

Deep Learning in Science

This is the first rigorous, self-contained treatment of the theory of deep learning. Starting with the foundations of the theory and building it up, this is essential reading for any scientists, instructors, and students interested in artificial intelligence and deep learning. It provides guidance on how to think about scientific questions, and leads readers through the history of the field and its fundamental connections to neuroscience. The author discusses many applications to beautiful problems in the natural sciences, in physics, chemistry, and biomedicine. Examples include the search for exotic particles and dark matter in experimental physics, the prediction of molecular properties and reaction outcomes in chemistry, and the prediction of protein structures and the diagnostic analysis of biomedical images in the natural sciences. The text is accompanied by a full set of exercises at different difficulty levels and encourages out-of-the-box thinking.

Pierre Baldi is Distinguished Professor of Computer Science at University of California, Irvine. His main research interest is understanding intelligence in brains and machines. He has made seminal contributions to the theory of deep learning and its applications to the natural sciences, and has written four other books.

Cambridge University Press
978-1-108-84535-9 — Deep Learning in Science
Pierre Baldi
Frontmatter
[More Information](#)

Deep Learning in Science

PIERRE BALDI

University of California, Irvine

CAMBRIDGE UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom
One Liberty Plaza, 20th Floor, New York, NY 10006, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India
79 Anson Road, #06–04/06, Singapore 079906

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning, and research at the highest international levels of excellence.

www.cambridge.org

Information on this title: www.cambridge.org/9781108845359

DOI: 10.1017/9781108955652

© Pierre Baldi 2021

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2021

Printed in Singapore by Markono Print Media Pte Ltd

A catalogue record for this publication is available from the British Library.

ISBN 978-1-108-84535-9 Hardback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

To Cristina, Julia Melody, and Marco Jazz

Cambridge University Press
978-1-108-84535-9 — Deep Learning in Science
Pierre Baldi
Frontmatter
[More Information](#)

Contents

	Preface	<i>page xi</i>
1	Introduction	1
	1.1 Carbon-Based and Silicon-Based Computing	1
	1.2 Early Beginnings Until the Late 1940s	4
	1.3 From 1950 to 1980	10
	1.4 From 1980 to Today	12
	1.5 Roadmap	14
	1.6 Exercises	15
2	Basic Concepts	16
	2.1 Synapses	16
	2.2 Units or Neurons	17
	2.3 Activations	17
	2.4 Transfer Functions	18
	2.5 Discrete versus Continuous Time	22
	2.6 Networks and Architectures	23
	2.7 Functional and Cardinal Capacity of Architectures	26
	2.8 The Bayesian Statistical Framework	28
	2.9 Information Theory	31
	2.10 Data and Learning Settings	33
	2.11 Learning Rules	35
	2.12 Computational Complexity Theory	36
	2.13 Exercises	37
3	Shallow Networks and Shallow Learning	41
	3.1 Supervised Shallow Networks and their Design	41
	3.2 Capacity of Shallow Networks	46
	3.3 Shallow Learning	52
	3.4 Extensions of Shallow Learning	56
	3.5 Exercises	58

4	Two-Layer Networks and Universal Approximation	63
	4.1 Functional Capacity	63
	4.2 Universal Approximation Properties	65
	4.3 The Capacity of $A(n, m, 1)$ Architectures	68
	4.4 Exercises	69
5	Autoencoders	71
	5.1 A General Autoencoder Framework	72
	5.2 General Autoencoder Properties	73
	5.3 Linear Autoencoders	75
	5.4 Non-Linear Autoencoders: Unrestricted Boolean Case	84
	5.5 Other Autoencoders and Autoencoder Properties	90
	5.6 Exercises	96
6	Deep Networks and Backpropagation	99
	6.1 Why Deep?	99
	6.2 Functional Capacity: Deep Linear Case	101
	6.3 Functional Capacity: Deep Unrestricted Boolean Case	102
	6.4 Cardinal Capacity: Deep Feedforward Architectures	103
	6.5 Other Notions of Capacity	104
	6.6 Learning by Backpropagation	105
	6.7 The Optimality of Backpropagation	109
	6.8 Architecture Design	111
	6.9 Practical Training Issues	114
	6.10 The Bias–Variance Decomposition	118
	6.11 Dropout	119
	6.12 Model Compression/Distillation and Dark Knowledge	124
	6.13 Multiplicative Interactions: Gating and Attention	125
	6.14 Unsupervised Learning and Generative Models	127
	6.15 Exercises	131
7	The Local Learning Principle	137
	7.1 Virtualization and Learning in the Machine	137
	7.2 The Neuronal View	138
	7.3 The Synaptic View: the Local Learning Principle	139
	7.4 Stratification of Learning Rules	141
	7.5 Deep Local Learning and its Fundamental Limitations	142
	7.6 Local Deep Learning: the Deep Learning Channel	144
	7.7 Local Deep Learning and Deep Targets Equivalence	147
	7.8 Exercises	149
8	The Deep Learning Channel	151
	8.1 Random Backpropagation (RBP) and its Variations	152
	8.2 Simulations of Random Backpropagation	154

