link reconstructions of individual cell morphologies and in-vivo physiological recordings to cell-type specific connectivity patterns (Potjans & Diesmann, 2014).

Like their single-scale counterparts, descriptive multiscale models use a fundamental presupposition and scale-specific assumptions. Consider again the multiscale model by Deco et al., (2013). Its fundamental presupposition is that "the relation between anatomical structure and functional [fMRI] correlations is strongly dependent on the local dynamics and the global dynamical state of the network" (Deco et al., 2013, p. 12,240). To implement this presupposition, Deco et al. use scale-specific assumptions to link structural and functional MRI data to parameters of the multiscale model (Fig. 4). First, they assume that the global dynamics are determined by connection strength C between two cortical areas, which is multiplied by the global coupling factor G. Second, they assume that the empirical functional connectivity patterns depend on local circuit activity, which is represented by the local excitatory strength w and the synaptic gating variable S. As pointed out above, fundamental presuppositions such as Deco et al.'s are revisable in light of further research into system organization that the descriptive model enables (see Sect. 3.2).

The descriptive character of multiscale connectomic models reveals the exploratory role of multiscale techniques in these models. In an exploratory context, the scale-specific assumptions which link data types and model parameters are preliminary, because the relation between discernable regularities at different scales is only poorly understood. The use of multiscale techniques helps researchers to justify these assumptions because they ensure that the parameter values of the multiscale model satisfy the fundamental presupposition.

For example: Deco et al. use homogenization and parametrization to justify that functional connectivity patterns depend on global and local brain dynamics. Consider first their use of homogenization. The synaptic gating variable S is a homogenized description of synaptic activity which is dominated by the receptor with the longest timescale (the NMDA receptor, Deco et al., 2013, p. 11,242). Furthermore, the simulated functional connectivity patterns generated with the Balloon-Windkessel model homogenize S, because "only gating variable correlations at slow time scales are transmitted through the [Balloon-Windkessel] model" (Deco et al., 2013, p. 11,246). This homogenization suggests that macroscale functional connectivity patterns in part reflect the slow dynamics of NMDA receptor activity (microscale) in cortical microcircuits (mesoscale).

I suggest that this exploratory use of homogenization helps *determine the reference* of upper-scale data patterns. Such reference determinations are tentative and revisable since in exploratory contexts, the relation between upper-scale data patterns and lower-scale features of the target system are only poorly understood. Nonetheless, homogenization at least temporarily fixes the reference of the upper- scale data patterns for the users of the model, just as operational definitions temporarily fix the reference of a scientific concept for its users (Feest, 2011, p. 403).

Consider now Deco et al.'s use of parametrization. The Balloon-Windkessel model alone can only simulate an fMRI time-course from S values of each region. It cannot couple these signals across brain regions. Thus parametrization is used to

set the *w* and *G* values to parameters which maximize the fit between simulated and empirical functional connectivity patterns. This suggests that besides NDMA receptor dynamics at long timescales, functional connectivity patterns also in part depend on the strength of recurrent excitatory connections *w* in cortical microcircuits, as well as dynamic processes reflected by the *G* parameter.

This link to lower-scale parameters is tentative. Further research can change which upper-scale data types should be used, or how exactly they should be used to parametrize a lower-scale model, and what the homogenized parameters themselves represent (Sect. 3.2). Yet the exploratory use of parametrization contributes to the overall aim of descriptive modelling: to discover patterns of organization that are relevant to many types of behavior of the target system. For example, Deco et al.'s parametrization reveals that *w* and *G* values lie near a critical point of two activity regimes. This information could be relevant to many types of cognitive or behavioral tasks where the brain switches from low to high activity states, e.g. allocating attention, response inhibition, working memory or mental rotation Shine & Poldrack, 2017; Burnston & Haueis, 2021, p. 136f.).

Abstracting from the details of the case, Table 1 describes the general characteristics of descriptive multiscale models, and how they contrast with explanatory multiscale models. Rather than defining two nonoverlapping sets of models, these characteristics systematize the pragmatic difference between two types of modeling activity. Whether a multiscale modeling schema is descriptive or explanatory

Table 1 Different types of multiscale models

	Descriptive multiscale modeling	Explanatory multiscale modeling
Aim of multiscale modeling	Discovery of patterns that could be relevant to different types of behaviors of the target system	Explanation of a particular type of behavior of the target system
Feature determination	Fundamental presupposition specifies overall organization of target system	Macroscale behavior determines explanatorily relevant regularities of the system
Utility of scale-specific models	Scale-specific modeling assumptions link data types to features realizing the overall organization	Scale-specific mathematical equations to model regular behaviors at each scale
Utility of upper-scale information	Upper-scale values are used to parametrize a lower-scale model across entire domain and justify scale-specific assumptions	Upper-scale boundary conditions are used to restrict lower-scale model domain
Utility of lower-scale information	Lower-scale information is homogenized to determine the referent of upper-scale data types	Lower-scale information is homogenized to explain upper-scale behavior

depends on whether researchers aim to explore patterns that could be relevant to many types of behavior, or whether they aim to explain one particular type of behavior exhibited by the target system. That behavior determines which scale-dependent regularities the explanatory multiscale model will describe.

