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Beyond planetary-scale feedback self-regulation: Gaia as an autopoietic system

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ABSTRACT

The Gaia hypothesis states that the Earth is an instance of life. However, appraisals of it tend to focus on the claim that life is a feedback self-regulator that controls Earth's chemistry and climate dynamics, yet, self-regulation by feedbacks is not a definitive characteristic of living systems. Here, we consider the characterization of biological systems as autopoietic systems (causally organized to self-produce through metabolic efficient closure) and then ask whether the Gaia hypothesis is a tractable question from this standpoint. A proof-of-concept based on Chemical Organization Theory (COT) and the Zero Deficiency Theorem (ZDT) applied on a simple but representative Earth's molecular reaction network supports the thesis of Gaia as an autopoietic system. We identify the formation of self-producing organizations within the reaction network, corresponding to recognizable scenarios of Earth's history. These results provide further opportunities to discuss how the instantiation of autopoiesis at the planetary scale could manifests central features of biological phenomenon, such as autonomy and anticipation, and what this implies for the further development of the Gaia theory, Earth's climate modelling and geoengineering.

1. Introduction

In the attempt to detect life on Mars (Hitchcock and Lovelock, 1967; Lovelock, 1965), the observation that Earth's atmosphere is a far-from-chemical-equilibrium product of metabolic activity led to the formulation of the Gaia hypothesis (Lovelock, 1972, 1979; Lovelock and Margulis, 1974). The Gaia hypothesis states that the Earth is an instance of life¹ (Lovelock, 1988, 2003a).

The pre-Gaian seminal contributions of Lovelock-Margulis's precursors Hutton, Vernadsky and Bogdanov, the father of geology, founder of the concept of biosphere and of systems theory (tektology) respectively, are quite important towards the Earth System thinking, but also towards the unifying ideas of geology and biology (Rispoli, 2020). While Hutton described the Earth as "not just a machine but also an organized body as it has regenerative power", Vernadsky (1945) suggested that "life is not a form of energy and is not merely a geological force, rather it is the geological force". Bogdanov saw that life and Earth constitute one complex system (Rispoli, 2020). Although these ideas are precursors towards a living Earth standpoint, it is nevertheless unclear whether they were key to the Gaia hypothesis formulation.

What is known is that the formulation of the Gaia hypothesis followed one of the key concepts that Schrödinger developed as an answer to the 'What is Life?' question: *negative entropy*² (Schrödinger, 1945). In Schrödinger's words, through this "marvellous faculty, [...] a living organism [...] 'feeds upon negative entropy' [...] to compensate the entropy increase it produces by living and thus [...] maintain[s] itself on a stationary

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¹ Here we refer to the term 'life' in reference to the following notion: "*life is not a property of living beings, the word life only evokes or names an invented abstract entity that we claim that must be there to sustain the living of a concrete singular living being*" (Maturana 2011, p. 147). That is, we consider life = living unity/system, an individual organism.

² "if I had been catering for them [physicists] alone I should have let the discussion turn on free energy instead. It is the more familiar notion in this context. But this highly technical term seemed linguistically too near to energy for making the average reader alive to the contrast between the two things" (Schrödinger, 1945).

and fairly low entropy level" (Schrödinger, 1945, p. 73). The Gaia hypothesis seizes on this explanatory framework to extend Schrödinger's characterization of living systems, hitherto pertaining solely to cells or multicellular organisms, up to the planetary scale (Lovelock, 1987; Margulis, 1990). Thus, its formulation involves fundamentally the Schrödinger's question "What is Life?" (Schrödinger, 1945), as Lovelock stated: "What is Life? [...] was, I would say, the book that most influenced my own thinking" (Lovelock, 1986, p. 646), or as the title of Margulis and Sagan's own book has (1995) in reference to Schrödinger's question. That is, different from the idea of unifying geology and biology from pre-Gaian precursors, the question 'What is Gaia?' amounts or it is equivalent to Schrödinger's question, 'What is Life?'. Hence, answer what Gaia is requires going beyond the notions of organism-environment, biotic-abiotic, biosphere-geosphere and/or biology-geology coupling. In a planetary context it is metabiotic (Clarke, 2020a). As Lovelock usually refers to it; "a single living entity capable of [self] maintaining [...] and endowed with faculties and powers far beyond those of its constituent parts" (Lovelock, 1979). Therefore an operational explanation of what life is, hence, the distinction between the living and the non-living is critical to taking the Gaia hypothesis at face value.

However, although biological systems in general can be recognized phenomenologically by empirical means and Schrödinger's free energy (negative entropy) is a fundamental piece of the puzzle, there is still no generally agreed answer to 'What is Life?' (Cornish-Bowden and Cárdenas, 2020). This indicates why the Gaia hypothesis, while always controversial and much disputed, has also grown unclear (Kirchner, 2002; Kleidon, 2002, 2004; Lenton and Wilkinson, 2003; Lovelock, 2003b; Margulis, 1993; Schneider, 1986; Schneider et al., 2004; Schneider and Boston, 1992; Volk, 2003). Moreover, the explanatory scope of current Gaia theory³ as purveyed by Earth scientists or Darwinists confines the Gaia hypothesis to its Darwinization (as expressed within the tenets of the modern synthesis's adaptationist programme of evolution with or without natural selection) or its mechanization (expressed with the tenets of the cybernetics, dynamical systems theory and self-organized far-from thermodynamics equilibrium) to fit the notion that Gaia is not a living phenomenon per-se, but an epiphenomenon or the effect of the sum of living systems on planetary feedbacks self-regulation (Rubin and Crucifix, 2019). Yet, self-regulation by feedbacks is not a definitive characteristic of living systems (Maturana, 2011; Rosen, 1985b).

Thus, these approaches have diverted attention and finally omitted the use of a universal generic characterization common to all living systems (Bernard, 1974; Friston, 2013; Maturana and Varela, 1980; Rosen, 1991; Schrödinger, 1945), to make the Gaia hypothesis tractable from a scientific standpoint. This paper shows that Gaia hypothesis is tractable from the clear-cut and operationalizable autopoietic characterization of biological systems. In Section 2, we outline the autopoietic characterization of living systems as refined by recent advances in metabolic theory. In section 3, we develop the thesis of Gaia as an autopoietic system and in section 4, we test it by applying chemical organization theory (COT) and the zero deficiency theorem (ZDT) in a simple but representative Earth system reaction network. Finally, section 5 discusses some key concluding remarks of the central feature of the autopoietic organization-autonomy-as inherent in Gaian behaviours and the implications of it for the Earth's climate modelling, geoengineering and the future of Gaia theory.

2. Living systems, autopoiesis and metabolic closure

The father of physiology, Claude Bernard, noted that "all the vital processes, varied as they are, have only one object, to conserve the uniformity of ... the internal milieu" (Bernard, 1974, p. 84). Since then, one of the common features broadly accepted as important to recognize living systems is how, despite forcing by environmental fluctuations and energic dissipation, they precisely conserve the uniformity of their internal milieu (their physiological boundaries) through the maintenance of their organization. Upon this notion of organization, later thinkers constructed the idea of the uniformity of the internal milieu primarily as fixing internal parameters at a 'set point' and using feedbacks to 'regulate' the values of these set-point parameters against deviation-errors. Walter Cannon named his error-correcting theory of regulation 'homeostasis' - stability through constancy (Cannon, 1929). Therefore, biological organization was thought to be captured by the concept of homeostasis, and its mathematical formulation was consolidated with the development of cybernetic systems and control theory. The core of these early cybernetic notions was stability through self-regulation by feedback mechanisms in which a system's behaviours seem, but are not, to be internally produced and automatically goal-oriented (Ashby, 1958; von Foerster, 1952; Wiener, 1948).

