

Review

Chemical Organization Theory as a General Modeling Framework for Self-Sustaining Systems

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Abstract: This paper summarizes and reviews Chemical Organization Theory (COT), a formalism for the analysis of complex, self-organizing systems across multiple disciplines. Its elements are resources and reactions. A reaction maps a set of resources onto another set, thus representing an elementary process that transforms resources into new resources. Reaction networks self-organize into invariant subnetworks, called ‘organizations’, which are attractors of their dynamics. These are characterized by closure (no new resources are added) and self-maintenance (no existing resources are lost). Thus, they provide a simple model of autopoiesis: the organization persistently recreates its own components. The resilience of organizations in the face of perturbations depends on properties such as the size of their basin of attraction and the redundancy of their reaction pathways. Application domains of COT include the origin of life, systems biology, cognition, ecology, Gaia theory, sustainability, consciousness, and social systems.

Keywords: chemical organization theory; self-organization; autopoiesis; resilience; reaction networks; sustainability



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1. Introduction

Complex adaptive systems [1,2] are systems consisting of many interacting components that exhibit some degree of self-organization: coherent patterns of organization spontaneously emerge out of the network of interactions [3]. Most of the phenomena we are confronted with in real life are such complex adaptive systems: people, organisms, societies, ecosystems, markets, cultures, etc. Great progress has been made in understanding the dynamics of such systems by means of multi-agent computer simulations [2]. However, on a more abstract, theoretical level, our understanding of self-organization and adaptation remains rather superficial and fragmented.

Part of the reason is that the conceptual and mathematical building blocks of our theories are poorly fitted to describe emergence and interaction. Traditional scientific models start by reducing a system to its static components and the properties in which these components can vary. The values of these variables define the state of the system. The evolution of the system is then represented as a time-parameterized trajectory in the thus predetermined state space, governed by a static equation. This approach makes it intrinsically difficult to understand the fundamental changes that result in the emergence of new components, properties, systems, or dynamics.

An alternative approach is to start from a *process metaphysics* [4,5] or *action ontology* [6,7]. Such a philosophy assumes that reality is not constituted out of static objects but out of processes or actions, and that objects and systems are merely stabilized (networks of) processes. While this perspective fits in with our most recent insights into complex adaptive systems, the problem is to represent processes in a way that allows precise modeling of such emergent systems [3].

This paper wishes to introduce a formalization of processes, namely the reaction networks used in what has been called *Chemical Organization Theory* (COT) [8–10]. In reaction networks and COT, the relation between states and dynamics is turned upside down. The processes are primary, in the form of ‘reactions’, which are the most fundamental elements of a reaction system. States only appear in a second stage, as the changing concentrations of the ‘molecules’ that the reactions are processing into other molecules. The molecules therefore are not static objects, but merely raw materials that are constantly being produced, consumed, and recreated by the reactions. In that sense, reaction networks form perhaps the first formalization of a process ontology that is both general and practical [11,12].

The general character means that COT can describe systems and processes in the most diverse disciplines—from elementary particle reactions via systems biology and cognitive science to the political organization of society. Its particular strength is that it provides an elegant mathematical method to define and construct *organizations*, i.e., self-sustaining networks of reactions within a larger network of potential interactions. As such, it is eminently suited to describe self-organization, autopoiesis, sustainability, resilience, and the emergence of complex systems out of simpler components.

Next to its broad foundation in process philosophy, COT derives its power from its concreteness and simplicity: basically, you can represent any process in the real world as a combination of reactions between suitably chosen ‘molecules’ and then start analyzing the resulting reaction system for self-maintenance, closure, and other observable properties. Moreover, COT models are intrinsically modular: it is trivial to add or to remove molecules or reactions from an existing model and (somewhat less trivial) see what effect that has on the emerging organizations. This makes it possible to model systems of great complexity, where you start with a simple model in order to get an intuitive grasp of what is going on, and then gradually add more detail and sophistication in order to achieve a more realistic representation.

Finally, COT focuses on what are the most important questions about a complex adaptive system: to what extent is it sustainable and resilient, i.e., able to maintain itself both autonomously and in the face of external perturbations? To what degree does it grow, remain the same, or perhaps diminish and decay? If it is perturbed to such a degree that it cannot maintain its present organization, which new type of organization is it likely to evolve into? How do its components and processes co-evolve, mutually adapt, and become coordinated into a symbiotic system? In summary, how does it self-organize into a robust, coherent whole?

The latter is perhaps the most important question in the whole of science and philosophy, and their applications to society. Practically all the phenomena we are confronted with—including matter, organisms, ecosystems, societies, and minds—are the result of self-organization producing complex wholes out of simpler components. Any general theory that would help us to understand, model, and control that process is likely to revolutionize our worldview, while opening up an endless variety of concrete applications.

The present paper wishes to make the case that COT, together with its future extensions, provides an exceptionally promising foundation for such a general theory. It will do that first by pointing out how the COT formalisms avoids the pitfalls of earlier approaches, then by offering a survey of existing and potential applications of COT to a broad variety of issues. It will do this in a simple, non-technical way, emphasizing the basic formalism and the core new insights, while avoiding some of the (relatively) more complex mathematical techniques required for a full implementation of COT.

2. Reaction Networks

As its name implies, the COT formalism [8] is inspired by chemistry, and the way it describes how chemical reactions transform molecules into new molecules. Therefore, it has inherited much of its terminology from chemistry, while being similar in its conceptualization to the emerging domain of systems chemistry [13,14]. In order to widen its appeal and to convince other scientists of its potential for transdisciplinary unification, it

may be wiser to replace some specifically chemical terms by more broadly applicable ones (and perhaps even rename the whole approach to the more neutral ‘Process Organization Theory’). The present paper will therefore replace some COT terms with new terms, while clearly pointing out the changes.

The basis of a COT model is a reaction network. It consists of two types of entities, which we will call *resources* (‘molecules’, ‘molecular species’, or ‘species’ in the traditional COT formulation) and *reactions*. A resource is an abstract representation of a specific kind of substance, entity, or, most generally, measurable phenomenon. Examples of resources are particular types of chemical substances, elementary particles, biological species, economic goods, human agents, messages, ideas, or decisions. All the resources in the model are assumed to be available in some shared container or workspace, which in COT is called the ‘reaction vessel’. This joint presence allows any resource to interact directly or indirectly with any other resource. Reactions denote elementary processes that create or destroy resources. They typically produce combinations of new resources out of combinations of existing resources. Yet, the simplest reactions just create or destroy a single resource.

