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Classification of Self-Organization and Emergence in Chemical and Biological Systems

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Most chemical and biological systems are complex, but the application of complex systems science to these fields is relatively new compared to the traditional reductionist approaches. Complexity can provide a new paradigm for understanding the behaviour of interesting chemical and biological systems, and new tools for studying, modelling, and simulating them. It is also likely that some very important, but very complicated systems may not be accessible by reductionist approaches. This paper provides a brief review of two important concepts in complexity, self-organization and emergence, and describes why they are relevant to chemical and biological systems.

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Introduction

Complex systems science (complexity science) provides a novel way of thinking about dynamic systems and is one of the most active and rapidly growing branches of science. Nonlinear behaviour, on which complexity depends, is deeply rooted in the fundamental laws of physics[1] so cuts across traditional scientific divisions, yielding deep insights into common mechanisms at play in diverse natural and artificial systems. Complex systems science provides a novel and alternative means of dealing with chemical and biological systems to the traditional reductionist methods in which most scientists are trained. The previous paper in this issue[2] provided a general overview of the importance of complex systems science in chemistry and biology.

According to Whitesides, almost everything in chemistry is complex.[3] Since everything in nature has a molecular or chemical basis, the core of all natural phenomena may be intrinsically complex. Two fundamental concepts in complex systems science are emergence and self-organization. Many systems in the natural world are self-organized (in whole or in part) and exhibit emergent behaviour. Although self-organization and emergence are intimately related, we provide separate overviews of these concepts to make the nature of the two clearer. We also describe in general terms how these processes (under the banner of complexity research) provide an insightful and unique conceptual framework for understanding, modelling, and predicting complex physical, chemical, and biological systems. As emergence and self-organization are still relatively poorly understood, our overview provides an introduction to these difficult concepts, a cautionary summary of their interrelations, and provides reading for those wishing to delve further.

Emergence

Emergence is a difficult but useful concept. It is typically described as a property of a system that is not reducible to, nor

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readily predictable from, the properties of individual system components. Such properties may therefore appear surprising or unexpected, at least from a reductionist perspective. Aristotle, over two millennia ago, captured the concept as 'the whole is something over and above its parts, and not just the sum of them all …'. Likewise, complexity research adopts a holistic systems perspective that is complementary to the traditional reductionist paradigm. In particular, systems biology is moving in this direction and we may be witnessing a paradigm shift in understanding the universe, as we realize that some laws of nature cannot be deduced by delving deeper into details.[4]

The relatively abstract nature of emergence has resulted in numerous ways of defining and classifying it being proposed. Emergence still lacks a clear, standard and widely accepted definition.[5–8] To some, the general concept describes an unproblematic relation among perfectly ordinary entities or properties, whereas to others it expresses an almost 'mysterious' relationship amongst the component entities.[9] In this paper, we provide a very simple and intuitive definition of what we consider to be the primary types of emergent phenomena.

Types of Emergence Exhibited by Physical Systems

Emergent properties reflect real, physical phenomena that exist regardless of an observer and regardless of the knowledge we may have about systems. To distinguish our classes from the numerous other classification systems in the literature, we label the classes 'simple' and 'complex' emergence. Simple emergence occurs in systems at or very close to thermodynamic equilibrium. Complex emergence exists in systems driven far from equilibrium by the input of matter and energy. We propose that a critical element in the transition from simple to complex emergence is the onset of self-organization (see below).

Simple Emergence

In chemistry and physics (less often in biology), there are systems that are close to equilibrium. Such systems, such as gases in closed vessels and many everyday objects such as tables, rocks and bottles of wine, possess many properties that are not exhibited by system components. For example, the table exhibits stability, a rock possesses rigidity, and wine exhibits fluidity. These simple collective properties are emergent in the sense that they are collective, and irreducible to single component parts. Other examples include the pressure and temperature of a gas at equilibrium.