However, for an alternative recognition of biological organization framed in terms of self-production by metabolic closure (autopoiesis and the (M,R)-system) (Letelier et al., 2003, 2011; Maturana and Varela, 1980; Rosen, 1991), the feedback is a reactive response (Louie, 2017; Nadin, 2010; Rosen, 1985a, 1985b). The feedback is an error-counteracting response, which takes place only when there is external perturbation sufficient to make the system's parameters deviate from externally pre-defined 'set points'. The feedback reactive response, thus, cannot accommodate constitutive anticipative and autonomous biological behaviour proper to biological systems (Louie, 2017; Maturana, 2011; Nadin, 2010; Rosen, 1985a, 1985b). When we consider the biological organization framed in terms of self-production by metabolic closure⁴ the conservation of physiological boundaries and maintenance of stability does not take place by error-correcting feedback responses, but instead, through cognition, autonomy, anticipation and/or active inference (Friston, 2013; Maturana, 2011; Rosen, 1985a; Varela, 1979). These central features of living systems, which are inherent to their metabolic closure and self-producing organization (Bich and Arnellos, 2012; Kirchhoff et al., 2018; Letelier et al., 2011; Louie, 2012, 2017; Maturana, 1980; Nadin, 2010; Rosen, 1991) are the means by which they maintain stable operations in face of fluctuations, dissipation and the second law of thermodynamics.

While the (M,R)-system outlines a formal system of self-producing organization of biological systems through metabolic efficient/operational closure, autopoiesis outlines the *causal realization* of it as a natural system. That is, autopoiesis is "not a philosophical proposition of a formalization of the phenomenon of life" (Maturana, 2011, p. 144). Nor is it a theory, model, or principle of biological organization. Rather, it "describes the molecular ... [dynamics] ... taking place in the realization of the living of living systems [such that] the molecular autopoiesis of a cell is its living in the continuous realization of their self-production without the participation of any organizing principle" (Maturana, 2011, p. 144, brackets are ours). Autopoiesis is characterized by a) self-production as "a network of processes of production (transformation and destruction) of components which: (i) through their interactions [openness to the flux of matter and energy] and transformations continuously regenerate and realize the network of processes (relations) that produced them; and (ii) constitute it (the system) as a concrete unity in space in which they (the components) exist by specifying the topological domain of its realization as such a network" (Maturana and Varela, 1980, p. 78, brackets are ours)

³ The distinction between the Gaia hypothesis, Gaia theory, and the Gaia phenomenon is crucial in determining that Gaia hypothesis has not been taken, so far, at face value (see Rubin and Crucifix 2019).

⁴ Closure does not refer to closed thermodynamic systems, but rather, to a circular organization of *efficient causes* (operators, constraints or boundary conditions) generated continually and internally within the system, an organization that fundamentally differs from biochemical or biogeochemical cycles in which circular organization refers to *material causes* (for details see Kauffman, 2019; Louie and Poli, 2011; Montévil and Mossio, 2015).



Fig. 1. A) Representation of Autopoietic operational -efficient- closure. Autopoiesis or self-production occurs when a molecular reaction network produces itself (thin central arrow) and a semipermeable boundary, which specifies the topological dynamics of the metabolic reaction network (arrows in both directions). Metabolic closure results from the interrelation between the metabolic network and the boundary. Metabolic closure renders an autopoietic system capable of selecting the matter and energy that enters and exits the system (dotted arrows). In this sense an autopoietic system is also an open system in relation to its environment [Adapted from Varela 2000, p. 55)] B) A schematic representation of Gaia as an autopoietic system organized on a planetary scale. The interdependence between the geo-hydro-biospheric metabolic network and atmosphere (arrows in both directions), in the sense that the geo-hydro-biospheric metabolic reaction network produces itself (thin central arrow) and the main components of the atmosphere (the Earth system's semipermeable boundary), and the atmosphere reciprocally specifies and allows the dynamics of the geo-hydro-biospheric metabolic reaction network, describes how Earth's autopoietic organization takes place on a planetary-scale.

(Fig. 1A), and by b) <u>metabolic (operational) closure</u>: "a closed domain of operational relations specified only with respect to the system organization that these relations constitute, and thus it defines a space whose dimensions are the relations of production of the components that realize it as a concrete biological unity" (Maturana and Varela, 1980, p. 97)(Fig. 1A). Thus, a biological system is alive when the circular efficient causality of the autopoietic organization is continuously realized.

Some authors have further established formal connections between autopoietic systems, (M,R)-systems (Letelier et al., 2003; Nomura, 2007; Zaretzky and Letelier, 2002; Rubin, 2017; Rubin and Crucifix, 2019), the minimization of variational free energy (active inference)(Friston, 2013; Rubin, 2017; Ramstead et al., 2018, Rubin et al., 2020) and chemical reaction networks (Contreras et al., 2011; Kreyssig et al., 2012; Veloz et al., 2011). Here we focus on the latter.

The relationship between autopoietic systems and chemical reaction networks dates back to the algorithmic implementation of what is known as computational autopoiesis (McMullin, 2004). In its initial implementation by Varela et al. (1974), computational autopoiesis is presented as a model using a rule-based system to simulate a reaction network with discrete dynamics in a two-dimensional grid. This implementation shows that a dynamical system based on simple rules can spontaneously develop a self-produced boundary. Around the same time, the foundational work of Feinberg and Horn (1974) formulated the zero deficiency theorem (ZDT), which links the structure of a reaction network to its ability to reach an asymptotically stable state. *Deficiency zero* basically means that such a network can regenerate autonomously all the complexes used up by its reactions from complexes produced by other reactions (see appendix A). ZDT also introduces the notion of complexes, which represent the collections of molecular species required to trigger (or produced by the occurrence of) reactions. If a reaction network is weakly reversible, it is possible to ensure that the differential equations that capture the reaction network's time evolution exhibit a dynamically stable regime for any choice of the kinetic parameters. ZDT is striking because it links two structural conditions (weak reversibility and zero deficiency), which are extremely simple to check for even with large reaction networks, to a dynamical property (asymptotic stability) that is extremely difficult to check for even with reaction networks of moderate size. For our purposes, the interest here is that the fundamental idea behind ZDT is similar to the self-production condition of autopoietic systems (Contreras et al., 2011; Kreyssig et al., 2012; Veloz et al., 2011). A tremendous number of explorations linking structure and stability of a similar kind have followed since the introduction of ZDT, resulting in the well-established deficiency theory of chemical reaction networks (Feinberg, 2019).

