Chemical Organization Theory as a modeling framework for self-organization, autopoiesis and resilience

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Abstract: Chemical Organization Theory (COT) is a recently developed formalism inspired by chemical reactions. Because of its simplicity, generality and power, COT seems able to tackle a wide variety of problems in the analysis of complex, self-organizing systems across multiple disciplines. The elements of the formalism are resources and reactions, where a reaction (which has the form $a + b + ... \rightarrow c + d + ...$) maps a combination of resources onto a new combination. The resources on the input side are "consumed" by the reaction, which "produces" the resources on the output side. Thus, a reaction represents an elementary process that transforms resources into new resources. Reaction networks tend to 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. Organizations can be more or less resilient in the face of perturbations, depending on properties such as the size of their basin of attraction or the redundancy of their reaction pathways. Concrete applications of organizations can be found in autocatalytic cycles, metabolic or genetic regulatory networks, ecosystems, sustainable development, and social systems.

Introduction

Complex adaptive systems are systems consisting of many interacting agents that exhibit some degree of self-organization (Holland, 2012): coherent patterns of organization spontaneously emerge out of the network of interactions. Most of the phenomena we are confronted with in real life are such complex adaptive systems: people, organisms, societies, ecosystems, markets, cultures... Great progress has been made in understanding the dynamics of such systems by means of multi-agent computer simulations (Miller & Page, 2007). However, on a more abstract, theoretical level, our understanding of self-organization and adaptation remains rather superficial and fragmented.

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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 analyzing a system into 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 represented as a timeparameterized 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* (Rescher, 1996; Whitehead, 1978) or *action ontology* (Heylighen, 2011; Turchin, 1993). Such a philosophy assumes that reality is not constituted out of static objects but out of dynamic processes or actions. It sees objects as merely stabilized, emergent networks of processes. While this perspective is consonant with our most recent insights into complex adaptive systems, the problem is to represent such processes in a way that is sufficiently general, explicit and concrete to allow precise modeling of such emergent systems.

This paper wishes to introduce a new formalization of processes, namely the reaction networks used in what has been called *Chemical Organization Theory* (COT) (Dittrich & Fenizio, 2007; Dittrich & Winter, 2008; Peter, Veloz, & Dittrich, 2011). In 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, COT appears to be the first formalization of a process ontology that is both fundamental and practical.

The fundamental character means that COT can describe systems and processes in *any* discipline—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, adaptive systems out of simpler components.

Next to its deep philosophical foundation, 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 and other properties. 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 truly most important questions about a complex adaptive system: in how far is it sustainable and resilient, i.e. able to maintain itself both

autonomously and in the face of external perturbations? In how far 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 organization? 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 material objects, 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 extremely 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 preliminary 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.

Reaction networks

As its name implies, the COT formalism (Dittrich & Fenizio, 2007) is inspired by chemistry, and the way it describes how chemical reactions recombine molecules into new molecules. Therefore, it has inherited much of its terminology from chemistry. 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 "Reactive Organization Theory"). The present paper will therefore replace some COT terms by new terms—however, 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, distinguishable phenomenon. Examples of resources are particular types of molecules, elementary particles, biological species, products, objects, tools, messages, words, ideas, or statements. 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 them to interact or react with each other. 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, a reaction network is defined by the 2-tuple $\langle M, R \rangle$, where $M = \{a, b, c, ...\}$ 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 transforms a particular subset X of M into another subset Y of M:

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

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:

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

The "+" symbol here represents a *conjunction* of the resources: x_1 and x_2 and ... 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

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:

$$2a + b \rightarrow 3c + d$$
,

or more generally:

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

For simplicity, we will here work only with ordinary sets, i.e. resources that only occur once in a reaction.

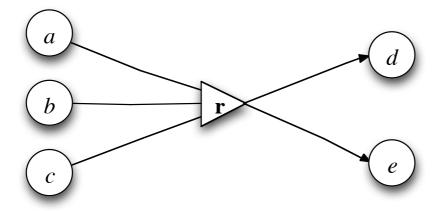


Fig. a depiction of the reaction r: $a + b + c \rightarrow d + e$

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 hypergraph* (Gallo, Longo, Pallottino, & Nguyen, 1993). 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:

 $r: x \to y$, 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.*

 $r_1: x \to y$ $r_2: x \to z$ $r_3: u \to y$

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 by "+", that plays the role of the conjunction. The juxtaposition of reactions plays the role of the disjunction. Consider the following reactions:

 $r_4: x + u \to y$ $r_5: w \to y$

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.

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 by the " \rightarrow " operator. This directly suggests the logical formalism of Horn clauses (Chandra & Harel, 1985). These have the following form:

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

This is to be read as "if a and b and ... are true, then x is true", or "x can be derived from the conjunction of a, b, ...". 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:

$$a+b+\ldots \rightarrow x+a+b+\ldots$$

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 all attempts to derive process, actions, dynamics or time from logic are bound to fail, in spite of a plethora of formalization attempts such as "dialectical logics", "process logics" or "dynamic logics" (see *e.g.* (Harel, Kozen, & Parikh, 1982; Ilyenkov, 2008; Van Benthem, 2007). 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.

