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Out-of-Equilibrium (Supra)molecular Systems and Materials: An Introduction

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1.1 General Description of the Field

1.1.1 Background, Motivation, and Interdisciplinary Nature of the Topic

What is life? What can we learn from living systems for the design of advanced (supra)molecular systems? What could the new properties of such systems be? Where will such systems find their applications in the future? And once we will have constructed such lifelike systems, will we better understand life itself? These are emerging and stimulating questions at the interface of biology, biological engineering, synthetic biology, origin-of-life research, molecular chemistry, supramolecular self-assembly, systems chemistry, nanoscience, and materials science. This book serves to be a switchboard for connecting conceptual advances in these disciplines to the overarching topic of out-of-equilibrium (supra)molecular systems engineering.

Living systems, first on foremost, inspire with their capability for self-organization leading to the formation of emergent functions such as self-regulation, adaptation, evolution, and self-replication. Examples can be extremely widespread across all scales: (i) development of human societies, (ii) predator/prey (fox/rabbit) oscillators on isolated islands, (iii) swarm behavior of flocks of bird or schools of fish, (iv) quorum sensing in certain bacteria that turn luminescent collectively upon reaching a critical population density, (v) morphogenesis in an embryo, or (vi) cell division. Many of the underlying molecular principles at the small scale have been unraveled by molecular biology in the recent decades. One of the key natural principles for complex and emergent behavior is the ability to make sense of a complex sensory landscape to define a precise output behavior. This is done via biological signaling reaction networks that provide localized computational power using principles such as autocatalytic activation, negative feedback loops, memory modules, timer clocks, and more. The circadian clock setting our day and night rhythm and its adaptation during long-distance travel (jet lag) is a formidable example to highlight how a biological reaction network regulates humans in an oscillating state between asleep

and awake and how this reaction network adapts to different time zones by changes in daylight settings (Figure 1.1) [3–5]. Understanding and mimicking such reaction networks to process signal inputs and to provide functional output is one key component for future out-of-equilibrium molecular systems [1, 6, 7]. This complex behavior does however not come for free, and energy needs to be spent to allow for it.

Erwin Schrodinger once said: "Living matter avoids to decay to equilibrium"[8]. This is a striking energetic description of living systems and is in stark contrast to how researchers have been organizing synthetic molecular systems in the past – with a focus toward equilibrium. The aspects of how life organizes matter to not decay to equilibrium heavily depend on the molecular machinery in the body. By often using the energy primarily provided through the hydrolysis of ATP (adenosine triphosphate) and GTP (guanosine triphosphate), living systems are able to perform work on their environment and establish active behavior. This, for instance, refers to the development of concentration gradients by powering ion pumps [9, 10], while other motor proteins are able to transport cargo (kinesin on microtubule tracks) [2, 11–15], lead to muscle contraction (actin/myosin) [11, 16, 17], or provide the flagellar motion propelling bacteria [9, 10, 18, 19] (Figure 1.1). Even when looking at structural proteins in the cytoskeleton, it is important to realize that microtubules and actin filaments are formed in a thermodynamically uphill-driven process consuming chemical energy [2, 20]. It is obvious that in some cases, the energy is just needed to execute a function or distribute resources in a cell, while for other cases the energy is in fact needed to build up a function. By driving a system energetically uphill and storing the energy, a system can react much faster. This is, for instance, seen in the ion gradients at our nerve cells, where the buildup of the action potential allows for very fast signal propagation by simple signal-induced opening of an ion channel – much faster than the comparably slow active ion pump transporter protein could provide a signal [9, 10]. Being in such a metastable energy-rich state is helpful for fast reactivity ("spun like a spring"). Similarly, driving self-assembling systems, such as the microtubules in our cytoskeleton, out of equilibrium, by coupling their structure formation processes to the dissipation of chemical fuels, allows to reach very unusual dynamics in the form of dynamic instabilities [21]. These dynamic instabilities with concurrent polymerization and depolymerization of the microtubule filaments, and recycling of the building blocks, enable the cytoskeleton to be in a flux-like, highly adaptive, dynamic steady state so that its structure can be quickly reconfigured to new sensory input. Even though it feels like a waste of energy to run such structures uphill in an energy-consuming way, the much faster capacity for adaptive reconfiguration is a key functional benefit [22, 23]. Understanding and controlling energy management and understanding how to reach controlled energy-driven nonequilibrium states are a second key aspect for the design of future out-of-equilibrium molecular systems.

