

# Brain Informatics and Health


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Informatics-enabled studies are transforming brain science. New methodologies enhance human interpretive powers when dealing with big data sets increasingly derived from advanced neuro-imaging technologies, including fMRI, PET, MEG, EEG and fNIRS, as well as from other sources like eye-tracking and from wearable, portable, micro and nano devices. New experimental methods, such as in to imaging, deep tissue imaging, opto-genetics and dense-electrode recording are generating massive amounts of brain data at very fine spatial and temporal resolutions. These technologies allow measuring, modeling, managing and mining of multiple forms of big brain data. Brain informatics & health related techniques for analyzing all the data will help achieve a better understanding of human thought, memory, learning, decision-making, emotion, consciousness and social behaviors. These methods also assist in building brain-inspired, human-level wisdom-computing paradigms and technologies, improving the treatment efficacy of mental health and brain disorders.

The Brain Informatics & Health (BIH) book series addresses the computational, cognitive, physiological, biological, physical, ecological and social perspectives of brain informatics as well as topics relating to brain health, mental health and well-being. It also welcomes emerging information technologies, including but not limited to Internet of Things (IoT), cloud computing, big data analytics and interactive knowledge discovery related to brain research. The BIH book series also encourages submissions that explore how advanced computing technologies are applied to and make a difference in various large-scale brain studies and their applications.

The series serves as a central source of reference for brain informatics and computational brain studies. The series aims to publish thorough and cohesive overviews on specific topics in brain informatics and health, as well as works that are larger in scope than survey articles and that will contain more detailed background information. The series also provides a single point of coverage of advanced and timely topics and a forum for topics that may not have reached a level of maturity to warrant a comprehensive textbook.


Daniele Caligiore · Samuele Carli

# Simulating the Brain

A Four-Step Method Using Ordinary  
Differential Equations and Python

 Springer

Daniele Caligiore  
Institute of Cognitive Sciences  
and Technologies  
Italian National Research Council  
Rome, Italy

Samuele Carli   
Entersys s.r.l.  
Padua, Italy

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*To Serena and Chiara*

—*Daniele Caligiore*

*Fascinating!*

—*Samuele Carli*

# Preface

When learning to build brain computational models using the method proposed in this book or other approaches, it is crucial to remember that a model, no matter how detailed or carefully constrained through data, is not reality. It does not matter whether the model represents the functioning of a single neuron or is a “system-level model” that considers the interactions between different areas of the brain and the interplay between the brain, body, and environment. Ultimately, it is still not reality. A model must simplify and capture the essence of reality. Through this simplification, the model becomes a tool that allows us to see and understand aspects of reality that would otherwise be difficult to grasp. A computational model is a tool for formulating new hypotheses about brain functioning or malfunctioning and exploring new paths that are challenging to pursue through reasoning or experiments alone.

Over the years, we have learned to create computational models at various levels of abstraction, ranging from connectionist models to more detailed biological models with spiking neurons and differential equations, as described in this book. We have come to believe that no single method of investigation—whether it be experiments, computer simulations using models, neurophysiology, or brain imaging—is inherently superior to another, nor is there an optimal level of abstraction for creating computational models to study the brain. A computational model that includes more detailed representations of the brain-body-environment system is not necessarily better than a more abstract model that captures general statistical properties and vice versa. The suitability of a model depends on the specific problem studied. A complex model often involves a greater number of free parameters to set, making it unmanageable and difficult to interpret.

Therefore, a model is a tool that can help you think about a problem in new ways compared to traditional “pen and paper” reasoning. However, two reasons make the computational model a unique and, in some ways, special tool compared to other techniques used to study brain, such as empirical experiments or brain imaging. To begin with, a model allows you to *operationalize a theoretical hypothesis* and bring it to life through a *computer simulation*. For instance, you might hypothesize that a lesion in brain area X causes an effect in area Y. With the model, you can verify if this occurs. But there is more. The simulation might reveal that in addition to affecting

area Y, the lesion in area X also causes changes in a third brain region, Z, which you had not considered. The simulation results prompt you to reflect on other factors. Computational models, particularly system-level models like those discussed in this book, can integrate and synthesize findings from various approaches and methodologies, such as behavioral experiments, brain imaging, genetic studies, and more. This *integrative capability* is another fundamental aspect that makes computational models a unique and valuable tool for studying the brain through a system-level approach that considers multiple factors.

Thus, the model enables a strongly *interdisciplinary approach* to investigate the brain, supporting an “original multi-methodological language”, facilitating synergistic interaction with colleagues from diverse backgrounds. This approach allows for the assimilation and transmission of trans-disciplinary knowledge and promotes *cross-fertilization* between different domains. The interdisciplinary viewpoint allows us to broaden the impact of our research to engage psychologists, neuroscientists, and clinicians aside from modelers. This process fosters innovative perspectives on brain research by promoting collaboration across disciplines like neuroscience, artificial intelligence, psychology, and cognitive science, as well as diverse scientific methods such as (neuro)computational modeling, simulations, machine learning, and experimental psychology. The system-level modeling technique showcased in this book supports this viewpoint.

We have developed an interdisciplinary methodology to design system-level brain models using systems of ordinary differential equations, which are to be solved and analyzed through simple Python scripts. These models could be successfully applied in many contexts: to study healthy and damaged brain functions and hence improve the current understanding of the system-level neural mechanisms underlying brain disorders, but also to discover, through computer simulation, new neural pathways that may be crucial for the emergence of pathologies, as well as the effects of possible new therapies acting on brain actors poorly investigated in traditional research. The main goal of this system-level perspective is to provide an operational hypothesis about the role played by a network of brain areas underlying a behavior: different classes of behaviors are generated by the interplay of various subsets of brain components rather than by specific components in isolation. The proposed method consists of four key steps: (i) designing the model architecture to represent interactions between distinct brain regions; (ii) formulating the system of ordinary differential equations derived from the architecture drawn in (i); (iii) developing a Python script to solve these equations; and (iv) identifying the model free parameters using optimization techniques, such as genetic algorithms or alternative methods, to generate one or more instances that accurately reproduce the target behavior under investigation.

