



HAL
open science

Introduction

Alvaro Moreno Bergareche, Matteo Mossio

► **To cite this version:**

Alvaro Moreno Bergareche, Matteo Mossio. Introduction. Biological Autonomy. A Philosophical and Theoretical Enquiry, Springer Netherlands, 2015, 978-94-017-9836-5. 10.1007/978-94-017-9837-2 . hal-01151449

HAL Id: hal-01151449

<https://hal.science/hal-01151449v1>

Submitted on 13 May 2015

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Alvaro Moreno • Matteo Mossio

Biological Autonomy

A Philosophical and Theoretical Enquiry

 Springer

Alvaro Moreno
IAS-Research Centre for Life,
Mind and Society
Departamento de Lógica y Filosofía
Universidad del País Vasco
Donostia – San Sebastian
Guipúzcoa, Spain

Matteo Mossio
Institut d'Histoire et de Philosophie des
Sciences et des Techniques (IHPST)
CNRS/Université Paris I/ENS
Paris, France

ISSN 2211-1948 ISSN 2211-1956 (electronic)
History, Philosophy and Theory of the Life Sciences
ISBN 978-94-017-9836-5 ISBN 978-94-017-9837-2 (eBook)
DOI 10.1007/978-94-017-9837-2

Library of Congress Control Number: 2015933996

Springer Dordrecht Heidelberg New York London
© Springer Science+Business Media Dordrecht 2015

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Printed on acid-free paper

Springer Science+Business Media B.V. Dordrecht is part of Springer Science+Business Media (www.springer.com)

Foreword

I am sitting with my grandchild in the park on a fading Australian summer afternoon. The sulphur-crested cockatoos screech as they squabble over the last of the sunlit eucalypt branches and she notices them as they fly over her, their powerful wings beating. “What is flying,” she asks, “and why can’t we do it?” For a moment I am tempted to respond to the latter question with “We don’t have the genes for flight”. But not only would this not help, indeed could not help, it also tears that question away from the initial one. While evolution as changes in gene frequencies can track the requisite gene changes involved, the actual features of organisms that make flight possible are left out. Genes can tell us about the appearance, spread and evolution of the *fact* of flight but they cannot in themselves tell us what flight actually *is*, namely the production of suitably spatially distributed and temporally coordinated thrust and lift. To understand that involves understanding, for example, how musculature must be recruited and organised to work wings that provide both lift and thrust, how skeletons must be both organised to effect tail-wing coordination, and be light enough to lift yet strong enough to brace the musculature in flight, to land on moving branches without fracturing legs, etc. and much more.

In short, it is to understand the internal organisation of birds. Without that we are blind to the internal consequences of genetic variation; and without that and ecological organisation, blind also to its external ecological consequences via the new sources of food and nests that become available, the spread of seeds via bird guts and the spread of plants that compete for bird feeding, and so on. Without such understanding the survival-of-the-fittest engine is left spinning its wheels, its simple idea of stochastic selection on populational variety left to sort rocks in a river and straws in the wind as well as gazelle on a savannah but without purchase on the nature and potential of evolving life.

There are three good reasons to read this book about how life is constituted. *First*, its organisational approach to organism is deeply informative, radically different from current orthodoxy and makes a crucial contribution at an important historical juncture in science. *Second*, it provides a detailed, powerful and ultimately elegant

model of the mutual development of scientific and philosophical understanding. *Third*, the pellucid, penetrating and parsimonious character of the writing makes a text dense in precisely characterised ideas quite accessible, including to a non-expert audience.

The last of these features is uncommon, the second is decidedly unusual and the first quite unique. They are all discussed a little further below. If you have an interest in understanding how our world works, or a specific interest in the foundations of biological science and/or philosophy of biology, or in organised complex systems more widely (robotics, cybernetics, intelligent agents, etc.) then this book is for you.

The book expounds and explores the claim that a distinctive organisation is the hallmark of life and that organisation ultimately provides a framework for understanding the evolution of life forms, of agency and of intelligence/intentionality. A quick review of chapter content can be found towards the close of the Introduction. As you might expect, it starts with the basics, closure and self-maintenance, then a complex form of closure called autonomy, the foundational organisation of all life, and then explores the still more complex topics just noted. Moreno especially has pursued the organisational approach consistently over decades and, with Mossio as collegial co-writer, this book is the summative outcome. I have helped to make the odd contribution to this position myself, partly on its systems foundations (organisation), but largely concerned with the adaptive roots of cognition (see references, this book), and in my view this book is unique in offering the first high quality conceptually integrated, empirically grounded, in depth exposition of this approach. It shows just how far the organisational perspective can take us in understanding the nature and evolution of life (answer: very far) and its exposition bids fair to remain the standard for some time to come.

The Organisational Approach

Listing genes and gene-trait associations tells you little about how the creatures that carry the genes are put together. The common presumption is that those latter answers come after the genetic work is done and will be found by studying the biochemical detail. Then whatever organisation there is will drop out as a consequence. But there is another, reverse possibility, one that has been largely neglected, namely that there are irreducible structures of nested correlated interactions, that is, organisations, that are key to understanding why the biochemical details are as they are, genomes included, and that such organisational design is as fundamental to understanding as is the biochemistry. That is the approach taken here.

Organisation (think car engines) happens when many different parts (cylinders, cam shafts, fuel injection ...) interact in specific, coordinated ways (cylinder rod rotates on cam shaft, fuel injected into cylinder, ...) so as to collectively support some global functioning (convert chemical potential energy into torque). It is roughly measured by the numbers of nested layers of different correlations

among different parts of a system. It is their functional contributions to the overall organisation of car engines that require the parts to have the shapes, sizes and material compositions they have. You can study these parts separately but unless you relate them to their organisation you will not understand their particular features. Organisation is not the same as order; pure crystals are highly ordered, so uniform they cannot show any organisation. Neither can gases, because they are too random to be organised. Organisation lies between the crystal and gas extremes but we don't have a good theory that tells us exactly where and why. Some may worry that talk of organisational constraints is too "airy fairy" and "metaphysical". But it is just the opposite, a matter of real dynamics found everywhere, from car engines to cellular "engines", for instance, the Krebs Cycle.

In this book the chief exemplar of an organised system is the living cell. The metabolism of a cell has to completely re-build the cell over time (that is its grand cycle). This is because, being material, a cell is a thermodynamic engine whose internal interactions degrade its innards which must then be replaced. But you don't get systematic self-replacement without being highly organised to do it: the particular materials and energy needed for each repair must be available at just the right location at just the right time, otherwise the cell will malfunction. In a cell more than 3,000 biochemical reactions are so organised that with each kind distinctively distributed throughout the cell their joint products re-make the cell, including themselves (and remove the thermodynamically unavoidable wastes), in the process also re-making the cell's capacity to extract from its environment the resources it needs. Thus at the heart of every cell is, and must be, a massive self-maintenance organisation cycle, operating under just the right constraints. This kind of organisation is called autonomy, with its core sense of self-governance applying all the way "up" from self-restriction by constraints to the more familiar socio-political notion.

Moreno and Mossio show that such organisation is central to cellular function, essentially defining all life. They also show that it is the necessary precursor to a well-defined evolutionary process, rather than the other way around. This is because the internal organisation of organisms secures the reproducibility of functionality which permits the inheritable traits, including those for mutant genomes, on which evolutionary selection operates. The interaction between evolutionary and developmental dynamics, in the context of epigenetic organisation, once mostly ignored but now richly studied, throws into stark relief the role of organism organisation in framing evolutionary process. All this is a relatively new perspective for evolutionary theorists, whose pure population statistics in themselves discourage awareness of organismal, communal and ecological organisation (cf. flight, above; albeit the theory has itself evolved significantly over the past 50 years). Moreno and Mossio lay out the issues with meticulous care.

Incidentally, it was the twin successes of the explorations of population genetics and molecular genetics that led to a century-long relative repression of biological organisation as an object of study, a repression that only really receded this century when molecular biology had exhausted simple gene sequencing and medicine simple gene-trait associations and both admitted the study of biosynthetic pathway

organisation as the next major challenge. Thus this book arrives on the scene at this epochal moment, just in time to provide a penetrating framework for understanding what is actually involved in such research.

On that score, note that the science of spatio-temporal organisation of interactions so as to generate global self-maintenance is itself in its infancy; we know relatively little about it, but just enough about the incredibly complex ways reactants are spatially arranged in cells to suppose it is going to be a large, complex and very difficult domain to understand. But it must come if ever we are to develop a thorough cellular biology and much else up to truly life-like robotics beyond the one-dimensional computer-in-a-box toys we focus on at present. (See also Hooker ed. *Philosophy of Complex Systems*, North Holland 2011 for further discussion.)

Multicellular Organisation

The emergence of a biochemical organisation capable of regenerative closure, the cell, is the first decisive step in the evolution of life. A subsequent giant step is the organisation of groups of cells to form multicellular organisms. These must organise their multicellular processes so that cellular metabolism is supported throughout, hence the presence of a cardiovascular system to deliver oxygen and nutrients where needed and remove wastes, the presence of renal and lymph systems to manage toxins and so on. In short, multicellularity requires a set of “higher” organisational layers on top of cellular ones to obtain a functional organism. (Again, we do not as yet understand a lot about such organisational constraints, e.g. respiration, that reach from individual cells across organs and other intermediate organisations, to the whole organism.) But there is a pay-off for all this overhead.

The distinctive twin advantages of multicellularity lie in its increased capacities for more complex behaviours and for more interactively open organisation, each feeding the other, even while closure must still be satisfied for their component cells. Once cellular communication develops to allow cell specialisation compatibly with cellular organisational coherence (as above), the way is thrown open to great increases in both behavioural complexity and interactive openness. The case of expanded behavioural repertoires is obvious enough. No single cell can fly, for the good reason that, whether or not it can muster thrust, it cannot control its surface shape so as to provide lift. But a collection of cells suitably specialised and interconnected can provide the musculature, cardiovascular support, surface controllability and so on to fly, powerfully and elegantly.

The case of greater interaction openness is perhaps less obvious but of even greater significance. Multicellularity has made possible increases in interaction-led adaption of both inner metabolism and outer environment. In the case of inner metabolism, multicellular organisms are able to suspend or adapt aspects of metabolic activity, from speeding up some processes (e.g. removing wastes before conflict) to slowing down and modifying others (e.g. hibernation in bears),

sometimes drastically (e.g. consuming internal organs for energy when fat stores are exhausted in stressful circumstances). Indeed, it is possible for existing organ systems to be entirely transformed in response to circumstances, as the metamorphosis of pupae into butterflies so beautifully illustrates. All of this requires over-arching organisational capacities. In the case of the outer environment, sensory cellular specialisation permits new ways of inward-bound interaction with the environment, leading to increased motor metabolic adaptiveness, from movement (e.g. sitting to running) to fasting, and to new ways of outward-bound interaction with the environment, like fight/flight, but also altering the environment to ease selection pressures (mouse holes for mice, etc.). Humans do not even internally manufacture all of their essential amino acids, relying on these open interaction systems to obtain them from their environment. (Which means that any constraint closures required for organism autonomy must be understood relatively to what can be regulated through external interaction and not only internal metabolic activity.) Just as with flight, all this also transforms ecological organisation.

In sum, if I might exploit a flight metaphor, when it comes to the expansion of life on the planet, it may be evolutionary selection that provides the thrust, but it is organisation that provides the lift. It is, as Howard Pattee taught us, the coordination of organisational constraints that makes possible the accumulating diversity and complexity of life. If organisation without evolution is impotent, evolution without organisation is blind.

Integration of Science and Philosophy

The dominant tradition in (meta-)philosophy is that philosophy and science are not to be integrated because philosophy provides an a priori normative framework for the analysis, conduct and evaluation of science whereas science constructs a posteriori empirical knowledge of the world by applying that framework. But in practice the development of understanding has rarely (really: never) happened like this. Philosophers have always borrowed ideas, theories and methods from science, and vice versa, each fertilising the other, unregarding of the proprieties of doing so. This has been a GOOD THING for both parties, each informing the other and keeping it on its toes. A minority naturalist (meta-)philosophy position would also applaud this intercourse as entirely appropriate. And that is what our authors consciously practice. Here is what they say (see Introduction): “. . . the approach developed in this book lies in between philosophy and theoretical biology. It deals with philosophical questions, like the nature of autonomy, agency and cognition, as well as their relations with concepts such as function, norms, teleology and many others; yet, it addresses these questions in close connection to, or even deeply entangled with, current scientific research.” What emerges from this rich process is a coherent, if unfinished, majestic view of life as a subtly mutually entangled, organised whole from molecules to macro-ecology.

On Chasing Hares

Like all really interesting books, this book is profoundly incomplete: it starts new hares (new lines of thought) running on almost every page. This leaves the curious and/or thoughtful reader to enjoy the pleasure of identifying them and deciding which ones to follow up. A fine example already occurs in Chap. 1, in the nature of the closure found in self-regeneration and its relation to dynamical constraints. This issue is central, for according to the book's story there is no function or organisation, properly so-called, without closure ("an organization is by definition closed and functional", Chap. 3) and hence no autonomy either. I have previously mentioned constraints five times, including in characterising autonomy itself, and closure thrice, as if both notions were well understood. Did you notice any hares leap?

Closure has been an issue in thinking about autonomous systems from the beginning (see the summary in their Chap. 1). Founders like Varela emphasised closure as the distinctive feature of biological organisation and made its discovery at multicellular levels the key requirement for understanding them, even though closure was hard to uncover (it was thought to characterise the immune and nervous systems) and seemed to pull against the increasing interactive and organisational openness that marks multicellularity (see above). Many (myself included) adopted a process model: processes are sequences of dynamical states and process closure occurs where these states cycle through a closed loop of states, returning each time to an initial state, e.g. the normal or "resting" metabolism state. The cellular Krebs cycle is again a useful example. The thermodynamic flow, another process, drives the cycling, thus reconciling openness (flow) with closure (cycling). But Moreno and Mossio find this unsatisfying (for reasons I leave to the reader to pursue) and have developed their own distinctive account on which it is constraints that are closed and not processes, which are open on account of the thermodynamic flow. By constraint closure is meant, roughly, that the constraints so interrelate as to reconstitute one another. (So there is still a process cycle, but it is among constraint conditions, leaving thermodynamic processes to remain open.) To make the distinction between constraints and processes really sharp, they require that constraints do not interact, in the sense of exchange energy/materials, with the thermodynamic flow, only shape its direction. Think of a river flowing between frictionless banks. For this reason, they characterise constraints as not being thermodynamic entities and in Chap. 2 they support that by arguing that they are emergent entities with respect to the thermodynamic flow.

What are constraints, these non-thermodynamic entities that somehow shape the flow while not being of it? In standard mathematical dynamics constraints appear in the application of dynamical models where, although not directly represented in the system dynamics flow equations, they apply forces that constrain the dynamical possibilities of the flow. When they do not interact with the flow (ironically for Moreno/Mossio) those forces can be calculated and, like all modelled forces, are grounded in physical configurations of matter and/or fields of the same sort as make

up the system being modelled, just located externally to it. But in autonomous systems all the matter/fields that give rise to those constraint forces have themselves to be assembled within the autonomous system itself in consequence of its constrained flow. Precisely that is the trick of autonomous self-regeneration, and a problem for understanding constraints.

For this means that constraints repeatedly degrade and have to be physically reconstructed, waste molecules literally replaced with new ones, etc. That is, the system itself must do work on its own constraints, or anyway on the matter/fields that give rise to them. Think of a real river that erodes and reconstructs its own banks as it flows. But that raises a first important issue: we have no workable methods for formulating the dynamics of systems that do work on their own constraints, the standard techniques of Lagrangian dynamics break down in this case. (See my “On the import of constraints in complex dynamical systems”, *Foundations of Physics*, 2013, and earlier in Hooker (2011) above.) So how exactly are we to understand these systems and their self-reconstituting constraints? (Hare 1) This issue applies much more widely than biology, of course, since the self-formation and transformation of internal constraints is a major feature of complex dynamics anywhere (Hare 2). And, as noted above, but not in the book, apparently multicellular closed constraints have to be understood relative to an organism’s interactional (agency) capacities, which itself depends on its functional, so closure, organisation (Hare 3).

And the manner in which Moreno/Mossio move to avoid facing the problem for autonomous dynamics (by requiring that constraints do no work and have none done on them) raises a second important issue: since constraints have to be reconstituted there are presumably periods of time when work is being done on at least some of them (on their supports): what kind of dynamics then applies to them and the flow? (Hare 4) These concerns are reinforced by a vivid picture in Chap. 3 of self-maintenance extended over time, for both intra-organism and inter-generational autonomous organisations, reinforced by the argument in Chap. 6 that developmental processes are necessary to multicellular constitution. (There is another group of hares loitering around these ideas.) But perhaps it also offers a way out in its conception of transmission of causal organisation over time that does not seem to require continuous satisfaction of closure (Hare 5). Even then, the hare 4 issue would remain to be addressed. And a further issue arises: considering time periods during which various proportions of constraints do not exist as such because they are doing work on some part of the system (including regenerating other constraints) and/or having work done on them (being regenerated), how large can those time spans be before system autonomy is considered disrupted and no longer explanatory of that system, and why? (Hare 6)

No doubt the authors will have anticipated such issues and been thinking about responses. (Their remarks on river banks and in a few other places reflect my earlier probings.) Irrespective, these questions should not be considered criticism of the book; to the contrary, they represent questions that could not be asked until the refined treatment of constraint closure Moreno and Mossio propose was available. And while there are lots of hares to startle, as there must inevitably be given our

ignorance and a penetrating book, the present book succeeds in blunting many of the criticisms (including mine) made of the organisational approach. For instance, theirs is a position that takes the nature and role of biological organisation far beyond simple self-organisation of the kind beloved of the complex-behaviour-from-simple-rules-among-many-components tradition in the physics of complex systems. Indeed, that latter kind of process includes forming crystal lattices and like, so in fact it has no direct relationship at all with the kind of nested-complementary-correlations-and-regulations-among-disparate-components that this book is concerned with. The former could in principle be extended to encompass biology via bringing all organic chemistry under atomic modelling, but even then “organisation” in “self-organisation” remains a misnomer. (Two more hares.) Again, the book’s position takes external interaction (individual and evolutionary) as seriously as internal organisation, whereas there are other traditions (discussed in the book) that are more closed-off to its importance, e.g. as illustrated above for understanding multicellular capacities. Nonetheless, we may still wonder whether the full extent of the interactive openness has been appreciated: what would their account of consuming internal organs under stress or adapting closure to environmental extraction of amino acids look like? (Another hare.) Finally, here the organisational approach is used to illuminate a thoroughly embodied approach to mind, for example with a deep connection developed to body plan, that counters the concern with “lifting off” an abstracted organisational pattern that has only nebulous connection to nervous system dynamics, organisation and functioning. However, there is still room to wonder about how neural phenomena characteristic of neural networks, whether distributed representations or waves, fit with organisation. (Another hare.) In these and like ways, this book represents a marked step forward in developing the organisational approach.