A related but different approach to deficiency theory starts from the idea that instead of focusing on the general structural properties of the reaction network (which approach neglects dynamic properties such as the values of the kinetic constants), one can focus on the possible reaction pathways that are dynamically feasible, and impose conditions on them that can be linked not only to stability, but to any desired behaviour of the network, such as increased production of biomass, degradation of toxic molecules, or resilience under kinetic perturbations, etc. This area of study is called Pathway Modelling (Rajvanshi and Venkatesh, 2013). It would be impossible to list even the most remarkable contributions in this monumental body of literature, but for the interested reader we point to the fact that there are, among others, several variants in this field, such as flux balance analysis (Orth et al., 2010), metabolic structural control analysis (Reder, 1988), metabolic pathway analysis (Klamt and Stelling, 2003), and structural kinetic modelling (Steuer et al., 2006). All these frameworks exploit the structures that pathways can take and relate them to some aspect of the dynamics of the reaction network. In the last decades there have been huge efforts to provide a unified reaction network theory that integrates all that is known in biochemistry (Kanehisa, 2002; Le Novere et al., 2006). Hence, pathway modelling can be applied to large-scale phenomena, and some recent efforts along this line have recently been proposed for biogeochemistry (Stüeken et al., 2016; Zerkle and Mikhail, 2017), attracting special attention in the context of the origin of life (Cleaves et al., 2019).

Chemical organization theory (COT) (Dittrich and Di Fenizio, 2007), stemming from the seminal work of Fontana and Buss (1994) who first used the untyped λ -calculus as a formalization of autopoietic systems, is one of the approaches that links the structure of reaction networks to their dynamics. COT has developed directly from pathway modelling and deficiency theory, and establishes a formal criterion for determining a reaction network to be operationally closed and stoichiometrically self-maintaining (see Appendix A). The parts of the reaction network that fulfil these two conditions, called organizations, contain all stable states that the reaction network can reach in the long term: For any long-term steady state that the reaction network reaches, the molecular species whose concentration is larger than zero-that is, the active part of the network—will be a chemical organization unit (Dittrich and Di Fenizio, 2007). However, depending on the kinetic constraints such as reaction rates or boundary conditions, some organizations become feasible but others not (Peter et al., 2010). Organizations can hence be characterized in terms of the possible ways, given particular kinetic constraints, that the consumed species (molecular components) are produced by reaction pathways. When comparing COT and ZDT, we observe that ZDT provides a more solid, but more stringent, criterion for identifying whether a reaction network reaches self-maintenance by metabolic closure. COT has been compared to frameworks such as (M,R)-systems and autocatalytic networks (Contreras et al., 2011; Hordijk et al., 2018) as a suitable method to explore the internal structures within networks that generate autopoietic operations, as represented both analytically and algorithmically by closure and self-maintenance (Centler et al., 2008; Speroni di Fenizio, 2015; Veloz et al., 2018).

Given the limitations of characterizing a living system as a mere feedback self-regulator, it has been suggested that the autopoietic organization presents the proper biological ground to address the Gaia hypothesis (von Foerster, 1975).⁵ Margulis stated: "Whereas the smallest recognizable autopoietic entity ... is a tiny bacterial cell the largest is Gaia' (Margulis, 1990, p. 861); 'planetary physiology ... is the autopoiesis of the cell write large" (Margulis and Sagan, 1995, p. 54). Numerous authors agree that autopoiesis is a plausible scenario for the organization of the Earth system (Capra, 1996; Capra and Luisi, 2014; Clarke, 2020a; Jantsch, 1980; Kazansky, 2002; Levchenko et al., 2012; Margulis, 1997; Margulis and Sagan, 1986; Onori and Visconti, 2012; Rubin and Crucifix, 2019; Sahtouris, 1996). However, so far, these authors appeal to intuition rather than to formal systems of inference. This has left the door open for some authors to downplay Margulis' notion of an "autopoietic Gaia" as an "Aquarian poetic vision" (Doolittle, 2017) rather than a scientific research programme. Thus, a serious examination of the question whether or not a rigorous relation exists between Gaia and autopoiesis is called for. In the next section, we develop arguments for the autopoietic, hence metabolic-closure, approach to the Gaia hypothesis.

3. Autopoiesis, Earth system and the Gaia hypothesis

The *reactive* paradigm of cybernetic control systems (Rosen, 1985a, 1985b) grew in popularity in the scientific thinking of the 1960s and 1970s and, quite naturally, Lovelock and Margulis (1974; 1974) provided the cybernetic standpoint of homeostasis as an explanatory framework to address the Gaia hypothesis. Later, Lovelock and Margulis acknowledged that Gaia returns to a *homeorhetic trajectory*, not to a homeostatic state.⁶ In this sense, "*Gaia … like the physiology of an embryo, is more homeorhetic, than homeostatic*" (Margulis, 1990, p. 866), and instead of homeostasis, "*Gaia's history is characterized by homeorhesis with periods of constancy punctuated by shifts to new, different states of constancy*" (Lovelock, 1991, p. 141).

Lovelock and Margulis also recognized the asymmetry between internal and external conditions as crucial to explain Gaia from a biologically grounded standpoint: "Different from a physicist, biochemist and neo-Darwinist's view ... [Gaia is] ... a bounded system that is open to a flux of energy and matter, and that is able to keep its internal conditions constant, despite changing external conditions" (Lovelock, 1991, p. 29, brackets are ours); "Cells and Gaia display a general property of autopoietic entities: as their surroundings change unpredictably, they maintain their structural integrity and internal organization" (Margulis, 1997, p. 267).

One of the conditions for the existence of the asymmetry between internal and external conditions in an autopoietic system is a selfproduced boundary (Maturana, 1980; Varela, 1979), which formulation resonates with Schrodinger's query, 'how can the events in space and time which take place within the spatial boundary of a living organism be accounted for by physics and chemistry? (Schrödinger, 1945, p. 2), which has also been one of the bases for formulating the Gaia hypothesis (Margulis and Lovelock, 1974, 1975). Thus, addressing the Gaia hypothesis from the biological-organizational standpoint amounts to recognizing a system that "specifies its own boundaries ... that defines the limits of the system in the same domain in which it specifies them through relations of production of components that generate these relations and define it as a unity" (Maturana and Varela, 1980, pp. 108–109). Thus, to determine whether Gaia is an autopoietic system, it is necessary to determine to what extent the Earth's atmosphere (the boundary) is self-produced by relations of molecular production of Earth's biotic and abiotic components (a planetary reaction network), and whether the latter specifies the topological dynamics of the former.

Today, it is generally accepted that the production of the principal components of the troposphere (the habitable boundary of the atmosphere), mainly, the cloud-forming aerosols (Dani and Loreto, 2017; Fröhlich-Nowoisky et al., 2016; Hughes et al., 2014), greenhouse gases (Conrad, 2009) and oxygen (Falkowski, 2006) are immediately related to metabolic activities (Lenton et al., 2018; Margulis and Lovelock, 1974). Stratospheric ozone, which blocks mutagenic UV rays from reaching the Earth surface, also is metabolically derived from oxygen released by photosynthesis (Falkowski, 2006). Most notably, methanogens (Bardgett et al., 2008), sulfate-reducing bacteria (Barton and Fauque, 2009) and subsurface cyanobacteria (Puente-Sánchez et al., 2018), which are the main producers of the main components governing Earth's climate dynamics, are involved in the self-production of the life-supporting and life-supported boundary layers of the atmosphere. Furthermore the chemical elements of the atmosphere derive from the modification, mobilization, and microbial transportation and deposition of geochemical elements of the lithosphere (Atekwana and Slater, 2009; McGenity, 2018; Tornos et al., 2018). These productions also involve the life-dependent hydrosphere (Harding and Margulis, 2009) and rely upon the entire integration of Earth dynamics through biogeochemical cycles (Falkowski et al., 2008). That is, there is evidence that the Gaia's boundary (the atmosphere) has been produced continuously by geometabolism (Lenton et al., 2018; Margulis and Lovelock, 1974) that at the same time has changed its topology specified by type of atmosphere⁷ (reductive or oxidative) (Falkowski, 2006).

