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Review

Unified representation of Life's basic properties by a 3-species Stochastic Cubic Autocatalytic Reaction-Diffusion system of equations

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Abstract

Today we can use physics to describe in great detail many of the phenomena intervening in the process of life. But no analogous unified description exists for the phenomenon of life itself. In spite of their complexity, all living creatures are out of equilibrium chemical systems sharing four fundamental properties: they (1) handle information, (2) metabolize, (3) self-reproduce and (4) evolve. This small number of features, which in terran life are implemented with biochemistry, point to an underlying simplicity that can be taken as a guide to motivate and implement a theoretical physics style unified description of life using tools from the non-equilibrium physical-chemistry of extended systems. Representing a system with general rules is a well stablished approach to model building and unification in physics, and we do this here to provide an abstract mathematical description of life. We start by reviewing the work of previous authors showing how the properties in the above list can be individually represented with stochastic reaction-diffusion kinetics using polynomial reaction terms. These include "switches" and computation, the kinetic representation of autocatalysis, Turing instability and adaptation in the presence of both deterministic and stochastic environments. Thinking of these properties as existing on a space-time lattice each of whose nodes are subject to a common mass-action kinetics compatible with the above, leads to a very rich dynamical system which, just as natural life, unifies the above properties and can therefore be interpreted as a high level or "outside-in" theoretical physics representation of life. Taking advantage of currently available advanced computational techniques and hardware, we compute the phase plane for this dynamical system both in the deterministic and stochastic cases. We do simulations and show numerically how the system works. We review how to extract useful information that can be mapped into emergent physical phenomena and attributes of importance in life such as the presence of a "membrane" or the time evolution of an individual system's negentropy or mass. Once these are available, we illustrate how to perform some basic phenomenology based on the model's numerical predictions. Applying the above to the idealization of the general Cell Division Cycle (CDC) given almost 25 years ago by Hunt and Murray, we show from the numerical simulations how this system executes a form of the idealized CDC. We also briefly discuss various simulations that show how other properties of living systems such as migration towards more favorable regions or the emergence of effective Lotka-Volterra populations are accounted for by this general and unified view from the "top" of the physics of life. The paper ends with some discussion, conclusions, and comments on some selected directions for future research. The mathematical techniques and powerful simulation tools we use are all well

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established and presented in a "didactical" style. We include a very rich but concise SI where the numerical details are thoroughly discussed in a way that anyone interested in studying or extending the results would be able to do so.

Keywords: Living systems; Turing instability; Top-down approach; Bottom-up approach; Non-linear reaction-diffusion equations; Properties of life

1. Introduction

Living systems (LS) involve thousands of finely tuned, delicately controlled and exquisitely synchronized chemical reactions and processes working together at many different temporal and spatial scales. Life on Earth, the only example of biology we know to date, is materially expressed through biochemistry [1]. It constitutes the highest level of complexity we know [2].

Today, using the tools of physics and physical chemistry, we are able to separately describe at the molecular level and in a highly detailed and successful form, many of the huge variety of phenomena pertaining to life (cf. for example [3] and [4]). Nonetheless an integrated physico-mathematical representation of life-itself as a unified cooperative molecular phenomenon is not available.

Prima facie, it would seem hopeless to attempt to describe the spectacular physico-chemical phenomenon of life as an analytical abstraction emerging from general principles [5].

However, starting in the first half of the 20-th century with the work of Lotka [6] and then Muller [7], Schrodinger [8] or Rashevsky [9], this was perceived to be an important objective as was for example later argued by Morowitz in e.g. [10] and [11]. And even though many of the elements and techniques needed to achieve this have been available for a long time, the fundamental question of providing a unified theoretical physics representation of life has been enshrouded by a considerable debate about "what is life" [12]. Indeed, to mention just a few of many important and foundational contributions, the work of Turing concerning pattern generation in reaction-diffusion systems [13], Sel'kov's work on the mathematical representation of glycolysis using non-linear chemical kinetics [14], Prigogine's [15] and other's (cf. e.g., [16]) work on self-organization in non-equilibrium systems, Eigen's approach to selection/adaptation using his hypercycle [17], Ganti's work on fluidic machines and his "chemoton" [5], together with Langton's [18] and Adami's [19] work on Artificial life, all provide an inspiring and useful trove of theoretical resources to apply in the ex-novo formulation of a mathematical or algorithmic description of the phenomenon of life as a whole, and its manifestation as living systems.

As we know, it is remarkable that independently of how "simple" or complex they are, all extant living systems are thermodynamically open chemical systems operating under the influence of internal and external fluctuations and share a small set of top-level properties.[1] These include (i) handling of Information, (ii) implementation of Metabolism (in reference to the harnessing of free-energy gradients and the production of the LS's molecular components from simpler molecules present as "food" in their environment), (iii) full LS-controlled and programmed system Self-replication (which amounts to programmed self-reproduction), and (iv) Evolution (both adaptive and non-adaptive) [2], [5], [12], [20], [21], [22], [23], [24], [25].