Meanwhile, there is the serious fun of chasing down such interesting and epistemically rewarding hares.

Conclusion

The authors describe my review of the draft of this book as, among other things, “relentlessly critical” (see closing remarks, Introduction). This is a compliment to both parties. A decade or more earlier I had entertained the prospect of a book on autonomy and discussed the idea with Moreno – on one occasion after an ocean swim near my Australian home and over a little local sauvignon blanc with freshly shucked Sydney Rock oysters, which he commented were “the best oysters I have ever tasted”. (The preceding year at his coastal village I ate the best turbot I had ever tasted.) I hopefully suggested that the book could begin by understanding life through a series of ever tightening dynamical and thermodynamical constraints culminating with a notion of autonomy as the unique allowed evolvable organisation, just as the Krebs Cycle is a solution to capturing free energy for the cell. “Go ahead!” he said, “Be quick! I shall eagerly await your analysis.” Of course, he knew better

from years of trying just how hard that scientific task would be, still impossibly hard today where, for example, simple chemical cell models are still under development. I should have paid more attention to the quiet twinkle in his eye.

But we can all pay attention to what has been achieved. This book has thrust and lift. It is a masterly account of the organisational foundations of life, a splendid flight in the firmament of conception and understanding.

Professor Emeritus of Philosophy
Fellow of the Australian Academy of Humanities
PhD (Physics, Sydney University)
PhD (Philosophy, York University, Canada)

Cliff Hooker

Contents

| | | |
|----------|--|----|
| 1 | Constraints and Organisational Closure | 1 |
| 1.1 | Biological Determination as Self-Constraint | 3 |
| 1.2 | The Thermodynamic Grounding of Autonomy | 6 |
| 1.2.1 | Kauffman's Work-Constraint Cycle | 9 |
| 1.3 | Constraints and Processes | 11 |
| 1.4 | From Self-Organisation to Biological Organisation | 15 |
| 1.5 | Dependence | 18 |
| 1.6 | Closure | 20 |
| 1.7 | A Word About Related Models | 24 |
| 1.8 | Regulation | 28 |
| 1.8.1 | Constitutive Stability | 31 |
| 1.8.2 | Regulation | 33 |
| 1.8.3 | Regulation and the Increase of Complexity | 36 |
| 1.8.4 | Towards Autonomy | 38 |
| 2 | Biological Emergence and Inter-level Causation | 39 |
| 2.1 | The Philosophical Challenge to Emergence | 41 |
| 2.2 | Irreducibility Versus Non-derivability | 43 |
| 2.3 | Irreducibility and Emergence | 44 |
| 2.3.1 | Supervenience and Constitution | 45 |
| 2.3.2 | A Reply to the Exclusion Argument | 47 |
| 2.4 | Constraints and Closure as Emergent Determinations | 49 |
| 2.5 | Inter-level Causation | 52 |
| 2.5.1 | Why We Do Not Need Nested Causation in Biology | 54 |
| 2.5.2 | Why We Might, After All, Need Nested Causation in Biology | 58 |
| 2.6 | Conclusions | 60 |
| 3 | Teleology, Normativity and Functionality | 63 |
| 3.1 | The Philosophical Debate | 65 |
| 3.1.1 | Dispositional Approaches | 65 |
| 3.1.2 | Aetiological Theories | 67 |

| | | |
|----------|---|------------|
| 3.2 | The Organisational Account of Functions | 69 |
| 3.2.1 | Teleology, Normativity and Self-Determination | 70 |
| 3.2.2 | Closure, Organisation and Functions | 71 |
| 3.3 | Implications | 74 |
| 3.3.1 | Cross-Generation Functions | 75 |
| 3.3.2 | Malfunctions | 81 |
| 4 | Agency | 89 |
| 4.1 | What Is Agency? | 91 |
| 4.2 | Minimal Agency | 94 |
| 4.3 | Adaptive Agency | 98 |
| 4.3.1 | The Specificity of Motility | 101 |
| 4.4 | Autonomy | 104 |
| 4.5 | Beyond Individuals: Networks of Autonomous Agents | 105 |
| 4.5.1 | Toward Cognition | 109 |
| 5 | Evolution: The Historical Dimension of Autonomy | 111 |
| 5.1 | A Preliminary Look Into the Origins of Darwinian Evolution | 115 |
| 5.2 | Replicative Molecules Versus Self-Maintaining Organisations | 117 |
| 5.3 | At the Origins of Organisation: The Emergence of Protocells | 120 |
| 5.4 | The Origins of Natural Selection | 124 |
| 5.5 | Early Forms of Template-Based Evolution | 126 |
| 5.6 | On the Nature of Template Constraints | 129 |
| 5.7 | The Emergence of Specialised Template Functions | 130 |
| 5.8 | The Emergence of Darwinian Evolution | 133 |
| 5.9 | Is Darwinian Evolution Open-Ended? | 135 |
| 5.10 | Conclusion: Integrating the Organisational and Evolutionary Dimensions | 138 |
| 6 | Organisms and Levels of Autonomy | 141 |
| 6.1 | The Concept of Multicellular Organism: Evolutionary and Organisational Views | 145 |
| 6.1.1 | The Evolutionary View | 146 |
| 6.1.2 | The Organisational View | 148 |
| 6.1.3 | Multicellularity and Autonomy | 152 |
| 6.2 | Comparative Analysis | 154 |
| 6.2.1 | Cyanobacterium Nostoc.Punctiforme | 154 |
| 6.2.2 | Volvox.Carteri | 155 |
| 6.2.3 | Strongylocentrotus.Purpuratus | 157 |
| 6.3 | Developmental Conditions for Highly Integrated Multicellular Organisations | 160 |
| 6.4 | Towards Higher-Level Autonomy | 164 |
| 7 | Cognition | 167 |
| 7.1 | Agency and Motility | 169 |
| 7.1.1 | The Relationship Between Multicellular Integration and Behavioural Agency | 170 |

- 7.1.2 Organisational Requirements for Complex Behavioural Agency 173
- 7.2 The Dynamical Decoupling of the Nervous System 175
- 7.3 The Evolution of the Nervous System 177
 - 7.3.1 Body Plans and the Complexification of the Nervous System 178
 - 7.3.2 Towards Further Decoupling: Autonomic and Sensorimotor Nervous Systems 180
- 7.4 The Appearance of Consciousness..... 183
- 7.5 Cognition and the Emergence of Neurodynamic Autonomy 187
- 7.6 Cognition and Social Interaction..... 189
- 7.7 Conclusions 192
- 8 Opening Conclusions 195**
- References..... 201**
- Index..... 219**

Introduction

Life as Autonomy

If we were to point out in a few words what characterises the phenomenon of life, we would probably mention the amazing plasticity and robustness of living systems, the innumerable ways they adapt, and their capacity to recover from adverse conditions. All these capacities have been on the surface of our planet since the origins of life, and for this reason we have become accustomed to seeing life as something almost “normal”. And yet, looking at it from a more global perspective, life is quite an extraordinary phenomenon. In a short period of time (compared to the history of the universe), in a very tiny portion of the cosmos, a set of entities has managed to attain extremely improbable configurations, to keep them in far-from-equilibrium conditions, and to thrive under these conditions: self-organising, proliferating, diversifying, and even increasing their complexity. Furthermore, this persistently organised system (or, rather, this global system formed by millions of local, individualised systems, which combine decay and reproduction) has been able to deploy a set of selective forces, modifying its environment so as to enhance its own maintenance. In a word, life seems to be at the same time an extraordinarily precarious (and improbable) phenomenon and a powerful, robust, and easily expansive one.

Actually, this astonishing capacity to maintain highly organised systems seems to be the easiest way to recognise universally living matter beyond the specificities of terrestrial life. Present-day theories estimate that the universe came into being 13.7 billion years ago, while our planet was formed approximately 9 billion years later. In this period of time, or perhaps later, forms of organisation similar to early living systems on our planet possibly appeared in other parts of the universe. Indeed, if life appeared on our planet when certain physicochemical conditions were met, other planets with similar conditions could also have once supported forms of life. This

raises the question of how we could recognise these hypothetical extra-terrestrial living systems, and what would be the essential features of *any* form of (possible) life. In the last decades, this question has been widely discussed.

For some (Cleland and Chyba 2007), it is impossible to say how such “essential features of life” should be conceived, because we only know life as it manifests itself on Earth. Yet, if what we mean by “life” is any material organisation that has evolved from non-living physicochemical systems (therefore obeying the universal laws of physics and chemistry) and has attained at least a degree of complexity capable of generating the properties we associate with the simplest forms of terrestrial life, we should be capable of recognising it anywhere in our universe, regardless of how differently these systems may be constituted (Ruiz-Mirazo et al. 2004). At the same time, the huge variety of life forms that have appeared during the very long history of life on our planet (Ward and Brownlee 2004) might downplay the argument that we have had access only to a unique example of life among a hypothetically huge set of extra-terrestrial biological systems. Be that as it may, when facing the question of the nature of life, we could not do otherwise than formulate theories based on – and tested against – life as we know it.

It is because of its capacity to achieve and maintain higher degrees of complexity that physical sciences find it very difficult to explain how life has originated. For this reason, the question of the origin of life is deeply entangled with the question of its very nature. Is there some law or principle in the physical world that allows explaining the emergence of life as a necessity or, as Monod (1970) thought, is the origin of life so unlikely that it is almost a miracle? How could inert matter originate something that seems to be so deeply different in its properties?

From the perspective of the physical sciences, explaining life is a highly challenging task because the more complex a system is, the less probable it becomes both in its appearance and its persistence. At first approximation, it might be easy to understand how simple building blocks may spontaneously generate composite stable structures (atoms, molecules, macromolecules . . .) due to different levels of forces (Simon 1969): as a result of these interactions, increasingly complex stable structures appear (endowed, in many cases, with new interactive properties, not present in their separate parts, such as superconductivity, chemical affinity . . .). As the complexity of the structures increases, however, its maintenance becomes a problem: thermal noise increases fragility and, moreover, the coincidence or coordination of many highly specific processes becomes increasingly unlikely.

It is true that recent advances in thermodynamics explain the formation of composite aggregates (called “dissipative structures”), whose parts are tied together without intrinsic forces, ensuring their cohesion in far-from-equilibrium conditions. However, as we will discuss at length in this book, these systems appear spontaneously and persist only when specific external boundary conditions are met and, more importantly, they lack internal complexity and functionality. In contrast, biology deals with highly complex systems, so that something more than initial conditions and fundamental laws seems to be required to explain a world of complex biological systems.

Assuming that nature does not make leaps and that, therefore, there is a continuum between non-living matter and life,¹ there should be explanatory principles of the transition from non-living to living matter. As Fry (2000) has pointed out, the fundamental problem of the origin of life lies in the tension between the principle of continuity and the difficulty of explaining the obvious differences between non-living and living matter. If the origin of life is a legitimate scientific question (and we think it is), one should look for a theory that bridges the gap between physics and biology. In particular, since living beings are made of the same constituents as non-living entities, what is the nature of the organisation that enables them to achieve, maintain, and propagate such a high degree of complexity? And what are the consequences of this extraordinary capacity?

On our planet, life has developed for a long period of time and has colonised the most diverse environments – from the deep oceans or even several kilometres under the Earth’s crust to the upper levels of the atmosphere; from the hottest environments (over 100°C) to extremely acid or radioactive ones. And if we consider life from an historical perspective, it is even more impressive how it has managed to adapt to the successive catastrophic events that have occurred on our planet during the last 3.5 billion years. Admittedly, only the simplest forms of life are capable of such extreme robustness and versatility; at the same time, these forms of life have also been able to innovate and evolve towards increasingly higher levels of complexity. Life, as it has developed on our planet, has gradually integrated more and more levels of organisation (from unicellular life to colonies, multicellular organisms and societies).²

How can we explain all this diversity and complexity? Ever since Dobzhansky’s (1973) famous dictum that “nothing in Biology makes sense except in the light of evolution”, mainstream thinking in biology has seen evolution by natural selection as the source of diversity at every level of biological organisation. Indeed, the unfolding of an evolutionary process by natural selection, based on heritable genetic mechanisms, allows life to explore many possible combinations and solutions in order to survive. And the evolution-centred view of life has been so dominant that the idea of organism (which played a key role in nineteenth century biology) has become almost dispensable (Morange 2003). However, in a very fundamental sense, we shall argue at length that the reality is rather the opposite: evolutionary mechanisms operate because they are embodied in the complex organisation of organisms. Thus, if we look for the roots of the impressive capacity of life to proliferate, to

¹Philosophically, this assumption amounts to adopting a monistic stance. Chapter. 2 is devoted to a detailed analysis of the position of the autonomous perspective developed in this book in the debate on emergence, reduction, and related issues.

²Nowadays we know that this process of diversification and complexification is not a contingent fact, but rather something “inscribed” in the evolutionary nature of life. As Gould (1994) has argued, evolution is not aimed towards an increase in complexity; in fact, life originates in the simplest form and many organisms have remained successfully as such. However, a few organisms occasionally introduced innovations, “thus extending the right tail in the distribution of complexity. Many always move to the left, but they are absorbed within space already occupied”.

create an enormous variety of forms, to adapt to completely different environments, and particularly, to increase its complexity, we shall focus on individual living entities, namely on organisms, because evolution³ as an explanatory mechanism actually presupposes the existence of organisms. As Varela (1979) pointed out,

evolutionary thought, through its emphasis on diversity, reproduction, and the species in order to explain the dynamics of change, has obscured the necessity of looking at the autonomous nature of living units for the understanding of biological phenomenology. Also I think that the maintenance of identity and the invariance of defining relations in the living unities are at the base of all possible ontogenetic and evolutionary transformation in biological systems (p. 5).

As Rosen also emphasised, the crucial question for understanding life lies in the nature of its organisation.⁴ It is true that any known living being cannot have appeared except as a result of a long history of reproductive events, since such a complex organisation can only be originated through an accumulative historical process and, furthermore, that its long-term sustainability also requires inter-generational entailments. This is clearly reflected in the fact that, in order to be operational, genetic components (which contribute to specify the metabolic machinery and organisation of single biological entities) must be shaped through a process that involves a large number of individual systems and many consecutive generations, or reproductive steps. Yet, this does not mean that the organisation of organisms should be neglected; on the contrary, a theory of living organisation is fundamental for understanding how these evolutionary mechanisms could have appeared and how they could work.

A theory of the living based on the concept of organism aims to review the concept of evolution and its role in a new way, attempting to overcome the dichotomy – and often opposition – between what since Mayr’s (1961) work is called the biology of proximate causes and that of ultimate causes. Our vindication of the central role played by the notion of organism in biology should be placed within this wider perspective, in which the explanatory emphasis is placed on organisation. As Hooker and Christensen (1999) have highlighted, in order to

³The term ‘evolution’ could be understood in a very broad sense, just as an historical process of causal entailments. However, since Darwin, the term evolution has acquired a more restrictive sense, referring to specific mechanisms of inheritance and several other conditions (see for example, Godfrey-Smith (2009)). We will discuss the relation between autonomy and evolution in Chap. 5; here, we use the more restrictive sense of the term.

⁴“We cannot answer the question (...) ‘Why is a machine alive?’ with the answer ‘Because its ancestors were alive’. Pedigrees, lineages, genealogies, and the like, are quite irrelevant to the basic question. Ever more insistently over the past century, and never more so than today, we hear the argument that biology *is* evolution; that living systems instantiate evolutionary processes rather than life; and ironically, that these processes are devoid of entailment, immune to natural law, and hence outside of science completely. To me it is easy to conceive of life, and hence biology, without evolution” (Rosen 1991: 254–55).

properly understand the evolution of biological systems, traditional approaches need to be embedded within a more general dynamical-organisational theory.⁵

Therefore, it is at the level of organisms, understood as cohesive and spatially bounded entities, that the biological domain's organised complexity is fundamentally expressed. Seen from the perspective of their relations with their environment, individual organisms are systems capable of acting for their own benefit, of constituting an identity that distinguishes them from their environment (at the same time as they continue interacting with it as open, far-from-equilibrium systems). This capacity of living beings to act for their own benefit follows from their peculiar form of organisation.