In explanatory contexts, the relations between scale-dependent regular behaviors are sufficiently well understood such that each can be modeled mathematically by a theoretical model. Each model can be connected by boundary conditions and homogenization to restrict the model domain and select lower-scale information that is explanatorily relevant to the upper-scale behavior. In exploratory contexts, the relevance of scale-dependent regularities and their relations is only poorly understood. Consequently, homogenization and parametrization are used to temporarily fix the reference of upper-scale data parameters to scale-specific features. Here, the focus is on features which realize the overall organization specified by the fundamental presupposition of the descriptive multiscale model.

3.2 Descriptive multiscale models of cortical gradients

The above account of descriptive multiscale modeling illuminates how connectomics researchers to explore the organization of *cortical gradients* across multiple scales (see Haueis 2021 for a detailed analysis). Here I focus specifically on the models of Wang et al., (2019) and Demirtaş et al., (2019) to support my claim that descriptive modelers use multiscale techniques to explore relations between scale-dependent patterns which are poorly understood.

Cortical gradients are systematic progressions of scale-specific features of brain organization across the entire cortex (Fig. 3). At the microscale, neuronal and myelin density is highest in primary sensory areas (e.g., primary visual or auditory cortex) and decreases systematically to lowest values in so-called "association areas" (e.g., areas in the default mode network or the frontoparietal control network). By contrast, dendritic spine density increases systematically from primary sensory to areas in the prefrontal cortex (Elston, 2003). At the mesoscale, connections between excitatory and inhibitory neuron types vary systematically between cortical areas (Beul & Hilgetag, 2015). At the macroscale, connectomics researchers recently discovered a *principal gradient* of functional connectivity—i.e. the axis of greatest variance in functional connectivity runs from primary sensory areas via attention networks to regions of the default mode network (Margulies et al., 2016).

Descriptive multiscale models of gradients pick these scale-specific features based on the fundamental presupposition that cortical gradients are related to a *hierarchy of information processing* in the brain. The basic idea is that an anatomical hierarchy of feedforward and feedback connections underlies a processing hierarchy of input/output relationships (Felleman and Van Essen 1991). Along the hierarchy, unimodal sensory representations are subsequently elaborated into more categorical and rule-based ones, integrating different types of information. This view of hierarchy is *representational* because different hierarchical levels are individuated by the *degree of abstraction* in representational content processed by cortical areas at that level (Burnston & Haueis, 2021). Different scale-specific gradient measures are assumed to relate to different aspects of the representational hierarchy, but they are commonly

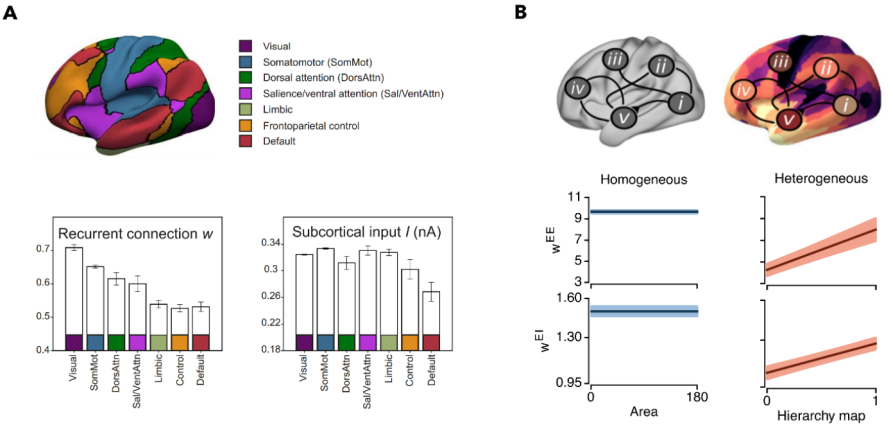

Fig. 5 Two parametrizations for multiscale modeling of cortical gradients. **A***Top*: Same macroscale network parcellation as shown in Figs. 3 and 4. *Bottom*: Parametrization results in high *w* values in sensory and low values in association areas; *I* values show the inverse pattern. Adapted from Wang et al., (2019, Fig. 2). **B.** Same network parcellation as in Wang et al., (2019) plus auditory network, five circled regions are shown to illustrate circuit differences across the brain. *Left*: A homogenous parametrization assigns uniform parameter values (y-axis) across 180 brain areas (x-axis) *Right*: A heterogenous parametrization based on MRI contrast values across the brain (x-axis) assigns low *w* values to primary sensory areas (dark colors in the brain map) and high values in association areas (bright colors). Adapted from Demirtaş et al., (2019, Figs. 1 and 2)

assumed to measure one and the same gradient of hierarchical information processing from primary sensory areas to association areas. This pattern of overall brain organization can be used to explain many types of neural function, such as information processing in sensory systems (Burnston & Haueis, 2021), or why the default mode network is more active in self-oriented than in goal-oriented tasks. (Margulies et al., 2016).