Tremendous progress has been made in the recent decades in synthetic (supra)molecular systems and materials, molecular machines and motors, self-assembly research, synthetic biology and chemical reaction network, as well as soft matter and bionanoscience, and materials research. Although a completely exhaustive picture is not the focus of this introduction, we wish to point to a few main developments that will also set the basis for the individual chapters of this book.
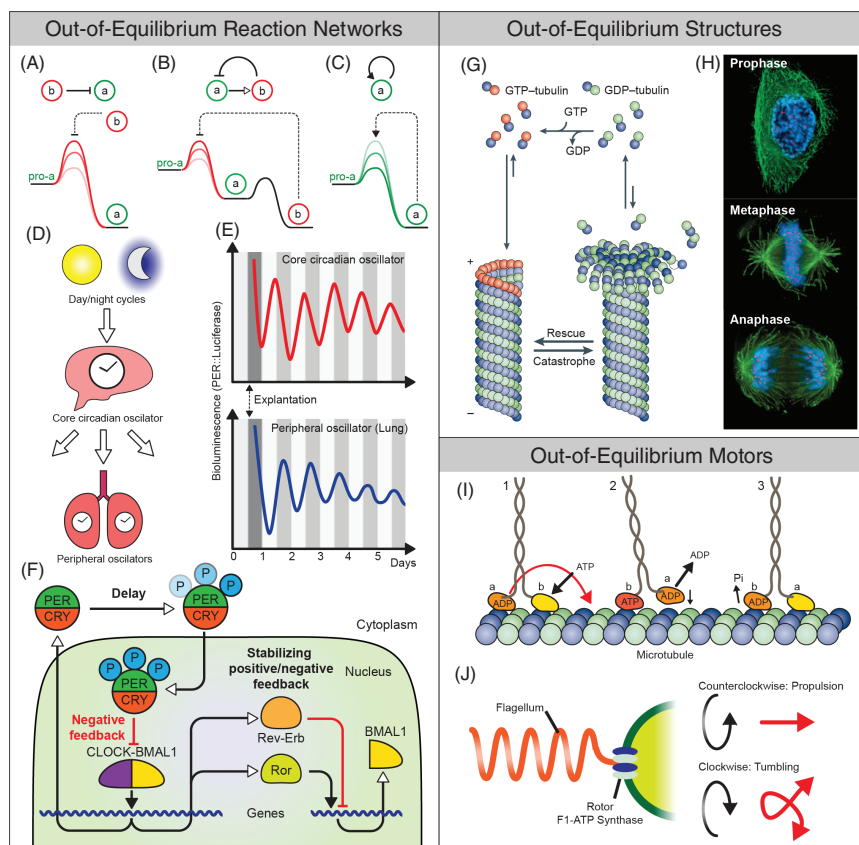
Figure 1.1 Selected out-of-equilibrium systems in living nature. 1. Biological regulatory networks for autonomous temporal control. (A) Schematic representation of the downregulation of "a" production by "b," symbolized by an arrow with a flat head (top), and an exemplarily corresponding reaction profile, where the amount of signal "b" is positively correlated with the activation barrier of formation of "a" (bottom). (B) Schematic representation and reaction rate profile of a delayed negative feedback, where the delay induced by the transformation of "a" into "b" is represented by an arrow with empty head. (C) Autocatalytic positive feedback for the formation of "a," symbolized by an arrow with a filled head (top), and the corresponding reaction profile, where "a" decreases its own activation barrier of formation (bottom). (D) Schematic representation of the hierarchical circadian network, in which the core clock synchronizes the metabolic clock in the lungs while being regulated by the day/night cycles. (E) Real-time visualization of PER2 gene (PER) expression using PER::luciferase fusion proteins in the suprachiasmatic nucleus (core oscillators) and in lungs (peripheral oscillators) in mice. Tissues were explanted at day 0.5; white and dark lines show day/night cycles. (F) Schematic representation of the feedback loops controlling circadian oscillations. 2. Out-of-equilibrium dissipative structures for microtubule self-assembly and dynamics. (G) Schematic representation of dynamic instabilities during microtubule polymerization. (H) Immunofluorescence images showing DNA (in blue) and microtubules (in green) during human cell division. Energy-driven molecular machines and motors: schematic representation of (I) the coordinated walk of kinesin motors on microtubules fueled by ATP hydrolysis and (J) the ATP-powered flagellar propulsion of bacteria. *Source:* (a–d, i, j) Merindol and Walther 2017 [1]. © 2017, Royal Society of Chemistry, (f–h) Cheeseman and Desai [2]. © Springer nature, (e) Yoo et al. [3]. (H) Reproduced from Merindol and Walther with permission from The Royal Society of Chemistry.