Living beings are systems continuously producing their own chemical components, and with these components they build their organs and functional parts. In a word, their organisation is maintaining itself. This is why living systems cannot stop their activity: they intrinsically tend to work or they disintegrate. Actually, this inherent tendency of living entities to promote their own existence – to act on their own behalf – could be related to the idea of the *conatus*, to which Spinoza (1677/2002) refers to designate the innate inclination of any entity to continue to exist and enhance itself.⁶

The root of this drive to persist lies in the principles of biological organisation. As Jonas (1966/2001) pointed out, the organisation of living systems is characterised by the inseparability between what they are – their “being” – and what they do – their “doing”. This feature is reflected in their metabolism, which consists of a set of processes that allow them to build and replace their structures, grow and reproduce, and respond to their environments. Metabolism is the ongoing activity by which living beings continuously self-produce (and eventually, re-produce), self-repair, and maintain themselves. Unlike the Cartesian argument (which has had so much influence during modernity⁷) that living beings are like man-made machines, Kant was the first author who defended the view that organisms are

⁵As a matter of fact, an organisational perspective seems to be taking shape in the new evolutionary developmental biology, which studies how the dynamics of development determine the phenotypic variation arising from genetic variation and how this affects phenotypic evolution (Laubichler and Maienschein 2007).

⁶As Spinoza (1677/2002) writes, “Each thing, insofar as it is in itself, endeavors to persist in its own being” (Ethics, part 3, prop. 6). This is understood as an intrinsic tendency or force to continue to exist. Striving to persevere is not merely something that a thing does in addition to other activities it might happen to undertake. Rather, striving is “nothing but the actual essence of the thing itself” (Ethics, part 3, prop. 7). See Duchesneau (1974) for an in-depth analysis of Spinoza's account of living systems, and a comparison with the Cartesian one.

⁷Actually, the Cartesian distinction between *res extensa* and *res cogitans*, which subsumed the biological domain within a global mechanistic vision of nature, facilitated a scientific research programme for studying living systems. It should be underscored that, while Descartes' metaphysical dualism is widely recognised and is a prominent feature of his *Meditations*, scholars in the past generation have also focused on the complexity of his natural philosophy, including his work in physiology, medicine but also on the passions, as displaying something very different: a more ‘integrated’ view of bodily function. See notably the essays collected in Gaukroger et al. (2000).

deeply different from machines because their parts and activities are non-separable, and the functions of these parts are not externally imposed, but rather intrinsically determined. According to Kant (1790/1987), since the activity performed by the parts of the organism is carried out for their own maintenance, organisms are intrinsically teleological. As he writes in the *Critique of Judgement*:

In such a product of nature each part, at the same time as it exists throughout all the others, is thought as existing with respect to the other parts and the whole, namely as instrument (organ). That is nevertheless not enough (because it could be merely an instrument of art, and represented as possible only as a purpose in general); the part is thought of as an organ producing the other parts (and consequently each part as producing the others reciprocally). Namely, the part cannot be any instrument of art, but only an instrument of nature, which provides the matter to all instruments (and even to those of art). It is then – and for this sole reason – that such a product, as organized and organizing itself, can be called a natural purpose (CJ, § 65).

This view allows him to open up a gap in the physical world, since organisms cannot be brought under the rules that apply to all other physical entities. Thus, Kant asks himself:

How purposes that are not ours, and that we also cannot attribute to nature (since we do not assume nature to be an intelligent being) yet are to constitute, or could constitute, a special kind of causality, or at least a quite distinct lawfulness of nature (CJ, § 61).

This “special” kind of causality is circular, namely, effects derive from the causes but, at the same time, generate them. The very organisation of living beings, in which the parts generate the whole, and, conversely, the whole produces and maintains the parts, shows a kind of intrinsic purpose. Kant grounds the idea of purposiveness (and teleology) in the holistic and circular organisation of biological organisms and, more precisely, in the fact that they are able to organise by themselves, to *self-organise*.⁸ Unlike artefacts, organisms are “natural purposes”: they are not produced or maintained by an external cause, but instead have the self-(re)producing and self-maintaining character that is revealed in the kinds of vital properties they display (reciprocal dependence of parts, capacity for self-repair and self-(re)production).

Today, some aspects of the Kantian perspective are undergoing resurgence. For example, the recent blossoming of systems biology (Kitano 2002; Science, *special issue* 2002; Bogeerd et al. 2007), focused on the complexity of biomolecular interaction networks, is much closer to a holistic or integrative conception of living systems than the reductionist views predominant in molecular biology. Thanks to the development of new scientific tools, these more holistic theories place the question of the organisation at the centre of biological research. This recent trend contrasts with the preceding history of biology, during which the Kantian view has often be seen as marginal (even through this view has been corrected by

⁸Actually, Kant has been one of first authors to use the term “self-organisation”. In Chap. 1, we will briefly mention how the meaning of this concept has progressively shifted during the 20th century.

the recent historiography, see for instance Huneman 2007; Richards 2000; Sloan 2002), essentially because it was thought to be at odds with the model of causality predominant in Newtonian science.

And yet, the Kantian perspective had continuity in the (mostly Continental) Biology of the nineteenth century, especially in the work of Goethe and Cuvier (Huneman 2006). In the first part of the twentieth century, many biologists were still convinced that the nature of living organisation – understood, following Kant’s inspiration, as the form in which the parts interact with each other to bring forth the properties of the whole – was one of the main issues of biology. This view was commonly labelled *organicism* (Wolfe 2010; see also Gilbert and Sarkar 2000). Organicism considers the observable structures of life, its overall organisation, and the properties and characteristics of its parts to be the result of the reciprocal interplay among all its components. The organicist tradition was influential in early twentieth century biology. During the twenties and thirties, a group of researchers, including Woodger, Needham, Waddington, and Wrinch, created the “Theoretical Biology Club”, whose objective was precisely to promote the organicist approach to biology. This movement – in which we can include other authors, like Bernal and Bertalanffy – was characterised by a predominant anti-reductionist and holistic inspiration (Etxeberria and Umerez 2006). Among these researchers, the name of Waddington is worth stressing because his work, after the Second World War, permitted the connection between the organicist movement of the thirties and the new tendencies of the sixties and seventies.

To understand the roots of the current blossoming of the “Kantian-inspired organicist ideas” in biology during the twentieth century, let us mention some other scientific trends, falling outside the frontiers of biology.

First, during the thirties and forties, a number of physicists associated with the development of quantum theory, interested in the nature of biological organisation, turned their attention to biology. Among these scientists, it is worth emphasising the name of Schrödinger, who gave his famous lectures “What Is Life?” in 1943 (Schrödinger 1944). Following this work, other quantum physicists addressed the problem of what characterises the specificity of living systems with regard to physical ones. Among these we can include researchers like von Neumann and Pauli. Interestingly, the advances in physics inspired new attempts to challenge reductionist assumptions. For example, Rashevsky, according to his disciple Rosen, defended

a principle that governs the way in which physical phenomena are organized, a principle that governs the organization of phenomena, rather than the phenomena themselves. Indeed, organization is precisely what relational biology is about (Rosen 1991: 113).

During the seventies, Rosen himself and Pattee (Umerez 2001) also developed an anti-reductionist view of the specific organisation of living systems, based on his analyses of the specific causation associated with emergent constraints that living systems generate (see further below).

Second, special emphasis should be put on the cybernetic movement. The cyberneticists were influenced by the work of the American physiologist Cannon

(1929) who, in the early 1930s, developed the concept of “homeostasis” (whose origins date back to the work of the French biologist Claude Bernard⁹) as a key feature of the organisation of living beings. According to Cannon, the idea of homeostasis expresses the tendency of living systems to actively maintain their identity, despite external perturbations or differences within their environment. During the 1970s, a new generation of cyberneticists, notably Von Förster, Ashby, and Maturana, created the so-called second-order cybernetics. This movement was especially interested in the study and mathematical modelling of biological systems, based on the ideas of recursivity and closure (Cahiers du CREA 1985). Second-order cybernetics is of special relevance for our purposes, since it constituted the scientific environment in which the theory of *autopoiesis* was elaborated (see below).

Third, after the work of Prigogine (1962), the idea of self-organisation in far-from-equilibrium conditions began to enter into scientific discourse in physics, which also helped the Kantian view to gain influence in biology. Yet, as we will discuss at length in Chap. 1, there is an important conceptual difference between the Prigoginian concept of (physical) self-organisation and the Kantian notion of (biological) organisation. As Fox Keller (2007) has pointed out, the kind of complexity of organisms resulting from an iterative processes of organisation that occur over time is completely different from the one-shot, order-for-free kind of self-organisation associated with some kind of non-linear dynamical systems. In particular, the former is constituted by functional parts, whereas the latter lacks functionality. The logic of the metabolism, for example, shows a functionally diversified organisation, clearly different in this sense from any physicochemical dissipative structure. In this sense, as we will see, what we need is a view of biological systems that goes beyond a generic vindication of an organisational-centred biology. What matters is the understanding of the *specificity* of the organisation of biological systems, which are not just self-organised systems.

In the second post-war period, both the New Synthesis in evolutionary biology and the revolution of Molecular Biology created a scientific atmosphere that was quite unprepared to accept organicist and Kantian views (Moreno et al. 2008). Accordingly, this tradition remained, until very recently, marginal in biology. In this context, however, Waddington was the main driver of a movement that advocated an organisational approach in biology, by reviving the “first” Theoretical Biology of the twenties and thirties (Etxeberria and Umercz 2006). This “second” Theoretical Biology was initially developed by several pioneering authors like Waddington himself (1968–1972), Rosen (1971, 1972, 1973, 1991), Piaget (1967), Maturana and Varela (1980), Pattee (1972, 1973), and Ganti (1973/2003, 1975). Many of these authors put strong emphasis on the idea that the constitutive organisation of biological systems realises a distinctive regime of causation, able not only of producing and maintaining the parts that contribute to the functioning of the system as an integrated, operational, and topologically distinct whole but also able

⁹See Bernard (1865) and (1878).

to promote the conditions of its own existence through its interaction with the environment. This is essentially what we call in this book *biological autonomy*.

To give a preliminary idea of what autonomy is about, let us mention one of its first and well-known accounts, the theory of *autopoiesis* proposed by the Chilean biologists Maturana and Varela in the early 1970s (Maturana and Varela 1973; Varela et al. 1974). In the theory of autopoiesis, although the concept of autonomy is applied to different specific biological domains (immune, neural . . . see Varela 1979), it characterises the fundamental feature of the living, namely, the autopoietic organisation. Autopoiesis refers to the capacity of self-production of biological metabolism, by emphasising (in a simplified and abstract way) its causal circularity – which Maturana and Varela called “operational closure”. In particular, their model describes the production of a physical boundary, which is conceived as a condition of possibility of the internal chemical network (because it ensures suitable concentrations for the maintenance of the component production network); in turn, the network maintains the physical boundary (because it is the component production network which produces the special self-assembling components that build the membrane). In their own terms (in which the cybernetic flavour is manifest):

An autopoietic machine is a machine organized (defined as a unity) as a network of processes of production (transformation and destruction) of components which: (i) through their interactions and transformations continuously regenerate and realize the network of processes (relations) that produced them; and (ii) constitute it (the machine) as a concrete unity in space in which they (the components) exist by specifying the topological domain of its realization as such a network (Maturana and Varela 1980: 78).

Thus, autopoiesis consists in a recursive process of component production that builds up its own physical border. The global network of component relations establishes self-maintaining dynamics, which bring about the constitution of the system as an operational unit. In short, physical border and metabolic processes are entwined in a cyclic, recursive production network and they together constitute the identity of the system. From this perspective, phenomena like tornadoes, whirlpools, and candle flames, which are to a certain degree self-organising and self-maintaining systems, are not autonomous, because they lack an internally produced physical boundary, and are not concrete topological units. In that sense, what distinguishes self-organisation from autonomy is that the former lacks an internal organisation complex enough to be recruited for deploying selective actions capable of actively ensuring the system’s maintenance.

For the purposes of this book, it is worth mentioning two lines of criticism that have been addressed to the theory of autopoiesis. On the one hand, autopoiesis conceives autonomy as a fundamental internal determination, defined by the operational closure between the production network and the physical border. In this model, interactions with the environment do not enter into the definition-constitution of the autonomous system; rather, the interactions with the environment – that Maturana and Varela called “structural couplings” – follow on from the specific internal identity of each autopoietic system. On the other hand, Maturana and Varela

define autonomy in rather abstract and functionalist terms: material and energetic aspects are considered as purely contingent to its realisation.

On both these issues, the framework that we will develop in this book takes a different path. The autonomous perspective, we hold, should take into account the “situatedness” of biological systems in their environment, as well as their “grounding” in thermodynamics. As a matter of fact, these issues have been at the centre of the most recent studies on biological autonomy, by authors like Hooker, Collier, Christensen, Bickhard, Kauffman, Juarrero, and the IAS Research Group,¹⁰ who have stressed that the interactive dimensions of autonomous systems in fact *derive* from the fact that they are thermodynamically open systems, in far-from-equilibrium conditions. As these authors have explained, since the constitutive organisation of biological systems exists only in far-from-equilibrium conditions, they must preserve an adequate interchange of matter and energy with their environment or they would disintegrate. For example, in Kauffman’s approach, the main condition required for considering a system autonomous is that it should be capable of performing what he calls “work-constraint cycles” (Kauffman 2000). As Maturana and Varela, Kauffman’s account envisages how autonomy can come out of the causal circularity of the system; yet, in his view, this circularity is understood not just in terms of abstract relations of component production but in explicit connection with the thermodynamic requirements that the system must meet to maintain itself.

In accordance with this literature, we will make in this book a conceptual distinction between two interrelated, and yet conceptually distinct, dimensions of biological autonomy: the *constitutive* one, which largely determines the identity of the system; and the *interactive* one, which, far from being a mere side effect of the constitutive dimension, deals with the inherent functional interactions that the organisms must maintain with the environment (Moreno et al. 2008). These two dimensions are intimately related and equally necessary. It might be illuminating to think of the example of the active transport of ions across the cell membrane, required to prevent osmotic crises. The cell can be maintained as long as ion transport is performed, but this interaction can only be carried out because there is a constitutive chemical organisation providing the membranous machinery that does the work. In particular, the emphasis on the interactive dimension implies, as we will stress repeatedly, that autonomy should not be confused with independence: an autonomous system must interact with its environment in order to maintain its organisation¹¹ (Ruiz-Mirazo and Moreno 2004). As we will discuss in Chap. 4, this is what grounds the agential dimension of autonomy.

¹⁰The IAS Research Group – to which the authors of this book belong – has been working since the last 25 years on autonomous perspective in biology, while extending it to other fields as cognition, society and bioethics. See also the end of this Introduction and footnote 6 in Chap. 1.

¹¹Hooker has recently defined autonomy as “the coordination of the internal metabolic interaction cycle and the external environmental interaction cycle so as the latter delivers energy and material components to the organism in a usable form and at the times and locations the former requires to complete its regeneration cycles, including regeneration of the autonomy capacity” Hooker (2013).

Again, there is a reciprocal dependence between what defines the conditions of existence of the system and the actions derived from its existence: from the autonomous perspective, in Jonas's terms, the system's *doing* and its *being* are two sides of the same coin (see also Moreno et al. 2008). In this view, the environment becomes a world full of significance: facts that from the outside may appear just as purely physical or chemical develop into positive, negative, or neutral influences on the system, depending on whether they contribute to, hinder or have no effect on the maintenance of its dynamic identity. Even the simplest living organism creates a set of preferential partitions of the world, converting interactions with their surrounding media into elementary values, as we will explain extensively in Chaps. 4 and 7. Von Uexküll (1982/1940) called this subjective meaningful world of each organism *Umwelt*. The interactive dimension of autonomy is where the nature of living systems as inventors of worlds with meaning becomes manifest (see also Hoffmeyer 1996). Indeed, this aspect was recognised by Weber and Varela (2002) who argued, following Jonas, that autonomy implies a meaningful relation with the environment.

The autonomous perspective that we develop here endeavours then to grasp the complexity of biological phenomena, by adequately accounting for their various dimensions, specificities, and relations with the physical and chemical domains. As we will discuss throughout the book, our framework differs in many ways from preceding related models, mainly because we aim at – simultaneously – enriching and specifying their central tenets, in close contact with current scientific theories. In the remainder of this introduction, let us give a synthetic overview of the ideas that we will be advocating.

First, the self-determination of the constitutive organisation remains the conceptual core of autonomy. We share with existing accounts of autonomy the idea that biological systems are constituted by a network of causal interactions that continuously re-establish their identity (see also Bechtel 2007). The aim of Chap. 1 will be to provide an explicit conceptual and (preliminarily) formal account of self-determination in terms of what we will label “closure of constraints”.

Biological systems determine (at least in part) themselves, we will contend, by constraining themselves: they generate and maintain a set of structures acting as constraints which, by harnessing and channelling the processes and reactions occurring in the system, contribute to sustain each other, and then the system itself. The core of biological organisation *is* the closure of constraints. We will discuss how the concept of closure allows specifying what kind of “circularity” is at work in the biological domain, and how it fundamentally differs from other “process loops” and self-organising phenomena in Physics and Chemistry. In particular, we will emphasise that biological closure requires taking into account, at the same time, the conceptual distinction, and yet inherent interdependence, between two causal regimes: the constraints themselves and the thermodynamic flow on which they act. In the autonomous perspective, closure (of constraints) and (thermodynamic) openness go hand in hand. Self-determination as closure constitutes the pivotal idea on which we will build our account of autonomy. A first step is made in the last section of Chap. 1, where we will claim that biological organisation, to

be such, requires regulation. The long-term preservation of biological organisms supposes the capacity to self-maintain not only in stable conditions but also, and crucially, before potentially deleterious internal or external perturbations. In such circumstances, regulatory capacities govern the transition towards a new viable situation, be it by countering the perturbations or by establishing a new constitutive organisation. In all cases, we will account for regulation in terms of a specific set of constraints, which contribute to the maintenance of the organisation *only* when its closure is being disrupted: accordingly, we will argue that regulatory constraints should be understood as being subject to *second-order* closure.