Complex Emergence

Many systems in nature are driven far from thermodynamic equilibrium by inputs of matter and energy. Such systems frequently display a characteristic order that arises when some instability point is crossed, and the system reaches a quasi-stable or meta-stable state that reflects both the driving force and any internal system constraints or behaviour. This order is termed self-organization. Collective properties of such systems that arise from this self-organization are termed complex emergent properties. Examples include the regular hexagonal convection cells that form when fluid in a shallow pan is heated uniformly,[10–12] selection of shortest pathways in ant mass-recruitment systems,[13–15] the dynamic instability of a population of microtubules attached to a microtubule organizing centre in a cell[16] (see below), and other more complicated phenomena such as weather patterns, ecosystems, and emotion. In abstract examples such as consciousness and self-awareness, the assumption that we make is that there is nothing vital or essentially mysterious in their emergence. In other words, if we possessed adequate knowledge of physics, chemistry, biology, and other relevant sciences, we could understand their emergence from the behaviour and interaction of all relevant component parts. Such assumptions in the past have proven worthwhile, although they may ultimately be shown to be lacking.

Detecting, Quantifying, and Exploiting Emergence

For emergence to be 'useful' it needs to fulfil a function—to be exploited—and thus requires the participation of an observer. Although it is far from clear how to quantify emergence, information theoretic approaches show promise in this regard. For example, Crutchfield and Shalizi developed a description of emergence in terms of what they called relative predictive efficiency.[17] If a complex system can be described at two levels of abstraction, perhaps a component, or agent, level and a higher level, emergence exists if the higher level description of the complex system has a higher predictive efficiency than the lower level. Predictive efficiency can be thought of as the ratio of how well the system can be modelled to the complexity of the model or system description used to make the prediction. Poorly predictive models, or those that predict well but are very complicated, will have a lower level of predictive efficiency. Clearly, this type of approach to quantifying and describing emergence depends on an observer willing and able to construct models of potentially emergent phenomena.

There is evidence from diverse sources that 'coarse graining' of a complex system can make computationally intractable problems accessible whilst still capturing essential features of the emergent properties.[18,19] For example, if the human brain paid attention to all available visual stimuli, it would be overwhelmed and become unable to function efficiently. Clearly, visual coarse graining occurs as much of the information we see is disregarded.

Crutchfield argued that emergence is ubiquitous in nature as it has strong adaptive advantages for living systems that employ it.[20] This idea is consistent with the idea of modelling at multiple levels of abstraction performed by an observer (essentially any organism with sensory capabilities that interacts with its environment and is not part of the system showing emergence). Crutchfield's suggestion that organisms make use of emergence to make sense of the world is congruent with Crutchfield and Shalizi's concept of emergence as a measure of relative predictive efficiency.[17] According to these ideas, organisms that exploit emergence to process sensory information to develop simplified models (abstractions) of their world should enjoy a competitive advantage over organisms that respond to raw sensory information alone.

Just as organisms have evolved to exploit emergent properties of complex systems through pattern recognition, coarse graining of information, and heuristics, researchers have begun to use pattern recognition and evolutionary methods to investigate complex biological systems, methods that have shown considerable promise. Such complexity-based methods allow the system to be described and modelled from the top-down at an appropriate level of detail or abstraction. Recognition of the complexity of many systems, and conscious exploitation of alternative, complexity-based paradigms for modelling and simulation, should allow more rapid progress in the future in modelling of complex systems. For example, medicinal chemists have been generating predictive models of emergent properties of biological systems for a considerable length of time but have only recently become aware of the emergent nature of these properties. This recognition allows complex, systems-based methods such as neural networks, agent-based models, and evolutionary methods to be used in a more disciplined, effective way. For example, in studies of quantitative structure–activity relationships (QSAR), we derive simple, predictive models of the response of complex proteins, cells, organs, and organisms to molecules. This is achieved using a coarse-grained representation of the molecules and a highly flexible method of modelling nonlinear interactions (a neural network) to model emergent biological responses, such as binding affinity, differentiation fate, or animal response.