The wide field of self-assembly with components from organic supramolecular chemistry, from polymer and colloid science, and from the biological domain has matured largely [24–34]. Researchers worldwide are able to design hierarchical and highly complex architectures from the bottom-up with an exquisite control over interactions and organization. However, all of these structures are typically designed by self-assembly and self-sorting toward thermodynamic equilibrium. This progress in experimental systems has been greatly assisted by developments in computer simulations that are able to predict and rationalize structural space using concepts of energy minimization. Such structures have become switchable by the integration of molecular switches, responsive macromolecules, or tunable colloidal interactions. Concurrently, this has given rise to the field of responsive materials that are able to change their function depending on an outside signal [35, 36]. Typically these materials switch under equilibrium conditions and are engineered for robust switching to minimize fatigue. Such concepts have deeply impacted materials science from photonics to biomaterials, and consumer products are in use based on such elaborate switches.

A special emphasis needs to be given to the progress made in the control of precision molecular switches that has culminated in the design and synthesis of sophisticated molecular machines – as recognized by the recent Nobel Prize for Chemistry in 2016 [37–39]. In terms of how these molecular switches react to external energy input, such as chemicals, light, pH, or redox potentials, they can be classified into reversible equilibrium switches and reversible metastable switches that can store a part of the energy in one configuration or into more advanced molecular motors that allow for a continuous operation with a nonreciprocal, cyclic trajectory. The latter is of particular importance, because it allows to break spatial and time-reversal symmetries and therefore to accumulate work in continued operation. Concurrently to the development of experimental approaches to such molecular machines and motors, advances in theory of nonequilibrium thermodynamics have delivered a further rationalization of their principles of operation [40, 41]. Progress in the direction of integrating such molecular switches, machines, and motors into macroscale materials is fascinating, but overall certainly rather at the beginning, and many discoveries toward molecularly controlled active systems can be expected [42, 43].

Feedback-controlled chemical reaction networks (CRNs) are intrinsic chemical out-of-equilibrium systems that provide the embodied intelligence in living systems [44–46]. Those are of profound relevance to ultimately empower molecular systems with the capacity for complex adaptation, learning, and interactivity. Nearly every chemist is familiar with the Belousov–Zhabotinsky (BZ) oscillator, which is a feedback-controlled redox oscillator that leads to spatiotemporal patterns in non-stirred reactors [47, 48]. Despite its serendipitous discovery in the 1950s, it continues to be a workhorse for implementing robust oscillatory behavior into materials [49]. The BZ reaction has been complemented by a diversity of other oscillators, and behavioral richness has been increased to show bistability or complex Turing patterns [1, 44, 50–52]. Although first important examples exist in coupling such CRNs to design autonomously behaving soft materials to make oscillating self-assemblies and pulsating and walking hydrogels or to preprogram dissipative self-assemblies

or transient materials, overall the connection of CRNs with functional materials is at its infancy, and major compatibility issues need to be addressed in the future [22, 23, 53–58].

A concurrent impetus is given from the biological domain, in particular from the fields of synthetic biology and biomolecular engineering [59]. Due to the fact that biological components such as cytoskeleton and motor proteins as well as enzymes can be rationally engineered and produced biotechnologically, possibilities have emerged to study complex systems using these components *ex vitro* with the aim for *de novo* engineering of minimalistic life and with the aim to design additional functions of no relevance to the biological world [60–67]. Additionally, fields such as peptide assembly and DNA nanoscience, with all the possibilities for manipulation of their nanostructures using enzymes and strand displacement reactions in the case of DNA, have matured considerably [68–72]. DNA computing devices are nowadays already able to move beyond binary logic and are able to make consensus decisions needed, for example, in threshold sensing [73–75].

1.1.2 From Equilibrium Self-Assembly to Far-From-Equilibrium Self-Organization

This part of the introductory chapter will set the scene to clarify the main terminology used in the field of nonequilibrium molecular systems by classifying self-assembling systems according to their energy landscapes. The individual chapters of this book will pick up upon these classifications and emphasize on different aspects of them in a more detailed manner. Classical **equilibrium self-assembly** is an energy minimization process in which the building blocks spontaneously assemble into an equilibrium state (Figure 1.2a,b). This process can be understood by computer simulations following concepts of energy minimization. When applied to mixtures of chemical building blocks, self-assembling processes under thermodynamic control have been instrumental to develop all kinds of powerful self-sorting systems [76–78] and have given birth to the rich research domain on dynamic combinatorial chemistry [79]. Self-assemblies can also be switchable by trigger/counter-trigger principles (e.g. pH, temperature, or redox potential), whereby the whole environment and energy landscape change, leading to a change of the self-assembled structure into a different energy minimum (Figure 1.2a) [53]. Robustness and minimum fatigue are typically desirable features of such systems, but at the same time these assets minimize their propensity toward an evolution of their response as needed for real adaptation concepts.