Does the autonomous perspective require appealing to some form of emergentism? In previous years, some authors have argued that accounts dealing with concepts like self-organisation, closure, constraints, autonomy, and related ones are indeed committed to the idea that biological organisation is an emergent determination. In Chap. 2, we deal with this issue, advocate a monistic stance, and provide a twofold argument. First we argue, against exclusion arguments, that closure can be consistently (with respect to our monistic assumption) understood as an emergent regime of causation, in the specific sense that the relatedness among its constituents provides it with distinctive and irreducible properties and causal powers. Second, although the closure of the constitutive organisation makes sense of the claim that “the very existence of the parts depends on their being involved in the whole”, we hold that closure does *not* imply inter-level causation, in the restrictive sense of a causal relation between the whole and its own parts (what we label “nested” causation). Yet, we leave room for appealing to nested causation in the biological domain, if relevant cases were identified and the adequate conceptual justification were provided.

With these clarifications in hand, Chap. 3 addresses the question of the distinctive emergent features of organisms by arguing, in particular, that the closure of constraints provides an adequate and naturalised grounding for the teleology, normativity, and functionality of biological organisation. When closure is realised, the existence of the organisation depends, as we have already emphasised, on the effects of its own activity: accordingly, biological systems are teleologically organised, in a specific and scientifically legitimate sense. Because of teleology, moreover, the activity of the organism has an “intrinsic relevance” which, we submit, generates the norms that the system is supposed to follow: the system must behave in a specific way, otherwise it would cease to exist. Hence biological organisation, because of closure, is inherently normative. And then, by grounding teleology and normativity, closure grounds also functionality in biological organisation: the causal effects produced by constraints subject to closure define biological functions. The general upshot of the analysis, at the end of Chap. 3, will be the deep theoretical binding between “closure”, “organisation”, and “functionality”: it will be our contention that, from the autonomous perspective, they are reciprocally defining concepts, which refer to the very same causal regime.

The constitutive dimension of closure, however, is not autonomy. As mentioned in the preceding pages, autonomy also includes an interactive dimension, dealing with the relations between the organism and its environment. We deal with the

interactive dimensions in Chap. 4, and refer to it as *agency*, characterised as a set of constraints subject to closure, exerting their causal effects on the boundary conditions of the whole system. At the end of the chapter, we argue that a system whose organisation realises closure, regulation, and agency, as defined in the first part of the book, is an autonomous system, and therefore a biological organism. More precisely, Chap. 4 elaborates on a definition of minimal autonomy that captures the essential features of biological organisation in its (relatively) most simple manifestations, typically in unicellular organisms.

What has the autonomous perspective to say about more complex organisations and specifically about multicellular organisms? One of the main weaknesses of the organisational tradition in biology is arguably the fact that it has never explicitly addressed the issue of higher *levels* of autonomy: How many levels of autonomy can be identified in the biological realm, and what are their mutual relations? In Chap. 6, we make a first step in this direction: we try to frame the issue of higher-level autonomy in precise terms and submit some explicit hypotheses on its features. The central idea will be that what matters for higher-level autonomy is *development*. More specifically, multicellular systems are relevant candidates as organisms when their organisation exerts a functional control over the development of unicellular components, so to induce their differentiation which, in turn, makes them apt to live only in the very specific environment constituted by the multicellular system: in a word, the control over development produces the relevant degree of *functional integration* that distinguishes multicellular organisms (as autonomous systems) from other kinds of multicellular systems. What about the relations between levels of autonomy? In spite of their differentiation (and then of the loss of some of their capacities), we will argue that unicellular constituents of higher-level organisms still meet the requirements of autonomy. In fact, the very possibility of higher-level autonomy seems to require that lower-level entities preserve an adequate degree of complexity: multicellular autonomy requires unicellular autonomy. One of the objectives of Chap. 6 (and partly of Chap. 4, last section) will be, by relying on an explicit definition of autonomy, to provide relevant criteria for examining different kinds of higher-level associations and organisations of autonomous systems and to compare them on theoretical grounds. In particular, our framework could allow locating them in a *continuum* of organised systems going from, at one extreme, those cases fulfilling only the requirements for closure (as ecosystems) to systems being progressively more integrated (as the cyanobacterium *Nostoc punctiforme*), up to genuine multicellular organisms (higher-level autonomous systems) at the other extreme.

The transition to multicellular autonomy paves the way towards cognition, which is possibly the most amazing innovation during the evolution of life. Cognition, as discussed in Chap. 7, is much more than a complex form of agency. It is better conceived as a radically new kind of autonomy whose specific features and dynamics go, qualitatively, far beyond multicellular autonomy, opening the way towards our own origins as human beings. In this sense, the analysis of cognition is related to the nuclear problem of the gap between the “biological” (broadly understood) and the “human” domains. Yet, the autonomous perspective strives

to understand and explain cognitive capacities in close connection to a bodily organisation, which is in turn the product of a long evolutionary process, through which new phenomena such as emotions or consciousness – and a world of meaning and values – have been generated. The appearance of cognition is the result of the evolution towards increasingly higher degrees of both constitutive and interactive complexity: in this sense, with all its specificities, cognition is still a “biogenic” (Lyon 2006) phenomenon. By framing the issue of cognition in these terms, we think that it can be better handled in naturalised terms, without underestimating the formidable difficulties that any satisfactory account of cognition has to face to understand its complex nature and phenomenological novelty. Accordingly, Chap. 7 is possibly the most ambitious and yet incomplete, since it sketches in a preliminary way many problems for which much more work will be required.

Autonomy, as conceived in this book, lies at the intersection between different dimensions, and specifically the constitutive and interactive ones, on which we put strong emphasis in the previous pages. Yet, this is not the whole story: autonomy also has a *historical* dimension. As we will discuss in Chap. 5, no adequate understanding of the emergence of autonomous systems (and specifically highly complex autonomous systems, as present biological organisms) can be obtained without taking into account the evolutionary process that brought them about. Autonomous systems are too complex to be spontaneous and cannot self-organise (in the sense of generate themselves) as dissipative systems do: their complexity requires an evolutionary process of accumulation and preservation. Yet, in addition to acknowledging the fundamental place of history in the autonomous perspective, we will submit two related ideas. First, the historical dimension does not have the same theoretical status as the constitutive and interactive ones: while the latter two *define* autonomy, the former does not. The reason is that we do not need history to understand what biological systems are, but rather to understand where they come from: these two questions are of course related, but conceptually distinct. Second, we will restate the relations between selection and organisation, by advocating the general picture according to which the evolution of biological systems stems from the mutual interplay between organisation and selection: this is because, as we will argue, organisation is a condition, and not only an outcome, of evolutionary processes.

Having outlined the central ideas of the book, let us point out that it is, of course, not our intention to develop an exhaustive account of biological autonomy, which would deal with all aspects and implications of the philosophical and theoretical framework. Rather, our ambition is to offer a coherent and integrated picture of the autonomous perspective, by focusing on what we think are some of its central tenets. Much more could (and hopefully will) be written on biological autonomy, but we hope that the ideas of this book can be a useful ground on which future investigations will rely.

This book is the result of a collaboration that goes far beyond that between the two authors. After having promoted (together with Julio Fernandez, Arantza Exteberria, and Jon Umerez), more than 20 years ago, the creation of the *IAS Research Centre for Life, Mind and Society*, at the University of the Basque Country,

in Donostia – San Sebastian, Alvaro Moreno has had since then the chance to work in this highly stimulating intellectual environment. In this respect, a special thought goes to Francisco Varela, who has been a fundamental source of inspiration for the creation of the *IAS Research* group and, for many years afterwards, a close collaborator and a friend.

Matteo Mossio joined the group in 2008 as a postdoctoral fellow and, after having moved back to Paris in 2011, maintains close collaborations with many of its members. Since the constitution of the *IAS Research* group its members have collectively developed the autonomous perspective in the biological, cognitive, biomedical, and ethical domain. The ideas developed in this book, then, are deeply grounded into the substantive and extensive philosophical and theoretical work undertaken by our colleagues and friends.¹²

It then goes without saying that we are intellectually indebted with many people. Let us thank first those who co-authored previous publications with (at least one of) us and allowed us to rework and use in this book some of the ideas advocated there: Argyris Arnellos, Xabier Barandiaran, Leonardo Bich, Maël Montévil, Kepa Ruiz-Mirazo, and Cristian Saborido. At the beginning of each chapter, we inserted a note in which we give the references of the specific publications from which some ideas and text portions have been taken and adapted.

We are sincerely grateful to the other members of the IAS Research Centre for continuous interactions, over the years, on a variety of topics related to this book: Antonio Casado da Rocha, Jesús Ibañez, Hanne de Jaegher, Asier Lasa, Ezequiel di Paolo, and Agustin Vicente. Also, we thank many other researchers with whom one of us (AM) has worked for a long time: Francisco Montero, Federico Morán, Juli Peretó, and more recently, Nei Nunes and Charbel El-Hani.

In Paris, the whole *Complexité et Information Morphologique Team* (CIM), at the Ecole Normale Supérieure, deserves a special mention. Some years ago, Giuseppe Longo created a small but very active interdisciplinary team, nourished by the talent of several young fellows: among them, let us thank with special emphasis Nicole Perret and Paul Villoutreix. We would also like to express our deepest gratitude to Giuseppe, a remarkably brilliant and profound scientist, for his wise guidance on – and unfailing support to – Matteo’s academic and scientific trajectory. Recently, Matteo has been invited, together with some of the CIM members, to join the new *Theory of Organisms* research group at the Ecole Normale Supérieure, supervised by Ana Soto. We warmly thank her, as well as Carlos Sonnenschein and Paul-Antoine Miquel, for this unique opportunity to engage in stimulating and quality discussions and exchanges.

Since Matteo’s appointment, the *Institut d’Histoire et Philosophie des Sciences et des Techniques* (IHPST) has constituted a privileged scientific environment and

¹²Over the years, the activities of the *IAS Research* group have received funding by both Basque and Spanish public institutions. This book, in particular, was supported by grant IT 590–13 of the Gobierno Vasco, and grant FFI2011-25665 of the Ministerio de Industria e Innovación.

provided him with ideal conditions of work. For that, we want to thank its director Jean Gayon, as well as all the members and colleagues who, in many cases, have become good friends.

Lastly, we are greatly indebted to those colleagues and friends who took the time to read and critically comment on early versions of the manuscript: Philippe Huneman, Johannes Martens, Arnaud Pocheville, and Charles Wolfe. In most cases, their observations and criticisms were decisive to highlight some of the weaknesses of the arguments and force us to improve their clarity and accuracy. In this respect, we owe a lot to Alicia Juarrero, who has not only made a number of precise and lucid comments on various ideas developed in the book but also crucially contributed to bringing the initial unstable language closer to correct English. We also want to warmly thank Juli Peretó for his help in the elaboration of many figures.

The final acknowledgements go to Cliff Hooker: his meticulous, lucid, and uncompromisingly critical reading of the entire manuscript has induced substantial changes (and, we hope, improvements!) in the formulation of the ideas, regarding both the form and the content. Last but not least, he has kindly written the best foreword we could expect.

Donostia – San Sebastian/Paris
October 7th 2014

References

- Abbott, N. (1995). Cerebrovascular organization and dynamics in cephalopods. In N. J. Abbott, R. Williamson, & L. Maddock (Eds.), *Cephalopod neurobiology*. Oxford: Oxford Science Publications.
- Adams, F. R. (1979). A goal-state theory of function attributions. *Canadian Journal of Philosophy*, 9, 493–518.
- Alexander, S. (1920). *Space, time and deity*. London: Macmillan.
- Allen, C., & Bekoff, M. (1995). Biological function, adaptation and natural design. *Philosophy of Science*, 62, 609–622.
- Allen, C., Bekoff, M., & Lauder, G. V. (Eds.). (1998). *Nature's purposes*. Cambridge, MA: MIT Press.
- Alon, U., Camarena, L., Surette, M. G., Aguera y Arcas, B., Liu, Y., Leiber, S., & Stock, J. B. (1998). Response regulator output in bacterial chemotaxis. *EMBO Journal*, 17(15), 4238–4248.
- Amundson, R. (2000). Against normal function. *Studies in History and Philosophy of Biological and Biomedical Sciences*, 31, 33–53.
- Anet, F. (2004). The place of metabolism in the origin of life. *Current Opinion in Chemical Biology*, 8, 654–659.
- Angerer, R. C., & Angerer, L. M. (2012). *Sea urchin embryo: specification of cell fates*. Chichester: ELS John Wiley & Sons.
- Arendt, D. (2008). The evolution of cell types in animals: emerging principles from molecular studies. *Nature Reviews Genetics*, 9(11), 868–882.
- Ariew, A. R., Cummins, R., & Perlman, M. (Eds.). (2002). *Functions*. Oxford: Oxford University Press.
- Arnellos, A., & Moreno, A. (2012). How functional differentiation originated in prebiotic evolution. *Ludus Vitalis*, 37, 1–23.
- Arnellos, A., & Moreno, A. (in press). Multicellular agency: an organizational view. *Biology & Philosophy*.
- Arnellos, A., Moreno, A., & Ruiz Mirazo, K. (2014). Organizational requirements for multicellular autonomy: insights from a comparative case study. *Biology & Philosophy*, 29, 851–884.
- Artiga, M. (2011). Re-organizing organizational accounts of function. *Applied Ontology*, 6(2), 105–124.
- Atkins, P. W. (1984). *The second law*. New York: Freeman.
- Barandiaran, X. (2008). *Mental life. A naturalized approach to the autonomy of cognitive agents*. Ph.D. dissertation, University of the Basque Country (UPV/EHU).
- Barandiaran, X., & Egbert, M. D. (2013). Norm-establishing and norm-following in autonomous agency. *Artificial Life Journal*, 20(1), 5–28.

- Barandiaran, X., & Moreno, A. (2006). On what makes certain dynamical systems cognitive. *Adaptive Behavior*, *14*, 171–185.
- Barandiaran, X., & Moreno, A. (2008). Adaptivity: from metabolism to behavior. *Adaptive Behavior*, *16*(5), 325–344.
- Barandiaran, X., Di Paolo, E., & Rohde, M. (2009). Defining agency. Individuality, normativity, asymmetry and spatio-temporality in action. *Journal of Adaptive Behavior*, *17*(5), 367–386.
- Barthal, I. B., Decety, J., & Mason, P. (2011). Empathy and pro-social behavior in rats. *Science*, *334*(6061), 1427–1430.
- Bechara, A. (2004). The role of emotion in decision-making: evidence from neurological patients with orbitofrontal damage. *Brain and Cognition*, *55*, 30–40.
- Bechtel, W. (2007). Biological mechanisms: organized to maintain autonomy. In F. Boogerd, F. Bruggeman, J. H. Hofmeyr, & H. V. Westerhoff (Eds.), *Systems biology. Philosophical foundations* (pp. 269–302). Amsterdam: Elsevier.
- Bedau, M. A. (1992). Goal-directed systems and the good. *The Monist*, *75*, 34–49.
- Bedau, M. A. (1996). The nature of life. In M. Boden (Ed.), *The philosophy of artificial life* (pp. 332–357). New York: Oxford University Press.
- Bell, G., & Mooers, A. O. (1997). Size and complexity among multicellular organisms. *Biological Journal of the Linnean Society*, *60*, 345–363.
- Benner, S. A. (1999). How small can a microorganism be? In *Size limits of very small microorganisms (Proceedings on a workshop)* (pp. 126–135). Washington, DC: National Academy Press.
- Ben-Tabou de-Leon, S., & Davidson, E. H. (2007). Gene regulation: gene control network in development. *Annual Review of Biophysics and Biomolecular Structure*, *36*, 191–212.
- Berger, S. L., Kouzarides, T., Shiekhattar, R., & Shilatifard, A. (2009). An operational definition of epigenetics. *Genes and Development*, *23*(7), 781–783.
- Berleman, J., & Kirby, J. (2009). Deciphering the hunting strategy of a bacterial wolfpack. *FEMS Microbiology Reviews*, *33*(5), 942–957.
- Bernard, C. (1865). *Introduction à l'étude de la médecine expérimentale*. Paris: Baillière.
- Bernard, C. (1878). *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux*. Paris: Baillière.
- Bich, L. (2012). Complex emergence and the living organization: an epistemological framework for biology. *Synthese*, *185*, 215–232.
- Bich, L., Moreno, M., Mossio, M., & Ruiz-Mirazo, K. (forthcoming). Biological regulation: controlling the system from within.
- Bickhard, M. H. (2000). Autonomy, function, and representation. *Communication and Cognition Artificial Intelligence*, *17*(3–4), 111–131.
- Bickhard, M. H. (2004). Process and emergence: normative function and representation. *Axiomathes – An International Journal in Ontology and Cognitive Systems*, *14*, 121–155.
- Bigelow, J., & Pargetter, R. (1987). Functions. *Journal of Philosophy*, *84*, 181–196. Reprinted in Buller, D. J. (1999). *Function, selection, and design* (pp. 97–114). Albany: SUNY Press.
- Bitbol, M. (2007). Ontology, matter and emergence. *Phenomenology and the Cognitive Science*, *6*, 293–307.
- Block, N. (2003). Do causal powers drain away? *Philosophy and Phenomenological Research*, *67*(1), 133–150.
- Bonner, J. T. (1988). *The evolution of complexity by means of natural selection*. Princeton: Princeton University Press.
- Bonner, J. T. (1999). The origins of multicellularity. *Integrative Biology*, *1*, 27–36.
- Bonner, J. T. (2000). *First signals. The evolution of multicellular development*. Princeton: Princeton University Press.
- Boogerd, F., Bruggeman, F., Hofmeyr, J.-H., & Westerhoff, H. V. (Eds.). (2007). *Systems biology. Philosophical foundations*. Amsterdam: Elsevier.
- Boorse, C. (1976). Wright on functions. *Philosophical Review*, *85*, 70–86.
- Boorse, C. (1977). Health as a theoretical concept. *Philosophy of Science*, *44*(4), 542–573.
- Boorse, C. (1997). A rebuttal on health. In J. M. Humber & R. F. Almeder (Eds.), *What is Disease?* (pp. 1–134). Totowa, NJ: Humana Press.