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, decrease in a implies increase in b. More generally, we can define the relation "a inhibits b" as:

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

This means that a enables a reaction r that consumes, but does not produce, 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 this case, we might say that *a* and *b* are competitors, respectively cooperators.

Inhibition is a negative causal influence; promotion is a positive one. However, note that the same resource can simultaneously inhibit and promote another resource via different reactions. In that case we need to investigate a more detailed, quantitative model of the reaction network in order to establish whether the overall relation is positive, negative or mixed. 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 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 (Sterman, 2000) is a very useful formalism for representing and analyzing networks of causal influences, and the positive and negative feedback loops they form. Compared to COT, however, it lacks the ability to combine different resources in a single reaction.

The interactions between reactions take place through their shared resources ("nodes" or "vertices" in traditional network terminology): the same resource can appear in input and output sets of different reactions. Because these resources are either consumed or produced by the reactions, different reactions can either facilitate each other (e.g. when the one produces a resource needed by the other) or hinder each other (when the one consumes a resource needed by the other). This creates a complex, non-linear dynamic of cooperation (mutual amplification or synergy), competition (mutual inhibition, conflict, or friction) and exploitation (growth of the one at the expense of the other). As we will show further, the general logic of self-organization, co-evolution and natural selection (Heylighen, 1992, 1999, 2008) ensures that this process moves 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.

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 (Maturana & Varela, 1980; Varela, 1979; Varela, Maturana, & Uribe, 1974). 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 (Benkö et al., 2009)—and a generalization of the more common but more restrictive model of an *autocatalytic set* (Hordijk, Hein, & Steel, 2010).

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: ∀ x ∈ M' for which ∃ r ∈ R such that x ∈ In(r) ⊆ M', ∃ r' ∈ R such that In(r') ⊆ M', and x ∈ Out(r').
- self-maintenance: this is a stronger form of the semi-self-maintenance condition, which states that each consumed resource x ∈ M' is not only produced by some other reaction in <M', R>, 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. This is necessary to establish the long-term maintenance of the resource set M, 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 the rate of a reaction is normally proportional to the concentration of its reactants: it increases whenever one of its input resources increases, and decreases whenever one of its input resources decreases. The flux vector then needs to be multiplied with the "stoichiometric matrix", specifying which reactions consume and which produce a particular resource, in order to calculate the net balance of consumption/production (Dittrich & Fenizio, 2007). A resource being produced by a reaction is listed as a positive number in the matrix; a resource being consumed is listed as a negative number. The product of flux vector and stoichiometric matrix then determines the net rate of production (production minus consumption) for each of the resources.

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 of the reaction network allow such self-maintaining flux vectors to exist, then the system will tend to automatically converge to the corresponding regime of self-maintenance. The reason is that resources that are consumed more than they are produced will decrease in concentration up to the point that the reactions consuming them slow down enough so that production (which is 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.

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 resources are added (closure) and no resources are removed (self-maintenance).

This 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 fundamental 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 different. 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 peculiar 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. Moreover, COT reformulates the rather difficult and confusing notion of autopoiesis as a simple mathematical property characterizing even simpler sets of resources and reactions.

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 $\rightarrow a$. 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 fluctuates in and out of existence.

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:

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

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.

 \rightarrow sunlight plants + sunlight + carbon dioxide + minerals \rightarrow plants + oxygen plants + animals + oxygen \rightarrow animals + carbon dioxide + detritus detritus + bacteria \rightarrow bacteria + carbon dioxide + minerals

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). 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 or facilitate a reaction, but are not themselves affected by it. In our more general interpretation, we may call them **agents** (Heylighen, 2011): 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.

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 plants + 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 by

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 (thus interrupting self-maintenance). Let us then try to better understand how organizations emerge.

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 reactions. 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 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* (Ashby, 1962; Heylighen, 2001, 2008): any dynamic system will eventually end up in an attractor (originally called "equilibrium" by Ashby), i.e. a stationary regime of activity that the system can enter but not leave. In the present, qualitative formulation of COT, such an attractor is defined as a particular 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 (Peter & Dittrich, 2011). 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 (Strogatz, 2000). Peter and Dittrich (2011) have shown that these dynamically stable regimes correspond in most cases to organizations. This means that while the selection 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 (Ashby, 1962), 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. 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 dependencies they all together constitute.

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 control the population numbers of the prey so that the prey cannot increase in population so much that they exhaust other species on which they depend—thus indirectly threatening their own survival. A classic example are the wolves that were reintroduced as top predators to the Yellowstone natural reserve (Ripple & Beschta, 2012): 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, increasing 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 dynamics. 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, mutual 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 to verify computationally—by analyzing the reaction network and checking whether each resource is produced at least as much as it is consumed, while no new resources are created.