Since the operation of a living system and its ensuing phenomenology are the result of the collective activity of its internal chemical components and the environment in which they operate, it makes sense to think of living systems abstractly in terms of the rules that apply to an extended chemical system [26], [27], [28] whose components interact in a way that is compatible with (or gives rise to) its collective properties.

Representing a system with general rules is of course a classical approach to model building in Physics [29]. Following this approach, the preceding reduced number of shared properties together with the non-equilibrium chemical character of all LSs can be exploited to obtain a general abstract description of LSs from first principles. Such an approach was at the foundation of various attempts to represent life and its chemical kinetics for example through

[1] Perhaps not coincidentally, starting with the tangled bank paragraph (which became "entangled" in later editions) in Darwin's Origin of Species, supplemented by H. Muller's work during the 1920s and 30s on genes and information, life is today widely considered to be an out of equilibrium physico-chemical phenomenon expressing these four basic properties [20].

Ganti's chemoton [5], by Langston's artificial life [18] or by Adami's AVIDA [19]. And of course it was also present in von Neumann's ideas on cellular automata [30].

Here without making any specific reference to biochemistry or its details, we review how the above properties can be individually represented using abstract chemical species that follow polynomial chemical kinetics which we then proceed to unify into a local reaction-diffusion kinetics. By assigning an instance of these kinetics to each of the nodes of a lattice, connecting the nodes by diffusion and using mass-action kinetics to represent the overall kinetics of a thermodynamically open system that ingests and processes some "food" and produces "waste" while subject to stochastic perturbations, we construct a minimal and mathematically compact dissipative physico-chemical reaction-diffusion model which unifies properties (i) through (iv).

This representation builds upon well understood notions of "switches" and their relevance for a general computation [31], the kinetic representation of auto-catalysis [32], [33], [34], the properties of reaction diffusion systems and the emergence of Turing patterns [35], [36], [28], as well as the implementation of adaptation [37], [38] in these systems in both deterministic and stochastic environments [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [54], [55]. In addition, the recent availability and access to high performance computing systems using graphics processors for numerical simulations, such as in CUDA [56] based machines, is another important component to study these systems in silico. They provide a relatively fast and efficient platform on which numerical experiments can be performed and the phenomenological predictions of the analytical, non-linear models, readily checked and understood.

The model that results after applying the reviewed material and principles, consists of a system of three coupled stochastic parabolic non-linear differential equations (SPANODES[2]) and harbors a surprisingly rich phenomenology which depends on the values of the free-parameters in the equations. Their numerical solutions for special parameter regions, where "domains" and mathematical metaphors of "membranes" self-organize and emerge, lead to a phenomenological description that includes simplified representations of some of the basic features of the universal Cell Division Cycle (CDC) [57] of extant biology. These equations apply to both non-homeostatic and homeostatic scenarios, lead to chemotactic behavior and cooperative self-organized behavior at the system level. They also give rise to populations described by Lotka-Volterra equations [58]. This tack at model building reflects a so-called "outside-in" or "top-down" [59] methodology for system building, where a set of essential top-level properties of the problem-system are described separately and then integrated into a single scheme that describes the full system.

This paper is organized as follows. We start by reviewing and motivating the introduction of a separate reaction or reaction-diffusion equation representation for each of the above properties. Then we present a unification of these properties via a system of three cubic autocatalytic reaction-diffusion (CARD) equations for three abstract "chemical" species existing in a stochastic environment (sCARD model), which we subsequently solve in a $2+1$ dimensional lattice and where the presence of a noisy environment is taken into account using additive noise terms. Important physical quantities such as entropy or system features, for example a self-organized "membrane", are identified and introduced for phenomenological discussion. We then proceed to test numerical predictions of the model which include the universal CDC, adaptive behavior, chemotaxis and elementary forms of adaptation and population dynamics. We end by offering some discussion, conclusions, and comment on directions for future research.

2. Representing mathematically the properties of life in the form of chemical-kinetics

Since chemistry is the vehicle with which natural life expresses its properties, in order to connect with theoretical chemistry we will first represent each of the four properties listed in the Introduction by means of chemical kinetics using qualitatively motivated and generic local reaction polynomials. Eventually, using mass action kinetics we will combine the above minimal algebraic requirements into a small set of three coupled kinetic equations obeyed by some abstract "chemical substances" which exist, diffuse, communicate and react in a spatial lattice. During their reaction they generate an abstract functioning, emergent, self-organized open "chemical system" whose solutions are capable of jointly displaying all the above properties. Of course, the description is valid at the "top-level", without providing any of the small-scale details.

[2] We thank the late Murray Gell-Mann for suggesting the SPANODE acronym for these equations.

(i) Information handling: its communication and processing.