- Boorse, C. (2002). A rebuttal on functions. In A. Ariew, R. Cummins, & M. Perlman (Eds.), *Functions* (pp. 63–112). Oxford: Oxford University Press.
- Bourgine, P., & Stewart, J. (2004). Autopoiesis and cognition. *Artificial Life*, *10*, 327–345.
- Bourgine, P., & Varela, F. J. (1992). *Toward a practice of autonomous systems*. Cambridge, MA: MIT Press/Bradford Books.
- Broad, C. D. (1925). *The mind and its place in nature*. London: Routledge and Kegan Paul.
- Brown, T. S. (1911). The intrinsic factors in the act of progression in the mammal. *Proceeding of the Royal Society London, Series B*, *84*, 308–319.
- Budin, I., & Szostak, J. W. (2011). Physical effects underlying the transition from primitive to modern cell membranes. *PNAS*, *108*(13), 5249–5254.
- Buller, D. J. (1999). *Function, selection, and design*. Albany: SUNY Press.
- Bullock, T. H., Bennett, M. V. L., Johnston, D., Josephson, R., Marder, E., & Fields, R. D. (2005). The neuron doctrine, redux. *Science*, *4–310*(5749), 791–793.
- Burge, T. (2009). Primitive agency and natural norms. *Philosophy and Phenomenological Research*, *79*(2), 251–278.
- Burge, T. (2010). *Origins of objectivity*. Oxford: Oxford University Press.
- Buss, L. W. (1987). *The evolution of individuality*. Princeton: Princeton University Press.
- Cahiers du CREA. (1985). *Histoires de cybernetique* (Vol. 7). Paris: Ecole Polytechnique.
- Campbell, D. T. (1974). Downward causation in hierarchically organized biological systems. In F. J. Ayala & T. Dobzhansky (Eds.), *Studies in the philosophy of biology* (pp. 179–186). Berkeley/Los Angeles: University of California Press.
- Campbell, R. J., & Bickhard, M. H. (2011). Physicalism, emergence and downward causation. *Axiomathes*, *21*(1), 33–56. Quotations from the online version: <http://www.lehigh.edu/~mhb0/physicalemergence.pdf>.
- Campbell, E. L., Summers, M. L., Christman, H., Martin, M. E., & Meeks, J. C. (2007). Global gene expression patterns of *Nostoc punctiforme* in steady-state dinitrogen-grown heterocyst-containing cultures and at single time points during the differentiation of akinetes and hormogonia. *Journal of Bacteriology*, *189*, 5247–5256.
- Canfield, J. (1964). Teleological explanation in biology. *British Journal for the Philosophy of Science*, *14*, 285–295.
- Cannon, W. B. (1929). Organisation for physiological homeostasis. *Physiological Reviews*, *9*(3), 399–431.
- Cárdenas, M. L., Letelier, J. C., Gutierrez, C., Cornish-Bowden, A., & Soto-Andrade, J. (2010). Closure to efficient causation, computability and artificial life. *Journal of Theoretical Biology*, *263*(1), 79–92.
- Carroll, S. B. (2001). Chance and necessity: the evolution of morphological complexity and diversity. *Nature*, *409*, 1102–1109.
- Centler, F., & Dittrich, P. (2007). Chemical organizations in atmospheric photochemistries: a new method to analyze chemical reaction networks. *Planetary and Space Science*, *55*(4), 413–428.
- Chandler, J. L. R., & Van De Vijver, G. (Eds.). (2000). *Closure: emergent organizations and their dynamics* (Vol. 901). New York: Annals of the New York Academy of Science.
- Chandrasekhar, S. (1961). *Hydrodynamic and hydromagnetic stability*. Oxford: Clarendon.
- Chiel, H., & Beer, R. (1997). The brain has a body: adaptive behaviour emerges from interactions of nervous system, body and environment. *Trends Neuroscience*, *20*, 553–557.
- Christensen, W. D. (2007). Volition and cognitive control. In D. Spurrett, H. Kincaid, L. Stephens, & D. Ross (Eds.), *Distributed cognition and the will: individual volition and social context* (pp. 255–287). Cambridge, MA: MIT Press.
- Christensen, W. D. (2012). Natural sources of normativity. *Studies in History and Philosophy of Science Part C*, *43*(1), 104–112.
- Christensen, W. D., & Bickhard, M. H. (2002). The process dynamics of normative function. *The Monist*, *85*(1), 3–28.
- Christensen, W. D., & Hooker, C. A. (2000). An interactivist-constructivist approach to intelligence: self-directed anticipative learning. *Philosophical Psychology*, *13*, 5–45.

- Christman, H. D., Campbell, E. L., & Meeks, J. C. (2011). Global transcription profiles of the nitrogen stress response resulting in heterocyst or hormogonium development in *Nostoc punctiforme*. *Journal of Bacteriology*, *193*(24), 6874–6886.
- Clarke, E. (2011). The problem of biological individuality. *Biological Theory*, *5*(4), 312–325.
- Clarke, E. (2013). The multiple realizability of biological individuals. *The Journal of Philosophy*, *8*, 413–435.
- Cleland, C., & Chyba, C. (2007). *Does life have a definition?* In W. T. Sullivan & J. A. Baross (Eds.), *Planets and life: The emerging science of astrobiology* (Ch. 5, pp. 119–131). Cambridge: Cambridge University Press. Reprinted in C. E. Cleland & M. A. Bedau (Eds.) *The nature of life: Classical and contemporary perspectives from philosophy and science*. Cambridge, 2010, pp. 326–339.
- Collier, J. D. (2000). Autonomy and process closure as the basis for functionality. In J. L. R. Chandler & G. van der Vijver (Eds.), *Closure: emergent organisations and their dynamics* (pp. 280–290). New York: Annals of the New York Academy of Sciences.
- Conrad, M. (1979). Bootstrapping on the adaptive landscape. *BioSystems*, *11*, 167–182.
- Costa, S., & Shaw, P. (2007). ‘Open minded’ cells: how cells can change fate. *Trends in Cell Biology*, *17*, 101–106.
- Craver, C. F. (2001). Role functions, mechanisms, and hierarchy. *Philosophy of Science*, *68*, 53–74.
- Craver, C. F., & Bechtel, W. (2007). Top-down causation without top-down causes. *Biology and Philosophy*, *22*, 547–563.
- Crick, F., & Koch, C. (1990). Towards a neurobiological theory of consciousness. *Seminars in the Neurosciences*, *2*, 263–275.
- Crutchfield, J. P. (1994). The calculi of emergence: computations, dynamics, and induction. *Physica D*, *75*, 11–54.
- Cummins, R. (1975). Functional analysis. *Journal of Philosophy*, *72*, 741–765. Reprinted in Buller, D. J. (1999). *Function, selection, and design* (pp. 57–83). Albany: SUNY Press.
- Cummins, R. (2002). Neo-teleology. In A. Ariew, R. Cummins, & M. Perlman (Eds.), *Functions* (pp. 157–172). Oxford: Oxford University Press.
- Dagg, J. (2003). Ecosystem organization as side-effects of replicator and interactor activities. *Biology and Philosophy*, *18*, 491–492. doi:[10.1023/A:1024128115666](https://doi.org/10.1023/A:1024128115666).
- Damasio, A. R. (1994). *Descartes’ error. Emotion, reason and the human brain*. New York: G.P. Putnam’s Sons.
- Damasio, A. R. (1999). *The feeling of what happens*. New York: Harcourt Brace and Company.
- Davidson, D. (1963). Actions, reasons, and causes. *The Journal of Philosophy*, *60*(23), 685–700.
- Davies, P. S. (1994). Troubles for direct proper functions. *Noûs*, *28*, 363–381.
- Davies, P. S. (2000). Malfunctions. *Biology and Philosophy*, *15*, 19–38.
- Davies, P. S. (2001). *Norms of nature. Naturalism and the nature of functions*. Cambridge, MA: MIT Press.
- Dawkins, R. (1976). *The selfish gene*. New York: Oxford University Press.
- Dawkins, R. (1982). *The extended phenotype: the long reach of the gene*. Oxford: Oxford University Press.
- De Duve, C. (2007). Chemistry and selection. *Chemistry and Biodiversity*, *4*(4), 574–583.
- De Groot, R. S., Wilson, M. A., & Boumans, R. (2002). A typology for the classification, description and valuation of ecosystem functions, goods and services. *Ecological Economics*, *41*, 393–408.
- De Jaegher, H., & Di Paolo, E. (2007). Participatory sense-making: an enactive approach to social cognition. *Phenomenology and the Cognitive Sciences*, *6*(4), 485–507.
- De Jaegher, H., Di Paolo, E., & Gallagher, S. (2010). Can social interaction constitute social cognition? *Trends in Cognitive Science*, *14*, 441–447.
- Deamer, D. W. (1997). The first living systems: a bioenergetic perspective. *Microbiology and Molecular Biology Reviews*, *61*(2), 239–261.
- Deamer, D. W. (2008). Origins of life: how leaky were primitive cells? *Nature*, *454*, 37–38.
- Deamer, D. W. (2009). On the origin of systems. Systems biology, synthetic biology and the origin of life. *EMBO Reports*, *10*(1), S1–S4.

- Delancey, C. (2006). Ontology and teleofunctions: a defense and revision of the systematic account of teleological explanation. *Synthese*, 150, 69–98.
- Dennett, D. (1986). *Kinds of minds: towards an understanding of consciousness*. New York: Basic Books.
- Di Paolo, E. A. (2005). Autopoiesis, adaptivity, teleology, agency. *Phenomenology and the Cognitive Sciences*, 4(4), 429–452.
- Di Paolo, E. A., & De Jaegher, H. (2012). The interactive brain hypothesis. *Frontiers in Human Neuroscience*, 6, 163.
- Dobzhansky, T. (1973). Nothing in biology makes sense except in the light of evolution. *American Biology Teacher*, 35, 125–129.
- Dretske, F. (1988). *Explaining behavior*. Cambridge, MA: MIT Press.
- Duchesneau, F. (1974). Du modèle cartésien au modèle spinoziste de l'être vivant. *Canadian Journal of Philosophy*, 3(4), 539–562.
- Edelman, G. (1987). *Neural Darwinism. The theory of neuronal group selection*. New York: Basic Books.
- Edelman, G. M. (1989). *The remembered present: a biological theory of consciousness*. New York: Basic Books.
- Edelman, G. M. (1992). *Brilliant air, brilliant fire: on the matter of mind*. New York: Basic Books.
- Edelman, D. B., & Seth, A. K. (2009). Animal consciousness: a synthetic approach. *Trends in Neuroscience*, 32(9), 476–484.
- Edelman, G. M., & Tononi, G. (2000). *Consciousness: how matter becomes imagination*. London: Penguin Books.
- Edin, B. (2008). Assigning biological functions: making sense of causal chains. *Synthese*, 161, 203–218.
- Eigen, M. (1971). Selforganization of matter and evolution of biological Macromolecules. *Naturwissenschaften*, 58(10), 465–523.
- Emmeche, C. (1992). Life as an abstract phenomenon: is artificial life possible? In F. Varela & P. Bourguine (Eds.), *Toward a practice of autonomous systems* (pp. 466–474). Cambridge, MA: MIT Press.
- Emmeche, C., Stjernfelt, F., & Köppe, S. (2000). Levels, emergence, and three versions of downward causation. In P. B. Andersen, C. Emmeche, N. O. Finnemann, & P. V. Christiansen (Eds.), *Downward causation. minds, bodies and matter* (pp. 13–34). Aarhus: Aarhus University Press.
- Engel, A. K., & Singer, W. (2001). Temporal binding and the neural correlates of sensory awareness. *Trends in Cognitive Sciences*, 5(1), 16–25.
- Ereshfsky, M., & Pedrosa, M. (2013). Biological individuality: the case of biofilms. *Biology and Philosophy*, 28(2), 331–349.
- Erickson, K., & Schulkin, J. (2003). Facial expressions of emotion: a cognitive neuroscience perspective. *Brain and Cognition*, 52(1), 52–60.
- Eschenmosser, A. (2007). The search for the chemistry of life's origin. *Tetrahedron*, 63, 12821–12844.
- Etzeberria, A., & Moreno, A. (2001). From complexity to simplicity: nature and symbols. *BioSystems*, 60(1–3), 149–157.
- Etzeberria, A., & Umerez, J. (2006). Organización y organismo en la Biología Teórica ¿Vuelta al organicismo? *Ludus Vitalis*, 26, 3–38.
- Farmer, J., Kauffman, S., & Packard, N. (1986). Autocatalytic replication of polymers. *Physica D*, 22, 50–67.
- Fell, D. (1997). *Understanding the control of metabolism*. London: Portland University Press.
- Flemming, H., & Wingender, J. (2010). The biofilm matrix. *Nature Reviews Microbiology*, 8, 623–633.
- Folse, H. J., 3rd, & Roughgarden, J. (2010). What is an individual organism? A multilevel selection perspective. *The Quarterly Review of Biology*, 85(4), 447–472.
- Fontana, W. (1992). Algorithmic chemistry. In C. G. Langton, C. Taylor, J. D. Farmer, & S. Rasmussen (Eds.), *Artificial life II* (pp. 159–209). Redwood City: Addison-Wesley.

- Fontana, W., Wagner, G., & Buss, L. W. (1994). Beyond digital naturalism. *Artificial Life*, 1(1/2), 211–227.
- Fox Keller, E. (2007). The disappearance of function from ‘self-organizing systems’. In F. Boogerd, F. Bruggeman, J.-H. Hofmeyr, & H. V. Westerhoff (Eds.), *Systems biology: philosophical foundations* (pp. 303–317). Amsterdam: Elsevier.
- Fox Keller, E. (2009). Self-organization, self-assembly, and the inherent activity of matter. In S. H. Otto (Ed.), *The Hans Rausing lecture 2009* (Uppsala University, Disciplinary Domain of Humanities and Social Sciences, Faculty of Arts, Department of History of Science and Ideas).
- Fox Keller, E. (2010). It is possible to reduce biological explanations to explanations in chemistry and/or physics? In F. J. Ayala & R. Arp (Eds.), *Contemporary debates in philosophy of biology* (pp. 19–31). Chichester: Wiley.
- Frankfurt, H. G. (1978). The problem of action. *American Philosophical Quarterly*, 15(2), 157–162.
- Fraser, O., & Bugnyar, T. (2010). Do ravens show consolation? Responses to distressed others. *PLoS ONE*, 5(5), 1–8.
- Fry, I. (2000). *The emergence of life on Earth: a historical and scientific overview*. London: Rutgers University Press.
- Fuchs, T., & De Jaegher, H. (2009). Enactive intersubjectivity: participatory sense-making and mutual incorporation. *Phenomenology and the Cognitive Sciences*, 8, 465–486.
- Ganti, T. (1975). Organization of chemical reactions into dividing and metabolizing units: the chemotons. *BioSystems*, 7, 15–21.
- Ganti, T. (1973/2003). *The principles of life*. Oxford: Oxford University Press.
- Gardner, A. (2009). Adaptation as organism design. *Biology Letters*, 5(6), 861–864.
- Gardner, A., & Grafen, A. (2009). Capturing the superorganism: a formal theory of group adaptation. *Journal of Evolutionary Biology*, 22(4), 659–671.
- Gaukroger, S., Schuster, J., & Sutton, J. (Eds.). (2000). *Descartes’ natural philosophy*. London: Routledge.
- Gayon, J. (2006). Les biologistes ont-ils besoin du concept de fonction? Perspective philosophique. *Comptes Rendus Palevol*, 5(3–4), 479–487.
- Gayon, J., & de Ricqlès, A. (Eds.). (2010). *Les fonctions: des organismes aux artefacts*. Paris: Presses Universitaires de France.
- Gerhart, J., & Kirschner, M. (1997). *Cells, embryos and evolution*. Malden: Blackwell Science.
- Gil, R., Silva, F. J., Peretó, J., & Moya, A. (2004). Determination of the core of a minimal bacteria gene set. *Microbiology and Molecular Biology Reviews*, 68, 518–537.
- Gilbert, S. F., & Sarkar, S. (2000). Embracing complexity: organicism for the 21st century. *Developmental Dynamics*, 219(1), 1–9.
- Glansdorff, P., & Prigogine, I. (1971). *Thermodynamics of structure, stability and fluctuations*. London: Wiley.
- Gloor, P. (1997). *The temporal lobe and limbic system*. New York: Oxford University Press.
- Godfrey-Smith, P. (1994). A modern history theory of functions. *Noûs*, 28, 344–362. Reprinted in Buller, D. J. (1999). *Function, selection, and design* (pp. 199–220). Albany: SUNY Press.
- Godfrey-Smith, P. (2009). *Darwinian populations and natural selection*. Oxford: Oxford University Press.
- Godfrey-Smith, P. (2010). *Thinking like an octopus*. Harvard Gazette, Oct 21.
- Godfrey-Smith, P. (2013). On being an octopus. Boston Review. <https://www.bostonreview.net/books-ideas/peter-godfrey-smith-being-octopus>
- Godfrey-Smith, P. (2014). *Philosophy of biology*. Princeton: Princeton University Press.
- Gommans, W., Mullen, S., & Maas, S. (2009). RNA editing: a driving force for adaptive evolution? *Bioessays*, 31(10), 1137–1145.
- Gould, S. J. (1988). On replacing the idea of progress with an operational notion of directionality. In N. H. Nitecki (Ed.), *Evolutionary progress* (pp. 319–338). Chicago: University of Chicago Press.
- Gould, S. J. (1994). The evolution of life on the Earth. *Scientific American*, Oct 85–91.9.