Formally, we will define a reaction network as the 2-tuple $\langle M, R \rangle$, where $M = \{a, b, c, \dots\}$ is the set of resources, and $R \subseteq P(M) \times P(M)$ is the set of reactions, where $P(M)$ denotes the power set (i.e., the set of all subsets) of M . Each reaction $r \in R$ maps a particular subset X of M onto another subset Y of M :

$$r: X \rightarrow Y: \{x_1, x_2, \dots \mid x_i \in M\} \rightarrow \{y_1, y_2, \dots \mid y_j \in M\}$$

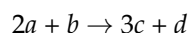
Note that the sets X and Y can be empty. We will call X the *input set* and Y the *output set* of r and denote them, respectively, $In(r)$ and $Out(r)$. We will call the elements of $In(r)$ the *reactants* of r , and the elements of $Out(r)$ its *products*. Borrowing the chemical notation for reactions, a reaction is conventionally written as:

$$r: x_1 + x_2 + \dots \rightarrow y_1 + y_2 + \dots$$

The ‘+’ symbol here represents a *conjunction* of the resources: x_1 and x_2 and \dots all need to be simultaneously present in $In(r)$ for the reaction to take place, while the reaction simultaneously produces y_1 and y_2 and \dots . If $In(r)$ is empty, the reaction will be written as:

$$\rightarrow y_1 + y_2 + \dots$$

Note that in traditional COT, it is assumed that $In(r)$ and $Out(r)$ are multisets. This means that the same element x_i can occur more than once (say n_i times) in $In(r)$. This is necessary to describe reactions of the form:



or more generally:

$$n_1x_1 + n_2x_2 + \dots \rightarrow m_1y_1 + m_2y_2 + \dots \quad \text{with } n_i, m_j \in \mathbb{N}$$

For simplicity, we will here just work with ordinary sets, i.e., resources that only occur once in a reaction. For a COT formulation in terms of multisets we refer the reader to [8,12].

2.1. Reaction Networks vs. Traditional Networks

The combined system $\langle M, R \rangle$ forms a network because the resources in M are linked to each other by the reactions in R that transform the ones into the others. But this is not a traditional network (i.e., a *directed graph*), in which a link connects a single element (‘node’, ‘vertex’) x to a single element y . A reaction connects a set X of elements to a set Y of elements. In mathematics, a network with this property is called a *directed bipartite graph*, or a *directed hypergraph* [15]. This appears to be the essential generalization that gives reaction

networks their power with respect to traditional network models. Let us try to explain how that happens.

A traditional network consists of nodes N and links L , with $L \subseteq N \times N$. Thus, $\langle L, N \rangle$ is a reaction network, but where the reactions $r \in L$ are limited to one input and one output:

$$r: x \rightarrow y, \text{ with } x, y \in N$$

A general reaction network provides much more richness and flexibility because it allows combinations of inputs to produce combinations of outputs, opening up an exponentially wider range of interacting processes. In a traditional network, the only way processes can ‘interact’ is by sharing input or output nodes, e.g.,

$$r_1: x \rightarrow y$$

$$r_2: x \rightarrow z$$

$$r_3: u \rightarrow y$$

Here, an initial state x can lead to y and/or to z via, respectively, r_1 and r_2 . This immediately creates an ambiguity: are r_1 and r_2 both taking place, producing y and z simultaneously? Or does the process make a choice between r_1 and r_2 , ending up in either y or z ? Similarly, y can be produced via r_1 and/or r_3 from x and/or u . Do we need both x and u , or is one of them sufficient to produce y ? The problem is that in traditional networks, there is no way to distinguish between conjunction (‘AND’) and disjunction (‘OR’) of nodes and links. Next to juxtaposition of links/reactions, there simply is no operator to express a different type of combination.

In reaction networks, we have an additional operator, denoted with ‘+’, that plays the role of the conjunction. The juxtaposition of reactions plays the role of the disjunction. Consider the following reactions:

$$r_4: x + u \rightarrow y$$

$$r_5: w \rightarrow y$$

This expresses unambiguously that in order to produce y we need either (x AND u), OR w . Now, different processes can interact in many ways to produce complex organizations, as we will see in further sections.

2.2. Reaction Networks and Propositional Logic

Interpretation of COT operators in terms of conjunction and disjunction points us towards formal, Boolean logic, where propositions can be combined in terms of these operators, together with the operators of implication and negation. Implication is naturally expressed with the ‘ \rightarrow ’ operator. This directly suggests the logical formalism of Horn clauses [16]. These have the following form:

$$a \ \& \ b \ \& \ \dots \rightarrow x$$

This is to be read as ‘if a and b and \dots are true, then x is true’, or ‘ x can be derived from the conjunction of a, b, \dots ’. The translation in terms of reaction networks requires a qualification, though, which is that if you derive the new proposition x from the conjunction of propositions on the input side of the inference, then the propositions on that side *remain* actual (they are not destroyed by the process). They therefore should properly be listed on the output side as well. This gives us the straightforward COT translation of a Horn clause:

$$a + b + \dots \rightarrow x + a + b + \dots$$

Note that in this interpretation, logical inference is a special type of reaction, namely one in which no ‘resources’ ever get consumed: inferences can only *add* true propositions to our knowledge, they cannot remove any. This is why logic is inherently static: nothing

really changes by making logical inferences; at most, we become aware of additional statements that were already true implicitly, but had not been proven yet. That is the fundamental reason why attempts to express process, action, or time with logic have not been very successful, in spite of a plethora of formalization attempts such as ‘dialectical logics’, ‘process logics’, or ‘dynamic logics’ (see, e.g., [17–19]). Insofar that these logics describe genuine changes in the state of the world, they have left the domain of logic proper and entered the domain of dynamics, which is more properly described by a formalism such as reaction networks.

2.3. Competition and Cooperation

Unlike logic, COT does not (as yet) incorporate a negation operator. However, reactions can express an implicit negative relation between two resources a and b : increase in a implies decrease in b . For this, we need to introduce the quantitative level of COT, where a resource is determined not only qualitatively by its presence or absence, but quantitatively by its amount or concentration in the reaction vessel. We can then define the relation ‘ a inhibits b ’ as:

$$\exists r \text{ such that } a, b \in \text{In}(r), b \notin \text{Out}(r)$$

This means that a enables a reaction r that consumes, but does not produce, b —thus reducing the concentration of b . The opposite relation, ‘ a promotes b ’ applies when a enables a reaction that produces, but does not consume, b . The relations of inhibition and promotion can be (but need not be) symmetric, in which case a and b inhibit or promote each other. In the latter case, we might say that a and b are competitors, respectively, cooperators. Note, however, that the same resource can simultaneously inhibit and promote another resource via different reactions. In that case, we need to use the more detailed, quantitative model of the reaction network, which allows us to calculate the net production of the different resources by summing the contribution of all reactions, and thus to determine whether the overall effect of a resource on another one is positive or negative.

Inhibition is a negative causal influence; promotion is a positive one. An uneven number of negative influences connected in a cycle (from a via a number of intermediate resources back to a) determines a *negative feedback* loop. Negative feedback suppresses deviations from an equilibrium level, thus producing a stabilization or an oscillation of the concentrations of the resources in the cycle around that level. A cycle with only positive influences, or an even number of negative influences, determines a positive feedback loop. Positive feedback produces an exponential growth of the resources in the cycle, which stabilizes only when they reach the ‘carrying capacity’ of the system, which is determined by the amount of external resources entering the cycle.

Systems dynamics [20] is a simple and useful formalism for representing and analyzing networks of such causal influences, and the positive and negative feedback loops they form. Moreover, system dynamics analyses processes in terms of *stocks* (equivalent to resource concentrations) and *flows* that add to or subtract from stocks (equivalent to reactions). Compared to COT, however, it lacks the ability to combine different resources in a single reaction: a system dynamics network only allows one-to-one connections between stocks.