Once information is available [60], it needs to be retrieved, communicated and be suitably transformed so that it can be used to implement the details it encodes for the expression of life's functions. The initial information which the LS uses or on which it acts must be available in some form accessible to the LS's chemistry. That is, it must be available in the form of molecules or materials and their arrangements that affect the chemistry in the LS.

A minimal architecture for implementing the communication of molecularly available information in a medium is of course provided by molecular collisions and diffusion [35], [61]. In general, transformation of information takes place by means of a computation, which is understood (cf., e.g., [62]) "as a path for information where it is (I) input, (II) subject to some mechanical (i.e. repetitive) processing and (III) output in some form ready for use" [63], [64], [65]. It goes from available stored information in a chemically available support to an actual physical representation. (This is a key aspect of how information enters in natural life during gene expression: the information contained in a gene's sequence is passed on to the mRNAs which express in the ribosome the information as an aminoacid sequence in a functional protein.)

Minimal information processing for a system to do a computation requires [31] the capability to perform both linear and non-linear transformations on the information available to the system. Using chemistry these transformations of the information can be achieved by processing the information through suitable combinations of chemically operated information processing automata such as gates, some of the simplest automata. That is, automata which transform the information-carrying molecules into other molecules (or physico-chemical responses) that change the state of the system. In fact, as is well known, any computation can be performed by using appropriately interconnected instances of AND, NAND, XOR gates, or by a network of multiple instances of interconnected universal NAND gates [66], [67].

Linear gates can be implemented with chemical kinetics [68] and suitably connected chemical feeds/interconnections within an appropriately "compartmentalized" and "cascaded" chemical system. Unfortunately, the use of gates in chemistry is very "costly", as even relatively simple computational operations can require a fairly large number of interconnected gates to process the information, which needs to be input, processed by the gates and output using diffusion which is a slow and inherently noisy process, and therefore error prone.

At this point it is important to recall that exactly the same computations can also be accomplished by combining instances of three linear gates together with appropriate fan-outs and a non-linear element [31] of the type of an ON/OFF switch.

As a matter of fact, non-linear chemical reactions themselves can act as much more powerful specialized chemical computing automata, such as Turing machines or other standard computer science automata capable of computing at the appropriate levels of complexity [64], [65]. These automata correspond to chemical reactions implementing operations at the molecular level, mostly avoiding diffusion, with fewer components and in a much more streamlined and less noisy processes. The switch is a fundamental component of these strategies.

It is easy to see how we can represent switching behavior using non-linear chemical kinetics. Indeed, a switch can be conceptually represented by a sigmoid function of its argument: as the independent variable, e.g. time, advances, the function stays near a zero constant value, and as time becomes closer to some specified value the first and second derivatives of the function grow until that value of time where the second derivative changes sign, and the first derivative eventually also vanishes. The net result is that the sigmoid "switches" from a zero value to some positive constant value. In other words, the concentration of the substance whose time evolution is sigmoidal has the potential to switch from zero to some finite value and trigger additional events. Chemical substances within a reaction network whose concentrations as a function of time evolve in the form of a sigmoid could in principle be used to represent a switch. For sigmoidal behavior, the kinetics for these substances can therefore be a combination of first and second order kinetics. (Interestingly, the above considerations concerning non-linear kinetics and sigmoidal behavior of concentrations also play a central role in the realization of Boltzmann machines, generative artificial intelligence models based on statistical physics [69] or in enzymatic processes through the Michaelis-Menten mechanism [70].

Thus, a necessary requirement for a spatially extended chemical system to handle information is that its kinetics be of the reaction-diffusion type [61], [13] with an appropriate reaction polynomial. Diffusion will enable the communication and linear superposition of concentrations of reactants and, if the reaction part of the kinetics polynomial reaction terms are linear and quadratic, we will have the necessary switch to fully represent the non-linear core of the computation.

(ii) Metabolism.

This property [33], [11] encompasses [71], [1] the synthesis by the LS of complex molecular components (such as lipids, sugars, nucleic acids or proteins constituting the extant natural LS) using simpler precursors that the LS finds in its environment. It includes the generation and maintenance of a critical free-energy gradient between the environment and the interior of the living-system. In this way the system "boots up" and the necessary out-of-equilibrium "chemical" processes can proceed [72], [73]. Metabolic processes in natural LSs occur under the control of its information processing machinery. This combination is an essential feature for the system to achieve homeostasis and to maintain the non-equilibrium state and structure necessary for life at the molecular level, together with information processing, and system self-replication and self-reproduction. Typically, this is accomplished by an autonomous, suitable and controlled combination of osmotic pressures, non-equilibrium chemistry and concentrations within the LS [74], [75].