To explore the relation between scale-specific gradients and hierarchical brain organization further, Wang et al., (2019) and Demirtaş et al., (2019) both developed modified versions of the multiscale modeling schema by Deco et al., (2013). The original schema assumes that mesoscale circuit architecture is homogeneous across the cortex (Fig. 4). Thus, Deco et al.'s parametrization chooses one *w* value and one *G* value for the mean dynamic field model to maximize the fit between simulated and empirical functional connectivity. By contrast, the modified schemas systematically vary circuit features across the cortex. Thus, the parametrizations choose different mesoscale parameter values for different regions of the brain. Wang et al.'s parametrization chooses heterogenous values for the recurrent connection strength *w* and the subcortical input *I*, whereas Demirtaş et al. leave *I* constant but split *w* into recurrent excitatory connections w^{EE} and excitatory-to-inhibitory connections w^{EI}. The resulting gradients in mesoscale circuit parameters are shown in Fig. 5.

Both multiscale models in Fig. 5 associate the gradient in *w* and *I* values with a representional hierarchy running from primary sensory to association areas. Surprisingly, however, the two parametrizations produce *opposing* trends for the *w* values: in

Demirtaş et al., (2019), both w^{EE} and w^{EI} values *increase* along the hierarchy, whereas in Wang et al., (2019), w values *decrease* from primary sensory to association areas.

It is unlikely that this discrepancy stems from one model being a poorer empirical fit to the data than the other. The parametrized values of both models correlate highly with several empirical measures of cortical gradients: MRI contrasts which indirectly measure differences in myelin density (so-called T_{1w}/T_{2w} maps, Wang et al., 2019, Fig. 4D, Demirtaş et al., 2019 Fig. 1E); estimates of neuronal density (Wang et al., 2019, Fig. 5) and dendritic spine density (Demirtaş et al., 2019, p. 10). Additionally, both models outperform the Deco et al., (2013) in terms of goodness of fit between simulated and empirical functional connectivity patterns. They also produce better correlations between functional and structural connectivity data. This increased fit is a robust result since Demirtas and Wang et al. use optimization procedures with different assumptions (hierarchical Monte Carlo versus dynamic causal modeling).[8]

I think that rather than reflecting poor empirical fit or being a methodological artefact, the discrepancy in *w* values arises from an *epistemic uncertainty* about the referent of upper-scale data patterns. Because it is partially unknown to which lower-scale features the upper-scale pattern is related, several parametrizations are plausible for a given descriptive multiscale model. Subtle differences between the Demirtaş and Wang parametrization justify different scale-specific assumptions that link macroscale data to meso- and microscale features of cortical organization. Demirtaş et al. parametrize w^{EE} and w^{EI} values with values from a hierarchical heterogeneity map (Fig. 5B upper right). The heterogeneity map is a conversion of the T_{1w}/T_{2w} map generated from MRI data. This parametrization justifies the assumption that increasing *w* values are linked to increases in *dendritic spine density* along the cortical hierarchy. Recent cross-species comparisons suggest that low $T1_w/T2_w$ values in human association cortex provide a homogenized description of increased dendritic spine density of excitatory neurons (Burt et al., 2018). The Demirtaş parametrization further justifies this proposal because high *w* values in association areas imply that neurons with more dendritic spines are able to receive an increased number of excitatory inputs.

In contrast to Demirtaş et al., Wang et al. parametrize *w* and *I* values directly with fMRI data and nowhere mention dendritic spine density to justify different *w* values. Instead, their parametrization justifies the scale-specific assumption that the principal gradient of functional connectivity reflects different *degrees of abstraction* along the representational hierarchy. First, high *I* and *w* values provide further justification of placing primary sensory areas at the 'concrete' end of the gradient of abstraction (Margulies et al., 2016). Circuits in primary sensory areas must quickly represent changes in the sensory environment. Strong subcortical inputs from the sensory periphery and strong connections for local processing support this functional role. Second, high *I* values but lower *w* values justify placing attentional networks in the middle of the gradient. Strong subcortical inputs support the representation of attentional targets because the allocation of attention depends on stimuli from the

[8] One might worry that these researchers are overfitting their model to spurious features of the particular dataset, which decreases descriptive power of both descriptive and explanatory models in neuroimaging. Wang et al., (2019, p. 8) acknowledge this limitation and Demirtaş et al., (2019, e9) run various tests to rule out overfitting.

environment (Wang et al., 2019, p. 8). Finally, low *I* values justify that the default mode and control networks are situated at the 'abstract' end of the gradient. Weak peripheral inputs imply "the lack of a direct flow of information from the external milieu" in these networks" (Wang et al., 2019, p. 7), whereas weak recurrent connections support their role in integrating information from many different systems.