The interactions between reactions take place through their shared resources: the same resource can appear in input and output sets of different reactions. Because these resources are either consumed or produced by the reactions, a reaction can facilitate another one (e.g., when the one produces a resource needed by the other) or hinder it (when the one consumes a resource needed by the other). This creates a network of ‘ecological’ relationships between reactions. These include *mutualism* (mutual amplification, cooperation, or synergy), *competition* (mutual inhibition, conflict, or friction), *predation or exploitation* (growth of the one at the expense of the other), and *commensalism* (growth of the one facilitated by the other, but without loss or gain for the other) [21]. As we will show further, the general logic of self-organization [7] explains why this complex non-linear dynamics tends to move towards a self-sustaining regime, as resources and reactions that do not fit in with the emerging system are eventually eliminated, while those that efficiently exploit the

more abundant resources grow and take over. This is the origin of the ‘organizations’ that we will now define.

3. Organizations

The most important new concept introduced by COT is an *organization*. This denotes a reaction system that is fundamentally self-sustaining: the resources it consumes are also the resources it produces, and vice versa. This means that although the system is intrinsically dynamic or process-based, constantly creating or destroying its own components, the complete set of components (resources) remains invariant, because what disappears in one reaction is recreated by another one, while no qualitatively new components are added.

This property is part of the definition of *autopoiesis* (‘self-production’), a concept that Maturana and Varela introduced to characterize living organisms [11,22–24]. The second defining property of autopoietic systems is that they produce their own topological boundary, such as the membrane that separates living cells from their environment. This property does not apply to organizations, and therefore organizations are more primitive than living systems. As such, they were introduced as a simple model for the origin of life out of interlocking cycles of chemical reactions [25]—and a generalization of the more common but more restrictive model of an *autocatalytic set* [26,27].

Consider a subnetwork $\langle M', R \rangle$ of a larger reaction network $\langle M, R \rangle$, i.e., $M' \subseteq M$. The formal definition of an organization is derived from three characteristics that such a reaction network $\langle M', R \rangle$ can have:

- **Closure:** This means that nothing new is generated; the only resources produced by the reactions are those that were already in the starting set M' : $\forall r \in R$ such that $In(r) \subseteq M'$, the requirement holds that $Out(r) \subseteq M'$.
- **Semi-self-maintenance:** This is the complementary condition that nothing existing is removed; each resource consumed by some reaction is produced again by some other reaction working on the same starting set: $\forall x \in M'$ for which $\exists r \in R$ such that $x \in In(r) \subseteq M'$, $\exists r' \in R$ such that $In(r') \subseteq M'$, and $x \in Out(r')$.
- **Self-maintenance:** This is a stronger form of the semi-self-maintenance condition, which states that each consumed resource $x \in M'$ is not only produced by some other reaction in $\langle M', R \rangle$, but that the amount produced is at least as large as the amount consumed.

The determination of self-maintenance is more complex than the other two conditions because it requires the introduction of a quantitative dynamics in the reaction network, which specifies the rate at which resources are consumed and produced by the different reactions. The standard dynamics for chemical reactions is based on a mass action kinetics [28,29], which assumes that the rate of a reaction is proportional to the concentration of the reactants. However, COT also allows using different types of dynamics, depending on the domain being modeled. Knowing these rates is necessary to establish the long-term maintenance of the resource set M' [8,10] because the reactions producing x may be slower than the ones consuming it, so that the concentration of x eventually goes to zero. The rate of each of the reactions defines the *flux vector*. Note that even without knowing the exact rates in a given state of the network, we may normally assume that the rate of a reaction increases when the concentration of its input resources increases (because there are more reactants to ‘feed’ the reaction) and decreases when that concentration decreases (this is anyway the case if we assume mass action kinetics).

In order to calculate the balance of consumption/production, we need to determine the *stoichiometric matrix* [8]. For each resource-reaction pair, this matrix specifies the net number of the resource produced by that reaction. This number is 1 if the resource is produced but not consumed, -1 if it is consumed but not produced, and 0 otherwise (in the multiset version of COT, the absolute values of these numbers can be larger than 1). The product of flux vector and stoichiometric matrix then determines the total net rate of production (production minus consumption) for each of the resources across all reactions.

The requirement for self-maintenance is that this rate is non-negative for all resources, i.e., all resources either increase or are conserved. The reaction network fulfils this condition if there exists a flux vector (i.e., list of reaction rates) for which this requirement holds. Note that if the constraints determined by the (qualitative) reaction network allow such self-maintaining flux vectors to exist, then it seems likely that the (quantitative) system will converge to the corresponding regime of self-maintenance. The reason is that resources that are consumed more than they are produced (no self-maintenance) will decrease in concentration up to the point that the reactions consuming them slow down enough so that production (which is normally not affected by the concentration of the products, only by the concentration of the resources consumed) compensates for consumption. For simplicity, we will not further discuss this quantitative aspect in the present qualitative description. Therefore, we will ignore the flux vector and the calculations that need to be performed on it in order to determine whether self-maintenance is possible for the given set of reactions, and just note that this requirement is easy to check computationally. Examples of how flux vectors are calculated can be found in [30], while [31] provides a detailed presentation.

We are now able to define the crucial concept of organization: a subset of resources and reactions $\langle M', R \rangle$ within a larger reaction network is an organization when it is closed and self-maintaining. This basically means that while the reactions in R are processing the resources in M' , they leave the set M' invariant: no new resources are added (closure) and no existing resources are removed (self-maintenance). Note that this does not exclude an overall input (resources entering the organization) or output (resources exiting the organization). These can be represented as reactions working on the empty set (which is by definition a subset of M'), such as $\rightarrow a$ (a is injected into the organization) or $b \rightarrow$ (b diffuses out of the organization). The only requirement is that a and b maintain a non-zero concentration in the organization.

Being an organization may seem a rather uninteresting property: nothing really changes. Most theories, models, and formalisms are based on invariant elements, so what is novel here? The essential contrast with classical modeling frameworks is that we started by assuming that *everything changes*: all resources are in a constant flux, being consumed by some reactions, produced by others, but by default processed into something else. The concept of organization establishes that stability can arise even within such ceaseless flux of transformations.

An organization is an *emergent system* that sustains itself by reprocessing its components, and thus constantly rebuilding its own structure. This is the essential property of living systems that Maturana and Varela have tried to capture with their concept of *autopoiesis*. What COT adds is that the same kind of emergent organization can arise in a wide variety of other domains outside of biology, on the sole condition that we have a sufficiently rich network of reactions and resources [12]. Moreover, COT reformulates the rather difficult and confusing notion of autopoiesis as a simple mathematical property characterizing even simpler sets of resources and reactions [11].

3.1. Some Examples

The simplest organization would consist of the single resource a and the single reaction $a \rightarrow a$. This would be the description of a resource that just maintains itself without interacting with anything else. The organization becomes slightly more interesting when we add the reaction $\rightarrow a$ (empty input set, single element output set). Here, a is not just maintained, it is also created out of nothing. We can make it more interesting by adding $a \rightarrow$. This means that a is not only produced or added, it is also removed from the 'reaction vessel'. This would describe a situation where some resource flows in and out of the reaction vessel.