- Gould, S. J. (2002). *The structure of evolutionary theory*. Cambridge, MA: Harvard University Press.
- Gould, S. J., & Lewontin, R. C. (1979). The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. *Proceedings of the Royal Society of London B*, 205, 581–598.
- Griesemer, J. R. (2002). What is “epi” about epigenetics? In L. Van Speybroeck, G. Van de Vijver, & D. De Waele (Eds.), *From epigenesis to epigenetics: the genome in context* (pp. 97–110). New York: New York Academy of Sciences.
- Griesemer, J. R., & Szathmáry, E. (2009). Ganti’s chemoton model and life criteria. In S. Rasmussen, M. A. Bedau, L. Chen, D. Deamer, D. C. Krakauer, & N. H. Packard (Eds.), *Protocells: bridging nonliving and living matter* (pp. 481–512). Cambridge, MA: MIT Press.
- Griffiths, P. E. (1993). Functional analysis and proper functions. *British Journal for the Philosophy of Science*, 44, 409–422. Reprinted in Buller, D. J. (1999). *Function, selection, and design* (pp. 143–158). Albany: SUNY Press.
- Griffiths, P. E. (2001). Genetic information: a metaphor in search of a theory. *Philosophy of Science*, 68(3), 394–412.
- Grosberg, R. K., & Strathmann, R. R. (2007). The evolution of multicellularity: a minor major transition. *Annual Review of Ecology, Evolution, Systematics*, 38, 621–654.
- Hallmann, A. (2011). Evolution of reproductive development in the volvocine algae. *Sexual Plant Reproduction*, 24, 97–112.
- Hanczyc, M., & Ikegami, T. (2010). Chemical basis for minimal cognition. *Artificial Life*, 16(3), 233–243.
- Hardcastle, V. G. (2002). On the normativity of functions. In A. Ariew, R. Cummins, & M. Perlman (Eds.), *Functions* (pp. 144–156). Oxford: Oxford University Press.
- Hartenstein, V. (2006). The neuroendocrine system in invertebrates: a developmental and evolutionary perspective. *Endocrinology*, 190, 555–570.
- Hempel, C. G. (1965). *Aspects of scientific explanation*. London: Collier Macmillan Publishers.
- Hempel, C. G., & Oppenheim, P. (1948). Studies in the logic of explanation. *Philosophy of Science*, 15, 135–175.
- Hertel, J., Lindemeyer, M., Missal, K., Fried, C., Tanzer, A., Flamm, C., Hofacker, I. L., & Stadler, P. F. (2006). The expansion of the metazoan microRNA repertoire. *BMC Genomics*, 7(1), 25.
- Hickman, C., Roberts, L., & Larson, A. (2001). *Integrated principles of zoology*. Boston: MacGraw-Hill.
- Hoffmeyer, J. (1996). *Signs of meaning in the universe*. Bloomington: Indiana University Press.
- Hoffmeyer, J. (1998). Life: the invention of externalism. In Farre, G., & Oksala, T. (Eds.), *Emergency, complexity, hierarchy, organization*. Selected and Edited Papers from the ECHO III Conference. Acta Polytechnica Scandinavica 91, Espoo, pp. 187–196.
- Hooker, C. (2004). Asymptotics, reduction and emergence. *British Journal for the Philosophy of Science*, 55(3), 435–479.
- Hooker, C. (2009). Interaction and bio-cognitive order. *Synthese*, 166, 513–546.
- Hooker, C. (2011). Introduction to philosophy of complex systems. Part A: Towards framing philosophy of complex systems. In C. A. Hooker (Ed.), *Philosophy of complex systems* (Handbook of the philosophy of science, Vol. 10, pp. 3–92). Amsterdam: North Holland/Elsevier.
- Hooker, C. (2013). On the import of constraints in complex dynamical systems. *Foundations of Science*, 18, 757–780.
- Hooker, C., & Christensen, W. (1999). The organisation of knowledge: beyond Campbell’s evolutionary epistemology. *Philosophy of Science*, 66(3), 237–249.
- Horibe, N., Hanczyc, M., & Ikegami, T. (2011). Mode switching and collective behavior in chemical oil droplets. *Entropy*, 13(3), 709–719.
- Hull, D. L. (1988). *Science as a process: an evolutionary account of the social and conceptual development of science*. Chicago: University of Chicago Press.
- Huneman, P. (2006). Naturalizing purpose: from comparative anatomy to the “adventures of reason”. *Studies in History and Philosophy of Life Sciences*, 37(4), 621–656.

- Huneman, P. (Ed.). (2007). *Understanding purpose? Kant and the philosophy of biology*. Rochester: University of Rochester Press.
- Jacobs, D. K., Nakanishi, N., Yuan, D., Camara, A., Nichols, S. A., & Hartenstein, V. (2007). Evolution of sensory structures in basal metazoa. *Integrative and Comparative Biology*, 47(5), 712–723.
- Jonas, H. (1966/2001). *The phenomenon of life: toward a philosophical biology*. Evanston: Northwestern University Press.
- Juarrero, A. (1999). *Dynamics in action: intentional behavior as a complex system*. Cambridge, MA: MIT Press.
- Juarrero, A. (2009). Top-down causation and autonomy in complex systems. In N. Murphy, G. Ellis, & T. O'Connor (Eds.), *Downward causation and the neurobiology of free will* (pp. 83–102). Berlin/Heidelberg: Springer.
- Kacian, D. L., Mills, D. R., Kramer, F. R., & Spiegelman, S. (1972). A replicating RNA molecule suitable for a detailed analysis of extracellular evolution and replication. *Proceedings of the National Academy of Sciences of the United States of America*, 69(10), 3038–3042.
- Kaiser, D. (2001). Building a multicellular organism. *Annual Review of Genetics*, 35, 103–123.
- Kandel, E. R. (1995). *Essentials of neural science and behavior*. Norwalk: Appleton and Lange.
- Kant, E. (1790/1987). *Critique of judgment*. Indianapolis: Hackett Publishing.
- Kauffman, S. (1986). Autocatalytic sets of proteins. *Journal of Theoretical Biology*, 119, 1–24.
- Kauffman, S. (2000). *Investigations*. Oxford: Oxford University Press.
- Keijzer, F., van Duijn, M., & Lyon, P. (2013). What nervous systems do: early evolution, input–output, and the skin brain thesis. *Adaptive Behavior*, 21(2), 67–85.
- Khushf, G. (2007). An agenda for future debate on concepts of health and disease. *Medicine, Health Care and Philosophy*, 10, 19–27.
- Kim, J. (1993). *Supervenience and mind: selected philosophical essays*. Cambridge: Cambridge University Press.
- Kim, J. (1997). Explanation, prediction and reduction in emergentism. *Intellectica*, 25(2), 45–57.
- Kim, J. (1998). *Mind in a physical world*. Cambridge, MA: MIT Press.
- Kim, J. (2003). Blocking causal drainage and other maintenance chores with mental causation. *Philosophy and Phenomenological Research*, 67(1), 151–176.
- Kim, J. (2006). Emergence: core ideas and issues. *Synthese*, 151(3), 547–559.
- Kim, J. (2010). *Essays in the metaphysics of mind*. Oxford: Oxford University Press.
- Kimura, M. (1968). Explanatory rate at the molecular level. *Nature*, 217, 624–626.
- Kirk, D. L. (1998). *Volvox: molecular-genetic origins of multicellularity and cellular differentiation* (Developmental and cell biology series). Cambridge: Cambridge University Press.
- Kirk, D. L. (2005). A twelve-step program for evolving multicellularity and a division of labor. *BioEssays*, 27, 299–310.
- Kirk, M. M., Ransick, A., McRae, S. E., & Kirk, D. L. (1993). The relationship between cell size and cell fate in *Volvox carteri*. *Journal of Cell Biology*, 123, 191–208.
- Kirschner, M., & Gerhart, J. (1998). Evolvability. *PNAS*, 95(15), 8420–8427.
- Kitano, H. (2002). Computational systems biology. *Nature*, 420, 206–210.
- Kitcher, P. (1993). Function and design. *Midwest Studies in Philosophy*, 18, 379–397.
- Koufopanou, V. (1994). The evolution of soma in the Vovocales. *American Naturalist*, 143, 907–931.
- Kozmik, Z., Ruzickova, J., Jonasova, K., Matsumoto, Y., Vopalensky, P., Kozmikova, I., Strnad, H., Kawamura, S., Piatigorsky, J., & Paces, V. (2008). Assembly of the cnidarian camera-type eye from vertebrate-like components. *Proceedings of the National Academy of Sciences of the United States of America*, 105, 8989–8993.
- Krohs, U. (2010). Dys-, Mal- et Non-: L'autre face de la fonctionnalité. In J. Gayon & A. De Ricqlès (Eds.), *Les fonctions: des organismes aux artefacts* (pp. 337–352). Paris: Presses Universitaires de France.
- Krohs, U. (2011). Functions and fixed types: biological and other functions in the post-adaptationist era. *Applied Ontology*, 6(2), 125–139.

- Kumar, K., Mella Herrera, A. R., & Golden, W. J. (2010). Cyanobacterial Heterocysts. Cold Spring Harb, *Perspect Biol*. doi: 10.1101/cshperspect.a000315.
- Kupiec, J. J., & Sonigo, P. (2000). *Ni Dieu ni gene. Pour une autre théorie de l'hérédité*. Paris: Seuil.
- Lagzi, I. (2013). Chemical robotics- chemotactic drug carriers. *Central European Journal of Medicine*, 8(4), 377–382.
- Laland, K., Sterelny, K., Odling-Smee, J., Hopitt, W., & Uller, T. (2011). Cause and effect in biology revisited: Is Mayr's proximate-ultimate dichotomy still useful? *Science*, 334(6062), 1512–1516.
- Laubichler, D., & Maienschein, J. (Eds.). (2007). *From embryology to evo-devo. A history of developmental evolution*. Cambridge, MA: MIT Press.
- Laughlin, R., & Pines, D. (2000). The theory of everything. *Proceedings of the National Academy of Science of the United States of America*, 97, 28–31.
- Laughlin, R., Pines, D., Schmalien, J., Stojkovic, B., & Wolynes, P. (2000). The middle way. *Proceedings of the National Academy of Science of the United States of America*, 97, 32–37.
- Ledoux, J. (1996). *The emotional brain: the mysterious underpinnings of emotional life*. New York: Simon & Schuster.
- Lengeler, J. W. (2000). Metabolic networks: a signal-oriented approach in cellular models. *Biological Chemistry*, 381, 911–920.
- Letelier, J.-C., Marin, J., & Mpodozis, J. (2003). Autopoietic and (M, R)-systems. *Journal of Theoretical Biology*, 222, 261–272.
- Letelier, J.-C., Soto-Andrade, J., Guíñez Abarzua, F., Cornish-Bowden, A., & Cardenas, M. L. (2006). Organizational invariance and metabolic closure: analysis in terms of (M, R)-systems. *Journal of Theoretical Biology*, 238, 949–961.
- Levi-Montalcini, R. L. (1999). *La galassia mente*. Milano: Baldini and Castoldi.
- Levy, A. (2011). Information in biology: a fictionalist account. *Noûs*, 45(4), 640–657.
- Lewis, M. D. (2005). Bridging emotion theory and neurobiology through dynamic systems modeling. *Behavioral and Brain Sciences*, 28(2), 169–194.
- Lewontin, R. C. (1970). The units of selection. *Annual Review of Ecology and Systematics*, 1, 1–18.
- Llinás, R., Ribary, U., Contreras, D., & Pedroarena, C. (1998). The neuronal basis for consciousness. *Philosophical Transactions of the Royal Society of London, Series B*, 353, 1841–1849.
- Lloyd Morgan, C. (1923). *Emergent evolution*. London: Williams and Norgate.
- Longo, G., & Montevil, M. (2014). *Perspectives on organism: biological time, symmetries and singularities*. Heidelberg: Springer.
- Losik, R., & Kaiser, D. (1997). Why and how bacteria communicate. *Scientific American*, 276(2), 68–73.
- Luisi, P. L. (2006). *The emergence of life: from chemical origins to synthetic biology*. Cambridge: Cambridge University Press.
- Luisi, P. L., Ferri, F., & Stano, P. (2006). Approaches to semi-synthetic minimal cells: a review. *Naturwissenschaften*, 93(1), 1–13.
- Lyon, P. (2006). The biogenic approach to cognition. *Cognitive Processing*, 7(1), 11–29.
- Manrubia, S., & Briones, C. (2007). Modular evolution and increase of functional complexity in RNA molecules. *RNA*, 13(1), 97–107.
- Mansy, S., Schrum, J. P., Krishnamurthy, M., Tobé, S., Treco, D. A., & Szostak, J. W. (2008). Template directed synthesis of a genetic polymer in a model protocell. *Nature*, 454, 122–126.
- Martin, W., & Russell, M. J. (2003). On the origins of cells: a hypothesis for the evolutionary transitions from abiotic geochemistry to chemoautotrophic prokaryotes, and from prokaryotes to nucleated cells. *Philosophical Transaction: Biological Science*, 358, 59–85.
- Mattick, J. (2004). The hidden genetic program of complex organisms. *Scientific American*, 291(4), 60–67.
- Maturana, H., & Varela, F. (1973). *De máquinas y seres Vivos – Una teoría sobre la organización biológica*. Santiago de Chile: Editorial Universitaria S.A.
- Maturana, H., & Varela, F. (1980). *Autopoiesis and cognition. The realization of the living*. Dordrecht: Reidel Publishing.

- Maturana, H., & Varela, F. (1987). *The tree of knowledge: the biological roots of human understanding*. Boston: Shambhala Publications.
- Maynard Smith, J. (1986). *The problems of biology*. Oxford: Oxford University Press.
- Maynard Smith, J., & Szathmari, E. (1995). *Major transitions in evolution*. Oxford: Oxford University Press.
- Maynard Smith, J., Burian, R., Kauffman, S., Alberch, P., Campbell, J., Goodwin, B., Lande, R., Raup, D., & Wolpert, L. (1985). Developmental constraints and evolution. *Quarterly Review of Biology*, 60, 265–287.
- Mayr, E. (1961). Cause and effect in biology: kinds of causes, predictability, and teleology are viewed by a practicing biologist. *Science*, 134, 1501–1506.
- Mayr, E. (2004). *What makes biology unique? Considerations on the autonomy of a scientific discipline*. Cambridge: Cambridge University Press.
- McAdams, H. H., & Arkin, A. (1997). Stochastic mechanisms in gene expression. *PNAS*, 94(3), 814–819.
- McFall-Ngai, M. J. (1999). Consequences of evolving with bacterial symbionts: insights from the Squid-Vibrio Associations. *Annual Review of Ecology and Systematics*, 30, 235–256.
- McGann, M., & De Jaegher, H. (2009). Self-other contingencies: enacting social perception. *Phenomenology and the Cognitive Sciences*, 8, 417–437.
- McLaughlin, B. P. (1992). The rise and fall of British emergentism. In A. Beckermann, H. Flohr, & J. Kim (Eds.), *Emergence or reduction? Essays on the prospects of nonreductive physicalism* (pp. 49–93). Berlin: Walter de Gruyter.
- McLaughlin, P. (2001). *What functions explain. Functional explanation and self-reproducing systems*. Cambridge: Cambridge University Press.
- McLaughlin, P. (2009). Functions and norms. In U. Krohs & P. Kroes (Eds.), *Functions in biological and artificial worlds. Comparative philosophical perspectives* (pp. 93–102). Cambridge, MA: MIT Press.
- McMullin, B. (1997). SCL: an artificial chemistry in Swarm. *Santa Fe Institute Working Paper* (SFI).
- McMullin, B., & Varela, F. J. (1997). Rediscovering computational autopoiesis. In P. Husbands & I. Harvey (Eds.), *Proceedings of the fourth European conference on artificial life* (pp. 38–47). Cambridge, MA: MIT Press.
- Melander, P. (1997). *Analyzing functions. An essay on a fundamental notion in biology*. Stockholm: Almkvist & Wiksell International.
- Meyer, L. M. N., Bomfim, G. C., & El-Hani, C. N. (2013). How to understand the gene in the 21st century. *Science Education*, 22(2), 345–374.
- Michod, R. E. (1999). *Darwinian dynamics: evolutionary transitions in fitness and individuality*. Princeton: Princeton University Press.
- Michod, R. E. (2005). On the transfer of fitness from the cell to the multicellular organism. *Biology and Philosophy*, 20, 967–987.
- Mill, J. S. (1843). *A system of logic*. London: Parker.
- Miller, R. V. (1998). Bacterial gene swapping in nature. *Scientific American*, 278(1), 66–71.
- Miller, M. B., & Bassler, B. L. (2001). Quorum sensing in bacteria. *Annual Review of Microbiology*, 55, 165–199.
- Millikan, R. G. (1984). *Language, thought, and other biological categories*. Cambridge, MA: MIT Press.
- Millikan, R. G. (1989). In defense of proper functions. *Philosophy of Science*, 56, 288–302.
- Millikan, R. G. (1993). Propensities, exaptations, and the brain. In R. G. Millikan (Ed.), *White queen psychology and other essays for Alice* (pp. 31–50). Cambridge, MA: MIT Press.
- Millikan, R. G. (2002). Biofunctions: two paradigms. In A. Ariew, R. Cummins, & M. Perlman (Eds.), *Functions* (pp. 113–143). Oxford: Oxford University Press.
- Mills, D. R., Peterson, R. L., & Spiegelman, S. (1967). An extracellular Darwinian experiment with a self-duplicating nucleic acid molecule. *Proceedings of the National Academy of Sciences of the United States of America*, 58(1), 217–224.