Self-Organization

Self-organization involves pattern formation via physical interaction of units to generate what is commonly a dynamic structure requiring constant energy input. It is an elegant and efficient way to generate complex architectures.[11,21–24] Self-organization has profound implications for our understanding of chemical and biological pattern formation,[1,10,21,22,25–35] although the concept is frequently overlooked in standard textbooks on chemistry and biology. A similar but distinct process, self-assembly, promises to be a valuable technological tool for nanoscience and nanotechnology, which attempts to understand and control the arrangement of material at nanometre scales. Self-organization (or more strictly, self-assembly) offers a powerful alternative to both top-down miniaturization and bottom-up nanofabrication approaches, bypassing tedious fabrication and manipulation procedures.[36] Self-organization is often used interchangeably with self-assembly, although we argue in another paper that the two concepts are distinct.[37] Whereas self-assembly implies an energy minimization to an equilibrium structure, absorption of energy is a pivotal factor in self-organization,[38] which is therefore a property of non-equilibrium systems.[39] Although self-organization depends upon energy input, the organized structures must not directly reflect this externally imposed order.[40] In other words, to be *self*-organized the formed structure must be an intrinsic property of the interactions of the components of the system, that may, however, be modulated to a degree by external interactions that any open, dissipative system necessarily has.

Despite confusion about how to best integrate ideas of self-organization into biology, 'bottom-up' organization is clearly important. For example, in the nervous system the number of cells and the number of connections far exceed the number of structural genes in the genome. There is no clear picture of how cells could create a properly wired central nervous system in the absence of self-organization.[16] It is clear that in many biological systems, self-organization provides a robust and flexible source of order that can be used to cope with variability.[16,21,22,24,41–44] We provide descriptions and examples of three important classes of self-organized processes prominent in chemistry and biology. Hopefully, appreciation of the ways in which self-organization interacts with other sources of order will provide clues to some of the most challenging scientific questions, such as how do stem cells 'choose' self-renewal or differentiation fates.

Self-Organization around a Template

In many types of self-organization, structures appear through amplification of random initial fluctuations. However, randomness can be detrimental, as structures may be required at specific locations and at specific times. For example tubulin, the cytoskeletal protein, undergoes a process of template-assisted self-organization around the microtubule organizing centre (MTOC) of cells. The MTOC provides a template upon which tubulin monomers self-assemble into microtubules, which participate in a larger, dynamic, dissipative self-organizing process.[16] Although the addition of tubulin to a growing microtubule structure is energetically favourable and spontaneous (self-assembly), tubulin is an enzyme as well as a structural protein. Tubulin hydrolyses GTP, providing an energy source that drives the energetically unfavourable disassembly process where tubulin monomers leave a partially assembled microtubule structure (collapse). During mitosis (cell division), when each chromosome must be connected to a MTOC, the exact position of each chromosome cannot be predicted as cells can differ considerably in morphology. The random exploration of cellular space during the dynamic, self-organized microtubule assembly process provides a mechanism by which the kinetochore of each chromosome can connect with the MTOC. Those microtubules that happen to contact a kinetochore are selectively captured and stabilized, while others eventually collapse.[16,45,46] This self-organizing process, which is constrained by the MTOC template, provides cells with flexibility and robustness, which is particularly useful given inevitable randomness in chromosome distribution and variability in cell morphology.[16] Rodionov et al.[47] tested the role of the MTOC as a template for self-organization. In the presence of a MTOC, microtubules showed dynamic instability indistinguishable from that which occurs naturally. In contrast, in the absence of a MTOC, microtubules 'tread-milled', which means that they both shrank and grew at similar rates at alternate ends.

Templates can come in a variety of forms, and need not be full-sized guides or moulds like Camazine et al.[22] incorrectly suggest.[48] Templates include gradients of any nature, as well as other environmental patterns that influence individual behaviour, contributing directly to the emergence of

patterning.[48] Of course, to be *self*-organized the characteristic features of the organization must not be derived solely from these templates. Another very important and intriguing example of template-assisted self-organization are regulatory networks. These encompass both the protein–gene interactions in the nucleus and cytoplasm, and extracellular protein–protein interactions.[49] Within eukaryotic cells, regulatory networks perform computational tasks, function as a kind of memory that contains information about the cell's surroundings[50] and facilitate information transfer between the plasma membrane and the genome, which acts as a template around which regulatory networks act. When self-organization is combined with the use of a template, biological systems can benefit from properties of self-organization (multistability, robustness, flexibility) while simultaneously enjoying enhanced predictability in time or space.[51]