For the simplest non-trivial organization, we need two resources $\{a, b\}$ that interact. They define an organization when the reactions form a cycle: $a \rightarrow b, b \rightarrow a$. This can be extended with an unlimited number of intermediate stages:

$$a \rightarrow b, b \rightarrow c, c \rightarrow d, \dots, z \rightarrow a$$

This is still too simple to be very useful, but we can make it more complex by considering reactions with more than one input or output, e.g.,

$$a + b \rightarrow c$$

$$c \rightarrow d + e + f$$

$$e \rightarrow a$$

$$d + f \rightarrow b$$

Here, an a and a b together are transformed into a c , which is then converted to d , e , and f , which again produce a and b , so that the cycle can start again. Let us make it more concrete by considering recognizable resources and reactions, in this case describing the organization of the Earth's ecosystem at an abstract level (this high-level view of Earth as an autopoietic system is similar to the Gaia hypothesis [32]).

$$\rightarrow \text{sunlight}$$

$$\text{plants} + \text{sunlight} + \text{carbon_dioxide} + \text{minerals} \rightarrow \text{plants} + \text{oxygen} + \text{heat}$$

$$\text{plants} + \text{animals} + \text{oxygen} \rightarrow \text{animals} + \text{carbon_dioxide} + \text{detritus} + \text{heat}$$

$$\text{detritus} + \text{bacteria} \rightarrow \text{bacteria} + \text{carbon_dioxide} + \text{minerals} + \text{heat}$$

$$\text{heat} \rightarrow$$

This describes the recycling of oxygen, carbon dioxide, and minerals by plants, animals, and bacteria, fueled by the energy of the sun (which enters the system from the outside, which is why the reaction producing it has no input within the system), while radiating heat into space. This is subtler than a simple cycle, because reactions require several inputs while producing several outputs that are all needed to sustain the organization. But the system is properly self-sustaining, as it produces all its essential components: nothing that is needed to sustain the organization gets lost; nothing new is added.

Note that some resources (such as *bacteria* in the last reaction) appear in both the input and output of a given reaction. That means that they are neither removed nor added by that reaction. Yet, they are necessary for the reaction to happen. In chemistry, such resources are called *catalysts*: they enable a reaction, but are not themselves affected by it. In our more general interpretation, we may call them *agents* [7]: they act on the other resources in the reactions, processing them into something else. For example, the bacteria are the agents that turn detritus into the carbon dioxide and minerals that are needed by the plants. The plants are the agents that transform these resources, with the help of sunlight, into oxygen (and more plants). The animals act on the plants and oxygen, converting them to detritus and carbon dioxide, which then again function as 'food' for, respectively, the bacteria and the plants.

3.2. Extending the Model

This model of global recycling is of course much too simple. To start with, it does not specify the relative proportions of the different resources produced and consumed. For example, plants do not produce just oxygen, they grow, thus producing *more* plants. In the multiset version of COT, the additional amount could be specified, e.g., by writing ' $2 \text{ plants} + \text{oxygen}$ ' on the output side of the reaction. While this may clarify the relative proportions, the actual rate of production would need the full, quantitative version of COT, which includes the rates of the different reactions as expressed with the flux vector. We will ignore these complications in the present introductory survey, and continue focusing on the power of COT for qualitative modeling.

Qualitatively, the simple model could be extended by noting some additional processes, such as *plants* \rightarrow *detritus* (plants die, thus producing matter to feed bacteria) and *animals* \rightarrow *detritus* (animals similarly die). We may also want to specify that it is not only bacteria that break down organic matter, but fungi as well, thus adding *fungi* + *detritus* \rightarrow *fungi* + *carbon dioxide* + *minerals*. But fungi are sometimes eaten by animals: *fungi* + *animals* \rightarrow *animals* + *carbon dioxide* + *detritus*.

A different kind of extension may occur by making the general resource categories more specific. For example, we could note that not all animals eat plants or fungi, but that some are carnivores. This leads us to split up the category ‘animals’ into the categories ‘carnivores’, ‘omnivores’, and ‘herbivores’, each characterized by its own specific reactions. In this way, we can go on adding reactions and the concomitant resources until we feel the model is detailed enough to include everything that seems relevant for a realist description.

But the crucial question remains: is the resulting network an organization? By adding a particular reaction, we may create a ‘source’ or a ‘sink’ for a particular resource, either injecting it into a system in which it was previously absent (thus interrupting closure), or removing it from the system faster than it can be produced (thus interrupting self-maintenance). Let us then try to better understand how organizations emerge.

4. Self-Organization

An arbitrary subset of a reaction network will in general not be an organization: its reactions working on its resources will produce additional resources (non-closure). These additional resources may react with some already present resources, producing even further new resources. Thus, every addition may activate reactions that produce further additions. However, this process of growth of the resource base must come to an end when there are no further resources that can be produced by reactions working on the already present resources. At that stage, all produced resources are already in the present set, and closure is reached. Thus, closure can be seen as an attractor of the dynamics defined by resource addition: it is the end point of the evolution, where further evolution stops.

Let us now apply the same reasoning for self-maintenance, starting from the previously reached closed set. Some of the resources present in that set will be consumed by the reactions, but not produced, or at least not produced in sufficient amounts to replace the amounts consumed. These resources will therefore disappear from the closed set. Note that this does not affect the closure, because loss of resources cannot add new resources. Without these resources, some of the reactions producing other resources will no longer be able to run. Therefore, the resources they otherwise produce will no longer be replaced if they are consumed by some other reaction. If no other reactions continue producing these resources, they too will disappear from the resource set, possibly triggering the disappearance of even further resources that depend on them for their production. Thus, resources disappear one-by-one from the set. However, this process too must come to an end, when the remaining resources do not depend for their production on resources that have been removed, but only on resources that are still being produced in sufficient amounts. Thus, self-maintenance too can be seen as an attractor of the dynamics defined by resource removal.

The process of resource addition ending in closure followed by resource removal ending in self-maintenance produces an invariant set of resources and reactions. This unchanging reaction network is by definition an organization.

This scenario for the spontaneous emergence of an organization illustrates the general *principle of self-organization* [33]: any dynamic system will eventually end up in an attractor (originally called ‘equilibrium’ by Ashby [33]), i.e., an invariant regime of activity defined as a subset of the system’s state space that the system can enter but not leave. In the present qualitative formulation of COT, such an attractor is defined as a subset of resources that is self-sustaining and therefore invariant.

To model the quantity of resources present at a particular moment, we must specify a dynamical law governing the rate with which resources are produced and consumed (this typically takes the form of a system of ordinary differential equations). In COT, it has

been proven that every fixed point (the simplest, 0-dimensional type of attractor) of such dynamics corresponds to an organization [34]. However, the opposite is not true: certain organizations cannot be realized as fixed points. Instead, we may encounter more complex attractors, exhibiting oscillatory regimes, limit cycles, and even chaotic behavior [35]. In [34], it was shown that these dynamically stable regimes correspond in most cases to organizations. This means that while the set of resources participating in an organization is invariant, the quantity of each resource can still vary according to some complex dynamics.

In the attractor regime produced by self-organization, the different components of the system (resources in this case) have mutually adapted [33], in the sense that the one no longer threatens to extinguish the other. They have co-evolved to a ‘symbiotic’ state, where they either more or less peacefully live next to each other, or actively help one another to be produced, thus sustaining their overall interaction [7]. This is the default state for an evolved ecosystem—such as a forest or a coral reef—in which the different species of plants and animals have adapted to the network of ecological dependencies they all constitute together [21].