Indeed, recent works that support the idea that metabolism involves not just the biosphere, but also the atmosphere, the hydrosphere, and the lithosphere⁸ (Goldford and Segrè, 2018; Jelen et al., 2016; Kim et al., 2019), therefore, a self-referential specification of the atmosphere from and to a planetary metabolic reaction network. This offers a plausible account of self-producing metabolic closure, hence, an autopoiteic organization on a planetary-scale (Fig. 1B). In other words, the continuous metabolic fabrication of the atmosphere (troposphere and stratosphere) in the same domain in which it continuously allows the metabolic reaction network (relations of production of components) amounts to recognizing the existence of a self-producing organization of the planetary domain, and hence, the recognition of Gaia as an autopoietic system (Fig. 1B). In the next section, we shall prove this, on formal theoretical grounds, by applying COT and the ZDT to a representative Earth's molecular reaction network.

4. Gaia, COT and ZDT

The seminal paper by Feinberg and Horn (1974) first presenting the Zero Deficiency Theorem (ZDT) discussed the possibility of applying the

⁵ For historical reasons, Heinz von Foerster, one of the main founders of firstand second-order cybernetics, was the first author, long before Doolittle and Dawkins, to publish not only this constructive critique of the Gaia hypothesis, but of the unnecessary relationship of first-order cybernetics with it.

⁶ Waddington preferred to distinguish between homeostasis and *homeorhesis*, because in a living system as opposed to a mechanical regulator what "*is being held constant* [uniform] *is not a single parameter but is a time-extended course of change, that is to say, a trajectory*" (Waddington, 1968, p. 12, p. 12).

⁷ Here we refer to the type of biospheres that has been changing and will surely change throughout the Gaia's ontogeny (see Sagan, 1990).

⁸ This aligns with Morowitz's arguments: "all organisms interact [are connected] through the gas-phase components that they take up from and give off to the atmosphere ... life, as individual organisms, persists over long geological periods only because of integrated processes of the atmosphere, the hydrosphere, the lithosphere, and the biosphere. In that sense life is a property of planets rather than individual organisms. This thought has been expressed in [...] the Gaia hypothesis" (Morowitz, 1993, pp. 5–6, brackets are ours). And "the metabolic character of life is a planetary phenomenon, no less than the atmosphere, hydrosphere, or geosphere" (Morowitz et al., 2008, p. 8).

ZDT far beyond cellular reaction networks, to ecological or other kinds of systems, and suggested that some ZDT systems are stable because they "*have their roots in ecological considerations*" (Feinberg and Horn, 1974, p. 785). For its part, COT has been applied to the characterization of self-producing behaviours not only in biochemical but also in ecological systems, and has recently been proposed as a general framework for the modelling of systems in which meta-structures operating at higher time-scales emerge (Veloz and Razeto-Barry, 2017). Our interest in ZDT and COT for an autopoietic account of the Gaia hypothesis lies here.

However, for a preliminary inference applying COT and ZDT with regard to Gaia as an autopoietic system, we should consider that all physical embodiments of autopoiesis, in any cellular, metacellular or planetary domain, must always be molecular: "There are autopoietic systems of higher order, integrated by [populated by] lower order autopoietic unities that may not be the components realizing them as autopoietic systems ... there are higher order autopoietic systems whose components are molecular entities produced through the autopoiesis of lower autopoietic unities" (Maturana, 1980, p. 53, brackets and underline are ours). This molecular realization of living systems is also pointed out as the realization of Gaia (Williams, 1996; Volk, 2004). Yet, this molecular embodiment does not mean that Gaia may be reduced altogether to the molecular phenomena of chemical reaction networks. Rather, it simply points out that the autopoietic organization of biological systems is an all-or-nothing phenomenon at the molecular level (Maturana, 1980). That is, life happens or not; Gaia occurs or not thanks to its autopoietic molecular organization. For example, although prokaryotic cells and metacellulars have different 'orders' of autopoietic organization, the 'livingness' of both is dependent of molecular components (e.g. CO2, CH4, CO, O2) regardless of their radically different phenomenology. Moreover, the Earth's climate dynamics largely depends on how such molecular components (CO_2, CH_4, O_2) are cycled by the interactions among enzymatic-constraint electron transfer reaction networks in the atmosphere, hydrosphere and geo-lithosphere (Falkowski, 2006). These networks act as planetary wires, ferrying oxidants and reductants across the Earth, which activities determine its unique habitable redox state (Jelen et al., 2016). As such, COT and ZDT provide fundamental approaches for testing the autopoietic molecular organization of planetary systems.

Here is a constructive method with the potential to identify whether a reaction network can be organized as an autopoietic system, in the context of the Gaia hypothesis. To test it, we selected—according to the geological history of the Earth (around 4.5 billion years) and of the evolution of microbial metabolisms (more than 3.5 billion years)—some critical molecular components of the Earth system and their geochemical (abiotic) and biochemical (biotic) reactions (Table 1). To study the generative properties of potential autopoietic organizations, the inflow of molecular component resources contains elements that are known, by the geological record, to be present from the Hadean-Archean Earth up to the Anthropocene epoch (Jelen et al., 2016; Schopf, 1983). Our aim is to show a proof-of-concept of the Gaia hypothesis through a metabolic-closure approach, that it is possible to identify a sequence of increasingly complicated reaction networks that plausibly describe the dynamical organization of Gaia as an autopoietic system.

Our analysis consists of identifying the organizations of the Earth system's reaction network shown in Table 1, and of computing the deficiency of such organizations, with the aim of determining whether or not their stability is certain in any dynamical setting (zero deficiency), or only under particular kinetic constrains (not zero deficiency).

Fig. 2 shows the COT analysis of the Earth system reaction network described in Table 1. It possesses four closed sets, of which three are self-maintained organizations. These may represent three structural scenarios of Gaia's ontogeny. The entire network (in cyan) could represent the Phanerozoic period during which the CO_2 , CH_4 , O_2 , H_2 O components, those largely involved in the dynamics of the atmosphere and hydrosphere, hence in the Earth's climate system, are self-produced. Other components such as CH_3 COOH (acetic acid), also fundamental

Table 1

A reaction network of molecular production of the Earth system's molecular components. In the left of the table are the stoichiometric equations and in the right the corresponding process of molecular production (synthesis and catalysis). This small but representative Earth's reaction network involves biotic and abiotic reactions that are known, by the geological record, to be present from the Hadean-Archean eon up to the Anthropocene epoch. The stoichiometric equations have been selected according to i) the geological records (around 4 billions of years ago), ii) the recapitulation of microbial metabolic evolution and diversification, and iii) the main greenhouses of the atmosphere (H₂O, CH₄,CO₂) and the reactions taking place at the interface between the lithosphere and hydrosphere. Some of the biotic reactions can happen abiotically, but only with high amounts of activation energy. For example, the reaction r_1 requires more than 150 °C, which is plausible abiotically around volcanic and vents activity.