The lesson to be drawn from this case study is that because descriptive modeling operates under considerable uncertainty, we should expect that scientists put forward multiple different proposals of how scale-dependent patterns are related. Given the sparse knowledge about interscalar relations, these proposals are often equally plausible (or implausible) at a given stage of research. One reason for this uncertainty is that upper-scale data patterns can be related to multiple different lower-scale features, or combinations of such features. In the connectomics case, functional connectivity fMRI patterns and $T1_w/T2_w$ maps are related to mesoscale circuit features such as recurrent connections, subcortical input, or microscale features such as dendritic spine density or myelin density.

Multiscale methods can reduce this uncertainty, because they temporarily fix the reference of the data patterns to certain features. Multiscale techniques also justify scale-specific assumptions about why certain features realize the fundamental presupposition of the descriptive model. In the case of cortical gradients, the relationship between different scale-specific features of hierarchical organization remains poorly understood. At this stage of research, the parametrizations of Wang et al. and Demirtaş et al. are both plausible because they temporarily fix the reference of mesoscale parameters to micro- and macroscale features which realize the hierarchical organization of the brain.

4 Exploratory functions of descriptive multiscale models

4.1 Descriptive multiscale models as sources of potential explanation

While descriptive multiscale modeling primarily aims to explore system organization at multiple scales, it also has an important relation to explanatory modeling. According to Gelfert (2014), one important exploratory function of models is that "they help us devise *potential explanations*, for example by envisaging scenarios that, if true, would give rise to the kinds of phenomena that constitute the explanandum" (Gelfert, 2014, p. 87). In exploratory models from physics, chemistry and biology, such potential explanations commonly—although certainly not exclusively—describe *possible mechanisms* which could produce the behavior of the target system (Gelfert, 2014, p. 89, p. 92; 2018, p. 258). How do descriptive multiscale models fulfil this exploratory role of being sources for potential explanation?

The idea that descriptive multiscale models describe possible mechanisms fits well with mechanistic accounts of discovery in the life sciences. According to such accounts, researchers use different epistemic activities such as experimentation or modeling to isolate patterns in the behavior of the target system from noise and background conditions, and to search for entities and activities at multiple scales to explain why these patterns occur (Kästner & Haueis, 2021). During discovery,

researchers put forward several potential explanations by describing how entities and activities at different scales might be organized such that the target system produces the pattern. According to mechanistic accounts, the exploratory function of models lies in constructing a space of possible mechanisms which can be explored by further experimentation and modeling (Craver, 2007, p. 112).

The multiscale modeling of cortical gradients fits this account insofar as Wang et al., (2019) and Demirtaş et al., (2019) describe possible mechanisms which could produce patterns of hierarchical brain organization. For example, Wang et al. describe possible circuit mechanisms which could explain why networks along the principal gradient represent information with different degrees of abstraction (Margulies et al., 2016). They argue that strong subcortical input and strong recurrent connections could explain why circuits in primary sensory areas represent simple features of external stimuli and are specialized in the local processing of sensory information. They also say that weak subcortical input and weak recurrent connections could explain why circuits in the default mode and control networks process self-related information that is removed from stimuli in the environment and integrate information from many different neural systems.

By contrast, Demirtaş et al., (2019) describe possible circuit mechanisms which could explain why the temporal duration at which networks integrate information increases along the cortical hierarchy (Chaudhuri et al. 2015). Their model suggests that low excitatory strength in primary sensory areas stems from the lower density of dendritic spines. This finding could explain why circuits in these areas are excited for shorter periods of time because their neurons can sum over fewer excitatory synaptic inputs. By contrast, the model relates high excitatory strengths in prefrontal areas to higher dendritic spine density. This finding could explain why circuits higher up in the hierarchy are active over longer timescales since their neurons can sum over many different synaptic inputs.

We can see here how these multiscale models construct a space of possible mechanisms which could explain patterns of hierarchical brain organization. Through parametrization and homogenization techniques, both models are constrained by empirical information from multiple scales. And while many model parameters (e.g., w and I and C parameters) can be physiologically interpreted, others represent filler terms (such as the global coupling factor G) to model neural entities and activities whose structure and function remains poorly understood. The fact that researchers can construct equally plausible but yet opposing parametrizations suggests that their models describe different possible mechanisms which could explain hierarchical patterns of organization.

This mapping of the exploratory function of multiscale connectomic models to mechanistic accounts certainly captures neuroscientists' intentions to "discover the mechanisms underlying the experimentally observed resting global brain dynamics" (Deco et al., 2013, p. 11244). But the mapping does not capture that descriptive multiscale models contain information relevant to multiple types of behavior of the target system. According to mechanistic accounts, multiscale models of mechanisms are always models *of* a particular phenomenon (Craver, 2006, p. 368). This requirement does not accommodate descriptive models because they do not select information based on its explanatory relevance to a particular type of behavior of the target sys-

tem. Descriptions of wiring diagrams, canonical microcircuits or cortical gradients do not explain any particular brain function or behavior of the organism. Yet these models are clearly more than mere data summaries. They describe patterns which can be used in multiple different explanations.