Conceptually, molecular self-replication may be thought of in terms of autocatalytic processes such as

$$\mathrm{U} + \mathrm{V} \xrightarrow{\lambda} 2\mathrm{V} \tag{1}$$

or

$$\mathrm{U} + 2\mathrm{V} \xrightarrow{\lambda} 3\mathrm{V} \tag{2}$$

whose stoichiometries imply that V catalyzes its own creation as it reacts with U. The chemical kinetics for these reactions requires at least a quadratic reaction kinetics (cubic for the second reaction) in order to implement "metabolism" in the way suggested by the above general considerations. (Note that autocatalysis in this system brings with it a feedback loop whose strength is the reaction rate constant λ.)

(iii) System self-replication.

Living Systems self-replicate as complete systems by means of internal cooperative processes that lead to one or more functional (but not necessarily identical) copies of the original system. Therefore, these processes must involve spatially extended and time dependent kinetics (and perhaps also include stochastic contributions). At an abstract mathematical physics level, we may think of system self-replication in terms of Turing structures subject to stochastic perturbations associated with internal and external noise affecting the LS [61], [76].

The Turing instability can lead from an initially homogeneous state to the emergence of inhomogeneous structures in the form of "domains" in space and time. This is well known, and is analogous to how we think of these structures as the foundation for the formation of geometrical patterns such as the "spots of a leopard" or as they manifest in morphogenesis [77], [78]. However, this requirement alone is not sufficient to capture the essentials of the kind of self-replication found in life: living systems also die and individuals undergo the CDC and self-replicate at fairly regular time intervals. Thus, in addition to the Turing instability mechanism, some kind of "clocking" behavior is needed, such as the one provided by a Hopf-type instability in non-linear dynamics. To implement this, we must then consider a cooperative regime in a multiple component system with a kinetics containing features of both the Turing and Hopf instabilities.

Since the Turing mechanism requires at least two-chemical species with different diffusion constants and at least one cubic interaction term between them [34], having a Turing instability is also a sufficient condition for a Hopf bifurcation [79], [80] which only requires quadratic interaction terms. Because of this we will concentrate on the former and require for the kinetics to involve at least two diffusing species with cubic reaction terms.

Self-replication in LSs is programmed, i.e., it is controlled by a system-intrinsic pre-established dynamical pattern. Therefore, to have programmed self-replication, it would be sufficient if the chemical species involved in the self-replication are, at least partially, also involved in the already discussed handling of information and the control of metabolism.

Finally, and before we turn to adaptation where the following is relevant, we note that the Turing instability mechanism holds within a finite continuous range of system parameters and not just for a single specific point in parameter space. In fact, the theory of Turing structures [61] predicts the existence of a range of stable wavelengths within which a system supports the Turing instability when the "required conditions" are met by both initial conditions and the ranges of values of the parameters in the system that control the instability.

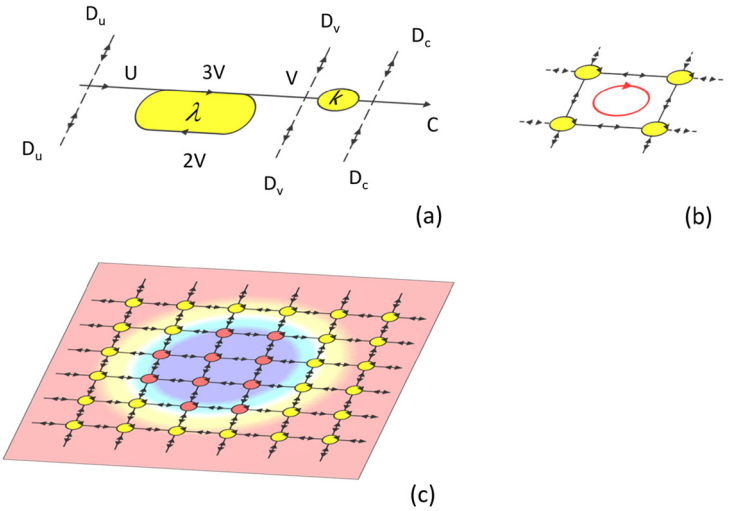

Fig. 1. (a) Unit cycle in the sCARD model including the influence of neighbors via diffusion and the inflow and outflow characteristic of the open system. The simplest diffusive hypercycle is depicted in (b) and corresponds with four unit cycles connected via diffusion. (c) Several sCARD cycles connected by diffusion (each one marked by a circle – red or yellow depending on whether they are located at the interior of the domain generated by the collective dynamics or its exterior). A cell-like domain is composed by many unit cycles (those marked in red) connected via diffusion. Thus, they constitute a form of diffusive hypercycle. In an actual simulation each of the pixels (such as can be seen in the figure) contains one sCARD cycle connected in the first instance to its four neighboring sCARD cycles. Running these simulations can be a demanding computational task.

(iv) Evolution.

Another fundamental feature of LSs is that they are susceptible to four so called "evolutionary forces" that make them experience both adaptive and non-adaptive evolution [23]. Adaptive evolution is non-stochastic and is associated with selection, one of the above "forces". Non-adaptive evolution is stochastic and arises from separate or concurrent action of the remaining three "forces": mutation, recombination and random genetic drift.