If appropriately designed and appropriately kinetically guided, such self-assembling systems can also end up in metastable states (Figure 1.2b). Depending on the energy barrier of the metastable energy well, **metastable self-assembled states** can remain kinetically trapped or can interconvert to the thermodynamic ground state with a certain temporal profile. Elaborate engineering of such kinetic traps is a principle of profound importance to the field of pathway complexity and kinetically controlled structure formation in supramolecular chemistry. This has given rise to landmark discoveries of autonomous interconversion of different
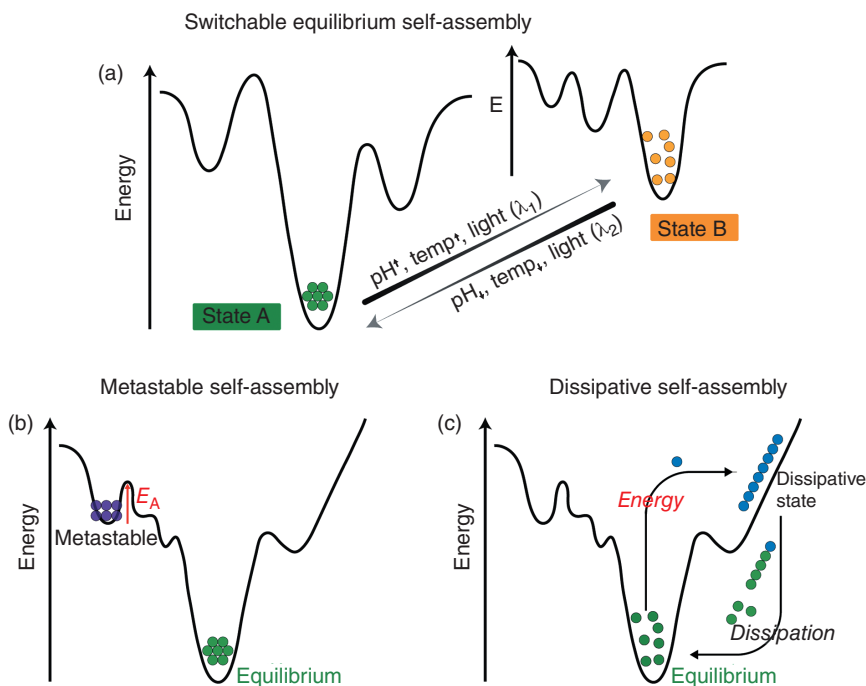
Figure 1.2 Differences in terms of energy landscapes between (a) classical switchable self-assembly, (b) kinetically controlled metastable self-assembly, and (c) dissipative self-assembly.

self-assembled supramolecular polymer structures and to the field of living supramolecular polymerization [80, 81]. Addressing specific kinetic pathways or specific metastable situations in an energy landscape has also been termed **directed self-assembly** (in particular with block copolymers) [82, 83]. It is important to emphasize that these states are non-dissipative, meaning that they do not require a constant input and dissipation of energy to sustain their functional state. They are out-of-equilibrium yet non-dissipative and purely kinetically trapped states.

In contrast, **dissipative self-assemblies** require a constant energy transduction to maintain a structural state (Figure 1.2c). The microtubules discussed above are a prime example for such a system [21]. Elaborate dynamics in the driven steady-state and strong out-of-equilibrium behavior can occur for kinetic asymmetry in the assembly and disassembly pathway if the system is able to store energy in the energy dissipative state [84]. When closed, meaning without energy and matter exchange, such systems – when, for instance, fueled with chemical fuels – will ultimately migrate back to the equilibrium state. This has given rise to the design of autonomous systems and transient self-assemblies with programmable lifetimes [22, 23, 53, 85–88]. Truly sustained nonequilibrium dissipative steady states can only be obtained in an open system that allows for constant exchange of energy and/or matter so that fuel and waste can be exchanged. Related to these dissipative self-assemblies driven by direct chemical fuels, there have also been notable

examples whereby a dissipative environment (e.g. a transient pH curve with negative feedback) organizes self-assemblies to follow this environment [1]. Next to chemically fueled systems, also light-fueled systems based on molecular machines (e.g. rotary motors developed by Feringa) or self-reverting photoswitches such as azobenzenes have contributed largely to the field of dissipative self-assembly and dissipative molecular materials design, whereby a functional state is only maintained upon constant irradiation and in which the decay to the thermodynamic ground state happens once the light is switched off [31, 38, 89]. Very closely related to such dissipative self-assemblies and systems is the field of active matter, where energy dissipation is used to drive motion, to organize patterns, and to perform work. The term active matter [90] has been mostly used for colloidal systems (or for research on bacteria behavior) with microscopically visible motion, but conceptually there is little difference to molecular systems driven by energy-dissipating molecular machinery.