Stoichiometric equations	Process of molecular production		
$r_1: S + H_2 \rightarrow H_2S$	Abiotic or Biotic hydrogen sufide synthesis		
$r_2:12H_2S + 6CO_2 \rightarrow C_6H_{12}O_6 + 6H_2O + 12S$	Biotic anoxic hydrogen sulphide chemosynthesis		
r_3 :2FeO + 3CO ₂ + H ₂ O \rightarrow Fe ₂ (CO ₃) ₃ + H ₂	Abiotic geochemical ferrous iron carbonate synthesis		
$r_4:CO_2 + 2H_2 \rightarrow CH_2O + H_2O$	Biotic anaerobic chemoautotrophic respiration		
r_5 :HCO ₃ + 4Fe(II) + 10H ₂ O \rightarrow CH ₂ O + 4Fe(OH) ₃ + 7H ⁺	Biotic anaerobic phototrophic ferrous iron oxidation		
$r_6:CO + H_2O \rightarrow CO_2 + H_2$	Biotic carboxydotrophogenesis		
$\begin{array}{l} r_{7}\text{:}3\text{CH}_{2}\text{O} + \text{H}_{2}\text{O} \rightarrow \text{CH}_{3}\text{COO}^{-} + \text{CO}_{2} + \\ 2\text{H}_{2} + \text{H}^{+} \end{array}$	Biotic fermentation		
$r_8:2\text{CO}_2 + 4\text{H}_2 \rightarrow \text{CH}_3\text{COOH} + 2\text{H}_2\text{O}$	Biotic anaerobic acetogenesis		
r_9 :CH ₃ COOH \rightarrow CH ₄ + CO ₂	Biotic anaerobic heterotrophic methanogenesis		
$r_{10}:CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O$	Biotic anaerobic chemoautotrophic methanogenesis		
$r_{11}:CH_4+SO_4^{2-} \rightarrow HCO_3^- + HS^- + H_2O$	Biotic reverse methanogenesis		
$r_{12}:CO_2 + H_2O \rightarrow CH_2O + O_2$	Biotic photosynthesis		
r_{13} :2H ₂ + O ₂ \rightarrow 2H ₂ O	Abiotic atmospheric water synthesis		
$r_{14}:3\mathrm{H}_2 + \mathrm{O}_2 + \mathrm{S} \rightarrow 2\mathrm{H}_2\mathrm{O} + \mathrm{H}_2\mathrm{S}$	Biotic aerobic sulfate reduction		
$r_{15}:2\mathrm{H}_{2}\mathrm{S}+\mathrm{O}_{2}\rightarrow 2\mathrm{S}+2\mathrm{H}_{2}\mathrm{O}$	Biotic aerobic chemoautotrophic respiration		
$r_{16}:C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$	Biotic aerobic heterotrophic respiration		

to all forms of life due to its relation with coenzyme A and with the metabolism of carbohydrates and fats, and HCO3, the key component for the ocean pH, are also self-produced. This network includes not only the other cyan and the green reaction networks, but also part of the red reaction network (Fig. 2). Interestingly, the red reaction network is closed but not self-maintaining, thus not an organization. However, the larger cyan network (whole network in Fig. 2B) seems to have gained the property of the red scenario through the incorporation of H_2 into its organization. Indeed, most of the reactions of the whole network organization produce H_2S directly and indirectly. This component is highly abundant since the late Archean Earth (Abramov and Mojzsis, 2009) and key in the current sulfur cycle. It is often produced from the microbial breakdown of organic matter in anaerobic conditions by sulfate-reducing bacteria, but also by volcanic activity. That is, the presence of H_2S is indicative of volcanic activity, and thus of tectonic, continental drift and geomorphological changes, which took place from the Proterozoic to the current phase of the Phanerozoic period. It has been proposed that the hydrological cycle itself is life-dependent, a Gaian contrivance established to prevent the escape of H_2 into space and thus out of the Earth system (Harding and Margulis, 2009). Additionally, the structure of the inner and outer layers of the continental plates appears to have been dominated by water-dependent continental drift (Lowman and Lowman, 2002). In short, the whole network, although very simple, has key self-produced elements by metabolic closure as represented by COT and may also represent current evolutionary changes in the Earth's climate system. So far, this reaction network can be considered as a toy model to represent Gaian autopoiesis.

The self-producing organization shown in cyan (Fig. 2B) shows a previous and intermediate scenario, which may correspond to the

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Fig. 2. A) The self-producing organization of the Earth system's molecular reaction network depicted by COT in the scenario in which $\emptyset \rightarrow C_6H_{12}O_6$ (glucose) is a necessary part of inflow. Circular nodes represent the component or chemical species (resources), while white square nodes represent the reactions. The yellow squares correspond to reactions associated with biotic activity, and the orange ones, with abiotic activity. Arrows go from reactants to products. Colors differentiate the dynamic properties of the resources. Green represents the inflow, red represents the set of species that, together with the inflow (green), form a closed sub-net that is not self-maintained. Cyan represents the species that together with the inflow (green) form the closed sub-network that is an organization. B) Structurally relevant sub-reaction networks of the COT analysis. The green sub-network corresponds to the inflow. The red sub-network corresponds to a closed but not self-maintaining system, thus not an organization, but still interesting because it reaches metabolic closure, but not self-production. The two cyan sub-networks correspond to two increasingly complex organizations. The one below is an intermediate scenario of the whole network, which represents today's Earth system.

Proterozoic eon, and hence to a plausible structure in this geological time-scale. Specially, the presence of CH_4 and O_2 and more sugars and acids can be explained by the transition from the Archean to the Proterozoic eons (from 4 to 2.5 billion years ago). In this transition, solar radiation alone was too weak (Bahcall et al., 2001; Gough, 1981) to maintain liquid water and ice-free conditions on Earth (Sagan and Mullen, 1972), and one plausible explanation is the warming produced by higher greenhouse gas concentrations in the atmosphere (Catling and Zahnle, 2020; Goldblatt and Zahnle, 2011). This greenhouse effect, by which greenhouse gases trap heat reflected from the Earth's surface, precisely involves CH_4 , which has stronger radiative forcing than CO_2 and is almost entirely metabolically produced (Conrad, 2009). CH₄ could have provided 10–12 °C of surface warming (Haqq-Misra et al., 2008) with levels ranging 10^2 to 10^4 times higher than modern amounts (Catling and Zahnle, 2020). The occurrence of O_2 in the self-sustained organization of the Earth system reaction network can be related to the shift from reductive to oxidative atmospheres-due to the advent of photosynthesis in the middle to late Archean period. The effective elimination of the methane greenhouse resulted in occasional glaciations and thus in the increase of planetary albedo related to climatic compensation against the increment of solar radiation. Moreover, the oxidative atmosphere and photosynthesis correspond to heterotrophic metabolism, and hence to the self-production of sugars and acids.

The smallest self-producing organization is formed by the inflow FeO, CO, SO_4^{2-} , FeII and $C_6 H_{12}O_6$ (in green), and suggests a planetary semi-chemoautotrophic scenario dominated by iron-sulfur and carbon, and hence a plausible incipient structure of Gaian autopoiesis. The role of iron-sulfur minerals in catalysing prebiotic reactions has been recognized as a potential pathway to form simple organic molecules, the first metabolic cycles (Wächtershäuser, 1990), and hence on carbon fixation (Fuchs, 2011). It is possible that this organization was a precursor to Gaia, since there is reasonable paleontological evidence of iron-sulfur availability in the early Archean Earth (Hazen, 2013) related to short peptide folds in primitive amino acids sequences (Eck and Dayhoff, 1966). Indeed, the contemporary planetary-scale electron-transfer reactions (Falkowski et al., 2008) employs no more than 400 oxidoreductase genes (evolved from deeply branching Precambrian lineages of methanogens) (Fuchs, 2011) of which approximately 60% contain Fe in the active site (Harel et al., 2012). This development is crucial for the evolution of the primitive pathways of carbon fixation

(Russell and Martin, 2004), and thus to the future Gaian aspects of Earth's climate dynamics.