For example: Wang et al. do not provide one, but three different potential explanations for how mesoscale circuit parameters could explain (i) how sensory networks represent external stimuli, (ii) how attention networks represent attentional targets, and (iii) how the default mode network represents self-related information (e.g., autobiographical memory). The fact that all three explanations mention 'representation' reflects that the model picks scale-specific features which realize fundamental presupposition of representational hierarchy. Similar points hold for Demirtas et al.'s use of dendritic spine density values to explain of different integration times along the cortical hierarchy. Mechanistic accounts rightfully stress that during scientific inquiry, researchers often provide multiple how-possibly models of the same mechanism. My account of descriptive multiscale modeling additionally highlights that scientists often use the same descriptive model in multiple (mechanistic) explanations. This insight suggests that descriptive models are not mere precursors of what will once be full-fledged explanatory models. They rather serve as stable repositories of information which exist alongside a multiplicity of explanatory models drawing on them.

4.2 Descriptive multiscale models as tools for reassessing the target system

Besides being usable in many different explanations, a descriptive multiscale model can also provide researchers with a better understanding of what target system the model actually describes. Gelfert (2014) argues that this exploratory function is important in early stages of inquiry when there is no well-defined theory under which the model of the target system can be subsumed:

> In order to delineate a target phenomenon and converge upon a set of relevant properties and relations (which may subsequently come to define the target system or phenomenon), we must operate with some preconception of which factors are significant or salient […]. At an early stage of inquiry, before the stability of the target phenomenon has been ascertained, our conception of the target phenomenon will necessarily be subject to revision (Gelfert, 2014, p. 93).

One example of reassessing the target system is Turing's exploratory model of biological pattern formation (Gelfert, 2018). Turing's model fell initially out of fashion in developmental biology because his choice of biological examples were not good target systems in which patterns are formed by local activation and long-range inhibition. But it nevertheless inspired subsequent experimental and theoretical research, which eventually did point out that this mechanism plays an important role for understanding how biological patterns form during biological development. This example illustrates a historical process in which a model "can go out of fashion and subsequently rebound" (Gelfert, 2014, p. 266) because researchers have revised their conception of the target system.

The case of multiscale gradient models supports Gelfert's analysis of this exploratory role, but additionally points out that reassessing the target system remains

important beyond the early stages of inquiry (Colaço, 2020). Like the Turing model, the discovery of the principal gradient of functional connectivity (Margulies et al., 2016) has reignited interest in the so-called *structural model*. This model is a "classical and hitherto largely overlooked theoretical framework" which posits that "the built-in architecture of the cortex varies systematically along the cortical landscape" (García-Cabezas et al., 2019, p. 1). This insight was already known to neuroanatomists in the 1960s but remained largely forgotten, as researchers meanwhile focused on the anatomical organization of individual areas and studied their contribution to cognitive functions in task-based neuroimaging experiments. Through the ascent of novel connectomics methods, researchers have realized that these areas are not only organized into large-scale networks, but also that these networks can be characterized by multiple scale-dependent features which change systematically across the cortex (Figs. 4 and 5). It is for this reason that the structural model has rebounded and is now part of several multiscale models of cortical gradients (Schmidt et al., 2018; Paquola et al., 2019; Wang et al., 2019).

These multiscale models go beyond the original structural model by connecting the gradient concept to hierarchical brain organization. A common assumption in these models is that there is only one gradient of hierarchical information processing, which runs from unimodal sensory to association areas. Gradients of scale-dependent features are related to different aspects of hierarchical information processing: microscale gradients of dendritic spine density relate to increased integration time across the representational hierarchy (Chaudhuri et al. 2015). Macroscale gradients of functional connectivity are related to differences in degree of abstraction (Margulies et al., 2016), while microscale gradients of neuronal density are related to increases in flexible changes to momentary task demands (Paquola et al., 2019). Importantly, the exploratory use of multiscale techniques shows that mesoscale features such as recurrent excitation strength vary along the representational hierarchy (Wang et al., 2019; Demirtaş et al., 2019). There is evidence that this gradient in circuit architecture runs from granular areas, which have a highly differentiated granular layer 4, to agranular areas which lack layer 4 altogether (Beul & Hilgetag, 2015).

It is this extension of the gradient concept to the mesoscale which could revise the assumption that that the cortex exhibits only one hierarchical gradient with a uniform spatial end-points. It is possible that the scale-dependent features do not cohere into one spatially uniform hierarchical gradient, but rather terminate in different endpoints of the cortex (Haueis, 2021). If Margulies et al. (2016) and Wang et al., (2019) are right, then the degree of abstraction could be highest in transmodal areas of association cortex such as the default mode network. By contrast, the best available anatomical evidence suggests that dendritic spine densities are highest in parts of the prefrontal cortex outside the default mode network (Elston, 2003). Therefore, integration time may be longest in areas which do not have the highest degrees of abstraction.