An Example

Let us illustrate the process of self-organization on an example of a reaction network that was randomly generated to include 10 reactions, each producing or consuming between 1 and 3 resources out of a 10-element resource set (see Table 1).

rl:	f	\rightarrow	f+g
r2:	j + a	\rightarrow	h
r3:	e + i + g	\rightarrow	е
r4:	a + g	\rightarrow	a+g+b
r5:	i + h	\rightarrow	c + a
r6:	а	\rightarrow	e+g+i
r7:	d	\rightarrow	a + d
r8:	e + c	\rightarrow	e + a
r9:	е	\rightarrow	f + d
<i>r10</i> :	е	\rightarrow	i + a

Table 1: *a* reaction network with 10 reactions $R = \{r_1, r_2, ..., r_{10}\}$ producing or consuming 10 resources $M = \{a, b, ..., i, j\}$

The process starts from an initial state, for which we can take an arbitrary subset of the resource set M, for example $\{d, h\}$. The only reaction applicable in this state is r_7 , which adds the resource a to the set, producing $\{a, d, h\}$. This new state enables r_6 , which adds e, g and i, thus producing the next state $\{a, d, e, g, h, i\}$. The presence of a and g activates reaction r_4 , which adds b to the set of resources: $\{a, b, d, e, g, h, i\}$. The presence of e activates r_9 which additionally produces f, resulting in $\{a, b, d, e, f, g, h, i\}$. The other enabled reactions ($e.g. r_{10}$ or r_3) merely add resources that are already there. The set has now become closed: no further resources can be added by applying any of the reactions.

From this set all the elements are produced by some reaction working on other resources in the set, except *h*. This resource can only be produced by r_2 , which requires the resource *j* that is not in the set. On the other hand, *h* is being consumed by r_5 . Therefore, *h* will eventually be eliminated from the set, leaving us with $\{a, b, d, e, f, g, i\} = A_1$. This 7-element set is closed and self-

maintaining and therefore an organization. It is the attractor reached by the reaction dynamics starting from the initial state $\{d, h\}$.

Let us now start from the state $\{f\}$. Only one reaction is applicable, r_1 , producing the new set $\{f, g\} = A_2$. This set is closed, because no further reactions can be applied to it, and self-maintaining, because r_1 continuously reproduces it. Therefore it is an organization, and an attractor of the dynamics.

Sustainability and resilience

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 either because all resources are recycled through the inherent reactions, 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" (Veloz, Reynaert, Rojas, & Dittrich, 2011). In the organization A_1 derived from the reaction network in Table 1, the resource *b* illustrates the property: it is produced by reaction r_4 , but not consumed by any other reaction. Organizations with overproduction fulfill the ideal of *sustainable development*: growth that can be sustained indefinitely.

Ecosystems are normally sustainable with an approximately constant level of resources. Economic systems, on the other hand, although they grow, are often unsustainable: they consume more of certain resources than they produce. Therefore, they are likely to 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 and cannot be renewed. Creating a sustainable economy means shifting to energy sources that are renewable, either through a dependable external input (e.g. solar energy) or through reprocessing within the network (e.g. biofuel derived from plants grown and harvested by the system).

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. In general, 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 vectors and stoichiometric matrices in order to establish in how far this reaction network is self-maintaining.

Complementary to the notion of sustainability is the one of *resilience*. Sustainability denotes the ability of the system to maintain and grow on its own, without outside interference. Resilience (Beigi, 2014; Holling, 1973; Walker, Holling, Carpenter, & Kinzig, 2004) broadens this notion to the ability to maintain the essential organization even in the face of serious outside disturbances. A resilient organization is one that will survive and recover from shocks induced by the environment.

In contrast, a vulnerable, fragile or brittle organization is one that is likely to disintegrate as soon as it encounters a serious disturbance.

In the qualitative version of COT, a disturbance can be represented as the removal of a resource that the organization relies upon, or as the introduction of a new resource that reacts with some of the existing resources, thus interfering with the network of reactions that defines the organization. In practice, 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. 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* (Heylighen & Joslyn, 2003).

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 dynamics is common in metabolic pathways and in ecosystem interactions. For example, if foxes eat more rabbits, less 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 dynamics 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 reactions consuming a resource necessarily slow down when that resource become scarcer (e.g. predation slows down when the prey population decreases), thus allowing other 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. One way to implement such capability is by means of a collection of resources that are either overproduced, or are not consumed by any of the reactions in the organization, and so remain in reserve. Each of these resources 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 (Ashby, 1958; Heylighen & Joslyn, 2003).

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.

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 resilient outcomes are more likely in the long run than vulnerable 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 (Heylighen, 2001). The larger the basin, the larger the probability that the starting point is 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 normally represent stable systems characterized by negative feedback, since a deviation from the attractor that remains within the basin is automatically counteracted by the descent back from basin into attractor.

In the example of the reaction system of Table 1, we found two attractors, the sets $A_1 = \{a, b, d, e, f, g, i\}$ and $A_2 = \{f, g\}$. The (qualitative) state space of this system is the power set P(M), i.e. the set of all possible combinations of elements from the 10-element set M. The size of that state space is $2^{10} = 1024$. With a computer program that simulates the dynamics of reaction systems, we found that the great majority of these states, namely 927, end up in the attractor A_1 . That means that this attractor has a very large basin. It is therefore very resilient: the probability that the combined removal or addition of any number of resources would make the system end up in a different attractor is only (1024 - 927) / 1024 = 9.4%. The probability that the removal or addition of a single resource would destroy the organization is actually zero: any resource removed from the organization can be reconstituted by other reactions working on different resources; the only resources in the organization. We may conclude that A_1 is a highly resilient organization.

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-toattractor 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 (Heylighen, 2001; Von Foerster, 1960), according to which increased variation ("noise") accelerates the self-organization of a stable configuration ("order").