For the ZDT test, we first notice that none of the three parts of the network that form an organization are weakly-reversible. Hence the ZDT does not apply to any of them. For a more detailed analysis, in Table 2, we show the values required to compute the deficiency of the organizations (see Appendix A). The only organization with zero deficiency is the inflow. If we had assumed outflow reactions for the inflow species, then the inflow would have been (trivially) weakly reversible and thus the zero deficiency theorem would have applied to it. The other two organizations (the cyan sets in Fig. 2B) have non-zero deficiency. Indeed, for the intermediate organization we have deficiency 2, and for the whole network the deficiency is 5. Hence, the most remarkable result here is that the non-trivial organizations are neither weakly reversible nor have zero deficiency. Even in case we add outflow reactions to the inflow, deficiency will remain different to zero for the cyan organizations in Fig. 2. This can be observed by simple inspection of the reactions in Table 1, and moreover, for the largest organization, the deficiency is greater than for the intermediate case. This strong absence of zerodeficiency theorem applicability occurs because the self-production of these networks does not occur at the level of complexes but at the level of molecular species, and such processes of self-production are distributed across the reaction pathways. The latter is an indication that the dynamical stability of Gaia over geological periods is due to appropriately well-linked, but not trivial, reaction pathways that self-produce the system.

Further research should concentrate on a more extended reaction network for the Earth system and on quantitative aspects with regard to climate dynamics and the self-producing constraints that allow stability at the level of molecular species in the absence of zero deficiency. However, for the aim of this paper, this proof-of-concept is sufficient to show how Gaia is the realization of self-production by metabolic closure–autopoiesis–across the Earth system.

5. Discussion: is Gaia an autonomous and anticipatory system?

Let us note now that biological autonomy and anticipation, which is given by the metabolic closure of self-production, is both a corollary aspect of the autopoietic organization and a more fundamental state of affairs than feedback self-regulation (Bich and Arnellos, 2012; Kirchhoff

Table 2

Deficiency analysis of organizations found for the organizations of our sample reaction network.

Organization	# reactions	# species	deficiency	# complexes	# of linkage clases	stoichiometric subspace
Whole net	21	20	5	38	17	16
Intermediate	17	18	2	30	13	15
Inflow	5	5	0	6	1	5

et al., 2018; Letelier et al., 2011; Louie, 2012, 2017; Maturana, 2011; Maturana and Varela, 1980; Nadin, 2010; Rosen, 1985a,b; Rubin, 2017; Varela, 1979, 2000). Applying COT and ZDT as two promising operational formalizations of autopoiesis—self-production by metabolic closure (Contreras et al., 2011; Kreyssig et al., 2012; Veloz et al., 2011), we presented a proof-of-concept by which Earth's molecular reaction network satisfies the conditions of an autopoietic organization. This suggests that self-production by metabolic closure may quite plausibly be the case at the planetary scale, and hence can establish a research program of the Gaia hypothesis beyond the feedbacks self-regulation.

Such a program would involve exploring the multiple approaches to metabolic pathway analyses (Klamt and Stelling, 2003; Orth et al., 2010; Steuer et al., 2006) in order to link the structure of Earth's molecular reaction network pathways to its dynamical properties at the various evolutionary scenarios. On the one hand, the latter involves identifying how to describe relevant systemic properties in the framework of pathway analysis such as autocatalysis (Hordijk et al., 2018). On the other hand, these methods could help us to understand the structure of large-scale biogeochemical reaction networks (Kanehisa, 2002; Le Novere et al., 2006), whose fast development needs to be complemented by appropriate and scalable inferential rules to apply metabolic pathway methods.

That is to say, one of the implications for understanding the Earth system from the characterization of autopoietic systems is the difference between structure and organization (Maturana and Varela, 1980; Nomura, 2006). The structure may undergo changes as long as the self-producing organization is preserved (Maturana 1980). Our results suggest that the persistence of Gaia may be associated to the conservation of the Earth system self-producing-autopoietic organization by different scenarios of structural change. Thus, under this framework, the so-called "tipping points" (Lenton et al., 2008) may be regarded as structural changes that so far did not cause the loss of the Earth system autopoietic organization. In other words, the system can go through different structural changes (extreme, abrupt, catastrophic) but preserve its living character-these events can be, so to speak, not fatal if we understand them as structural changes. Indeed, Earth's history has been punctuated by several structural changes associated with massive biodiversity losses (Barnosky et al., 2011), planetesimal impacts, geomorphological and atmospheric composition changes (Falkowski, 2006). However, the Gaia phenomenon has persisted, thus the living character of the Earth system. This touches on the definition of what could be a "critical" disturbance for Gaia. Are the "planetary boundaries" (Rockström et al., 2009) critical for planetary self-producing organization? What sort of perturbations can be disruptive to Gaia's autopoietic organization?

Another implication of Gaia as an autopoietic system is associated with the notion of "Earth stewardship" (Steffen et al., 2018).⁹ In this notion it is assumed that the Earth can be "controlled" to be maintained on a "safe" trajectory by anthropogenic "input" mechanisms. This consists in developing strategies of mitigation and geoengineering to avoid triggering runaway feedbacks and tipping points. Thus, it is based on feedback control theory, the reactive paradigm view of the Earth system. However, our results indicate the Gaia's ability to preserve autonomously its own self-producing organisation through metabolic closure. So, does the "Earth stewardship" could be the same if the Earth is an autonomous system? For example, under the idea of the feedback, it has been proposed to 'mitigate' climate change by releasing sulfate aerosols into the atmosphere to increase the planetary albedo and thus diminish solar warming of the planet. This feedback is intended to compensate for the increase in downwelling long-wave radiation caused by greenhouse gas emissions. However, in an biological -autopoietic- system, the structural change caused by such feedback perturbation is expected to have many correlative changes, not necessarily just the one predicted by the control model (Maturana, 1980; Rosen, 1985a). This implies that Gaia's response to any given perturbation may involve a potentially large number of unpredictable structural changes to preserve the system's autopoietic organisation. Here is a first formal argument for the intuition that solar radiation management may lead to unforeseeable repercussions due to the autonomous Gaian responses of the Earth system. More stringent arguments related to biological organization (Louie, 2020) may have consequences on geoengineering¹⁰ and on the relevance of current simulations of the Earth's climate system (for a brief discussion see section 6 of Rubin and Crucifix, 2019).