Targeting truly **self-organizing far-from-equilibrium systems** requires to improve information processing and feedback control in such dissipative systems, whereupon spatiotemporal patterns occur that form based on interacting entities without a central organizing authority. These patterns can, for instance, form from seemingly random fluctuations that are amplified by positive feedback (e.g. autocatalysis, cross-catalysis), and they are maintained and spatiotemporally regulated by a feedback network. In molecular systems this requires on the one hand an organization of CRNs to harbor increasingly complex regulatory modules and on the other hand a constant energy input to continuously drive structure formation beyond bifurcation points. Such systems have been described theoretically by the Brussels' school and others building on Prigogine's seminal work on nonequilibrium thermodynamics [91]. Truly emergent behaviors such as ultrasensitivity, reaction–diffusion patterns, stable oscillations, bistability, synchronization, and collective motion occur. The term far-from-equilibrium behavior should be restricted to such systems and not be used for dissipative out-of-equilibrium self-assemblies discussed above.

1.1.3 From Responsive Materials to Adaptive and Interactive Materials Systems with Life like Behavior

Following the key advances on a system level, we will witness in the near future a disruptive paradigm change in the design of functional soft materials. At present functional and responsive soft materials are designed to feature reliable switching mechanisms, similar to the switchable self-assemblies discussed above (Figure 1.2a), between two or more functional states with high reliability and minimum fatigue. However, beyond these passively responsive materials lie the fields of truly adaptive and interactive materials that provide entirely new property profiles that have to be described as behavioral materials or better behavioral materials systems [6]. Such materials systems will in long term be able to sense, adapt, communicate, learn, evolve and replicate, and take the present-day "dead" (equilibrium) responsive materials to a more interactive, intelligent, and lifelike state (Figure 1.3). Even
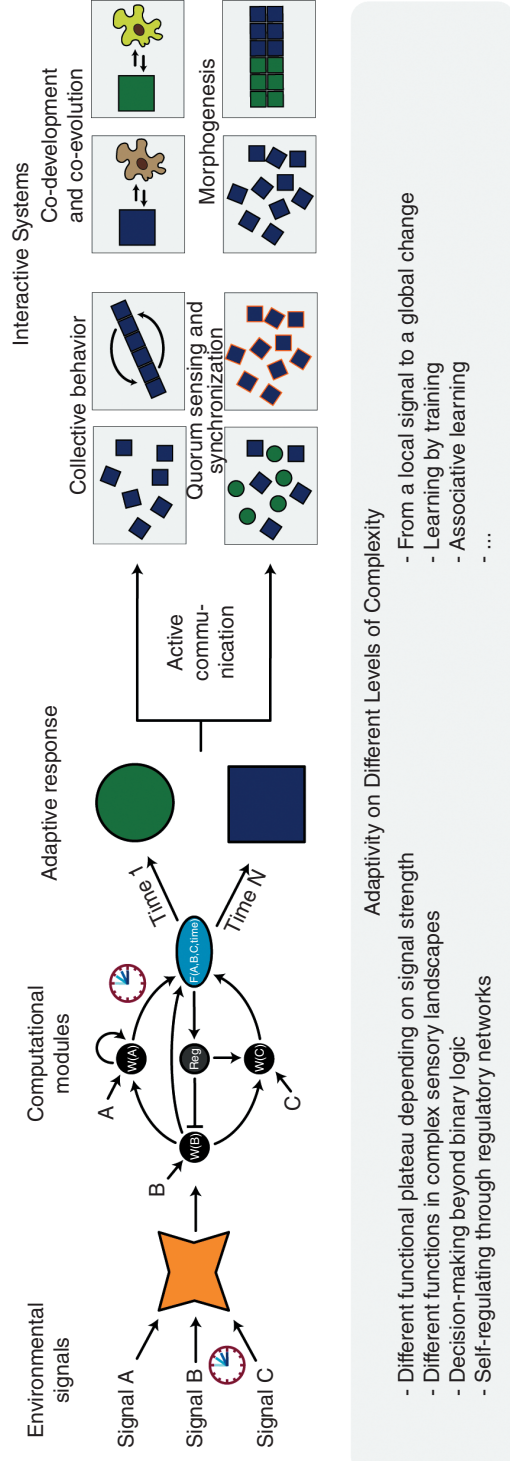
Figure 1.3 Pathways toward adaptive and interactive systems and materials systems requiring energized out-of-equilibrium concepts for embodied intelligence and active communication. *Source:* Walther [6]. Licensed Under CC BY 4.0.

though this is a profound paradigm change compared with current state of the art, the understanding of molecular biological mechanisms and the design of synthetic out-of-equilibrium molecular systems are improving quickly, and transductions toward lifelike materials systems may soon become a reality.