To incorporate selection in the model, we may think of the interior of the LS as made up of a lattice with multiple nodes each of which is endowed with the autocatalytic features already included in the representation of the previous properties (i)-(iii). We may then assume the nodes to be interconnected into a network configuration which implements some form of hypercycle [17] which is well known to lead to a mathematical description of selection and its consequence, adaptation [81]. To represent this scenario in our model we follow [82], and consider a situation where in addition to the internal chemical reaction feedbacks within each node leading to local autocatalysis, we can implement a configuration where each instance of the local autocatalytic dynamics (node) feeds from and feeds into at least two more local instances. This is possible if the local instances of autocatalysis (in the nodes) are interconnected in a grid with at least two spatial dimensions as depicted in Fig. 1. The above interconnection of nodes can be implemented via diffusive couplings among the nodes. In this way, adaptive evolution can be incorporated in the mathematical model by imagining that the represented LS is made up by a lattice with a "large" number of diffusively interconnected, locally autocatalytic nodes incorporating all the properties discussed thus far. The resulting collective dynamics would represent the LS behavior. We will call these multi-node domains "cell-like" when their dynamical changes concomitantly show the basic properties of LSs.

Note that since the process of "being alive" involves metabolism this collective dynamics takes place in a growing (and eventually self-replicating) system. That is, the number of nodes inside a "cell-like" domain changes with the passage of time due to the combined action of metabolism and the diffusion of reactive species.

But living systems exist in internally and externally ordered and disordered environments [83]. These circumstances can be incorporated into the mathematical model by introducing space and time dependent noisy (i.e. stochastic) contributions to the LS kinetics which can potentially represent sources of stochasticity affecting the LS. In principle, using these we can model the effects of stochastic contributions to non-adaptive evolution.

Noisy reactant feeds to a chemical reaction generate local stochastic variations in molecular concentrations (additive noise) which propagate to the reaction and diffusion constants. This is directly caused by multiplicative noise

and indirectly, through additive noise. Such variations affect LS kinetics in ways that depend on noise structure and the spatio-temporal scales at which the noise acts [41], [84]. In general, these modifications are a reflection of the specific statistical properties of the noise, and translate (via the renormalization group) [85], [27] [86], [40] into scale dependent changes to the reaction and diffusion constants of the nodes.

We can expect that these effects will manifest downstream in the detailed properties of the Turing patterns themselves and finally propagate to the population of LSs. In fact, given a noisy environment, some of the noise-modified patterns will be more efficient at using the available resources in their autocatalysis and replication. These domains and their daughters will mix with the currently dominating domains and give rise to a "pool" of initially coexisting and more stable and efficient Turing patterns within a population of "cell-like" domains which compete better for resources.

Thus, we see that when the above diffusive hypercycle topology [17], [82] and system response to noise are combined, they provide a mathematical physics and chemistry scenario with the necessary components to incorporate the basic ingredients to represent (of course in a limited and primitive way) some of the basic effects of both adaptive and non-adaptive evolutionary "forces" [23].

3. Hierarchical interrelation of the individual basic properties of living systems and their unification into a system of three cubic autocatalytic and stochastic reaction-diffusion equations

Expressed with biochemistry in natural life the above four properties are interlocked, interdependent and, of course, unified by the existence of life itself.

Prior to general evolution of the LS as an individual (property 4 common to all LSs) or as a member of a population, the system must be capable of self–replicating (property 3). To self-replicate, the LS must construct the necessary parts for its descendants to be able to boot-up within the restrictions imposed by the laws of chemistry and physics and without incurring any "catastrophic" losses due to excessive modifications of its basic information contents. It has to do all this in such a way that it can adapt to changes that may have taken place in its environment or in its own internal chemistry or structure. Self–replication in a natural living system requires the staging and synchronization of many processes. This is done and controlled by the LS itself using simpler parts obtained from its environment to assemble and synthesize the more complex working parts of the LS itself (property 2). The preceding is autonomously orchestrated and executed by the LS according to information contained in some plan existing in the system (property 1). That is, evolution (4) requires self-replication (3) which in turn requires construction of parts based on simpler parts and their self-assembly (2) based on information (1).

These properties and the processes attendant to their implementation play various roles during the execution of the (universal) Cell Division Cycle (CDC), the set of processes that take place in the LS and whose generic features are shared by all extant living systems [57].

The above suggests a hierarchical interdependence among the properties which we can use for the construction of a "simple", "high level" mathematical scheme (i.e., a scheme where each explicit mathematical step corresponds to several non-explicit internal steps), or model, capable of simultaneously encompassing and expressing the dynamical features of all the above properties with a small set of unifying equations. (Representing a system starting with general rules is of course a classical approach to unified model building in Theoretical High Energy Physics. In the context of computer science this would correspond to a "top-down" approach [59].)