Dynamic Activity Patterns, Excitable Media, and Direct Communication

In self-organized systems generally, communication between the system components (agents) can be either direct or indirect. The majority of examples of self-organization in chemistry, and a considerable number in biology, fall into the class of *dynamic activity patterns* or excitable media, where communication is largely direct. Such systems typically comprise component parts that exhibit two or more alternative states, with transitions between these states dependent on an intrinsic probability or some function of interaction. For example, Halley and Burd[44] studied groups of feeding Argentine ants, where individuals could be simply classified as either 'feeding' or 'disturbed'. In the absence of any externally imposed disturbance (for example, by an experimenter[52]), most ants are motionless and feeding. The arrival of ants at the food meant that some ants wandered around the group in haphazard directions, disturbing feeding ants. These disturbances comprised a background dynamic activity pattern that is characterized by a simple power law (log–log plot of frequency of disturbance versus size of disturbance is linear).[44] In other words, most of the time disturbances remained small and local, comprising only one or two additional ants. This 'subcritical' background disturbance level in which disturbances amplified to some extent but rarely affected the entire group constituted a type of swarm, or collective, intelligence. At this subcritical point, groups seemed to find a good compromise between rapid response to danger and excessive disturbance.[44]

Another broad class of this type of self-organization via direct communication are described as reaction diffusion processes. The Belousov–Zhabotinsky (BZ) reaction is a well-known chemical example that displays concentric ring patterns that travel outwards from centres that arise spontaneously. Alternatively, if reagents are kept well mixed, the whole system oscillates from one state to the other, a curious organization considering most chemical reactions in the laboratory do not generally display dynamic patterns or spatial order. The order of the BZ reaction arises from an autocatalytic chemical reaction and molecular diffusion. Similar reaction–diffusion examples exist in nature, and may be responsible for important processes, such as morphogenesis, and striped patterning of animal coats. Such processes can be simulated by cellular automata and agent-based modelling methods, which will be described in Polley et al.[53]

External Memory Systems, Stigmergy, and Indirect Communication

In contrast to the previous example of self-organization based on direct communication, this class of self-organization relies on indirect communication among system components. Such organization is particularly important in biology, as individual animals have limited memory and cognitive capabilities and some information must be stored in external environments rather than in individual minds. The process of storing information in the environment, using it as an external memory resource,[54] is called 'stigmergy' and was originally introduced by Grassé to explain some aspects of termite behaviour.[55] Another example is the laying down of pheromone trails by ants. Successive ants respond to the pheromone information in the environment, modify their behaviour, then reinforce pheromone cues that are the most useful. Hence, self-organization can emerge as individuals communicate indirectly through dynamically evolving environments.[21,56–59]

Although stigmergy was introduced in the context of social insects, the idea can be generalized to describe how simple agents can produce a wide range of organized behaviours through exploitation of the environment as an external memory source and means of communication.[51,56,60,61] Interesting examples of this include routing in telecommunication networks, task allocation in multi-robot systems, and exploratory data analysis.[51,60,61]

Summary

Most interesting systems in chemistry and biology are complex, exhibiting emergent properties and self-organization. To fully understand many complex chemical and biological processes, we must appreciate how self-organized pattern formation emerges from the properties and interactions of system components and other sources of order, such as environmental templates. For example, an important contemporary problem is how the behaviour of stem cells (e.g. differentiation, lineage choice, self-renewal) emerges from smaller scale processes and interactions. This problem is likely to involve several types of self-organization, one of which may be the self-organization of the regulatory network around the genome. However, the environment external to stem cells is also crucial for behaviour, and the cytokine regulatory network may act as a kind of external memory that is both updated by, and interacts with, the regulatory network. In addition, stem cells may communicate with other cells or the environment through cell–cell and cell–extracellular matrix contacts. Thorough understanding and control of stem cell behaviour may ultimately require all components of these self-organized processes to be understood and modelled. This complexity may explain why it has been so difficult in the past to control stem cell behaviour.

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