	8.3 Understanding Random Backpropagation	155
	8.4 Mathematical Analysis of Random Backpropagation	157
	8.5 Further Remarks About Learning Channels	162
	8.6 Circular Autoencoders	164
	8.7 Recirculation: Locality in Both Space and Time	165
	8.8 Simulations of Recirculation	167
	8.9 Recirculation is Random Backpropagation	168
	8.10 Mathematical Analysis of Recirculation	170
	8.11 Exercises	173
9	Recurrent Networks	177
	9.1 Recurrent Networks	177
	9.2 Cardinal Capacity of Recurrent Networks	178
	9.3 Symmetric Connections: The Hopfield Model	179
	9.4 Symmetric Connections: Boltzmann Machines	182
	9.5 Exercises	185
10	Recursive Networks	189
	10.1 Variable-Size Structured Data	189
	10.2 Recursive Networks and Design	190
	10.3 Relationships between Inner and Outer Approaches	199
	10.4 Exercises	201
11	Applications in Physics	204
	11.1 Deep Learning in the Physical Sciences	204
	11.2 Antimatter Physics	208
	11.3 High Energy Collider Physics	214
	11.4 Neutrino Physics	224
	11.5 Dark Matter Physics	228
	11.6 Cosmology and Astrophysics	230
	11.7 Climate Physics	233
	11.8 Incorporating Physics Knowledge and Constraints	235
	11.9 Conclusion: Theoretical Physics	237
12	Applications in Chemistry	239
	12.1 Chemical Data and Chemical Space	240
	12.2 Prediction of Small Molecule Properties	242
	12.3 Prediction of Chemical Reactions	245
13	Applications in Biology and Medicine	257
	13.1 Biomedical Data	257
	13.2 Life in a Nutshell	258
	13.3 Deep Learning in Proteomics	261
	13.4 Deep Learning in Genomics and Transcriptomics	268

x	Contents	
	13.5 Deep Learning in Biomedical Imaging	270
	13.6 Deep Learning in Health Care	273
14	Conclusion	275
	14.1 Explainability and the Black-Box Question	275
	14.2 ANNs versus BNNs	277
Appendix A	Reinforcement Learning and Deep Reinforcement Learning	282
	A.1 Brief History and Background	282
	A.2 Main Algorithmic Approaches	287
	A.3 Limitations and Open Problems	298
	A.4 Other Directions of Research	302
	A.5 Deep Reinforcement Learning	303
	A.6 Exercises	306
Appendix B	Hints and Remarks for Selected Exercises	308
	References	313
	Index	365

Preface

By and large, this book grew out of research conducted in my group as well as classes and lectures given at the University of California, Irvine (UCI) and elsewhere over the years. It can be used as a textbook for an undergraduate or graduate course in machine learning, or as an introduction to the topic for scientists from other fields. Basic prerequisites for understanding the material include college-level algebra, calculus, and probability. Familiarity with information theory, statistics, coding theory, and computational complexity at an elementary level are also helpful. I have striven to focus primarily on fundamental principles and provide a treatment that is both self-contained and rigorous, sometimes referring to the literature for well-known technical results, or to the exercises, which are an integral part of the book.

In writing this book, one of my goals has been to provide a rigorous treatment from first principles, as much as possible, in a still rapidly evolving field. This is one of the meanings of “in science” in the title. In this regard, the flow of the book is dictated primarily by complexity issues, going from shallow networks in their different forms, to deep feedforward networks, to recurrent and recursive networks. Two-layer networks, of which autoencoders are the prototypical example, provide the hinge between shallow and deep learning. For each kind of network, it is useful to consider special “hardware” cases, such as networks of linear units. Contrary to widespread belief, the linear case is often interesting and far from trivial. But this is not the only case where using a particular hardware model is helpful. Another example is the use of unrestricted Boolean units, another model that may seem trivial at first sight, but which leads to useful insights for both autoencoders and deep architectures. Yet another important example is provided by networks of linear or polynomial threshold gates.