In the example of Table 1, the organization A_2 has a basin containing only 2 states out of the 1024 possible ones, namely the states $\{f\}$ and $\{f, g\}$. Practically any resource change pushes the organization out of its basin into a different basin, and thus eventually into a different attractor—most likely the attractor A_1 . For example, adding the resource *a* to A_2 would immediately enable reactions r_4 and r_6 , producing the additional resources *b*, *e* and *i*, which would in turn enable reactions r_9 and r_{10} , eventually producing all the resources that make up the larger and more resilient organization A_1 .

The shifting from one attractor to a similar, neighboring one can be seen as a higher process of evolution, in which the system adapts to changing conditions by changing its organization, but in such a way as to maintain continuity by keeping most of its resources. Note that a "sideward shift" to an overlapping organization normally happens as a combination of two "vertical" shifts, one "upward" that adds resources (e.g. from A_2 to A_1), and one "downward" that removes resources (Matsumaru, di Fenizio, Centler, & Dittrich, 2006). 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* (Aldana, Balleza, Kauffman, & Resendiz, 2007; Beigi, 2014).

What is as yet unclear is how such organizations are precisely organized: what kinds of arrangements of reactions make up a resilient whole? A theoretical decomposition of organizations (Veloz et al., 2011) 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 but without making them dependent on each other. Such decomposition makes it possible to identify where in the network a disturbance would have the strongest effect. For example, a perturbation happening in a small subnetwork may not affect the bulk of the organization.

A more detailed analysis is likely to come from simulations, in which reactions systems are randomly generated and then allowed to settle into an attractor. The corresponding organizations are then repeatedly perturbed by generating a variety of random disturbances. We can then compare the organizations that were easily destroyed by disturbances with those that proved to be particularly resilient. This may allow us to formalize the aspects of resilience that (Walker et al., 2004) have called *precariousness* (nearness of the organization to the border of its attraction basin, i.e. minimum number of changes needed to switch attractors) and *resistance* (effort needed to move the organization out of its basin). The latter might be measured as the minimum amount of resources that need to be added to, or removed from, the organization in order to make it shift to a different organization.

Another source of inspiration for understanding resilience are 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 (Matias Rodrigues & Wagner, 2009). A likely reason is the redundancy—or more precisely *degeneracy* (Edelman & Gally, 2001)—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. For example, the organization A_1 depends on two critical resources, *a* and *e*, that together produce most of the other resources in the organization (see Table 1). However, both *a* and *e* can be produced by more than one reaction, so if one of such reactions would be disabled (e.g. r_3 through the removal of the resource *g*), the main processes can still continue (e.g. *a* can still be produced by reactions r_4 and r_7). Such degeneracy is one of the factors that explain the remarkable resilience and evolvability of living systems (Aldana et al., 2007): 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.

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 (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 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 $a: b + c \rightarrow d, f \rightarrow g + h, ...$ 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 catalyses, the richer its "skill set" or "toolbox" of condition-action rules, and therefore the greater its power in manipulating its environment. 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:

$$S + In(S) \rightarrow S + Out(S)$$

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

S:
$$a + b \rightarrow c + d + e$$

The fact that S is itself constituted of a network of resources and reactions does not really make any difference when seem 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 (Rasmussen, Baas, Mayer, Nilsson, & Olesen, 2001) and metasystem transitions (Heylighen, 1995; Turchin, 1995; Maynard Smith & Szathmáry, 1997) 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 (Peter et al., 2011), 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.

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 (Matsumaru, Centler, Fenizio, & Dittrich, 2006) and the chemistry of a planetary atmosphere (Centler & Dittrich, 2007). 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 (Fernando & Rowe, 2008). Previously, this problem of the origin of life had been approached by looking for *autocatalytic cycles* of chemical reactions (Hordijk, Hein, & Steel, 2010; Maynard Smith & Szathmáry, 1997; Vasas, Szathmáry, & Santos, 2010). 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.

A related application domain is the study of metabolic networks in existing organisms, such as the bacterium E. Coli (Centler, di Fenizio, Matsumaru, & Dittrich, 2007). This domain has recently attracted a lot of attention under the label of *systems biology*, but still lacks an integrated theoretic framework (Machado et al., 2011)—which COT may be able to provide (Kaleta, Centler, & Dittrich, 2006). 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) (Aldana et al., 2007). 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 active gene 2 + protein $1 \rightarrow$ non-active gene 2 non-active gene 3 + protein $1 \rightarrow$ active gene 3 (protein expression of an active gene) (expressed protein deactivates gene) (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" (Matsumaru, Centler, di Fenizio, & Dittrich, 2005). 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 (Kaleta, Richter, & Dittrich, 2009) or to program distributed artefacts (Matsumaru, Hinze, & Dittrich, 2009), 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 or not a set of resources is an organization is a Linear Programming problem, whose computational complexity is polynomial, but of 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 (Centler, Kaleta, di Fenizio, & Dittrich, 2008). These algorithms were later extended to their parallelized counterparts (Centler, Christoph, Pietro, & Peter, 2010). 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 (Veloz et al., 2011). 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 (Veloz, 2010), namely Petri Nets (Murata, 1989), 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 (Dittrich & Winter, 2005) or political decisions (Dittrich & Winter, 2008). 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 (1986, 1995). Another application of Luhmann's social theory is a framework to study the evolution of cooperation (Veloz, Razeto-Barry, Dittrich, & Fajardo, 2014). This problem is usually studied from an agent-based perspective. The reaction network model does not include individual agents, but models agents' decisions as resources. Decisions 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 (Nowak, 2006) without assuming agents.