Additionally, the mesoscale granular-to-agranular gradient terminates in paralimbic areas of the cortex, which show an increased presence of molecules which enhance synaptic plasticity mechanisms. According to the structural model, these mechanisms enhance the capacity to switch information processing flexibly according to momentary task demands. This suggests that the capacity for flexible information processing

may reach peak levels in paralimbic areas. But these areas process visceral, gustatory and olfactory inputs, and thus do not represent information with the highest degree of abstraction (Haueis, 2021).

If this divergence of the endpoints of scale-dependent gradient descriptions can be confirmed by further studies, then multiscale descriptive modeling could revise our understanding of the brain as a hierarchical system. While Gelfert's description of this exploratory role uses 'target system' and 'phenomenon' interchangeably, I think is it is better to distinguish these notions in the context of descriptive modeling. If we revise our conception of the brain as a hierarchical system, we need to also revise our characterization of *multiple* phenomena which can be explained using descriptive models of hierarchical organization.

Moreover, the multiscale modeling of hierarchical gradients reveals that the exploratory reassessment of target systems proceeds beyond the early stages of inquiry. The concept of hierarchy is one of the most well-known and established organizational principles in systems neuroscience. Yet, the concept has recently evolved due to new methods being used to study brain networks (Burnston & Haueis, 2021). Together with the gradient concept, these advances have allowed neuroscientists to explore different senses in which the brain can be described as a hierarchical system, and whose relations to each other we are just beginning to understand (Hilgetag & Goulas, 2020). The case study of multiscale gradient models suggests that the use of multiscale techniques is one important tool by which scientists continue to improve their understanding of the target system. Descriptive multiscale modeling can thus function as a tool for reassessing the target system beyond the early stages of inquiry.

5 Conclusions

This paper introduced the notion of a descriptive multiscale model to highlight that the exploratory function of multiscale modeling should stand alongside its role in explanation. I illustrated the exploratory role of such models by discussing examples of descriptive models in data-driven neuroscience, specifically connectomic models of cortical gradients. These models do not aim to select information that is relevant to one type of behavior of the target system. Rather, researchers use multiscale techniques to describe scale-dependent patterns to better understand the relation between upper-scale data patterns and lower-scale features which realize an overall organization of the target system. Because that organization is relevant to many types of behaviors, information in descriptive multiscale models can be used in many different explanations.

Because of this explanatory pluripotency, descriptive multiscale models should not be seen as mere precursors to how-actually models of a target behavior. They rather act as repositories of information that can be used in all explanations which reference the overall organization of the target system specified in the fundamental presupposition of a particular descriptive model. Besides being a source of potential explanation, descriptive multiscale models can serve as tools to reassess the target system. In the case of cortical gradients the existence of scale-specific gradients could revise our conception that the representational hierarchy has one unique end-

point in the cortex. While it is too early to tell how this revision will pan out, the case of cortical gradients highlights that exploratory uses of multiscale modeling are an integral feature of scientific practice. An adequate philosophical understanding of multiscale models should account for the specifics of exploratory uses rather than simply assimilate them to explanatory modeling.

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References

Ankeny, R. A. (2000). Fashioning Descriptive Models in Biology: Of Worms and Wiring Diagrams. *Philosophy of Science*, 67, S260–S272. https://doi.org/10.1086/392824

Bastos, A. M., Vezoli, J., Bosman, C. A., Schoffelen, J. M., Oostenveld, R., Dowdall, J. R., et al. (2015). Visual Areas exert Feedforward and Feedback Influences through Distinct Frequency channels. *Neuron*, 85, 390–401. https://doi.org/10.1016/j.neuron.2014.12.018

Batterman, R. W. (2013). The Tyranny of Scales. In R. Batterman (Ed.), *The Oxford Handbook of Philosophy of Physics* (pp. 255–286). Oxford: Oxford University Press

Batterman, R. W. (2019). Universality and RG Explanations. *Perspectives on Science*, 27, 26–47. https://doi.org/10.1162/posc_a_00298

Batterman, R., & Green, S. (2021). Steel and Bone. Mesoscale Modeling and Middle-Out Strategies in Physics and Biology. *Synthese 199*, 1159–1184. https://doi.org/10.1007/s11229-020-02769-y

Beul, S. F., & Hilgetag, C. C. (2015). Towards a "Canonical" Agranular Cortical Microcircuit. *Frontiers in Neuroanatomy*, 8, 165. https://doi.org/10.3389/fnana.2014.00165

Bursten, J. R. (2016). Smaller than a Breadbox: Scale and Natural Kinds. *The British Journal for the Philosophy of Science*, 81, axw022. https://doi.org/10.1093/bjps/axw022

Burnston, D. (2019). Getting over Atomism: Functional decomposition in complex neural systems. *The British Journal of Philosophy of Science*. https://doi.org/10.1093/bjps/axz039

Burnston, D., & Haueis, P. (2021). Evolving Concepts of "Hierarchy" in Systems Neuroscience. In M. Viola, & F. Calzavarini (Eds.), *Neural Mechanisms: New Challenges in the Philosophy of Neuroscience* (pp. 113–141). Cham: Springer. https://doi.org/10.1007/978-3-030-54092-0_6