- Monod, J. (1970). *Le hasard et la nécessité. Essai sur la philosophie naturelle de la biologie moderne*. Paris: éditions du Seuil.
- Montévil, M., & Mossio, M. (2015). Biological organisation as closure of constraints. *Journal of Theoretical Biology*, 372, 179–191.
- Morán, F., Moreno, A., Montero, F., & Minch, E. (1997). Further steps towards a realistic description of the essence of life. In C. G. Langton & K. Shimohara (Eds.), *Artificial life V (Proceedings of the 5th international workshop on the synthesis and simulation of living systems)* (pp. 255–263). London: MIT Press.
- Morange, M. (2003). *La vie expliquée ? 50 ans après la double hélice*. Paris: Odile Jacob. Eng trans. (2008). *Life explained*. New Haven: Yale University Press.
- Moreno, A. (2007). A systemic approach to the origin of biological organization. In F. Boogerd, J. H. Bruggeman, H. V. Hofmeyr, & H. Westerhoff (Eds.), *Systems biology. Philosophical foundations* (pp. 243–268). Dordrecht: Elsevier.
- Moreno, A., & Etxeberria, A. (2005). Agency in natural and artificial systems. *Artificial Life*, 11(1–2), 161–175.
- Moreno, A., & Fernández, J. (1990). Structural limits for evolutive capacities in molecular complex systems. *Biology Forum*, 83(2/3), 335–347.
- Moreno, A., & Lasa, A. (2003). From basic adaptivity to early mind. *Evolution and Cognition*, 9(1), 12–30.
- Moreno, A., & Ruiz Mirazo, K. (1999). Metabolism and the problem of its universalization. *BioSystems*, 49(1), 45–61.
- Moreno, A., & Ruiz-Mirazo, K. (2009). The problem of the emergence of functional diversity in prebiotic evolution. *Biology and Philosophy*, 24(5), 585–605.
- Moreno, A., & Umerez, J. (2000). Downward causation at the core of living organization. In P. B. Anderson, C. Emmeche, N. O. Finnemann, & P. V. Christiansen (Eds.), *Downward causation* (pp. 99–117). Aarhus: Aarhus University Press.
- Moreno, A., Etxeberria, A., & Umerez, J. (1994). Universality without matter? In R. A. Brooks & P. Maes (Eds.), *Artificial life IV (Proceedings of the 4th international workshop on the synthesis and simulation of living systems)* (pp. 406–410). London: MIT Press.
- Moreno, A., Etxeberria, A., & Umerez, J. (2008). The autonomy of biological individuals and artificial models. *BioSystems*, 91(2), 309–319.
- Moreno, A., Ruiz-Mirazo, K., & Barandiaran, X. E. (2011). The impact of the paradigm of complexity on the foundational frameworks of biology and cognitive science. In C. A. Hooker, D. V. Gabbay, P. Thagard, & J. Woods (Eds.), *Handbook of the philosophy of science (Philosophy of complex systems)*, pp. 311–333. Amsterdam: Elsevier.
- Moreno, A., Umerez, J., & Ibáñez, J. (1997). Cognition and life. *The Autonomy of Cognition Brain & Cognition*, 34(1), 107–129. Academic Press.
- Morowitz, H. J. (1968). *Energy flow in biology*. New York: Academic Press.
- Morowitz, H. J. (1992). *Beginnings of cellular life*. New Haven: Yale University Press.
- Mossio, M. (2013). Closure, causal. In W. Dubitzky, O. Wolkenhauer, K.-H. Cho, & H. Yokota (Eds.), *Encyclopedia of systems biology* (pp. 415–418). New York: Springer.
- Mossio, M., & Moreno, A. (2010). Organizational closure in biological organisms. *History and Philosophy of the Life Sciences*, 32(2–3), 269–288.
- Mossio, M., Bich, L., & Moreno, A. (2013). Emergence, closure and inter-level causation in biological systems. *Erkenntnis*, 78(2), 153–178.
- Mossio, M., Longo, G., & Stewart, J. (2009a). A computable expression of closure to efficient causation. *Journal of Theoretical Biology*, 257(3), 489–498.
- Mossio, M., Saborido, C., & Moreno, A. (2009b). An organizational account of biological functions. *British Journal for the Philosophy of Science*, 60, 813–841.
- Nagel, E. (1961). *The structure of science*. London: Routledge & Kegan Paul.
- Nagel, E. (1977). Teleology revisited. *Journal of Philosophy*, 74, 261–301.
- Neander, K. (1980). Teleology in biology. *Paper presented to the AAP conference*, Christchurch, New Zealand.

- Neander, K. (1991). Function as selected effects: the conceptual analyst's defense. *Philosophy of Science*, 58, 168–184.
- Neander, K. (1995). Misrepresenting and malfunctioning. *Philosophical Studies*, 79, 109–141.
- Nedelcu, A. M., & Michod, R. E. (2004). Evolvability, modularity, and individuality during the transition to multicellularity in volvocalean green algae. In G. Wagner & G. Schlosser (Eds.), *Modularity in development and evolution* (pp. 468–489). Chicago: University of Chicago Press.
- Neihardt, F. (Ed.). (1996). *Escherichia coli and salmonella: cellular and molecular biology*. Washington, DC: American Society for Microbiology.
- Newell, A. (1980). Physical symbol systems. *Cognitive Science*, 4, 135–183.
- Nicolis, G., & Prigogine, I. (1977). *Self-organisation in non-equilibrium systems: from dissipative structures to order through fluctuation*. New York: Wiley.
- Nilsson, S., & Holmgren, S. (Eds.). (1994). *Comparative physiology and evolution of the autonomic nervous system*. Chur: Harwood Academic Publishers.
- Nissen, L. (1980). Nagel's self-regulation analysis of teleology. *Philosophical Forum*, 12, 128–138.
- Nunes, N., Moreno, A., & El Hani, C. (2014). Function in ecology: an organizational approach. *Biology and Philosophy*, 29(1), 123–141.
- Oehlenschläger, F., & Eigen, M. (1997). 30 years later—a new approach to Sol Spiegelman's and Leslie Orgel's in vitro evolutionary studies. Dedicated to Leslie Orgel on the occasion of his 70th birthday. *Origins of Life and Evolution of the Biosphere*, 27(5–6), 437–457.
- Oliveri, P., Tu, Q., & Davidson, E. H. (2008). Global regulatory logic for specification of an embryonic cell lineage. *Proceedings of the National Academy of Sciences of the United States of America*, 105, 5955–5962.
- Oyama, S. (2002). The nurturing of natures. In A. Grunwald, M. Gutmann, & E. Neumann-Held (Eds.), *On human nature. Anthropological, biological and philosophical foundations* (pp. 163–170). New York: Springer.
- Panksepp, J. B., & Lahvis, G. P. (2011). Rodent empathy and affective neuroscience. *Neuroscience and Biobehavioral Reviews*, 35, 1864–1875.
- Pattee, H. H. (1972). Laws and constraints, symbols and languages. In C. H. Waddington (Ed.), *Towards a theoretical biology* (Vol. 4). Edinburgh: Edinburgh University Press.
- Pattee, H. H. (1973). The physical basis and origin of hierarchical control. In H. H. Pattee (Ed.), *Hierarchy theory* (pp. 73–108). New York: Braziller.
- Pattee, H. H. (1977). Dynamic and linguistic modes of complex systems. *International Journal of General Systems*, 3, 259–266.
- Pattee, H. H. (1982). Cell psychology: an evolutionary approach to the symbol-matter problem. *Cognition and Brain Theory*, 4, 325–341.
- Pattee, H. H. (2007). Laws, constraints, and the modeling relation – History and interpretations. *Chemistry and Biodiversity*, 4, 2272–2295.
- Pepper, J. W., & Herron, M. D. (2008). Does biology need an organism concept? *Biological Reviews*, 83(4), 621–627.
- Pereto, J. (2005). Controversies on the origin of life. *International Microbiology*, 8, 23–31.
- Perlman, R. L. (2000). The concept of the organism in physiology. *Theory in Bioscience*, 119, 174–186.
- Pessoa, L. (2008). On the relationship between emotion and cognition nature reviews. *Nature Reviews Neuroscience*, 9(2), 148–158.
- Peter, I., & Davidson, E. H. (2009). Genomic control of patterning. *International Journal of Developmental Biology*, 53, 707–716.
- Peter, I., & Davidson, E. H. (2010). The endoderm gene regulatory network in sea urchin embryos up to mid-blastula stage. *Developmental Biology*, 340(2), 188–199.
- Peter, I., & Davidson, E. H. (2011). A gene regulatory network controlling the embryonic specification of endoderm. *Nature*, 474, 635–639.
- Piaget, J. (1967). *Biologie et connaissance*. Paris: Éditions de la Pléiade.

- Piedrafita, G., Montero, F., Morán, F., Cárdenas, M. L., & Cornish-Bowden, A. (2010). A simple self-maintaining metabolic system: robustness, autocatalysis, bistability. *PLoS Computational Biology*, *6*(8), e1000872.
- Pigliucci, M., & Muller, G. (Eds.). (2010). *Evolution: the extended synthesis*. Cambridge, MA: MIT Press.
- Porges, S. (1997). Emotion: an evolutionary by-product of the neural regulation of the autonomic nervous system. In C. S. Carter, B. Kirkpatrick, & I. I. Lederhendler (Eds.), *The integrative neurobiology of affiliation* (Vol. 807, pp. 62–67). New York: Annals of the New York Academy of Sciences.
- Powers, W. T. (1973). *Behavior: the control of perception*. Chicago: Aldine de Gruyter.
- Price, T., Qvarnström, A., & Irwin, D. (2003). The role of phenotypic plasticity in driving genetic evolution. *Proceedings of the Royal Society of London B*, *270*, 1433–1440.
- Prigogine, I. (1962). *Introduction to nonequilibrium thermodynamics*. New York: Wiley-Interscience.
- Pross, A. (2003). The driving force for life's emergence: kinetic and thermodynamic considerations. *Journal of Theoretical Biology*, *220*(3), 393–406.
- Queller, D. C., & Strassmann, J. E. (2009). Beyond society: the evolution of organismality. *Philosophical Transactions Royal Society, B: Biological Sciences*, *364*, 3143–3155.
- Raff, R. (1996). *The shape of life*. Chicago: University of Chicago Press.
- Rasmussen, S., Bedau, M. A., Liaohai, C., Deamer, D., Krakauer, D. C., Packhard, N. H., & Stadler, P. F. (Eds.). (2008). *Protocells: bridging nonliving and living matter*. Cambridge, MA: MIT Press.
- Richards, R. J. (2000). Kant and Blumenbach on the Bildungstrieb: a historical misunderstanding. *Studies in History and Philosophy of Biology and Biomedical Science*, *31*(1), 11–32.
- Rokas, A. (2008). The origins of multicellularity and the early history of the genetic toolkit for animal development. *Annual Review of Genetics*, *42*, 235–251.
- Rosen, R. (1971). Some realizations of (M, R)-systems and their interpretation. *Bulletin of Mathematical Biophysics*, *33*, 303–319.
- Rosen, R. (1972). Some relational cell models: the metabolism-repair systems. In R. Rosen (Ed.), *Foundations of mathematical biology* (Vol. II, pp. 217–253). New York: Academic Press.
- Rosen, R. (1973). On the dynamical realizations of (M, R)-systems. *Bulletin of Mathematical Biophysics*, *35*, 1–9.
- Rosen, R. (1978). *Fundamentals of measurement and representation of natural systems*. New York: North Holland.
- Rosen, R. (1991). *Life itself: A comprehensive enquiry into the nature, origin and fabrication of life*. New York: Columbia University Press.
- Rosenbluth, A., Wiener, N., & Bigelow, J. (1943). Behavior, purpose and teleology. *Philosophy of Science*, *10*, 18–24.
- Rosslinbroich, B. (2014). *On the origin of autonomy. A new look at the major transitions in evolution*. Cham: Springer.
- Ruiz-Mirazo, K. (2001). *Condiciones físicas para la aparición de sistemas autónomos con capacidades evolutivas abiertas*. Ph.D. dissertation, University of the Basque Country.
- Ruiz-Mirazo, K. (2011). Protocell. In M. Gargaud, R. Amils, J. Cernicharo Quintanilla, H. J. Cleaves, W. M. Irvine, D. Pinti, & M. Viso (Eds.), *Encyclopedia of astrobiology* (Vol. 3, pp. 1353–1354). Heidelberg: Springer.
- Ruiz Mirazo, K., Briones, C., & Escosura, A. (2013). Prebiotic systems chemistry: new perspectives for the origins of life. *Chemical Reviews*, *114*(1), 285–366. 2014.
- Ruiz-Mirazo, K., & Mavelli, F. (2007). Simulation model for functionalized vesicles: lipid-peptide integration in minimal protocells. In F. Almeida e Costa, L. M. Rocha, I. Harvey, & A. Coutinho (Eds.), *ECAL 2007*, Lisbon, Portugal, 10–14 Sept 2007. Proceedings (Lecture notes in computer science 4648, pp. 32–41). Heidelberg: Springer.

- Ruiz-Mirazo, K., & Mavelli, F. (2008). Towards 'basic autonomy': stochastic simulations of minimal lipid-peptide cells. *BioSystems*, 91(2), 374–387.
- Ruiz-Mirazo, K., & Moreno, A. (2004). Basic autonomy as a fundamental step in the synthesis of life. *Artificial Life*, 10(3), 235–259.
- Ruiz-Mirazo, K., & Moreno, A. (2006). On the origins of information and its relevance for biological complexity. *Biological Theory*, 1(3), 227–229.
- Ruiz-Mirazo, K., & Moreno, A. (2009). New century biology could do with a universal definition of life. In G. Terzis & R. Arp (Eds.), *Information and living systems: essays in philosophy of biology*. Cambridge, MA: MIT Press.
- Ruiz-Mirazo, K., & Moreno, A. (2012). Autonomy in evolution: from minimal to complex life. *Synthese*, 185(1), 21–52.
- Ruiz-Mirazo, K., Etxeberria, A., Moreno, A., & Ibañez, J. (2000). Organisms and their place in biology. *Theory in Biosciences*, 119, 43–67.
- Ruiz-Mirazo, K., Peretó, J., & Moreno, A. (2004). A universal definition of life: autonomy and open-ended evolution. *Origins of Life and Evolution of the Biosphere*, 34(3), 323–346.
- Ruiz-Mirazo, K., Umeréz, J., & Moreno, A. (2008). Enabling conditions for open-ended evolution. *Biology and Philosophy*, 23(1), 67–85.
- Ruse, M. (1971). Functional statements in biology. *Philosophy of Science*, 38, 87–95.
- Saborido, C. (2012). *Funcionalidad y organización en biología. Reformulación del concepto de función biológica desde una perspectiva organizacional*. Ph.D. dissertation. University of the Basque Country.
- Saborido, C., Mossio, M., & Moreno, A. (2011). Biological organization and cross-generation functions. *The British Journal for the Philosophy of Science*, 62, 583–606.
- Saborido, C., & Moreno, A. (2015). Biological pathology from an organizational perspective. *Journal of Theoretical Medicine and Bioethics*, 36(1), 86–95.
- Saborido, C., Moreno, A., González-Moreno, M., & Hernández, J. C. (2014). Organizational malfunctions and the notions of health and disease. In M. Lemoine & E. Giroux (Eds.), *Naturalism in philosophy of health: issues, limits and implications*. In Press, Springer.
- Salmon, W. C. (1998). *Causality and explanation*. Oxford: Oxford University Press.
- Santelices, B. (1999). How many kinds of individual are there? *Trends in Ecology & Evolution*, 14(4), 152–155.
- Sartenaer, O. (2013). *Émergence et réduction. Analyse épistémologique de la dynamique des systèmes naturels*. Ph.D. dissertation. Université Catholique de Louvain.
- Schlosser, G. (1998). Self-re-production and functionality: a systems-theoretical approach to teleological explanation. *Synthese*, 116, 303–354.
- Schramme, T. (2007). A qualified defence of a naturalist theory of health. *Medicine, Health Care and Philosophy*, 10, 11–17.
- Schrödinger, E. (1944). *What is life? The physical aspect of the living cell*. Cambridge: Cambridge University Press.
- Science. (2002). *Special Issue on Systems Biology*, 295, 5560, 1589–1780.
- Segré, D., & Lancet, D. (2000). Composing life. *EMBO Reports*, 1(3), 217–222.
- Segré, D., Ben-Eli, D., Deamer, D., & Lancet, D. (2001). The lipid world. *Origins of Life and Evolution of the Biosphere*, 31, 119–145.
- Seipel, K., & Schmid, V. (2005). Evolution of striated muscle: Jellyfish and the origin of triploblasty. *Developmental Biology*, 282, 14–26.
- Sengupta, S., Ibele, M., & Sen, A. (2012). Fantastic voyage: designing self-powered nanorobots. *Angewandte Chemie International Edition*, 51(34), 8434–8445.
- Seth, A. K. (2009). Brain mechanisms of consciousness in humans and other animals. In S. Atlason & P. Helgadóttir (Eds.), *Veit efnið af andanum* (pp. 47–72). Reykjavík: University of Iceland Press.
- Shani, I. (2012). Setting the bar for cognitive agency: or how minimally autonomous can an autonomous agent be? *New Ideas in Psychology*, 31(2), 151–165.
- Shapiro, J. A. (1998). Thinking about bacterial populations as multicellular organisms. *Annual Review of Microbiology*, 52, 81–104.