We have alluded several times at the as yet unexplored potential for applying COT to problems in ecology, sustainable development, and the resilience of social and ecological systems. A related issue is the understanding of business ecosystems (Moore, 1996; Nachira, Nicolai, Dini, Le Louarn, & Leon, 2007; Peltoniemi, 2006), 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 such multi-resource reactions make the emergence of stable organizations easier rather than more difficult.

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 (Veloz, 2014). 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 (Helbing, 2013; Helbing, Bishop, Conte, Lukowicz, & McCarthy, 2012)

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 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 (Maturana & Varela, 1980), intelligence, and intentionality (Heylighen, 2011). 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".

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 individual human beings that we tend to see as the sole possessors of minds. Examples are the intelligence exhibited by insect societies, plants (Trewavas, 2005), bacterial colonies (Ben-Jacob, Becker, Shapira, & Levine, 2004), human organizations, the self-regulating planetary ecosystem—i.e. "Gaia" (Free & Barton, 2007)—, and the Internet in its function as a "Global Brain" (Heylighen, 2007). In all these cases, intelligence is *distributed* (Heylighen, 2014): 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 (Dehaene, 2014; Dehaene, Kerszberg, & Changeux, 1998). 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: $a + b + ... \rightarrow e + f + ...$, 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 (Dehaene et al., 1998), 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 shift 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".

Conclusion

Chemical Organization Theory (COT) proposes a very promising new formalism for the modeling of complex, self-organizing systems. Its power results from several highly beneficial 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

- COT models are intrinsically **modular**: it is easy to add (or remove) components, 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 realworld 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 problems in about all scientific and social disciplines, and in particular to **multidisciplinary** issues, such as interactions between ecological, economical, 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 all the 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.
- 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
- these organizations can be easily analyzed for further properties, and in particular for the characteristics that make them more or less **resilient** in the face of perturbations: overproduction of resources, latitude of the basin of attraction, precariousness, feedback, degeneracy of pathways, evolvability...
- as such, COT is a very 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 **sustainable development**, 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 will obviously be 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 (Peter & Dittrich, 2011), 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) are self-sustaining and resilient.

The COT formalism is hardly a decade old and as yet has only been actively investigated by a handful of scientists. 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. In collaboration with other COT researchers, we intend to further develop these different aspects in a series of subsequent papers. We hope that after reading this paper, others may become as enthusiastic as we are in joining this enterprise, and thus potentially revolutionizing our conception of complex, self-organizing systems.

References

- Aldana, M., Balleza, E., Kauffman, S., & Resendiz, O. (2007). Robustness and evolvability in genetic regulatory networks. *Journal of Theoretical Biology*, 245(3), 433–448. doi:10.1016/j.jtbi.2006.10.027
- Ashby, W. R. (1958). Requisite variety and its implications for the control of complex systems. *Cybernetica*, *1*(2), 83–99.
- Ashby, W. R. (1962). Principles of the self-organizing system. In H. von Foerster & G. W. Zopf (Eds.), *Principles of Self-Organization* (pp. 255–278). Pergamon Press. Retrieved from http://csis.pace.edu/~marchese/CS396x/Computing/Ashby.pdf
- Beigi, S. (2014). *Mindfulness Engineering: A Unifying Theory of Resilience for Volatile, Uncertain, Complex and Ambiguous (VUCA) World* (PhD thesis). University of Bristol, Bristol, UK.
- Ben-Jacob, E., Becker, I., Shapira, Y., & Levine, H. (2004). Bacterial linguistic communication and social intelligence. *Trends in Microbiology*, 12(8), 366–372.
- Benkö, G., Centler, F., Dittrich, P., Flamm, C., Stadler, B. M. ., & Stadler, P. F. (2009). A topological approach to chemical organizations. *Artificial Life*, 15(1), 71–88. Retrieved from http://www.mitpressjournals.org/doi/abs/10.1162/artl.2009.15.1.15105
- Centler, F., Christoph, K., Pietro, S. di F., & Peter, D. (2010). A parallel algorithm to compute chemical organizations in biological networks. *Bioinformatics*, 26(14), 1788–1789.
- Centler, F., di Fenizio, P. S., Matsumaru, N., & Dittrich, P. (2007). Chemical organizations in the central sugar metabolism of Escherichia Coli. *Mathematical Modeling of Biological Systems, Volume I* (pp. 105–119). Springer. Retrieved from http://link.springer.com/chapter/10.1007/978-0-8176-4558-8_10
- Centler, F., & Dittrich, P. (2007). Chemical organizations in atmospheric photochemistries—A new method to analyze chemical reaction networks. *Planetary and Space Science*, 55(4), 413–428. Retrieved from http://www.sciencedirect.com/science/article/pii/S0032063306002339
- Centler, F., Kaleta, C., di Fenizio, P. S., & Dittrich, P. (2008). Computing chemical organizations in biological networks. *Bioinformatics*, 24(14), 1611–1618. Retrieved from http://bioinformatics.oxfordjournals.org/content/24/14/1611.short
- Chandra, A. K., & Harel, D. (1985). Horn clause queries and generalizations. *The Journal of Logic Programming*, 2(1), 1–15. doi:10.1016/0743-1066(85)90002-0

Dehaene, S. (2014). Consciousness and the Brain: Deciphering How the Brain Codes Our Thoughts. Penguin.