While some of these species are competitors, or predators (exploiters) of other species, they will normally not consume more of their prey than what is produced from other resources in the ecosystem. Predation may actually regulate the population numbers of the prey. This can prevent the problem where the prey increases so much in population that they exhaust other species on which they depend, thus indirectly threatening their own survival. A classic example of this regulatory function is found in the wolves that were reintroduced as top predators to the Yellowstone natural reserve [36]: their presence reduced the number of deer, thus allowing vegetation that the deer were consuming to recover. This in turn helped other species dependent on that vegetation to increase in number, boosting the overall diversity and sustainability of the ecosystem.

As we noted about organizations in general, the population of a species (i.e., quantity of the corresponding resource) in such an ecosystem is likely to fluctuate over time—e.g., following the classic predator–prey dynamics that leads to periodic increases and decreases, or following a more chaotic dynamic. But on the qualitative level, each of the species should be able to be reproduced at a rate sufficient for it not to disappear altogether, because this would entail a potentially radical reorganization of the ecosystem.

The relations between the different resources and reactions in an organization form a similar web of exploitation, competition, and cooperation—or, more generally, ecological dependencies—that has stabilized into a self-sustaining network. Depending on the number and type of reactions, this network can be very complex. However, its defining features of closure and self-maintenance are easy to formulate mathematically and verify computationally by analyzing the reaction network and checking whether each resource can be produced at least as much as it is consumed, while no new resources are created.

5. Sustainability and Resilience

Organizations generally require a sufficient input to self-maintain. In environments with such an input, an organization is by definition a self-sustaining, and therefore *sustainable*, system. That means that it can maintain perpetually, without ever running out of the resources that it needs to function—because all resources are recycled through the inherent reactions and/or because there is a dependable input from outside the system (represented by reactions of the form: $\rightarrow a$).

Many organizations do not just maintain, they *grow*, because they produce more of certain resources than they consume. Such resources are said in COT to be ‘overproduced’ [37]. Organizations with overproduction fulfill the ideal of *sustainable development*: growth that can be sustained without exhausting its environment.

While this may seem paradoxical, we should note that the COT formalism does not a priori assume any conservation law for resources [25], as one would expect for material or energetic resources. That is because the formalism is intended to be more flexible than traditional chemical or physical models. This allows it for example to model informational

resources, such as knowledge, decisions, or messages, which do not obey a conservation law, or hybrid material-informational resources, such as economic products. This also helps us to simplify our models by ignoring ever-present inputs (such as air or sunlight) or outputs (such as dissipated heat or waste). Still, it is possible to impose conservation on a particular set of reactions if that would help to make the model more realistic.

Ecosystems are normally sustainable with an approximately constant level of resources, externally supplemented by energy from the sun. Economic systems, on the other hand, although they grow, are often unsustainable: they consume more of certain resources than they produce. Therefore, they may collapse when the resource reserve is eventually exhausted. For example, our present economy is largely relying for its energy on fossil fuels that are in limited supply. Creating a sustainable economy means shifting to energy sources that are renewable through a dependable external input (e.g., solar energy) or through reprocessing within the network (e.g., energy produced from waste).

In this example, the cause of unsustainability is easy to identify as it resides in a single type of resource (fossil fuel), and therefore the solution is obvious: replacing this resource by other, renewable resources. More generally, sustainability is an emergent property dependent on the reactions between all the resources used, because a shortfall in one resource may be compensated by the increased production of another resource performing a similar function. It is here that we need the more sophisticated quantitative formalism of COT with its flux vector and stoichiometric matrix in order to establish under which conditions the reaction network is self-maintaining.

In previous work, we have developed a more complex example of a sustainable farm to illustrate such analysis [30]. The model includes resources such as water, cows, grain, grass, milk, chickens, eggs, and dung, with only water as an external input (from rain), and milk, eggs, and grain as external output leaving the farm. It includes reactions such as $water + grass + cows \rightarrow cows + dung + milk$. It shows under which conditions this network of reactions is self-maintaining and thus sustainable. It also shows which subsets of this set of resources can form self-maintaining organizations. For example, it demonstrates that the farm could still be sustainable without chickens and eggs.

Complementary to the notion of sustainability is the one of *resilience*. Sustainability denotes the ability of the system to maintain on its own without outside interference. Resilience [30,38–40] broadens this notion to the ability to maintain the essential organization even in the face of serious outside disturbances. A resilient system is one that will survive and recover from shocks induced by the environment. In contrast, a vulnerable or fragile system is one that is likely to disintegrate when it encounters an intense disturbance, such as an earthquake or a traumatic event.

In the sustainable farm example [30], we have also made an analysis of how different types of disturbances can affect the sustainability of the farm. Some of the disturbances affect the amount of available resources—e.g., some of the cows may die. Others affect the rate of certain reactions, such as a reduction in the amount of rain falling. Yet, others introduce new resources with the corresponding reactions they trigger, such as an introduction of mice in the farm that eat some of the grains.

In the qualitative version of COT, a disturbance can be represented as the removal of a resource that the organization relies upon (e.g., cows), or as the introduction of a new resource (e.g., mice) that reacts with some of the existing resources (e.g., grain), thus interfering with the network of reactions that defines the organization. Both types of disturbances may reduce the availability of certain resources that are part of the organization, either by removing them at the input stage or by inhibiting them via internal reactions. To survive such a disturbance, a resilient organization will need to either suppress the disturbing resources before they interfere with the organization's critical 'metabolism', or to replace the lost resources before their absence makes further self-maintenance impossible [11]. In other words, the organization will need to counteract or compensate the disturbance and/or its effects on the network of reactions so as to minimize the deviation from the viable configuration. This defines the cybernetic process of *regulation* or *control* [11].

The simplest method of control is *buffering*: maintaining a large enough reserve of resources so that temporary reductions in availability have little effect. This can be achieved by organizations that increase their resource base through overproduction of the most crucial resources.

The next method is *negative feedback*: organizing the network of reactions in such a way that deviations from the desired concentration of resources are automatically counteracted after each cycle of consumption and production. For example, a reduced supply of a particular resource may automatically trigger an increased net production of that resource. This kind of dynamic is common in metabolic pathways and in ecosystem interactions. For example, if foxes eat more rabbits, fewer rabbits will be left, and therefore some of the foxes will starve. A reduction in the number of predators will then let the rabbit population recover. Such a dynamic follows naturally from our earlier observation that reaction rates normally increase together with the concentration of their reactants. This creates an implicit negative feedback because the reactions consuming a resource necessarily slow down when that resource becomes scarcer (e.g., predation slows down when the prey population decreases), thus allowing the reactions producing that resource (e.g., reproduction of the prey population) to catch up.

The third basic control method is *feedforward*: neutralizing the disturbance *before* it has had the chance to perturb the functioning of the system. This can be achieved by reactions that consume the disturbing resource before it could have interfered with other, vital resources. The tricky part here is that these neutralizing reactions will only be enabled when a disturbance is present for them to react with. This means that for most of the time, these reactions will remain ‘dormant’: the organization has the potential to react, but will only do so when the right condition is present [11]. One way to implement such capability is by maintaining a collection of resources that can react with a particular disturbance, either getting consumed in the process, or, preferably, functioning as a catalyst that remains in the system after the reaction. The larger the variety of such potential ‘neutralizers’ contained in the organization, the larger the variety of disturbances it can survive. This implements Ashby’s law of requisite variety [11,41].