From the previous discussion of the individual properties and their mathematical representation, such mathematical model must, at least, be cubic autocatalytic. This part of the model supports self-replication, involves at least two "substances", which we can identify as representing the inner part V of the LS and its "food" U and includes metabolism. Furthermore, since an additive shift of a concentration by a constant can generate quadratic kinetics from cubic kinetics, a cubic autocatalytic kinetics could simultaneously incorporate metabolism and (system) self-replication kinetics. With this choice of kinetics, we are also including in the model some form of computation (property 1) and, if the kinetics is of the reaction-diffusion type, we also incorporate a means for the communication of information (required by properties 1 and 4). Furthermore, since the system must be thermodynamically open and spatially extended, we will "feed" it matter from an external source in the form of a species U which also participates in the "chemical" kinetics at the system-level.

But living systems degrade, and to model a less than 100% efficiency in the overall operation of the system, we will allow for the accumulation of some chemically inert ("waste") matter in the system. This will be a third "substance"

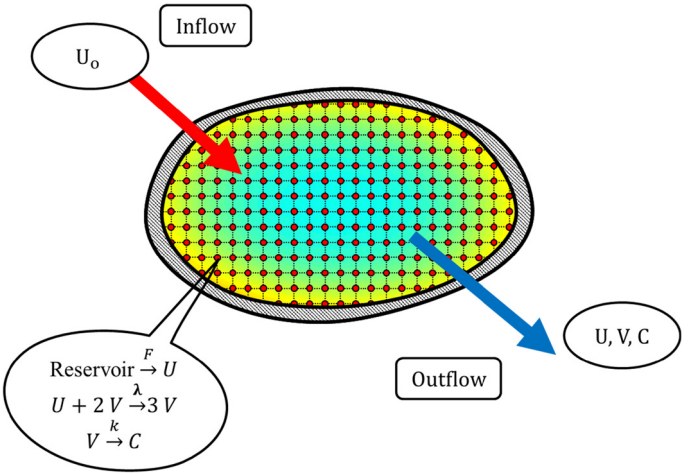

Fig. 2. Idealized representation of a generic out of equilibrium open system where substance U inflows at a rate F, interacts with V through an autocatalytic process and some of the autocatalytically produced V is converted into a "waste" product C (CARD model). In order to keep the total volume balanced, the same amount of chemicals that enters the system must leave. For the stochastic version of the CARD model (sCARD) the inflow and outflow have an additively noisy contribution. Red circles inside the shadowed membrane-like boundary mark the spatial units that constitute the domain.

C generated after the decay with a rate k of molecules of the V-species. Finally, in order to keep the mass balance in the system we will let some amount of matter to be removed from the system. This general scheme is illustrated in Fig. 2.

A simple kinetics satisfying all the above general requirements is provided by the three reactions

$$\text{Reservoir} \xrightarrow{F} \text{U}; \qquad \text{U} + 2\text{V} \xrightarrow{\lambda} 3\text{V}; \qquad \text{V} \xrightarrow{k} \text{C} \tag{3}$$

augmented with diffusion and stochastic contributions occurring at the interconnected nodes of a lattice. The space and time coordinates of the lattice points will be denoted by $\mathbf{r}$ and t. The concentration of the chemical species will have values $u\,(\mathbf{r}, t)$, $v\,(\mathbf{r}, t)$, and $c\,(\mathbf{r}, t)$.

(Note that this set of reactions constitute the simplest autocatalytic process that exhibits a Turing instability. And also that the same degree of nonlinearity is achieved by considering an autocatalytic reaction such as $\text{U} + \text{V} \xrightarrow{\lambda} 2\text{V}$ together with cross diffusion [54], a combination which is known to effectively increase the nonlinearity by one degree in the order of the reaction polynomial. It is important to also bear in mind that the time-dependent model can exist in 2 or more spatial dimensions. Because of practical reasons in the computer simulations presented here we restricted ourselves to two spatial dimensions plus time. We expect this to be appropriate, as we are not computing here any critical exponents or quantities with asymptotic regimes strongly dependent on the dimensionality of space.)

Figs. 1a and 1b present a sketch of the mechanism described by Eqs. (3). Using the law of mass-action and introducing a stochastic environment for the above kinetics lead to the following set of three stochastic reaction-diffusion partial differential equations

$$\frac{\partial \text{u}}{\partial \text{t}} = -\lambda \text{uv}^2 + \text{F}\,(\text{u}_0 - \text{u}) + \eta_u + \text{D}_\text{u}\nabla^2\text{u} \tag{4a}$$

$$\frac{\partial \text{v}}{\partial \text{t}} = +\lambda \text{uv}^2 - (\text{F} + \text{k})\,\text{v} + \eta_v + \text{D}_\text{v}\nabla^2\text{v} \tag{4b}$$

$$\frac{\partial \text{c}}{\partial \text{t}} = \text{kv} - \text{Fc} + \eta_c + \text{D}_\text{c}\nabla^2\text{c} \tag{4c}$$

operating locally at the nodes of the lattice introduced earlier during the discussion of evolution, property 4.