- Dehaene, S., Kerszberg, M., & Changeux, J. P. (1998). A neuronal model of a global workspace in effortful cognitive tasks. *Proceedings of the National Academy of Sciences*, 95(24), 14529.
- Dittrich, P., & Fenizio, P. S. di. (2007). Chemical Organisation Theory. *Bulletin of Mathematical Biology*, 69(4), 1199–1231. doi:10.1007/s11538-006-9130-8
- Dittrich, P., & Winter, L. (2005). Reaction networks as a formal mechanism to explain social phenomena. *Proc. Fourth Int. Workshop on Agent-Based Approaches in Economics and Social Complex Systems* (AESCS 2005) (pp. 9–13). Retrieved from http://users.minet.uni-jena.de/~dittrich/p/DW2005.pdf
- Dittrich, P., & Winter, L. (2008). Chemical organizations in a toy model of the political system. Advances in Complex Systems, 11(04), 609. doi:10.1142/S0219525908001878
- Edelman, G. M., & Gally, J. A. (2001). Degeneracy and complexity in biological systems. *Proceedings of the National Academy of Sciences*, 98(24), 13763–13768.
- Fernando, C., & Rowe, J. (2008). The origin of autonomous agents by natural selection. *Biosystems*, 91(2), 355–373. Retrieved from http://www.sciencedirect.com/science/article/pii/S0303264707001050
- Free, A., & Barton, N. H. (2007). Do evolution and ecology need the Gaia hypothesis? *Trends in Ecology & Evolution*, 22(11), 611–619. doi:10.1016/j.tree.2007.07.007
- Gallo, G., Longo, G., Pallottino, S., & Nguyen, S. (1993). Directed hypergraphs and applications. *Discrete Applied Mathematics*, 42(2-3), 177–201.
- Harel, D., Kozen, D., & Parikh, R. (1982). Process logic: Expressiveness, decidability, completeness. *Journal* of computer and system sciences, 25(2), 144–170. Retrieved from http://www.sciencedirect.com/science/article/pii/0022000082900034
- Helbing, D. (2013). Globally networked risks and how to respond. *Nature*, 497(7447), 51–59. Retrieved from http://www.nature.com/nature/journal/v497/n7447/abs/nature12047.html
- Helbing, D., Bishop, S., Conte, R., Lukowicz, P., & McCarthy, J. B. (2012). FuturICT: Participatory computing to understand and manage our complex world in a more sustainable and resilient way. *European Physical Journal Special Topics*, 214, 11–39. Retrieved from http://adsabs.harvard.edu/abs/2012EPJST.214...11H
- Heylighen, F. (1992). Principles of Systems and Cybernetics: an evolutionary perspective. *Cybernetics and Systems'* 92 (pp. 3–10). Retrieved from http://cyberneticscockpit.com/global/documents/principlescybsys.pdf
- Heylighen, F. (1995). (Meta)systems as constraints on variation— a classification and natural history of metasystem transitions. *World Futures*, 45(1), 59–85. doi:10.1080/02604027.1995.9972554
- Heylighen, F. (1999). The growth of structural and functional complexity during evolution. In F. Heylighen, J. Bollen, & A. Riegler (Eds.), *The evolution of complexity* (pp. 17–44). Springer. Retrieved from http://pcp.vub.ac.be/Papers/ComplexityGrowth.pdf
- Heylighen, F. (2001). The science of self-organization and adaptivity. *The Encyclopedia of Life Support Systems*, 5(3), 253–280. Retrieved from http://cleamc11.vub.ac.be/papers/EOLSS-Self-Organiz.pdf
- Heylighen, F. (2007). The Global Superorganism: an evolutionary-cybernetic model of the emerging network society. Social Evolution & History, 6(1), 58–119. Retrieved from http://pcp.vub.ac.be/papers/Superorganism.pdf
- Heylighen, F. (2008). Complexity and Self-organization. *Encyclopedia of Library and Information Sciences,* eds. MJ Bates & MN Maack Taylor & Francis. Retrieved from http://pespmcl.vub.ac.be/Papers/ELIS-complexity.pdf
- Heylighen, F. (2011). Self-organization of complex, intelligent systems: an action ontology for transdisciplinary integration. *Integral Review*. Retrieved from http://pespmc1.vub.ac.be/Papers/ECCO-paradigm.pdf