Key traits of adaptive materials are sketched at the bottom of Figure 1.3. Adaptation in the materials world may refer to adaptation to distinct functional plateaus in complex sensory landscapes, threshold sensing, homeostasis, training, and learning as evolutionary trades or to the ability to make decisions. It is obvious that this requires to improve the computational abilities of such materials systems, which requires an "embodied intelligence." Such an embodied intelligence can be provided by out-of-equilibrium CRNs, and such CRNs can also provide the possibilities to embed memory functions so that a materials system can remember its past and adapt its answers to a future outcome. Such memory functions in future metabolic materials systems are highly challenging [92–94] but ultimately needed for a behavioral evolution of materials systems to provide self-regulation, evolution, and learning effects.

One of the decisive aspects to transition toward interactive systems and materials systems is to implement active communication between intrinsically adaptive entities or between an adaptive entity and an adaptive surrounding [6]. This may, for instance, appear particularly relevant for computing delivery devices *in vivo* or for establishing communication of a hydrogel biomaterial with cells to provide interactive cell niche materials. This requires to go beyond established concepts of passive response and necessitates to provide active feedback, which can include the emission of chemical counter-messengers, or physical counter-stimuli, which in turn will induce a secondary response of the interacting entity in a system. Ultimately, both entities should in fact adapt continuously toward each other's signaling and signal processing systems to arrive at crosswise regulation and self-regulation. It is obvious that this will require even greater advances in the computational abilities of materials and systems to provide an adaptive communication as the entities evolve jointly, leading potentially as an ultimate goal to biosynthetic hybrid morphogenesis (co-development and coevolution).

1.1.4 An Outlook on Challenges Ahead

Some of the challenges that emerge from the considerations above and from the conclusion of the chapters within this book can be summarized as follows. We still need a better understanding for how to rationally design out-of-equilibrium systems and for how to modulate and manipulate energy landscapes. Interestingly, aspects such as evolution and self-replication are emerging across a diversity of disciplines, from RNA nanoscience to supramolecular polymers, but very generic principles are not derived as of yet [95–97]. Additionally, although much progress has been made for homogeneous systems, addressing the involvement of spatial domains with respect to compartmentalization or to include competitive reaction–diffusion processes is still rather underdeveloped but overall presents a key aspect when targeting communication and morphogenesis. On the energy transduction side, synthetic

principles for the handling of energy sources are still rather simplistic. Certainly, light or chemo-driven molecular motors are emerging; however, they fall short of the sophistication and efficiency provided by their biological analogs both at their own scale (pumping, transport of cargo, catalysis, programing) and also regarding the transduction of motion to larger length scales, as well as in their coupling with larger chemical systems [98–101]. Much can be learned however already on the systems level from the repurposing of biological energy-driven molecular machinery in *ex vivo* systems, but those may in many cases not be applicable to real-world material problems. This motivates very profoundly the research for synthetic molecular machines and motors that can operate in a human needs-centered materials world. In addition, we are also faced with the challenge that the fundamental development of nonequilibrium thermodynamics to better understand and classify the nature of synthetic out-of-equilibrium systems and materials requires new descriptive approaches. Along these lines it is also obvious that the system features of synthetic CRNs have been diversified tremendously, in particular in, but not limited to, synthetic biology. Aspects such as consensus decisions and even simplistic aspects of learning can be implemented on a reaction network level [1, 44, 73–75, 102]. Although this sheds important light on origin-of-life aspects and on how life operates and has implications for the engineering of synthetic cells [60, 103], the connection to the materials science world is still underdeveloped – which is however a critical step toward an implementation into future technologies of societal relevance.

One way to tackle these aspects in future will be to bring together the approaches from different disciplines in a more focused manner. Hence, the further integration of the contributing fields, for instance, materials science and systems chemistry, materials science and synthetic biology, molecular and biological machines, bottom-up supramolecular systems design with top-down 3D printing for spatial compartmentalization, as well as theory, simulations, and experiments will be of outstanding relevance to lay the foundation for adaptive and interactive next-generation materials systems. This book emphasizes this cross-disciplinary thinking and highlights the diversity of approaches for out-of-equilibrium (supra)molecular systems originating from different fields to foster an integrative understanding and fertilize new approaches also bridging disciplines. The field of out-of-equilibrium molecular systems engineering is young and vibrant, and many opportunities for groundbreaking discoveries present themselves. The best is yet to come, and it will be interesting how the fields of lifelike out-of-equilibrium systems will develop in the coming decade and beyond.