Burt, J. B., Demirtaş, M., Eckner, W. J., Navejar, N. M., Ji, J. L., Martin, W. J., et al. (2018). Hierarchy of Transcriptomic Specialization across Human Cortex captured by Structural Neuroimaging Topography. *Nature Neuroscience*, 21, 1251–1259. https://doi.org/10.1038/s41593-018-0195-0

Chaudhuri, R., Knoblauch, K., Gariel, M. A., Kennedy, H., & Wang, X. J. (2015). A Large-Scale Circuit Mechanism for Hierarchical Dynamical Processing in the Primate Cortex. *Neuron*, 88(2), 419–431. https://doi.org/10.1016/j.neuron.2015.09.008

Colaço, D. (2020). Recharacterizing Scientific Phenomena. *European Journal for Philosophy of Science*, 10, 735. https://doi.org/10.1007/s13194-020-0279-z

Craver, C. F. (2006). When Mechanistic Models Explain. *Synthese*, 153, 355–376. https://doi.org/10.1007/s11229-006-9097-x

Craver, C. F. (2007). *Explaining the Brain. Mechanisms and the Mosaic Unity of Neuroscience*. Oxford: Oxford University Press

Deco, G., Ponce-Alvarez, A., Mantini, D., Romani, G. L., Hagmann, P., & Corbetta, M. (2013). Resting-state Functional Connectivity Emerges from Structurally and Dynamically Shaped Slow Linear Fluctuations. *Journal of Neuroscience*, 33, 11239–11252. https://doi.org/10.1523/JNEUROSCI.1091-13.2013

Demirtaş, M., Burt, J. B., Helmer, M., Ji, J. L., Adkinson, B. D., Glasser, M. F., et al. (2019). Hierarchical Heterogeneity across Human Cortex Shapes Large-Scale Neural Dynamics. *Neuron*, 101, 1181–1194e13. https://doi.org/10.1016/j.neuron.2019.01.017

Douglas, R. D., & Martin, K. A. (1992). In Search of the Canonical Microcircuits of Neocortex. In R. Lent (Ed.), *The Visual System From Genesis to Maturity* (pp. 213–232). New York: Springer

Elston, G. N. (2003). Cortex, Cognition and the Cell: New Insights into the Pyramidal Neuron and Prefrontal Function. *Cerebral Cortex*, 13, 1124–1138. https://doi.org/10.1093/cercor/bhg093

Feest, U. (2011). Remembering (Short-Term) Memory: Oscillations of an Epistemic Thing. *Erkenntnis 75*(3), 391–411. https://doi.org/10.1007/s10670-011-9341-8

Felleman, D. J., & van Essen, D. C. (1991). Distributed Hierarchical Processing in the Primate Cerebral Cortex. *Cerebral Cortex*, 1, 1–47. https://doi.org/10.1093/cercor/1.1.1

Fellous, J. M., Tiesinga, P. H. E., Thomas, P. J., & Sejnowski, T. J. (2004). Discovering Spike Patterns in Neuronal Responses. *Journal of Neuroscience*, 24, 2989–3001. https://doi.org/10.1523/JNEUROSCI.4649-03.2004

García-Cabezas, M., Zikopoulos, B., & Barbas, H. (2019). The Structural Model: A Theory Linking Connections, Plasticity, Pathology, Development, and Evolution of the Cortex. *Brain Structure and Function*, 224(3), 985–1008. https://doi.org/10.1007/s00429-019-01841-9

Gelfert, A. (2014). *How to Do Science with Models*. Cham: Springer

Gelfert, A. (2018). Models in Search of Targets: Exploratory Modelling and the Case of Turing Patterns. In A. Christian, D. Hommen, N. Retzlaff, & G. Schurz (Eds.), *Philosophy of Science: European Studies in Philosophy of Science 9* (pp. 245–269). Cham: Springer

Green, S., & Batterman, R. W. (2017). Biology meets physics: Reductionism and multi-scale modeling of morphogenesis. *Studies in History and Philosophy of Biological and Biomedical Sciences*, 61, 20–34. https://doi.org/10.1016/j.shpsc.2016.12.003

Haueis, P. (2018). Beyond Cognitive Myopia: A Patchwork Approach to the Concept of Neural Function. *Synthese 195*(12), 5373–5402. https://doi.org/10.1007/s11229-018-01991-z

Haueis, P. (2021). Multiscale Modeling of Cortical Gradients: The Role of Mesoscale Circuits for Linking Macro- and Microscale Gradients of Cortical Organization and Hierarchical Information Processing. *NeuroImage 232*. https://doi.org/10.1016/j.neuroimage.2021.117846

Haueis, P., & Slaby, J. (2017). Connectomes as Constitutively Epistemic Objects. Critical Perspectives on Modelling in Current Neuroanatomy. In T. Mahfoud, S. McLean and N. Rose (eds.). Progress in Brain Research Vol 233: *The Making and Use of Animal Models in Neuroscience and Psychiatry*. (pp. 149–177). Amsterdam: Academic Press. https://doi.org/10.1016/bs.pbr.2017.05.002