An example of such a collection of neutralizers are the genes of an organism that are activated via a particular molecular pathway whenever the cell encounters a particular disturbance. Once activated, these genes produce enzymes catalyzing reactions that neutralize the disturbance. But as long as a specific disturbance does not occur, the genes remain non-active snippets of DNA. Other examples of ‘dormant neutralizers’ are antibodies, which are produced by the immune system in large quantities only in case of infection, and the armed forces of a country, which are mobilized only if the country is attacked.

6. The Evolution of Resilience

We have argued that arbitrary networks of reactions will self-organize to produce sustainable organizations, for the simple reason that organizations are attractors of their dynamics. It is less obvious that these organizations would also be resilient. However, evolutionary reasoning shows that robust or resilient outcomes are more likely in the long run than fragile ones.

First, any dynamical process starts from some point in the state space of the system, while eventually settling down in some attractor region within that space. Attractors are surrounded by basins of attraction, i.e., subsets of the state space from which all states lead into the attractor [42]. The larger the basin, the larger the probability that the starting point would be in that basin. Therefore, the system is a priori more likely to end up in an attractor with a large basin than in one with a small basin. The larger the basin, the smaller the probability that a disturbance pushing the system out of its attractor would also push it out of the basin, and therefore the more resilient the organization corresponding to the attractor. The size of the basin corresponds to what in [40] has been called the *latitude* aspect of resilience. Large basins normally represent stable systems characterized

by negative feedback, because a deviation from the attractor that remains within the basin is automatically counteracted by the descent back from basin into attractor.

The higher a priori probability of starting from a large basin does not exclude the possibility of ending up in an unstable attractor, characterized by a small (or empty) basin. However, these unstable attractors will normally not survive long, as nearly any perturbation will push the system out of that attractor's basin into the basin of a different attractor. After a number of such attractor-to-attractor shifts the probability increases that the eventual attractor will have a large basin, and therefore be stable. This very general, abstract reasoning makes it plausible that systems that are regularly perturbed will eventually settle down in a stable, resilient organization. This is an application of the *order from noise* principle [43], according to which increased variation ('noise') accelerates the self-organization of a stable configuration ('order').

We have tested out this scenario in a computer simulation [30], where networks of randomly generated reactions were first allowed to settle into one of their self-sustaining organizations, and then subjected to various random perturbations. What we found was a little more subtle than the simplest form of the scenario. Under continuing perturbations, the system did not settle into a single large attractor, but rather tended to repeatedly shift between a cluster or family of related attractors [44]. These attractors corresponded to largely overlapping organizations (meaning that they shared most of their resources).

The shifting from one attractor to a similar, neighboring one can be seen as a higher-order process of evolution, in which the system adapts to changing conditions by changing its organization (i.e., its set of resources), but in such a way as to maintain a continuity of identity by keeping most of its resources the same. Note that a 'sideward shift' to an overlapping organization normally happens as a combination of two 'vertical' shifts, one 'upward' that adds resources and one 'downward' that removes resources [45]. The ability of the system to undergo such minimal shifts of organization in response to great disturbances exemplifies a higher level of resilience that may be called *evolvability* [46], because it allows the organization to evolve into a new organization while keeping most its components and structures intact.

What needs to be investigated further is how such organizations are precisely organized: what kinds of arrangements of reactions make up a resilient whole? A theoretical decomposition of organizations [37] shows that complex organizations tend to be *modular*, i.e., they consist of subnetworks whose self-maintenance is independent of the self-maintenance of other subnetworks. Overproduced molecules and catalysts function as 'boundaries' that connect the subnetworks, however, without making them dependent on each other. Such decomposition makes it possible to delimit the effects of a perturbation. For example, a perturbation happening in a small subnetwork will leave the bulk of the organization intact.

Another source of inspiration for understanding resilience is the metabolic networks used by real organisms. These appear to be surprisingly robust in the face of random mutations removing or adding gene-regulated reactions [47]. A likely reason is the redundancy—or more precisely *degeneracy* [48]—of pathways for producing critical resources: there is a variety of independent mechanisms that perform partly different, partly the same functions. Thus, the loss of a pathway through mutation is simply compensated by more activity in other pathways that perform the same function [11]. Such degeneracy is one of the factors that explain the remarkable resilience and evolvability of living systems [46]: they can afford to undergo a lot of variation without losing their essential ability to self-maintain. This allows them to explore an immense space of largely overlapping organizations, and thus to discover ever more resilient and adaptive ones.

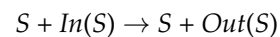
7. Agents and Topological Structures

A priori, the world of reaction networks does not have any spatial structures or boundaries: all resources and reactions are supposed to be mixed within the same 'reaction vessel' where everything can react with everything else. Most real-world models assume

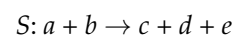
some kind of subdivision of the elements of the model into objects, systems, or spatial regions. Typical simulations of complex adaptive systems (CAS) start with agents located in the cells or vertices of some discrete topological structure, such as a lattice or network. Coordinated groups of agents may form systems that function as ‘superagents’ at a higher hierarchical level. Without going into the necessary mathematical details of the construction, we will here argue that such spatial and hierarchical differentiation can be introduced into COT models without essential changes in the formalism.

First, as we already noted, the concept of agent is easily reinterpreted in COT as a catalyst [7]—i.e., a resource a that is necessary to enable a reaction, but that is not itself affected by the reaction it triggers: $a + b + c \rightarrow a + d$. This can be read as ‘agent a processes $b + c$ into d ’. Since an agent can catalyze several independent reactions (e.g., $a + f \rightarrow a + g + h$), it will be characterized by a list of ‘condition-action rules’ of the form $a: b + c \rightarrow d, f \rightarrow g + h$, etc. The input of the reaction without the catalyst here functions as the condition to which the agent will react, while the output of the reaction without the catalyst functions as the action that the agent performs whenever it encounters that condition. Thus, an agent a ‘acts’ by transforming some initial condition ($b + c$) it encounters into some subsequent condition (d). This characterization of agents as bundles of condition–action rules is the basis for common multi-agent simulations of CAS. The larger the set of reactions an agent catalyzes, the richer its ‘skill set’ or ‘toolbox’ of condition–action rules, and therefore the greater its power in manipulating its environment [7,11].

To define superagents, we may note that complex organizations often contain suborganizations: subsets of their resource set that are able to autonomously self-sustain while exchanging some of these resources with other processes or suborganizations within the larger organization. These exchanged resources can be categorized as either input, $In(S)$, or output, $Out(S)$, of the suborganization S . This allows us to summarize the activity of S by the following ‘higher-order’ reaction:



Suppose that $In(S) = \{a, b\}$ and $Out(S) = \{c, d, e\}$, then we can write this as a more conventional condition-action rule:



The fact that S is itself constituted of a network of resources and reactions does not really make any difference when seen from the outside. S behaves like a ‘black box’ which processes a given input ($a + b$) into a specific output ($c + d + e$). If S is sufficiently resilient, it can maintain itself even when the input changes, producing a correspondingly changed output of ‘waste products’. This means that S behaves like a higher-order agent, capable of executing a range of condition–action rules, while itself remaining invariant. The larger organization of which S is a subset may itself be embedded in a network of reactions, thus defining an agent of an even higher order. While we still need to investigate this construction mathematically, this appears to open the door to the modeling of the *dynamical hierarchies* [49] and *metasystem transitions* [50] that characterize the multilevel self-organization that we see in the evolution of life and society.