This four-step method has been progressively integrated into the courses we teach at the interdisciplinary “Advanced School in Artificial Intelligence (AS-AI)<sup>1</sup>” directed and co-founded by the first author of this book and promoted by the Institute

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<sup>1</sup> [www.as-ai.org](http://www.as-ai.org).

of Cognitive Sciences and Technologies of the Italian National Research Council<sup>2</sup> and by AI2Life srl.<sup>3</sup> AS-AI is open to students with any background and actively supports inter-disciplinary collaboration. The idea for this book emerged from this interdisciplinary framework, emphasizing the importance of collaboration and the exchange of ideas across scientific fields. The book is designed for anyone interested in using Python and ordinary differential equations to simulate different aspects of reality, regardless of their background. In addition to explaining the methodology for building system-level brain computational models, the book also includes examples from other dynamic complex systems, such as those in physics and social sciences. While rigorous mathematical proofs of many topics discussed are beyond the scope of this work—since they remain open research areas requiring advanced mathematical expertise—the essential elements needed for critical analysis and self-assessment are presented in a simplified and practical manner. For those interested in delving deeper, extensive references are provided. This textbook is a comprehensive resource, providing everything needed to learn from the ground up. It covers essential mathematical concepts—ranging from foundational topics for beginners to insights on advanced subjects for more experienced readers—as well as fundamental computing and collaboration tools indispensable for interdisciplinary, team-based research. Additionally, it introduces the basics of Python programming and equips readers with the skills to design, simulate, visualize, and interpret models of the brain and other complex systems. These abilities are honed through numerous hands-on examples, explained step-by-step.

**Keywords:** Brain simulation, Digital twin, Hands-on examples, Interdisciplinary, Network neuroscience, Numerical models, Python, Ordinary differential equations, System-level modeling.

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Mentioning all the incredible friends and collaborators that accompanied me during this journey, and everything they did with me and for me, would require a book of its

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<sup>2</sup> [www.istc.cnr.it](http://www.istc.cnr.it).

<sup>3</sup> [www.ai2life.com](http://www.ai2life.com).

own. You know who you are, and I'm sure you also know how grateful I am. Thank you! Osobitné poďakovanie patrí mojej úžasnej manželke Ine, e grazie a mamma e babbo!

Rome, Italy  
Padua, Italy

Daniele Caligiore  
Samuele Carli

**Competing Interests** The authors have no competing interests to declare that are relevant to the content of this manuscript.

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## About the Authors

**Daniele Caligiore** is a Research Director at the Institute of Cognitive Sciences and Technologies (ISTC) of the Italian National Research Council (CNR), where he coordinates the Computational and Translational Neuroscience Laboratory (CTNLab). This interdisciplinary research group leverages artificial intelligence (AI) and computational neuroscience to study brain function and behavior. The CTNLab ultimate goal is to discover new clinical applications and therapies for neurodegenerative diseases. He is the director and co-founder of the Advanced School in Artificial Intelligence (AS-AI), a postgraduate institution supported by ISTC, dedicated to the interdisciplinary study and application of AI. Additionally, he teaches “Artificial Intelligence Systems in Social Contexts” at the Libera Università Maria Santissima Assunta (LUMSA) in Rome. Daniele earned his Master’s Degree in Electronic Engineering from the University of Catania in 2003 and a PhD in Biomedical Engineering from the University Campus Bio-Medico of Rome in 2011. He has been a visiting scholar at the University of Plymouth, the University of Bologna, and the University of Southern California. With over 90 scientific articles published in international journals, conference proceedings, and book chapters, Daniele has also contributed to numerous international research projects in artificial intelligence and neuroscience. He serves on the Scientific Secretariat of the CNR Commission for Ethics and Integrity in Research and is an expert evaluator of research project proposals in AI and neuroscience for the Italian Ministry of University and Research (MUR) and the European Commission. Additionally, he is a founding member of AI2Life, a spin-off of ISTC-CNR, which aims to promote the use of AI to foster social development and individual well-being. Daniele is the author of interdisciplinary books, including “*IA istruzioni per l’uso*” and “*Curarsi con l’Intelligenza Artificiale*”, both published by il Mulino, and “*Healing with Artificial Intelligence*”, published by Routledge Taylor & Francis.

**Samuele Carli** is a seasoned Senior Developer and Entrepreneur with over 25 years of professional experience. Throughout his career, he has contributed to a diverse array of projects across scientific research, industry, and business domains, taking on roles ranging from developer to project manager and coordinator. He holds a

Master of Science degree in Computer Science from Università degli Studi di Firenze, specializing in numerical analysis, computer simulation, and artificial intelligence. His expertise includes work on machine learning applications for data analysis at CERN (the European Organization for Nuclear Research). Currently, he collaborates as a researcher with CTNLab and ISTC-CNR, focusing on brain modeling and simulation in the context of neurodegenerative diseases. In addition to his research endeavors, Samuele teaches courses on numerical optimization at the Advanced School in Artificial Intelligence. He is also the co-founder and Chief Technology Officer of Entersys S.r.l., a company dedicated to small enterprise management and the development of AI-driven and data-centric solutions for enterprise resource planning and management.

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