- Heylighen, F. (2014). Challenge Propagation: Towards a theory of distributed intelligence and the global brain. *Spanda Journal*, *V*(2), 51–63. Retrieved from http://cleamc11.vub.ac.be/papers/ChallengePropagation-Spanda.pdf
- Heylighen, F., & Joslyn, C. (2003). Cybernetics and Second-Order Cybernetics. In Robert A. Meyers (Ed.), *Encyclopedia of Physical Science and Technology* (3rd ed., Vol. 4, pp. 155–169). New York: Academic Press. Retrieved from http://pespmc1.vub.ac.be/Papers/cybernetics-EPST.pdf
- Holland, J. H. (2012). Signals and Boundaries: Building Blocks for Complex Adaptive Systems. Cambridge, Mass: The MIT Press.
- Holling, C. S. (1973). Resilience and stability of ecological systems. *Annual review of ecology and systematics*, 1–23.
- Hordijk, W., Hein, J., & Steel, M. (2010). Autocatalytic sets and the origin of life. *Entropy*, *12*(7), 1733–1742. Retrieved from http://www.mdpi.com/1099-4300/12/7/1733
- Ilyenkov, E. V. (2008). *Dialectical Logic; Essays on its History and Theory*. Aakar Books. Retrieved from http://books.google.be/books?hl=en&lr=&id=0KIhjQizSkYC&oi=fnd&pg=PA5&dq=%E2%80%9Cd ialectical+logic%E2%80%9D+OR+%E2%80%9Cprocess+logic%E2%80%9D+OR+%E2%80%9Cdy namic+logic%E2%80%9D&ots=E8052FwIoC&sig=oQ9Y99VUQrnpKqwyHGn137ArjJU
- Kaleta, C., Centler, F., & Dittrich, P. (2006). Analyzing molecular reaction networks. *Molecular* biotechnology, 34(2), 117–123.
- Kaleta, C., Richter, S., & Dittrich, P. (2009). Using chemical organization theory for model checking. *Bioinformatics*, 25(15), 1915–1922. Retrieved from http://bioinformatics.oxfordjournals.org/content/25/15/1915.short
- Luhmann, N. (1986). The autopoiesis of social systems. *Sociocybernetic paradoxes*, 172–192. Retrieved from http://books.google.be/books?hl=en&lr=&id=2Yfys20NPAoC&oi=fnd&pg=PA172&dq=Luhmann& ots=E5hsDIDSAG&sig=rGBVijKWKxrLU2NTkVWizu6rZko
- Luhmann, N. (1995). Social systems. Stanford University Press. Retrieved from http://books.google.be/books?hl=en&lr=&id=zVZQW4gxXk4C&oi=fnd&pg=PR9&dq=Luhmann&ot s=7EEKk78LVS&sig=GNMqh5YJn54eoK_BQzuRzrgFdOI
- Machado, D., Costa, R. S., Rocha, M., Ferreira, E. C., Tidor, B., & Rocha, I. (2011). Modeling formalisms in systems biology. *AMB Express*, *1*(1), 1–14. Retrieved from http://www.biomedcentral.com/content/pdf/2191-0855-1-45.pdf
- Matias Rodrigues, J. F., & Wagner, A. (2009). Evolutionary Plasticity and Innovations in Complex Metabolic Reaction Networks. *PLoS Comput Biol*, 5(12), e1000613. doi:10.1371/journal.pcbi.1000613
- Matsumaru, N., Centler, F., di Fenizio, P. S., & Dittrich, P. (2005). Chemical organization theory as a theoretical base for chemical computing. *Proceedings of the 2005 Workshop on Unconventional Computing: From Cellular Automata to Wetware* (pp. 75–88). Luniver Press. Retrieved from http://books.google.be/books?hl=en&lr=&id=ZCabr1UUUKcC&oi=fnd&pg=PA75&dq=%22chemic al+organization+theory%22+%22Towards+a+theory+of+constructive+dynamical+systems%22+sper oni+networks+Dittrich&ots=h0Z iPOVcJ&sig=ua85T0kCnZ2HA9oGmgZG6PDCcNY
- Matsumaru, N., Centler, F., Fenizio, P. S. di, & Dittrich, P. (2006). Chemical organization theory applied to virus dynamics. *it-Information Technology*, *48*(3/2006), 154–160. Retrieved from http://www.degruyter.com/view/j/itit.2006.48.issue-3 2006/itit.2006.48.3.154/itit.2006.48.3.154.xml
- Matsumaru, N., di Fenizio, P. S., Centler, F., & Dittrich, P. (2006). On the evolution of chemical organizations. *Proc. of the 7th German Workshop of Artificial Life* (pp. 135–146). Retrieved from http://books.google.be/books?hl=en&lr=&id=3kuT8-FpBCQC&oi=fnd&pg=PA135&dq=%22chemical+organizations%22+reaction+networks&ots=zBQd OG4pej&sig=4ob_uZNuqBZAmegXKjxVvom3R9c
- Matsumaru, N., Hinze, T., & Dittrich, P. (2009). Organization-oriented Chemical Programming of Distributed Artifacts. *International Journal of Nanotechnology and Molecular Computation (IJNMC)*, 1(4), 1–19.