In general, autopoietic systems cannot be modelled, hence 'controlled' by using feedback control theory without causing side effects because living systems are not input-output cybernetic systems (Maturana and Varela, 1980; Nomura, 2006). The identification of the autopoietic organization in the Earth system by COT and ZDT suggest reconsidering the control theory approach for one of biological organization (Casti, 2002), hence a shifts on our understanding of the character of Earth system towards autonomy and anticipation. Anticipatory behaviour¹¹ seems to be relevant to any level of biological self-producing organization. From microbes (Mitchell et al., 2009), to fungi (Siegal, 2015), to trees (Calvo and Friston, 2017). For example at the regional scale, the Amazonian trees anticipate the dry season, they bring moist air in from the ocean by increasing their rate of evapotranspiration (Wright et al., 2017) and releasing cloud-forming organic aerosols (Pöhlker et al., 2012). But how could our way of modelling the Earth system change, if anticipation is a Gaian-planetary-phenomenon? Recent advances on Gaia theory may allow us to understand anticipation on a planetary scale by identifying a Markov blanket -autopoieticboundary for the Earth's climate system (Rubin et al., 2020; Rubin and Crucifix, 2017). This suggests that any attempt of "Earth stewardship" may involve making inferences from Gaia's own inference. That is, one would have to understand what kind of anticipatory models Gaia has in

⁹ Margulis writes in a letter on 1989 "The title of your series, Stewardship of the Land, seems repulsively anthropocentric to me, even though your intentions are laudable. We humans aren't stewards of anything exept our flimsy ships, but we are inordinately arrogant...especially scientists (footnote 33 of Clarck, 2020, p. 14)

¹⁰ For a brief epistemological discussion related to the contrast of Gaia as a cybernetic system or as a biological -autopoietic, hence autonomous- system and the implications of geoengineering based on the former idea see (Clarck, 2020b; Givens, 2018; Lovelock and Rapley, 2007; Shepherd et al., 2007).

¹¹ Living systems are cognitive systems with capacities to learn and remember through their ontogeny and phylogeny (Bateson, 1979; Maturana and Mpodozis, 2000). Throughout this development, living beings build anticipatory dynamic models of themselves and their environment that make them predict future fluctuations (Rosen, 1985; Louie, 2017; Friston, 2013). These models are inherent to the self-producing organization and rather differ from feedback error-counteracting reactive cybernetic systems (Louie, 2012; Maturana, 2011; Rosen 1985b). That is, anticipation involves self-reference (Varela 1979) and feedforward rather than feedback loops (Louie, 2012; Rosen, 1978).

her own cognitive domain to face dissipation and external fluctuation (Rubin et al., 2020). This touches the point of whether a form of memory, inherent in the anticipatory models of living systems, at the planetary scale should be different from the cellular or metacellular scale. As the organization of self-production in different 'orders' or scales of biological unities implies different structural realizations (Maturana and Varela 1980), we think that the anticipatory models of Gaia can be structurally determined operating in the short and long term. The former established as the metabolic capacity and structure of the biosphere as a single rhizome network (Raoult, 2010; Williams, 1996) possessing a relatively stable set of key central enzymes (for example, Rubisco, glutamine synthetase, etc.) capable of influencing of the major redox reactions and electron transfer of Earth chemistry (Falkowski et al., 2008; Jelen et al., 2016). The structure of the biospheric rhizome network, in general, should work in a distributed, parallel, scattered way in diversity, richness, abundance and connectivity (trophic and symbiotic relationships of eukaryotic and prokaryotic systems in the ocean, continents, deep subsoil and atmosphere) (Stolz, 2016). The latter, which operates in the long term, must be fundamentally associated with the geomorphology that determines the dynamic interplay between lithosphere (orography), ocean and atmosphere that continuously ensures climatic regularities and climatic changes.

Although the range of COT and ZDT, so far, does not include cognition or anticipation and is limited to identifying an autopoietic organization of a representative reaction network of the Earth system, nevertheless, it reaffirms the biological bases from which to address the Gaia hypothesis at face value.

6. Coda: biologizing the Gaia theory

This paper outlines the key explanatory scope of autopoiesis in relation to the Gaia hypothesis. This approach rests upon self-production by metabolic closure as more fundamental than self-regulation by feedback mechanisms. Equipped with COT and ZDT as a workable operational formalization of self-production by metabolic closure, we presented a proof-of-concept by which Earth's molecular reaction network, composed by biotic and abiotic reactions, satisfies the metabolic closure of the autopoietic organization and shows different scenarios that resemble the history of the Earth itself.

Based on the COT analysis of the Earth's molecular reaction network, we conclude that it is possible to establish a link between the autopoietic organizations identified for such networks and the different scenarios of the Earth's history. Since organizations as defined by COT entail

Appendix A

Reaction Networks Basics

structures integrated by autopoietic closure, the links between organizations and Earth's evolutionary scenarios may resemble a kind of ontogenetic process of the Earth altogether.

Based on the ZDT analysis, we conclude that the stability of the organizations of Earth's molecular reaction networks is due to the selfproduction of species by reaction processes, and not by self-production of complexes in the sense of ZDT. The inapplicability of the zero deficiency theorem to the Gaian system occurs because the self-production of these networks does not occur at the level of complexes but at the level of molecular species, in a distributed manner across reaction pathways. The latter is an indication that the dynamical stability of Gaia persisted over geological periods due to appropriately well-linked, but not trivial, reaction pathways that self-produce the system.

These results provide the possibility of an entirely new research programme to understand Earth dynamics beyond identify selfregulatory feedbacks, but in terms of identify critical feedforward elements of self-producing organization on a planetary scale. This will open the discussion on how the central feature of autopoiesis—autonomy—could manifest itself at the planetary scale, and whether in future developments of the Gaia theory and Earth system science notions such as Earth 'stewardship' or control-theoretical geoengineering will need to be placed on radically different—specifically, autopoietic—foundations.

Declaration of competing interest

All authors have seen and approved the final version here submitted. The authors also have no conflict of interest. The authors declare that all prevailing local, national and international regulations and conventions, and normal scientific ethical practices have been respected. All authors are consent this article is given for publication in BioSystem.

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A reaction network is defined by a set of *components* $M = \{m_1, ..., m_n\}$ and a set of *reactions* $R = \{r_1, ..., r_n\}$, where each reaction r_i is a transformation of a subset $A \subseteq M$ to another subset $B \subseteq M$:

$$r_i: A \to B = \{a_1, a_2, \dots, a_i \in M\} \to \{b_1, b_2, \dots, b_j \in M\}$$

The subset $A = \text{supp}(r_i)$ in known as the *support* or *reactants* of r_i and $B = \text{prod}(r_i)$ as its *product*. All element of A are in conjunction via the "+" symbol. Which represents that the reaction can take place (*triggered*) if and only if all the elements of A are simultaneously present. When the reaction occurs, the reactants of r_i are *consumed* to form the *products* B that emerge from *the reaction*. Moreover, A and B can be multisets, *i.e.* each element m_i participating in a reaction r_j can be consumed or produced in a different amount (say c_{ij}). Hence, we describe a reaction as of:

$$r_i = c_{i1}\mathbf{m}_1 + \cdots + c_{in}\mathbf{m}_n \rightarrow p_{i1}\mathbf{m}_1 + \cdots + p_{in}\mathbf{m}_n$$

With c_{ij} and $p_{ij} \in N_0$. These coefficients define the stoichiometry of the reactions, which encapsulates the structural dynamics of the reaction network.