To introduce a topology, we need to create the equivalent of ‘cells’ separated by membranes or boundaries. One way to achieve this in COT is to label resources with indices that indicate the specific cell in which the resource is located [10], while adding the constraint that resources can only react with resources that reside in the same cell (i.e., that have the same label). Topological structure can then be introduced as a network of ‘neighboring’ relations between cells, meaning that a resource can diffuse from a cell to a neighboring one via a reaction that merely changes the label but otherwise maintains the resource type: $x_{cell1} \rightarrow x_{cell2}$. By diffusing from neighbor to neighbor, resources or agents can in principle propagate throughout the whole topology.

A shortcoming of this construction is that the labeling must be introduced by the modeler. A perhaps more elegant approach is to view non-overlapping suborganizations as spatially separated, i.e., as residing in different cells, and their exchange of resources as processes of diffusion between neighbors. To make this realistic, we would need a large number of essentially equivalent suborganizations (or some less strictly defined distinguishable modules within a reaction network), playing a role similar to the cells of a multicellular organism. The resources of each cell, while a priori distinct, would play essentially the same role, and in that respect behave similarly to the resources in the previous construction that are merely distinguished by their labels. While apparently more complex, the advantage of such a construction is that the ‘cells’ would self-organize out of the network of reactions, instead of being imposed by the modeler.

To make this approach more concrete, we need further research into the possible structures and topologies of reaction networks and organizations. We here merely suggest that it is possible to introduce more complex entities, such as agents, hierarchies, cells, and topologies, into the COT formalism, while maintaining the conceptual and mathematical simplicity of resources and reactions.

8. Concrete Applications

After explaining some of the most important capabilities of COT on an abstract level, we wish to provide a brief survey of existing and future application domains.

Most obviously, COT has been used to simulate networks of chemical reactions, with a focus on the emergence of stable systems. The first examples were models of virus dynamics [51] and the chemistry of a planetary atmosphere [52]. The initial inspiration for the development of COT was to model how such chemical networks could develop the degree of autonomy that we associate with simple living systems [53]. Previously, this problem of the origin of life had been approached by looking for *autocatalytic cycles* of chemical reactions [26,54]. These are a more specialized type of organizations, which are both more difficult to build by evolution and less flexible and resilient than more general chemical organizations [27].

A related application domain is the study of metabolic networks in existing organisms, such as the bacterium *E. coli* [55]. This domain has recently attracted a lot of attention under the label of *systems biology*, but still lacks an integrated theoretic framework [56]—which COT may be able to provide [57]. A classic problem within this domain is the modeling of gene regulatory networks, in which genes activate or deactivate each other via the proteins they produce. These networks can settle into a variety of attractors characterized by specific patterns of expressed and dormant genes. Different attractors are assumed to correspond to different cell types (such as liver cells, bone cells, or neurons), or cell fates (such as apoptosis, quiescence, or proliferation) [46]. The reaching of such attractors is commonly modeled by means of Random Boolean Networks, a highly abstract formalism whose main advantage is that its dynamics is easy to simulate. But COT suggests a model that seems both simpler and more realistic, in which the attractors are the organizations that emerge from a network of reactions with the following form:

active gene 1 \rightarrow active gene 1 + protein 1 (*protein expression of an active gene*)

active gene 2 + protein 1 \rightarrow non-active gene 2 (*expressed protein deactivates gene*)

non-active gene 3 + protein 1 \rightarrow active gene 3 (*expressed protein activates gene*)

Because the reactions defining COT are intrinsically abstract, computable processes, they can be used as a foundation for a new method of computation, based on ‘artificial chemistries’ [58]. Here, the input of a chemical program is a list of resource concentrations. Because the dynamics of a reaction network settles in organizations, it is possible to build reaction networks where reactions play the role of complex logical gates, and organizations represent the final state of the computation. Such ‘chemical computation’ can, for instance,

be used to check models [59] or to program distributed artefacts [60], helping them to coordinate their actions.

Modeling complex systems with many variables of course cannot be done manually. Yet, COT lends itself readily to the development of simple, modular computer programs that can examine a wide range of possible situations, and that are easy to extend or update. An important issue here is how the algorithmic complexity of COT models grows as the number of resources and reactions increases. A basic result is that verifying whether a set of resources is an organization is a Linear Programming problem, whose computational complexity is polynomial, albeit of a degree higher than 2. This motivated a first algorithmic study that builds the set of organizations of a given reaction network from a bottom-top approach that adds resources until an organization is found, and an intricate method that combines flux vectors of previously known organizations [61]. These algorithms were later extended to their parallelized counterparts [62]. The computational complexity of these methods is at first sight exponential because every subset of resources could in principle be an organization. However, it is possible to decompose organizations into subnetworks that are independently self-maintaining [37]. This technique could permit the classification of types of reaction networks in terms of how complex it is to compute their set of organizations. Note, also, that reaction networks are structurally equivalent to a formalism studied in distributed processing, namely Petri Nets [63], about which there is extensive algorithmic research.

Once we make abstraction of the molecules that originally inspired COT, the application domain immediately extends to the social sciences, where the resources to be processed by reactions can, e.g., be economic goods [64] or political decisions [9]. In the latter case, the self-sustaining network of decisions producing further decisions provides a simple formal model of the notoriously difficult theory of autopoietic social systems developed by Niklas Luhmann [65,66]. Another application of Luhmann's social theory is a framework to study the evolution of cooperation [67]. This problem is usually studied from an agent-based perspective. The reaction network models agents' decisions as resources that interact to produce new decisions together with the payoffs generated by the agents' interaction. This model manages to reconstruct the known conditions for the evolution of cooperation [68]—yet without including individual agents! More generally, COT can help us to develop an integrative view of social organizations as autopoietic, self-organizing, and complex adaptive systems [69].

We have alluded several times to the potential for applying COT to problems in ecology [21], sustainable development [30], and the resilience of social and ecological systems. A related issue is the understanding of business ecosystems [70–72], an approach that sees companies producing and consuming different goods and services as forming a symbiotic, co-evolving network, where the ones provide the resources for the others. Existing formalisms in ecosystem modeling, such as food webs or systems dynamics, tend to be limited to networks of one-to-one interactions, in which one variable (e.g., a predator population) positively or negatively affects another variable (e.g., a prey population). In COT, we can examine how several resources in combination produce a combination of other resources. While this at first sight makes modeling more complicated, the mathematics of COT shows that it actually becomes easier to model the emergence of stable organizations.

A general advantage of COT is that you can freely mix resources of very different types, such as organisms, chemicals, economic goods, and even human decisions [12]. This makes it eminently suitable for modeling the truly complex social–technological–economical–ecological–physical systems that surround us, such as cities, businesses, regions, or our planetary society. This is the objective of the new approach of global systems science [73,74].