In the above, the D_i are the diffusion constants for each species. The space and time dependent random functions $\eta_\text{u}\,(\mathbf{r}, t)$, $\eta_\text{v}\,(\mathbf{r}, t)$ and $\eta_\text{c}\,(\mathbf{r}, t)$ are additive-noise terms modulating the rates of change in concentrations for each of the participating chemical species [40]. The origin of these fluctuations may be internal (such as in the cases of

rate constants) or external or localized at the interface between the LS and its environment (for example leading to fluctuations of the feeding rates). Depending on the values of the reaction parameters F and k and the specific nature of the noises, these kinetics can lead to a variety of cooperative regimes (resulting in order and organization) or to destructive regimes (for example preventing the formation of ordered structures in the medium).

From now on we will refer to the system modelled by Eqs. (4a), (4b) and (4c) in the lattice as the sCARD (acronym for stochastic Cubic Autocatalytic Reaction-Diffusion) model.

For the sake of completeness, we note that the above kinetics (without the chemical species C) has a long pedigree. Cubic autocatalysis was explored by Higgins [87] and then by Sel'kov [14] as a coarse-grained description in time of the chemical kinetics of glycolysis. A variant of this two chemical-species model was also considered by the Brussels' school to model the kinetics of the Belousov-Zhabotinsky (BZ) reaction [88], which eventually gave way to the now widely accepted (Field, Köros and Noyes), or FKN, relatively simplified kinetics [89] of this beautiful, non-biochemical reaction originally introduced by Belousov to imitate the Krebs cycle without biochemistry. In the early 1980's, cubic autocatalysis saw a resurgence in the form of the Gray-Scott model of autocatalysis [90], [91] which was applied to combustion and later was reformulated by Pearson [39] as a two-species reaction-diffusion model. Using computer simulations, Pearson discovered the existence of a rich set of geometrical patterns in this deterministic version of cubic autocatalysis. The stochastic version of the model was studied in the early 2000s by Lesmes et al. [40] who numerically found the existence of collective population regimes that provided numerical evidence of system adaptation to noisy environments. (We also note that it can be shown that the 3-species variant of the Oregonator model is mathematically equivalent to the above sCARD equations without the diffusion or stochastic terms.)

4. Numerical simulations and measurement of computed physical quantities

In order to determine the various possible behaviors represented in this model, we next introduce the necessary tools to build numerically the phase plane for the model in Eqs. (4a), (4b), (4c) and describe how to measure physical quantities such as mass and entropy and detect an emergent membrane.

Using F and k as its coordinates, one can compute a phase plane diagram mapping out the collective behavior of the configurations predicted in the absence of noise by Eqs. (4) (see Fig. S2). A similar, but in some aspects extended, phase portrait is obtained simulating the stochastic version of Eqs. (4) and is presented in Fig. 3. Each point in these phase diagrams corresponds to independent simulations of Eqs. (4). In all cases, we initially set the full integration domain to the steady state except for a small square region in the center of the integration domain (side equal to 1 s.u.) that at $t = 0$ we chose to have the value (u, v, c) = (0.5, 0.25, 0) and on which we superimposed an uniformly distributed noise with a zero mean value and 0.01 maximum amplitude (for details see the ESI).

The result of the simulations collected in these phase diagrams illustrates the existence of a rich variety of behaviors that include what we call "cell-like" behavior. This behavior occurs for parameter values within an intermediate region between the Turing and the pure Hopf regions (examples of it are shown in Fig. 3, SI Fig. S2 and movie S5 in the ESI).

The "cell-like" area corresponds to a region of phase space where, at least qualitatively, the behavior of the domains generated by our equations turns out to be very similar to the overall generic behavior observed in extant living cells during the CDC as shown in Fig. 5a below [57]. Examples of such behavior are shown in Fig. 3, SI Fig. S2 and movies S1 and S2 in the ESI. Here, spontaneous splitting of a domain into new domains in both the CARD and sCARD versions takes place with the process repeating for the newly generated daughter domains (see Fig. 4, first column).