1.2   Description of the Book Content

The chapters of this book have been classified by subgroups including biological and bioinspired molecular reaction networks (Chapters 2–4), supramolecular polymers and self-assemblies from kinetic traps to out-of-equilibrium self-assemblies and dynamic combinatorial libraries (Chapters 5–8), light-controlled chemical reactions

and self-assemblies (Chapters 9–10), and artificial and biological molecular machines (Chapters 11–13).

Chapter 2: Jean-Christophe Galas and André Estevez-Torres, *Learning from Embryo Development to Engineer Self-Organizing Materials*

In Chapter 2, Jean-Christophe Galas, André Estevez-Torres, and coworkers introduce recent concepts learned from embryogenesis in living organisms – which typically transforms an amorphous mass into a highly differentiated structure – and show how they could be implemented for the self-fabrication of out-of-equilibrium materials. In particular, they review the formation of highly ordered concentration patterns by out-of-equilibrium reaction–diffusion processes, as well as the chemomechanical transduction pathways used to generate spatially addressed forces. They then describe experimental achievements and discuss the perspectives offered by soft chemical and biochemical systems that can display a rich variety of dynamical behaviors going from force-induced pattern formation to movement and deformation of macroscopic materials.

Chapter 3: Annette F. Taylor, *From Clocks to Synchrony: The Design of Bioinspired Self-Regulation in Chemical Systems*

In Chapter 3, Annette Taylor deeply discusses the impact of feedback loops in complex reaction networks. She shows how network architectures and reaction kinetics are instrumental to generate and govern self-regulated processes in living organisms, in which internal feedback mechanisms can give access to multiple possible states under out-of-equilibrium dissipative conditions. In particular, the author discusses the generation of nonlinear functional aspects of high interests including autocatalysis, chemical oscillations, clock reactions, far-from-equilibrium phase diagrams, waves, and collective behaviors. Finally she shows how chemists can build on these self-organization principles to access emergent functional properties in order to design novel types of complex interacting materials.

Chapter 4: Sergey N. Semenov, *De novo Design of Chemical Reaction Networks and Oscillators and Their Relation to Emergent Properties*

Sergey Semenov details in a fourth chapter the different types of emergent properties produced by out-of-equilibrium CRNs in well-mixed solutions or in flow systems. The author provides guidelines to design them *de novo* by playing on parameters such as stoichiometry, connectivity and network motifs, kinetics, molecular structures, autocatalysis and cross-catalysis, inhibition, and allosteric modulation. He also highlights future directions of investigations, including compartmentalization, and of possible implementations, in particular toward signal treatment, computation, and open-ended Darwinian evolution.

Chapter 5: Kazunori Sugiyasu, *Kinetically Controlled Supramolecular Polymerization*

In another direction, the fifth chapter written by Kazunori Sugiyasu opens the discussion on the recently introduced methodologies that can provide a kinetic control over supramolecular polymerization processes. These methodologies are mandatory to reach supramolecular polymers with potentially defined molecular weight and microstructure, but they are also challenging because noncovalent bonds in one-dimensional objects and in solution are most of the time formed

under thermodynamic control. This translation toward a kinetic regime can however be afforded by making use of nucleation–elongation mechanisms of very high cooperativity and up to the achievement of living supramolecular polymerization by fully controlling the initial nucleation step.

Chapter 6: Jan H. van Esch and Rink Eelkema, *Chemically Fueled, Transient Supramolecular Polymers*

In the following chapter, Jan van Esch, Rink Eelkema and coworker discuss examples of dissipative supramolecular polymerizations leading to transient 1D assemblies that can only maintain their structures out of equilibrium in the presence of a chemical fuel. As it is the case in biology with the polymerization of microtubules using GTP as an energy source, chemically fueled artificial systems couple their supramolecular assembly with a CRN in which formation competes with degradation. Interestingly, such coupling when properly engineered opens new possibilities for the generation of emergent behaviors of the supramolecular structures such as bifurcation, oscillation, and adaptation.