To further illustrate the power and generality of COT, we wish to briefly suggest some more speculative applications. The section on resilience noted that a highly evolved organization is likely to exhibit a variety of regulatory mechanisms characteristic of a cybernetic or autopoietic system. Such a system acts like a goal-directed agent [42] that aims to sustain its essential organization while suppressing any disturbances that may push

it away from this goal. That means that it exhibits not just the most basic features of life, but of cognition [11,22], intelligence, and intentionality. Like all living systems, the implicit goal or intention of an organization is to maintain and grow. To achieve this, it needs to produce the right actions for the right conditions (e.g., produce the right resource to neutralize a particular disturbance, or to exploit a particular input). This means that it implicitly follows a system of ‘condition–action rules’ that play the role of the organization’s ‘knowledge’ on how to act in its environment. The capability of ‘computing’ the right combination of action(s) to solve a given problem constitutes the organization’s ‘intelligence’. To do this, it needs to ‘perceive’ what is going on in its environment. For example, a unicellular organism will sense the presence of certain resources (such as food) or disturbances (such as toxins) when the corresponding molecules diffuse into the cell, and respond by activating the right combination of genes to produce the enzymes that will catalyze the reactions for effectively dealing with this condition. In this way, an organization can be seen as a rudimentary ‘intelligence’ or ‘mind’ [11].

Because this abstract conceptualization is independent of any specific substrate—such as a brain—it is applicable to systems that exhibit intelligent behavior, but that are otherwise very different from the human individuals that we tend to see as the sole possessors of minds. Examples are the intelligence exhibited by insect societies, plants [75], bacterial colonies [76], human organizations, the self-regulating planetary ecosystem—i.e., ‘Gaia’ [32,77]—and the Internet in its function as a ‘Global Brain’ [78]. In all these cases, intelligence is *distributed*: it is not localized in some central decision-making component, but it emerges from the coordinated interactions between many agents and resources working in parallel. Providing simple models of such self-organizing, distributed organization is precisely the strength of COT.

Even the human brain is a complex, distributed network, where all the important features such as intelligence, intentionality, and consciousness are emergent rather than localized in some specific neuron or assembly of neurons. Recently, great progress has been made in understanding consciousness as a coherent pattern of activity taking control of the ‘global neuronal workspace’ in the brain [79,80]. For conscious processing of thoughts, we need to maintain a pattern of activity long enough in our working memory so that it can be examined and processed by different brain modules. This is intrinsically difficult, because neural activation cannot stay in the same place: a neuron that is excited by an electrical signal (‘action potential’) cannot retain that electrical charge, but must pass it on to one or more neighboring neurons via its outgoing axon ending in synapses. If a sufficient number of incoming synapses pass on a signal, the newly reached neurons will become activated as well, passing on this activation via their outgoing synapses to further neurons. This transmission of activation can be described as a reaction of the form: $a + b + \dots \rightarrow e + f + \dots$, where a , b , etc., are the initially activated neurons whose combined activation is necessary to activate the subsequent neurons e , f , etc. We may say that the activation of a and b is ‘consumed’ by the reaction in order to ‘produce’ the activation of e and f .

What the neuronal workspace theory proposes is that conscious patterns of activation—in contrast to subconscious or subliminal processes—are to some degree self-sustaining: activation that leaves a neuron comes back to it at a later stage after having propagated through some complex, closed network. This creates coherent assemblies of neurons that are firing in a synchronized, cyclic manner, so as to keep the idea ‘alive’ long enough for it to be monitored and processed in a controlled, focused manner—the hallmark of consciousness. Mathematical models of this process have been built [79], but they are rather complicated, making many ad hoc assumptions about specific neurophysiological properties and structures, while being able to simulate only the most basic dynamics of a neuronal assembly reaching ‘ignition’ (self-sustaining activation). By interpreting coherent neuronal activation patterns as organizations, we may reach a simpler, broader, and more qualitative understanding of the different conscious patterns that the brain can produce. Moreover, we may be able to model how such patterns can evolve into different

but overlapping patterns as new stimuli make them deviate from their initial organization, thus producing a ‘train of thought’ or ‘stream of consciousness’ [81].

9. Conclusions

Chemical Organization Theory (COT) proposes a very powerful formalism for the modeling of complex, self-organizing systems. Its power results from several advantageous properties:

- The components of the formalism—resources and the reactions that map combinations of resources onto new combinations—are extremely simple and intuitive. This makes it easy even for people without mathematical background to start expressing their understanding of a system in the form of a COT model.
- Reaction networks are intrinsically modular: it is easy to add (or remove) resources and reactions, and thus to develop an increasingly realistic model of a complex system.
- These components are so general that they can be used to represent a wide variety of real-world objects and variables, including particles, molecules, biological species, economic goods, technological infrastructures, human or animal agents, ideas, and decisions. This makes it possible to apply COT to modeling systems in the most diverse scientific and social disciplines [12], and in particular to multidisciplinary issues, such as interactions between ecological, economic, social, and technological systems.
- COT models are easy to analyze computationally: entering a set of reactions into an appropriate computer program will allow you to quickly discover the different possible outcomes together with the conditions under which they can arise.
- The COT formalism is intrinsically dynamic, starting from reactions rather than from static objects or properties. This makes it particularly suitable for describing systems characterized by an on-going creation, process, or flow of resources. Such systems, which include organisms, ecosystems, societies, and brains, are intrinsically difficult to fit in a traditional, Newtonian framework [7].
- COT shows how such dynamic networks of production and consumption tend to spontaneously settle into invariant ‘organizations’, thus providing a simple model of the hitherto difficult-to-understand phenomena of self-organization and autopoiesis that produce self-sustaining systems [11].
- These organizations can be easily analyzed for further properties, and in particular for the characteristics that make them more or less resilient [30] in the face of perturbations: overproduction of resources, latitude of the basin of attraction, precariousness, feedback, degeneracy of pathways, evolvability, etc.
- As such, COT is a promising approach to a range of notoriously difficult problems, including the origin of life, the modeling of metabolic and genetic regulatory networks in systems biology, the resilience of ecosystems, the formalization of sustainability, the self-organization of socio-economic systems, and even the dynamics of consciousness.

One of the reasons why COT manages to achieve so much with so few assumptions is that the formalism consists of two levels: the very simple qualitative level listing the resources and reactions active in a particular network or organization, and the more advanced quantitative level (which we have largely ignored in this introductory survey) examining the rates of the reactions and the changing concentrations of the resources. Precise modeling at the quantitative level is of course more difficult, both analytically and numerically, but that does not prevent us from deriving clear, unambiguous results by just examining the qualitative level. While the qualitative model can be seen as a mere ‘abstraction’ of the full quantitative dynamics [34], its algebraic properties are so strong that many non-trivial properties can be established at this level without need to determine quantitative dependencies or concentrations. These properties can be used to simplify the model to such a degree that it not only becomes intuitively easier to grasp, but easier to turn into a computable quantitative model without need for unrealistic simplifications. Moreover, in many cases, we do not need to know the full quantitative dynamics, but just need to establish which combinations of reactions and resources (such as species in

an ecosystem, or active genes in a genetic regulatory network) form a self-sustaining and resilient whole.

The COT formalism is hardly two decades old and has as yet only been investigated by a relatively small number of researchers. Thus, there is of course still a lot of work that needs to be done, both in further clarifying its mathematical and conceptual foundations and in applying it to concrete problems. Yet, the results we have reviewed here illustrate the power and flexibility of this formal framework. We hope that after reading this paper, others may become as enthusiastic as we are in applying COT to various domains, and thus potentially revolutionizing our conception of complex, self-organizing systems.

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