Retrieved from http://www.igi-global.com/article/organization-oriented-chemical-programming-distributed/40362

- Maturana, H. R., & Varela, F. J. (1980). Autopoiesis and Cognition: The Realization of the Living. D Reidel Pub Co.
- Maynard Smith, J., & Szathmáry, E. (1997). The major transitions in evolution. Oxford University Press, USA.
- Miller, J. H., & Page, S. E. (2007). Complex Adaptive Systems: An Introduction to Computational Models of Social Life. Princeton, N.J: Princeton University Press.
- Moore, J. F. (1996). *The death of competition: leadership and strategy in the age of business ecosystems.* HarperBusiness New York.
- Murata, T. (1989). Petri nets: Properties, analysis and applications. *Proceedings of the IEEE*, 77(4), 541–580. doi:10.1109/5.24143
- Nachira, F., Nicolai, A., Dini, P., Le Louarn, M., & Leon, L. R. (2007). Digital business ecosystems. Retrieved from http://www.digital-ecosystems.org/events/2006.06-sardegna/nachira-sardegna-ict.pdf
- Peltoniemi, M. (2006). Preliminary theoretical framework for the study of business ecosystems. *Emergence:* Complexity & Organization, 8(1).
- Peter, S., & Dittrich, P. (2011). On the Relation between Organizations and Limit Sets in Chemical Reaction Systems. *Advances in Complex Systems*, 14(01), 77–96. doi:10.1142/S0219525911002895
- Peter, S., Veloz, T., & Dittrich, P. (2011). Feasibility of Organizations-A Refinement of Chemical Organization Theory with Application to P Systems. *Membrane Computing* (pp. 325–337). Springer. Retrieved from http://link.springer.com/chapter/10.1007/978-3-642-18123-8 25
- Rasmussen, S., Baas, N. A., Mayer, B., Nilsson, M., & Olesen, M. W. (2001). Ansatz for dynamical hierarchies. *Artificial Life*, 7(4), 329–353.
- Rescher, N. (1996). Process metaphysics: An introduction to process philosophy. State Univ of New York Pr.
- Ripple, W. J., & Beschta, R. L. (2012). Trophic cascades in Yellowstone: The first 15years after wolf reintroduction. *Biological Conservation*, 145(1), 205–213. Retrieved from http://www.sciencedirect.com/science/article/pii/S0006320711004046
- Sterman, J. D. (2000). Business Dynamics: Systems Thinking and Modeling for a Complex World. Irwin McGraw-Hill.
- Strogatz, S. H. (2000). Nonlinear dynamics and chaos: With applications to physics, biology, chemistry, and engineering. Westview Pr.
- Trewavas, A. (2005). Plant intelligence. Naturwissenschaften, 92(9), 401-413.
- Turchin, V. (1995). A dialogue on metasystem transition. *World Futures*, 45, 5–57. Retrieved from http://pespmc1.vub.ac.be/papers/Turchin/dialog.pdf
- Turchin, V. F. (1993). The Cybernetic Ontology of Action. Kybernetes, 22(2), 10-30. doi:10.1108/eb005960
- Van Benthem, J. (2007). Dynamic logic for belief revision. *Journal of Applied Non-Classical Logics*, 17(2), 129–155. Retrieved from http://www.tandfonline.com/doi/abs/10.3166/jancl.17.129-155
- Varela, F. J. (1979). Principles of Biological Autonomy. North Holland.
- Varela, F. J., Maturana, H. R., & Uribe, R. (1974). Autopoiesis: the organization of living systems, its characterization and a model. *Biosystems*, 5(4), 187–196.
- Vasas, V., Szathmáry, E., & Santos, M. (2010). Lack of evolvability in self-sustaining autocatalytic networks constraints metabolism-first scenarios for the origin of life. *Proceedings of the National Academy of Sciences*, 107(4), 1470–1475. Retrieved from http://www.pnas.org/content/107/4/1470.short

- Veloz, T. (2010). *A computational study of Algebraic Chemistry*. Universidad de Chile, Santiago. Retrieved from http://www.tesis.uchile.cl/tesis/uchile/2010/cf-veloz tg/pdfAmont/cf-veloz tg.pdf
- Veloz, T. (2014). Teoría de organizaciones químicas: un lenguaje formal para la autopoiesis y el medio ambiente. Autopoiesis: Un concepto vivo. (Razeto-Barry, P. & Ramos-Jiliberto, R.). Santiago, Chile: Editorial Nueva Civilización.
- Veloz, T., Razeto-Barry, P., Dittrich, P., & Fajardo, A. (2014). Reaction networks and evolutionary game theory. *Journal of mathematical biology*, 68(1-2), 181–206. Retrieved from http://link.springer.com/article/10.1007/s00285-012-0626-6
- Veloz, T., Reynaert, B., Rojas, D., & Dittrich, P. (2011). A decomposition theorem in chemical organizations. Proc. of European Conference in Artificial Life (in press). LNCS Springer. Retrieved from https://mitp-web2.mit.edu/sites/default/files/titles/alife/0262297140chap123.pdf
- Von Foerster, H. (1960). On self-organizing systems and their environments. *Self-organizing systems* (pp. 31–50). Retrieved from http://e1020.pbworks.com/f/fulltext.pdf
- Walker, B., Holling, C. S., Carpenter, S. R., & Kinzig, A. (2004). Resilience, adaptability and transformability in social–ecological systems. *Ecology and society*, *9*(2), 5.
- Whitehead, A. N. (1978). Process and Reality: An Essay in Cosmology Ed. David Ray Griffin and Donald W. Sherburne. Free Press, New York.[PR].