- Shepherd, G. M. (1994). *Neurobiology* (3rd ed.). New York: Oxford University press.
- Sherrington, C. S. (1947). *The integrative action of the nervous system* (2nd ed.). New Haven: Yale University Press.
- Sherwood, L. (1997). *Human physiology*. Belmont: Wadsworth Publishing Company.
- Silberstein, M., & McGeever, J. (1999). The search for ontological emergence. *Philosophical Quarterly*, 50(195), 182–200.
- Simon, H. (1969). *The sciences of the artificial*. Cambridge, MA: MIT Press.
- Simons, P. J. (1981). The role of electricity in plant movements. *New Phytologist*, 87, 11–37.
- Skewes, J., & Hooker, C. (2009). Bio-agency and the problem of action. *Biology and Philosophy*, 24(3), 283–300.
- Sloan, P. (2002). Preforming the categories: eighteenth-century generation theory and the biological roots of Kant's a-priori. *Journal of the History of Philosophy*, 40, 229–253.
- Smithers, T. (1997). Autonomy in robots and other agents. *Brain and Cognition*, 34, 88–106.
- Sober, E. (Ed.). (2006). *Conceptual issues in evolutionary biology*. Cambridge, MA: MIT Press.
- Soto, A. M., Sonnenschein, C., & Miquel, P. A. (2008). On physicalism and downward causation in developmental and cancer biology. *Acta Biotheoretica*, 56, 257–274.
- Sperry, R. W. (1969). A modified concept of consciousness. *Psychological Review*, 76(6), 532–536.
- Spinoza, B. (1677/2002). *Ethics*. In Complete works translated by Samuel Shirley and others. Indianapolis: Hackett Publication Company.
- Srere, P. A. (1984). Why are enzymes so big? *Trends in Biochemical Sciences*, 9, 387–390.
- Stephan, A. (1992). Emergence – a systematic view on its historical facets. In A. Beckermann, H. Flohr, & J. Kim (Eds.), *Emergence or reduction? Essays on the prospects of nonreductive physicalism* (pp. 25–48). Berlin: Walter de Gruyter.
- Sterelny, K., & Griffiths, P. (1999). *Sex and death. An introduction to philosophy of biology*. Chicago: The University of Chicago Press.
- Stewart, J. (1996). Cognition=life: implications for higher-level cognition. *Behavioral Processes*, 35, 311–326.
- Storer, T., Usinger, R., Stebbins, R., & Nybakken, J. (1979). *General zoology*. New York: McGraw-Hill.
- Strassmann, J. E., & Queller, D. C. (2010). The social organism: congresses, parties and committees. *Evolution*, 64(3), 605–616.
- Szathmáry, E. (2000). The evolution of replicators. *Philosophical Transactions of the Royal Society of London B*, 355, 1669–1676.
- Szathmáry, E. (2006). The origin of replicators and reproducers. *Philosophical Transactions of the Royal Society B*, 361, 1761–1776.
- Szathmáry, E., & Maynard Smith, J. (1997). From replicators to reproducers: the first major transitions leading to life. *Journal of Theoretical Biology*, 187, 555–571.
- Taft, R. J., Pheasant, M., & Mattick, J. S. (2007). The relationship between non-protein-coding DNA and eukaryotic complexity. *BioEssays*, 29, 288–297.
- Teller, P. (1986). Relational holism and quantum mechanics. *The British Journal for the Philosophy of Science*, 37, 71–81.
- Thompson, E. (2007). *Mind in life. Biology, phenomenology, and the sciences of mind*. Cambridge, MA: Harvard University Press.
- Tononi, G., & Edelman, G. M. (1998). Consciousness and complexity. *Science*, 262, 1846–1851.
- Tononi, G., Sporns, O., & Edelman, G. M. (1999). Measures of degeneracy and redundancy in biological networks. *Proceedings of the National Academy of Sciences USA*, 96, 3257–3262.
- Trewavas, A. (2003). Aspects of plant intelligence. *Annals of Botany*, 92, 1–20.
- Turrone, F., Ribbera, A., Foroni, E., van Sinderen, D., & Ventura, M. (2008). Human gut microbiota and bifidobacteria: from composition to functionality. *Antonie van Leeuwenhoek*, 94(1), 35–50.
- Umerez, J. (1994). *Jerarquías Autónomas. Un estudio sobre el origen y la naturaleza de los procesos de control y de formación de niveles en sistemas naturales complejos*. Ph.D. dissertation. Donostia/San Sebastian: University of the Basque Country.
- Umerez, J. (1995). Semantic closure: a guiding notion to ground artificial life. *Advances in artificial life*, 929, 77–94.

- Umerez, J. (2001). Howard Pattee's theoretical biology—a radical epistemological stance to approach life, evolution and complexity. *Biosystems*, 60(1), 159–177.
- Umerez, J., & Mossio, M. (2013). Constraint. In W. Dubitzky, O. Wolkenhauer, K.-H. Cho, & H. Yokota (Eds.), *Encyclopedia of systems biology* (pp. 490–493). New York: Springer.
- Van Dujin, M., Keijzer, F., & Franjen, D. (2006). Principles of minimal cognition: casting cognition as sensorimotor coordination. *Adaptive Behavior*, 14(2), 157–170.
- Van Gulick, R. (2001). Reduction, emergence and other recent options on the mind/body problem: a philosophical overview. *Journal of Consciousness Studies*, 8(9–10), 1–34.
- Varela, F. J. (1979). *Principles of biological autonomy*. New York: North Holland.
- Varela, F. J. (1981). Autonomy and autopoiesis. In G. Roth & H. Schwegler (Eds.), *Self-organizing systems: an interdisciplinary approach* (pp. 14–24). Frankfurt/New York: Campus Verlag.
- Varela, F. J. (1997). Patterns of life: intertwining identity and cognition. *Brain and Cognition*, 34, 72–87.
- Varela, F. J., Maturana, H., & Uribe, R. (1974). Autopoiesis: the organisation of living systems, its characterization and a model. *BioSystems*, 5, 187–196.
- Vasas, V., Fernando, C., Santos, M., & Kauffman, S. (2012). Evolution before genes. *Biol Direct*, 7–1.
- Vicente, A. (2011). Current physics and 'the physical'. *The British Journal for the Philosophy of Science*, 62(2), 393–416.
- Vieira, F. S., & El-Hani, C. (2008). Downward determination: a philosophical step in the way to a dynamic account of emergence. *Cybernetics and Human Knowing*, 15(3–4), 145–147.
- Virchow, R. (1858/1978). *Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre*. English translation, Cellular pathology. special ed., 204–207. John Churchill London, UK.
- Vogel, S. (1988). *Life's devices: the physical world of animals and plants*. Princeton: Princeton University Press.
- Von Uexküll, J. (1982/1940). The theory of meaning. *Semiotica*, 42(1), 25–82.
- Waddington, C. H. (1968–1972). *Towards a theoretical biology*. 4 vols. Edinburgh: Edinburgh University Press.
- Wagner, G. P., & Altenberg, L. (1996). Complex adaptations and the evolution of evolvability. *Evolution*, 50(3), 967–976.
- Walsh, D. M. (1996). Fitness and function. *British Journal for the Philosophy of Science*, 47, 553–574.
- Walsh, D. M., & Ariew, A. (1996). A taxonomy of functions. *Canadian Journal of Philosophy*, 26, 493–514. Reprinted in Buller, D. J. (1999). *Function, selection, and design* (pp. 257–279). Albany: SUNY Press.
- Ward, P., & Brownlee, D. (2004). *Rare earth: why complex life is uncommon in the universe*. New York: Copernicus Books.
- Weber, A., & Varela, F. (2002). Life after Kant: natural purposes and the autopoietic foundations of biological individuality. *Phenomenology and the Cognitive Sciences*, 1, 97–125.
- Wicken, J. S. (1987). *Evolution, thermodynamics and information. Extending the Darwinian program*. Oxford: Oxford University Press.
- Wilson, J. (1999). *Biological individuality. The individuation and persistence of living entities*. Cambridge: Cambridge University Press.
- Wilson, J. (2000). Ontological butchery: organism concepts and biological generalizations. *Philosophy of Science*, 67, 301–311.
- Wilson, D. S., & Sober, E. (1989). Reviving the superorganism. *Journal of Theoretical Biology*, 136, 337–356.
- Wimsatt, W. (2002). Functional organisation, functional inference, and functional analogy. In A. Ariew, R. Cummins, & M. Perlman (Eds.), *Functions* (pp. 174–221). Oxford: Oxford University Press.
- Winther, R. (2006). Parts and theories in compositional. *Biology and Philosophy*, 21(4), 471–499.
- Woese, C. (2002). On the evolution of cells. *Proceedings of the National Academy of Science*, 99(13), 8742–8747.

- Wolfe, C. (2010). Do organisms have an ontological status? *History and Philosophy of the Life Sciences*, 32(2–3), 195–232.
- Wolpert, L., & Szathmary, E. (2002). Multicellularity: evolution and the egg. *Nature*, 420, 745.
- Wouters, A. G. (2005). The function debate in philosophy. *Acta Biotheoretica*, 53(2), 123–151.
- Wright, L. (1973). Functions. *Philosophical Review*, 82, 139–168.
- Wright, L. (1976). *Teleological explanations: an etiological analysis of goals and functions*. Berkeley: University of California Press.
- Young, K. D. (2006). The selective value of bacterial shape. *Microbiology and Molecular Biology Reviews*, 70(3), 660–703.
- Zaretsky, A., & Letelier, J. C. (2002). Metabolic networks from (M,R) systems and autopoiesis perspective. *Journal of Biological Structures*, 10(3), 265–280.
- Zepik, H., Blöchliger, E., & Luisi, P. L. (2001). A chemical model of homeostasis *Angew. Chemie Int*, 40(1), 199–202.
- Ziemke, T. (2003). What's that thing called embodiment? In *Proceedings of the 25th Annual Meeting of the Cognitive Science Society*.
- Zullo, L., Sumbre, G., Agnisola, C., Flash, T., & Hochner, B. (2009). Nonsomatotopic organization of the higher motor centers in octopus. *Current Biology*, 19, 1632–1636.

Index

A

- Agency, 91–93
 - adaptive, 38, 98–101, 103, 105, 109, 132, 169, 199
 - behavioural, 102–104, 109, 169–175, 192
 - minimal, 92–98
- Agents, 89–93
 - cognitive, 167, 168, 193
 - vs. replicators, 95–97
 - strong vs. weak interactions, 106
- Autonomy, 104–105
 - constitutive dimension, xxviii, xxx, 1, 65, 89, 114, 115, 196
 - historical dimension, xxxii, 81, 111–139, 197, 198
 - interactive dimension, xxviii, xxix, xxx, 38, 89, 90, 94, 114, 115, 197
 - levels, 164, 165, 200
 - minimal, 105, 164
 - neurodynamic, 187–189, 191
 - and organisms, 104–105
- Autopoiesis, xxvi, xxvii, 3, 7, 24, 25

B

- Bénard cells, 16, 55, 72
- Biological units, 112, 113
- Body plan, xii, 104, 134, 163, 178–180, 187, 192

C

- Causal closure (Kim), 42
- Causal drainage, 42, 43, 47
- Causal inheritance. *See* Inclusivity of levels

- Chemotaxis, 97, 98, 100–102
- Closure, 20–24
 - algebraic notion, 3
 - as a biological invariant, 23, 24
 - catalytic, 25, 28
 - “Closure Thesis”, 1–3
 - context-dependence, 23
 - as a criterion of individuation, 23, 79
 - and functionality, xxx, 51, 63, 71, 72, 198, 200
 - generative nature, 57–58
 - and holism, xxiv, 23
 - and openness, xxix, 6, 11, 27, 105
 - levels, 143, 144, 153, 200
 - and mutual dependence, 2, 4, 5, 20, 72
 - orders, 28, 34–38, 74, 83–86, 143, 153
 - and organisation, 6, 23, 71, 72
 - vs. physical cycles, 4
 - physical/functional boundaries, 4, 23
 - as a principle of order, 23, 197, 198
 - and regimes of self-maintenance, 33, 74, 82–85
 - semantic (Pattee), 21, 131
 - statistical (Pattee), 21
 - temporal continuity, 78, 79
 - temporal instances, 79, 80
 - Varela’s organisational/operational closure, 3
 - and variability, 4, 24, 198, 199
- Cognition
 - minimal, 167, 169, 188, 189
 - and social interaction, 189–191
- Compartmentalisation, 121–123, 136
- Configuration, 12, 15, 16, 40, 45–50, 53–57, 59, 60, 123

Constitution, 45–48
 Constitutive stability, 31–33, 36, 37, 99
 Constraint, 11–15
 causal role, 5, 11, 12, 15, 39
 conservation, 11–15, 20, 34, 39
 enabling/limiting, 14, 178
 intra- vs. *inter-*cellular, 152
 and processes, 6, 11–15, 20, 27
 relevant aspects, 11–14, 19, 20
 time scale, 11–15, 18–20, 22, 34, 37, 50, 79

D

Delancey's "splitting account" of functions, 75, 76
 Dependence between constraints, 18–20
 dependence between constraints vs. dependence between processes, 19
 direct, 19
 enabling vs. dependent constraints, 19
 Development
 aggregation vs. differentiation, 149, 150
 and control, 152, 153, 157
 developmental functions (constraints), 144, 145, 152, 160
 Dispositional approaches to function
 goal contribution approach, 66
 propensity view, 67
 systemic approach, 66
 Dissipative structure. *See* Self-organisation

E

Ecological organisations, 105–108
 Emergence, 44–49
 emergence base, 43–45, 47, 49, 51, 52, 54, 55
 resultant vs. emergent properties, 43
 Emotions, xxxii, 183–192, 198
 Etiological approaches to function
 epiphenomenalism, 41, 47, 68, 86
 evolutionary causal loop, 68
 modern history theory, 69
 selected effect theories, 68, 70
 Wright's account, 67, 68
 Evolutionary processes
 "open-ended", 115, 135–137
 and organisation, 111–115

F

Fitness
 alignment of, 148, 154
 export of, 148, 154

Formal causation, 53, 56, 58
 Function, 71–74
 and biological explanations, 63
 cross-generation, 74–81
 and integration, xxxi, 103, 124, 142, 144, 149–153, 183–185, 188, 189
 interactive, 90, 93, 108, 128, 165, 170, 173
 and normativity, xxx, 4, 64, 70, 71, 93, 197
 reproduction, 75, 80, 81
 structure vs. effects, 74
 and teleology, xxx, 64, 70, 71, 93, 197
 Functional presuppositions, 84, 85

G

Ganti's chemoton, 25, 26, 29, 30
 Genetic code, 131
 Genetic templates-based organisation (GTBO), 133, 135, 136

H

Homeostasis, xxvi, 173, 181

I

Inclusivity of levels, 42, 44–46, 54, 59
 Independence, xxviii, 6, 17, 23, 89, 97, 114, 197, 198
 Inheritance, 124
 statistical, 125, 126
 template-based, 129
 Inter-level causation. *See* Nested causation
 Irreducibility (functional), 41, 45, 46
 vs. non-derivability (epistemological), 43–44

K

Kim's exclusion argument, 40–42

M

Malfunctions, 81–87
 and adaptivity, 83
 degrees, 83, 85–87
 and nonfunctions, 82
 organisational vs. bio-statistical accounts, 83
 and the origins of norms, 86
 and regulation, 83–85
 Metabolism, 28, 29, 36, 131
 metabolic decoupling, 34, 102, 161–163
 proto-metabolism, 29, 96, 99, 128
 Monism, xxi, xxx, 40, 45, 47, 49, 54, 56, 58, 59

- Motility, 94, 101–104, 156, 169–175, 179, 180, 192
 social motility, 171
- Multicellular organisms
 evolutionary view, 146–148
 organisational view, 148–152
- N**
- Naturalisation, 64, 65, 71, 92
- Nervous system, 174
 autonomic vs. sensorimotor, 180–183
 dynamical decoupling, 175–177
 dynamic core, 185, 189
 embodiment, 175, 177–179, 187, 192
- Nested causation, 40
 and inter-level causation, 52–61
 ontological, epistemological, heuristic justification, 58–60
 synchronic vs. diachronic, 54
 wheel example (sperry), 53
- O**
- Organicism, xxv
- Organisation. *See* Closure
- Organisation-induced transmission of variation, 29–30, 119–120
- Organised complexity, 72
 increase, 29–30, 33, 36, 37, 113, 115–116, 122–127, 136–139
 vs. material complexity, 72
 vs. structural complexity, 122–123, 126–129
- Organisms
 as “clusters of adaptations”, 111, 112
 as units of autonomy, 113
- P**
- Primary consciousness, 184–187, 191
- Protocells, 115, 120–130
- R**
- Re-entrant signalling, 185
- Reflexive catalysis, 25
- Regulation
 and adaptivity, 31, 36
 and autonomy, 38
 and complexity, 30, 36–37
 and decoupling, 34
 second-order closure, xxx, 35–37, 83, 86, 153
 second-order constraints, 35, 36, 89
 second-order norms, 36, 38
 triggering, 34, 83
- Relatedness, xxx, 46–52, 197
- Replicator, 95–97, 117, 118
- Rosen’s closure to efficient causation, 26, 27
- S**
- Self-determination, xxix, 1, 6, 10, 15–18, 51, 69–73, 104, 189, 196, 197
 as self-constraint, 5, 50
- Self-organisation, xxiv, xxvi, 15–18
 and autonomy, xxvii, 17, 18, 114, 198
 interplay with self-assembly, 123
 Kantian view of organisms, xxvi
- Self-reproduction, 25, 75, 120, 123, 134
- Spiegelman’s monster, 97, 118
- Spinoza’s conatus, xxiii
- Supervenience, 41
 relational mereological supervenience (constitutive vs. non constitutive interpretation), 45, 46, 59
 supervenience base, 44–46, 48, 54
- T**
- Templates, 25, 31, 32, 95, 96, 115, 117, 126–133, 138, 199
- Thermodynamic grounding, 6–10
 Kauffman’s work-constraint cycle, xxviii, 9–11
- U**
- Umwelt, xxix
- Unicellular bottleneck, 147, 148
- V**
- Views in the origin of life
 “metabolism-first”, 117
 “replication-first”, 117, 118