From here, we are able to define the *stoichiometry matrix* $\mathbf{S} = (s_{ij})$, a matrix with $(n \times m)$ dimensions, where $m = |\mathbf{M}|$ and $n = |\mathbf{R}|$. Here the $s_{ij} = p_{ij} - c_{ij}$ coefficients denote the number of components of type *i* is produced $(s_{ij} > 0)$, consumed $(s_{ij} < 0)$, or unchanged $(s_{ij} = 0)$ in reaction *j*. In this way, the dynamics of a reaction network in a specific time-interval can be specified by the occurrence v_i of each chemical reaction r_i during such time-interval

Moreover, it is possible to obtain a dynamical equation for the concentration of the components $\mathbf{x} = (x_1, ..., x_n)$ of a reaction network described as follows:

$$\frac{d\mathbf{x}}{dt} = S \cdot \mathbf{v},\tag{1}$$

Where ν is a vector specifying the rate of occurrence of each reaction. To fix ideas, let's consider an example where M = {*a*,*b*} and R:

 $r_1: \emptyset \to a$

 $r_2:a + b \rightarrow 2b$

We can see that $s_{11} = 1 - 0$, $s_{21} = 0 - 0$, $s_{12} = 0 - 1$ and $s_{22} = 2 - 1$. which results in S = ((1, -1), (0, 1)).

Zero Deficiency Theorem

Note that each a specific collection of reactants is needed for each reaction to trigger. And the reaction also produces another specific collection of products. These specific collections are called *complexes*.

For example, the complexes for r_2 are a + b and 2b, acting as reactants and products respectively. The ZDT basically states that if complexes acting as reactants act as well as products then the network is going to reach equilibrium.

Let *C* be set of complexes of a reaction network, and *G* be the directed graph with nodes given by the complexes *C* and directed edges given by the reactions $r_i = \nu_k \rightarrow \nu_k'$, with. $\nu_k, \nu'_k \in C$.

Let G_1, \ldots, G_l denote the connected components of G. $\{G_i\}$ are the linkage classes of the reaction network. Let l = # of linkage classes.

A chemical reaction network (M, R) with a set of complexes *C* is called *weakly reversible* if for any reaction $\nu_k \rightarrow \nu_k'$, there is a sequence of directed reactions beginning with ν_k' as a source complex and ending with ν_k as a product complex.

Let s = dim(S) be the dimension of the stoichiometric subspace of *S*.

The **deficiency** of a chemical reaction network (M,R), is $\delta = |C| - l - s$, where |C| is the number of complexes, l is the number of linkage classes of the network graph, and s is the dimension of the stoichiometric subspace of the network.

The Deficiency Zero Theorem of Feinberg (Feinberg, 1979) states that for (M, R) a chemical reaction network with deterministic mass-action kinetics that.

1. Is weakly reversible,

2. Its deficiency is equal to zero.

We have that, for any choice of rate constants κ , within each positive stoichiometric compatibility class c there is precisely one equilibrium value, x_c , satisfying $S_c \cdot v_c(x_c) = 0$, where $S_c \cdot v_c$ and x_c are the stoichiometric matrix, the flux vector and the state of the system restricted to the compatibility class c, and that such equilibrium is locally asymptotically stable (relative to its compatibility class).

We make use the CrnPy library (Tornos et al., 2018) for the calculation of the deficiency, number of linkage classes, number of complexes and stoichiometric subspace of the subnets that satisfy the organization property.

Organization

We would like to describe subsystems of our reaction networks in terms of their ability to persist in the long-term. An *organization* can be understood as a subsystem of a reaction network such that all its components are able to persist in the long-term. Under the COT framework, it is necessary for a reaction network to satisfy certain conditions to fulfill that property:

- We say a set $C \subseteq M$ is *closed* if for all $r \in R$ such that $supp(r) \subseteq C$, then $prod(r) \subseteq C$. This can be understood as that *no novel components* can be generated. In other words, the components produced are already present in the reactive part. We can also define the *closure* $C = G_{CL}(S)$ of a set S as the smallest closed set that contains S. This operation can be performed by adding products of *the* reactions that can be triggered from the set S. Formally, these products are defined by $P = \bigcup_i prod(r_i)$ such that $supp(r_i) \subseteq S$, and the discovery of which possible new reactions can be triggered is formally specified by determining which r_i not considered already are such that $supp(r_i) \subseteq S \cup P$. The latter process can be repeated recursively until no new reactions can be triggered (this process safely terminates as the reaction set is finite).
- A set $C \subseteq M$ is *semi-self-maintained* if $\forall x \in C$ such that $\exists r \in \mathbb{R}$ with $x \in \text{supp}(r)$ then must $\exists r^0 \in \mathbb{R}$ such that $x \in \text{prod}(r^0)$. This property realizes that any component that is consumed by some reaction, must be produced by some other (self-produced).
- Let's consider $C \subseteq M$ semi-self-maintained, and $R_C \subseteq R$ to all reaction $r \in R$ such that $supp(r) \subseteq C$. Considering C and R_C we can construct the stoichiometric matrix S of this sub-network. In this way we define C is *self-maintained* if condition $S \cdot v \ge 0$ with v > 0. Considering the latter condition and equation (1), the concentration of the components will either increase or remain zero, and therefore we ensure that no component will be depleted in the long-term. The latter is equivalent to say that the amount of components produced by triggering the reactions at the rates specified by v is greater or equal than what is necessary to trigger v. The computation to test if a closed set is an organization, can be solved using linear programming (Dantzig, 1998).

Therefore, an organization is such when a subset *C* satisfies the property of self-maintenance and closure. So, it does not consume something that is not produced enough, and its components persist under long-term dynamics.

Methods

We already mentioned the feasibility of a reaction network being an organization was calculated by means of linear programming (LP). The proposed LP methodology consists in finding which creation and destruction components reactions are necessary to add to the network, so it achieves a stable dynamic (also known as flux balance analysis). If S is our stoichiometric matrix, we consider the following *E* matrix as:

$\mathbf{E} = [\operatorname{diag}(1), \operatorname{diag}(-1), S]$

Where diag(*x*) is a diagonal matrix with *x* values in his diagonal and with dimension ($n \times n$) such that $n = |\mathbf{M}|$. For this new stoichiometric matrix *E* we wish to analyze which components are necessary required as inflow and outflow in such a way that E is considered stable i.e.:

 $Ev^e = 0$

(2)

Here v^e is the related flow vector. This process can be understood as which of these components are added to the inflow or outflow, by means of v^e . If a flux vector component $v^e_i = 0$ is turned off in such way that condition (2) holds, those components are not considered as inflow or outflow of the stable network *E*. Our imposition on v^e for LP is such that the components associated with the original stoichiometric matrix *S* are greater than zero. Thus, the original reaction network is always present. We arbitrarily impose that they should be greater that one. This can be done without loss of generality given the linearity of equation $S \cdot v \ge 0$. If v is solution then λv is also solution for any $\lambda \in \mathbb{R}^+$. Therefore, the optimization problem to find the feasibility of being an organization relay on minimizing:

$\min(C \cdot \mathbf{v} \mathbf{e})$

By holding,

$$Ev^e = 0$$

 $v^e \ge h$

h is such that the $S \cdot v \ge 0$ condition is satisfied:

$$h_i = \{ \begin{array}{c} 0 \ if \ 1 \le i \le 2|M| \\ 1 \ else \end{array}$$

The C vector associated to the cost function is:

$$C_i = \{ \begin{array}{c} 1 \ if \ 1 \leq i \leq |M| \\ 0 \ else \end{array}$$

Therefore, the only consideration cost for this minimization problem, is to require components in the inflow reaction. The R code of this program and for the respective Earth system reaction networks (*sbml* folder) can be found in the following *Github* repository https://github.com/pmaldon a/Gaia_RN.

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