Heinzle, J., Hepp, K., & Martin, K. A. C. (2007). A Microcircuit Model of the Frontal ye fields. *The Journal of Neuroscience*, 27, 9341–9353. https://doi.org/10.1523/JNEUROSCI.0974-07.2007

Hilgetag, C. C., & Goulas, A. (2020). 'Hierarchy' in the Organization of Brain Networks. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 375*(1796), 2019.0319. https://doi.org/10.1098/rstb.2019.0319

Hillerbrand, R. (2015). Explanation Via Micro-reduction: On the Role of Scale Separation for Quantitative Modelling. In B. Falkenburg, & M. Morrison (Eds.), *Why More Is Different.: Philosophical Issues in Condensed Matter Physics and Complex Systems* (81 vol., pp. 69–87). Berlin, Heidelberg: Springer Berlin Heidelberg

Kästner, L., & Haueis, P. (2021). Discovering Patterns: On the Norms of Mechanistic Inquiry. *Erkenntnis 86*(6), 1635–1660. https://doi.org/10.1007/s10670-019-00174-7

Kuehn, C. (2016). Moment Closure – a Brief Review. In E. Schöll, S. Klapp, & P. Hövel (Eds.), *Control of Self-organizing Nonlinear Systems. Understanding Complex Systems* (pp. 253–271). Cham: Springer. https://doi.org/10.1007/978-3-319-28028-8_13

Margulies, D. S., Ghosh, S. S., Goulas, A., Falkiewicz, M., Huntenburg, J. M., Langs, G., et al. (2016). Situating the Default-Mode Network along a Principal Gradient of Macroscale Cortical Organization. *Proceedings of the National Academy of Sciences of the United States of America*, 113, 12574–12579. https://doi.org/10.1073/pnas.1608282113

McCaffrey, J., & Danks, D. (2017). Mixtures and Psychological Inference with Resting State fMRI. *The British Journal for the Philosophy of Science*. https://doi.org/10.1093/bjps/axx053

Morrison, M. (2018). Turbulence, Emergence and Multi-Scale Modelling. *Synthese*, 109(5), https://doi.org/10.1007/s11229-018-1825-5

Paquola, C., De Wael, V., Wagstyl, R., Bethlehem, K., Hong, R. A. I., Seidlitz, S. J., J., et al. (2019). Microstructural and Functional Gradients are Increasingly Dissociated in Transmodal Cortices. *PLoS Biology*, 17, e3000284. https://doi.org/10.1371/journal.pbio.3000284

Potjans, T. C., & Diesmann, M. (2014). The Cell-Type Specific Cortical Microcircuit: Relating Structure and Activity in a Full-Scale Spiking Network Model. *Cerebral Cortex*, 24, 785–806. https://doi.org/10.1093/cercor/bhs358

Rodriguez, R., & Tuckwell, H. (1996). Statistical Properties of Stochastic Nonlinear Dynamical Models of Single Spiking Neurons and Neural Networks. *Physics Review E Statistical Nonlinear Soft Matter Physics*, 54(5), 5585–5590. https://doi.org/10.1103/physreve.54.5585

Shine, J. M., & Poldrack, R. A. (2017). Principles of Dynamic Network Reconfiguration Across Diverse Brain States *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2017.08.010

Serban, M. (2020). Exploring Modularity in Biological Networks. *Philosophical Transactions of the Royal Society B*, 375(1796), https://doi.org/10.1098/rstb.2019.0316

Schmidt, M., Bakker, R., Hilgetag, C. C., Diesmann, M., & van Albada, S. J. (2018). Multi-scale Account of the Network Structure of Macaque Visual Cortex. *Brain Structure & Function*, 223, 1409–1435. https://doi.org/10.1007/s00429-017-1554-4

Silberstein, M., & Chemero, A. (2013). Constraints on Localization and Decomposition as Explanatory Strategies in the Biological Sciences. *Philosophy of Science*, 80(5), 958–970. https://doi.org/10.1086/674533

Wang, P., Kong, R., Kong, X., Liégeois, R., Orban, C., Deco, G., et al. (2019). Inversion of a Large-scale Circuit Model Reveals a Cortical Hierarchy in the Dynamic Resting Human brain. *Science Advances*, 5, eaat7854. https://doi.org/10.1126/sciadv.aat7854

Wilholt, T. (2005). Explaining Models: Theoretical and Phenomenological Models and their Role for the First Explanation of the Hydrogen Spectrum. *Foundations of Chemistry*, 7, 149–167. https://doi.org/10.1007/s10698-004-5958-x

Wilson, M. (2017). *Physics Avoidance. Essays on Conceptual Strategy*. Oxford: Clarendon Press

Zednik, C. (2018). Models and Mechanisms in Network Neuroscience. *Philosophical Psychology*, 32(1), https://doi.org/10.1080/09515089.2018.1512