A second characteristic of this book is its connection to biology. Neural networks, deep learning, and the entire field of AI are deeply rooted in biology, in trying to understand how the brain works and the space of possible strategies to replicate and surpass its capabilities. This is evident in Turing’s foundational work on Turing machines, guided by the fundamental intuition of a brain capable of having only a finite number of states [736] and in the vocabulary of computer science, which is full of words clearly rooted in biology such as AI, machine learning, memory, computer vision, computer virus, genetic algorithms, and so forth. It is regrettable to see young students and practitioners of machine learning misled to believe that artificial neural networks have little to do with biology, or that machine learning is the set of techniques used to maximize engineering or business goals, such as advertising revenues for search engines. In addition, not only computers and neural networks are inspired by biology, but they are of course also being

successfully used to analyze biological data, for instance high-throughput omic data, and through one of these surprising self-recursions only mankind seems to have produced, the results of these bioinformatics and systems biology analyses are progressively informing our understanding of the brain, helping to reveal for instance key gene expression and protein mechanisms involved in synaptic formation and biological memory.

A third characteristic of this book is precisely in the applications. The second meaning of “in science” in the title is “for science”. I have focused on applications of deep learning to the natural sciences – primarily physics, chemistry, and biology for the past three decades or so. These applications are expanding rapidly today, but were almost nonexistent in the 1980s. Plenty of textbooks and other material can be found dealing with applications of neural networks to problems in engineering and other related areas.

A fourth characteristic is the emphasis placed on storage, specifically on the neural-style of information storage, in fundamental contrast to the Turing-style of information storage, ironically introduced by Turing precisely while thinking about the brain. This theme goes together with the importance of recognizing the virtualization process hidden behind most of today’s neural network applications. In most applications of neural networks today, there are no neurons and no synapses, only their digital mirage. This comes at a price that can only be understood by thinking about “learning in the machine”, as opposed to machine learning. In a physical neural system, learning rules must be local both in space and time. Among other things, this locality principle helps clarify the relationship between Hebbian learning and backpropagation and explains why Hebbian learning applied to feedforward convolutional architectures has never worked. It also naturally leads to random backpropagation and recirculation algorithms, important topics that are poorly known because they are not particularly useful for current applications. For readers primarily interested in applications, or for courses with tight time limitations, I recommend using the abbreviated sequence of chapters: 2, 3, 6, and 10, covering most of the practical aspects.

Finally, the field of neural networks has been polluted by fads and a significant amount of cronyism and collusion over the past few decades, that a fragmented, multigenerational, and often unaware community could do little to stop. Cronyism and collusion are nothing new in human affairs, but they have distorted and slowed down the development of the field through the subtle control and manipulation of conferences, publications, academic and corporate research departments, and other avenues of power and dissemination. Readers should read more widely, check what has been published – where and when – and decide for themselves which results are supported by mathematical proofs or sound simulations, and which are not. In the end, towering over human affairs, all that matters are the beauty of deep learning and the underlying mysteries it is intimately connected to: from whether silicon can be conscious to the fundamental nature of the universe.

About the Exercises

The exercises vary in difficulty substantially. Should you become frustrated at trying to solve one of them, remind yourself that it is only when you are struggling with a problem that your brain is really learning something.

In order to solve some of the problems in the book, or more broadly to think about scientific and other questions, I recommend that my students systematically try at least four different approaches. The first of course is to simplify. When a question seems too difficult at first, look for special or simpler cases. When trying to understand a theorem, look at the case of “small n ”, or fix the values of certain parameters, or switch to the linear case, or try to interpolate. The second is the opposite way of thinking: generalize, abstract, or extrapolate. Are there other situations that bear some similarity to the current problem? How can a result be applied to more general cases? Can the conditions under which a theorem is true be relaxed? The third way of thinking is “to take the limit”, to look at what happens at the boundaries of a certain domain, under extreme conditions, to let n go to zero, or to infinity. And finally, the fourth way is always to invert, look at things somehow from an opposite perspective. Thus, for example, when thinking about an autoencoder, one may want first to simplify it by studying how to solve the top layer given the lower layer, which is usually an easier problem; and then to invert this approach by studying how the lower layer can be solved given the top layer, which is usually a harder problem.

Of course these four principles are not a panacea to every situation and, for instance, identifying the right form of “inversion” in a given situation may not be obvious. However, the discipline of trying to apply these four principles in a systematic manner can be helpful and, incidentally, remains a major challenge for Artificial Intelligence (AI).

Acknowledgments

The number of people I am indebted to keeps growing every year, and I can only mention a few of them.