Chapter 7: Leonard Prins, *Design of Chemical Fuel-Driven Self-Assembly Processes*

As reviewed by Leonard Prins and coworkers in Chapter 7, chemical fuel-driven supramolecular systems can be also encountered in various types of transient self-assemblies of higher dimensionalities, including micelles, vesicles, and colloids. An interesting extension of this approach by the authors was directed toward the design of temporal control over transiently active gold nanoparticles for fluorescent signal generation, catalysis, and self-assembly. In this general context, they discuss in depth the concepts that sustain the transfer of energy from a chemical fuel to a self-assembly process, and they establish a distinction between limit situations such as self-assembly under dissipative conditions, dissipative self-assembly, and driven self-assembly

Chapter 8: Sijbren Otto, *Dynamic Combinatorial Chemistry Out of Equilibrium*

Chapter 8, written by Sijbren Otto and coworker, is dedicated to the coupling of out-of-equilibrium situations with dynamic combinatorial libraries. Such libraries are adaptive chemical systems that can recombine their numerous building blocks depending on internal factors or external effectors. The concepts were originally implemented at thermodynamic equilibrium toward the design of receptors, ligands, replicators, and complex shuffling materials. The discussion of the recent literature shows further involvement of irreversible reactions within the library members, of their kinetic trap, and of energy-fueled dynamic libraries. These advances highlight the potential of these combined approaches to access truly adaptive and evolving systems.

Chapter 9: Rafal Klajn, *Controlling Self-Assembly of Nanoparticles Using Light*

In Chapter 9, Rafal Klajn and coworkers detail the use of light to control the remote self-assembly of functionalized nanoparticles and microparticles. A variety of systems is described by paying a particular attention to the molecular level, which, for instance, involves photoswitchable molecules, photodimerization reactions, photoacids and photobases, thermoresponsive polymers, and photoredox receptor–ligand complexes. Future directions are also discussed including nonspherical nanoparticles, use of lower energy wavelengths, selectivity in

multidynamic systems, and self-assemblies at interfaces or in confined spaces, as well as in biological environment.

Chapter 10: Stefan Hecht and Michael Kathan, *Photoswitchable Components to Drive Molecular Systems Away from Global Thermodynamic Minimum by Light*

When properly engineered, photoswitchable components are very general and powerful tools to drive functional molecular systems away from equilibrium. This is the interesting demonstration made by Stefan Hecht and Michael Kathan in the 10th chapter of this book. After describing key differences between thermodynamic and photodynamic equilibria, the authors detail through different examples of the literature how photochromic molecules can be coupled to sustainable chemical reactions, molecular motions, and self-assemblies. Interestingly, they highlight how such systems can be precisely manipulated by energy powering rather than by simple gating.

Chapter 11: Alberto Credi, *Out-of-Equilibrium Threaded and Interlocked Molecular Structures*

As shown by Alberto Credi and coworkers in the following chapter, out-of-equilibrium situations can be now implemented in fully synthetic machines based on threated and interlocked molecules. After explaining the terminologies used to describe mechanically interlocked molecules and their chemical access, they discuss how they can move their substructures on long range and in a preferential direction upon energy supply when properly making use of ratcheting mechanisms. This precise modulation of the potential energy surface can lead to interesting functional features under dissipative conditions, such as the autonomous cycling of mechanical work giving access to molecular motors and pumps.

Chapter 12: Ben L. Feringa, *Light-Driven Rotary Molecular Motors for Out-of-Equilibrium Systems*

In Chapter 12, Ben Feringa and coworkers state that despite the plethora of ingenious synthetic chemical systems that have been designed so far to produce motion, most of them are limited to reversible (switching) events that do not generate increasing work upon back-and-forth actuation. The authors then discuss how photochemical excitation can be an efficient source of energy to actuate light-driven rotary motors that perform work. After describing in details the functioning principles that sustain their unidirectional rotation and tune their frequency, they describe their out-of-equilibrium properties through various examples of the literature, including when working in collective systems. They finally highlight their future potential as they now enter an era in which they can play a role not only at nanoscale but also at macroscale.

Chapter 13: Henry Hess, *Design of Active Nanosystems Incorporating Biomolecular Motors*

In a final chapter, we return to a biological system, where Henry Hess and coworker introduce the functioning principles used by biomolecular motors to produce a mechanical work from fuel consumption and how they can be engineered and incorporated in active nanosystems. In particular, the authors discuss the interactions between protein motors and cytoskeleton components and their responses to external stimuli. They finally show how functions can be implemented from these dynamic constructs, such as for delivering cargo, for sensing, and for

controlling the passive and active formation of patterns and of high-order structures capable of motion.

Overall, with this outstanding ensemble of contributions by the best specialists worldwide, diverse but coherent views of present achievements and future outlooks encompass this nascent field of research. We hope that, as a reader, this book will answer to some of your questions and will stimulate your imagination. We are particularly grateful to Wiley, which was instrumental in giving birth to the first existing book dedicated to this fascinating scientific domain.

Acknowledgments

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