- As a graduate student at Caltech (1983-1986) and visiting lecturer at UCSD (1986-1988), I was fortunate to be able to participate and contribute to the early beginnings of neural networks in the 1980s. Being at those two universities, which were the hotbeds of neural networks research at the time, resulted to a large extent from a series of chance encounters with several individuals, of whom I can only mention two: Brian Ekin and Gill Williamson. Brian, who I met by chance in Paris, told me to apply to Caltech, a name I had never heard before. And while bartending for an alumni reunion in the basement of the Caltech Athenaeum, I met Gill Williamson who was a Professor at UCSD and, while still sober, offered me my first academic job.
- From those early times, I wish also to acknowledge two kind mentors – Edward Posner and Walter Heiligenberg – both of whom died prematurely in tragic transportation accidents; as well as some of my early collaborators and friends including: Amir Atiya, Eric Baum, Joachim Buhmann, Yves Chauvin, Paolo Frasconi, Kurt Hornik, Ron Meir, Fernando Pineda, Yosi Rinott, and Santosh Venkatesh.
- From more recent times, I wish to acknowledge past and present faculty colleagues at UCI in AI and machine learning, including: Rina Dechter, Charles Fowlkes, Roy Fox, Richard Granger, Alexander Ihler, Dennis Kibler, Richard Lathrop, Stephan

Mandt, Eric Mjølness, Ioannis Panageas, Michael Pazzani, Deva Ramanan, Sameer Singh, Padhraic Smyth, Erik Sudderth, Max Welling, and Xiaohui Xie.

- Successful applications of deep learning to the sciences vitally require interdisciplinary collaborations. I am deeply grateful to all my collaborators from the natural sciences. Among the current active ones at UCI, I only have space to mention: Roman Vershynin (Mathematics) and Babak Shahbaba (Statistics), Daniel Whiteson and Jianming Bian, together with Simona Murgia, Franklin Dollar, and Steven Barwick (Physics), Michael Pritchard (Earth Sciences), David Van Vranken and Ann Marie Carlton (Chemistry), and Paolo Sassone-Corsi, Marcelo Wood, and Amal Alachkar (Biology). As I was about to send the final draft to Cambridge University Press, Paolo unexpectedly died and I wish to honor his memory here. He was an outstanding scientist, friend, and collaborator.
- Together with my external collaborators, I am also deeply grateful to current and past students and postdoctoral fellows in my research group, who have contributed in so many ways to this book over the years, including: Forest Agostinelli, Alessio Andronico, Chloe Azencott, Kevin Bache, Pierre-François Baisnée, Ryan Benz, Vincenzo Bonnici, Martin Brandon, Andrew Brethorst, Jocelyne Bruand, Francesco Ceccarelli, Nicholas Ceglia, Ivan Chang, Jonathan Chen, Siwei Chen, Jianlin Cheng, Davide Chicco, Julian Collado, Kenneth Daily, Ekaterina Deyneka, Pietro Di Lena, Yimeng Dou, David Fooshee, Clovis Galliez, Steven Hampson, Lars Hertel, Qian-Nan Hu, Raja Jurdak, Matt Kayala, John B. Lanier, Christine Lee, Lingge Li, Erik Linstead, Junze Liu, Yadong Lu, Alessandro Lusci, Christophe Magnan, Antonio Maratea, Stephen McAleer, Ken Nagata, Francesco Napolitano, Ramzi Nasr, Jordan Ott, Vishal Patel, Gianluca Pollastri, Liva Ralaivola, Arlo Randall, Paul Rigor, Alex Sadovsky, Peter Sadowski, Muntaha Samad, Hiroto Saigo, Siyu Shao, Alexander Shmakov, Suman Sundaresh, S. Joshua Swamidass, Mike Sweredoski, Amin Tavakoli, Gregor Urban, Alessandro Vullo, Eric Wang, Lin Wu, Yu Liu, and Michael Zeller.
- I am equally grateful to Janet Ko, who has assisted me and other faculty, for so many years with her loyalty and outstanding administrative skills, always shielding scientific research from bureaucracy.
- As far as the book itself is directly concerned, two chapters and the appendix reuse material from three previously published articles [72, 634, 262] and I thank the publishers – Springer and Annual Reviews – for their permissions. I wish also to thank Annie Vogel-Cierna for providing me two of the microscopy images in the last chapter.
- This book was finished during the COVID-19 pandemic. It has been a real pleasure to work with the staff of Cambridge University Press, and in particular with David Tranah. I thank them for their outstanding support and professionalism, and their deep understanding of academic publishing.
- Last but not least, I am deeply grateful to my close friends and to my family.