These numerical simulations correspond to the emergence of dynamical spatial domains inside a medium [92], [93], [94], [95]. They show features such as the generation of an all-important semi-permeable "boundary" that we can think of as a mathematical representation for the cell membrane of a "simple" natural living system, a "protocell" or the overall interfacial boundary of a coacervate. The emergence of such a membrane generates an all important free-energy gradient between the inside and the outside of the domain. This semi-permeable boundary makes the domain an open system and plays an important role in the dissipative use of the available free energy both inside and outside of the domain. We can think of the membrane as the locus of the points where the net diffusive transport between domain and environment has a gradient and its divergence becomes small. That is, the locus of points $(\mathbf{r}, t)$ in physical space where the quantity $\Phi(\mathbf{r}, t)$ defined by

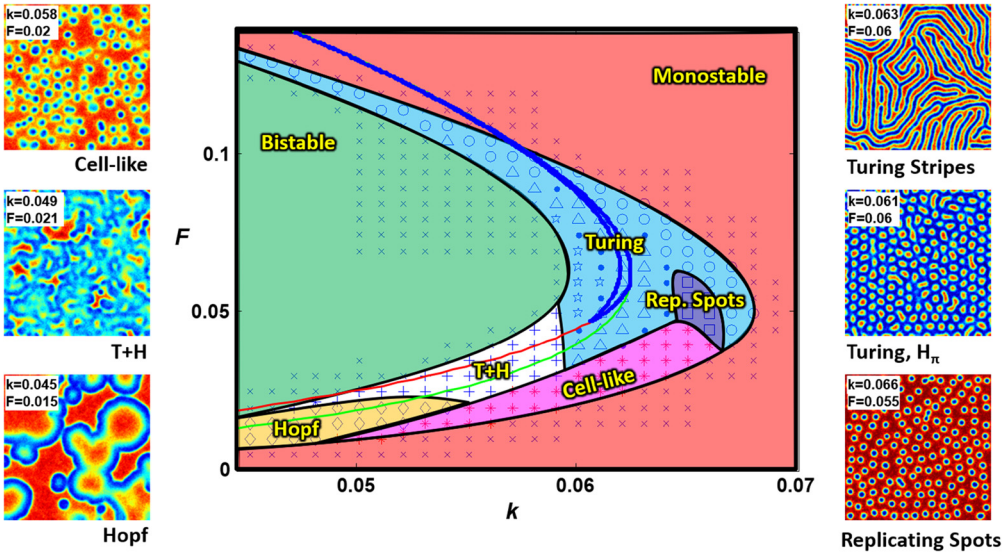

Fig. 3. Phase diagram for the sCARD system. Green, red and blue lines are theoretically calculated from linear stability analysis and absence of noise (green line is Hopf curve and Hopf domain is between green and red lines, region limited by the blue lines corresponds with the Turing regime). All colored regions marked in the figure were calculated from numerical simulations (thus, boundaries are just a guide for the eyes). The integration domain was a lattice of 501x501 mesh points ($\Delta x = 1$, $\Delta t = 0.1$). Model parameters: Du = 1, Dv = Dc = 0.5. Additive noise is considered only in the u variable with a zero mean value and a standard deviation of 0.20. Actual simulations are marked in the diagram with the different points: x = homogeneous steady state, ○ = Turing spots, □ = replicating spots, ● = mix of Turing spots and stripes, △ = Turing stripes, ★ = inverted Turing spots, ◇ = Hopf structures, + = mixed Turing-Hopf modes, * = cell-like behavior. The panels at both sides of the phase diagram present examples of the different solutions observed for different parameter values.

$$\Phi(\mathbf{r}, t) = \sum_{s=u,v,c} D_s \nabla^2 [s(\mathbf{r}, t)] \tag{5}$$

becomes very small. (In this equation D_s represents the diffusion constant for species s = U, V, C). This is a function of space and time and a two-dimensional plot of $\Phi(\boldsymbol{r}, t)$ is also shown in Fig. 4. By construction, it is the surface on which the divergence of the concentration gradients becomes very small. Note that the values of the concentrations where the net spatial diffusive transport vanishes (shown in pale yellow in Fig. 4) correspond with the values of the concentrations at the boundary separating the inside of our domains from their outside, and therefore acts as an effective "membrane". Note also that the membrane does not stay at the same spatial location but moves and evolves as the "cell-like" domain grows. This motion can be understood in terms of a phase wave triggered by a wave instability (recall that a Hopf instability is also present in the model) [61]. We also note that the membrane continues expanding until the domain size becomes too large to be compatible with the characteristic Turing wavelength, at which point the spherical symmetry is broken and, eventually, domain division takes place.

Measuring physical properties in a "cell-like" domain.

We can measure and track in time the values of physical quantities during the simulations of the dynamical time-evolution of the domains and the overall system processes they generate. These include self-replication, a process where two new, and almost identical, structures, emerge at approximately periodic time intervals from one particular "mother" structure. This observed form of "programmed self-replication" [71] is, of course, controlled by the dynamical equations in Eqs. (4) and the values of their parameters. At this level of abstraction, we can think of it as "programmed" because once given the specific parameter values in the equations and the initial conditions, the observed behavior is specific to those values. As mentioned earlier, these parameters are modified in the presence of noise perturbations. The modifications are approximately described by the dynamical renormalization group [40] and correspond to slightly shifted, scale dependent parameters.

Once the membrane is defined, as for example in Eq. (5) above, the size of a "cell-like" domain is determined by the straightforward measurement of the area contained within its membrane. Similarly, the "mass" of material ("chemical

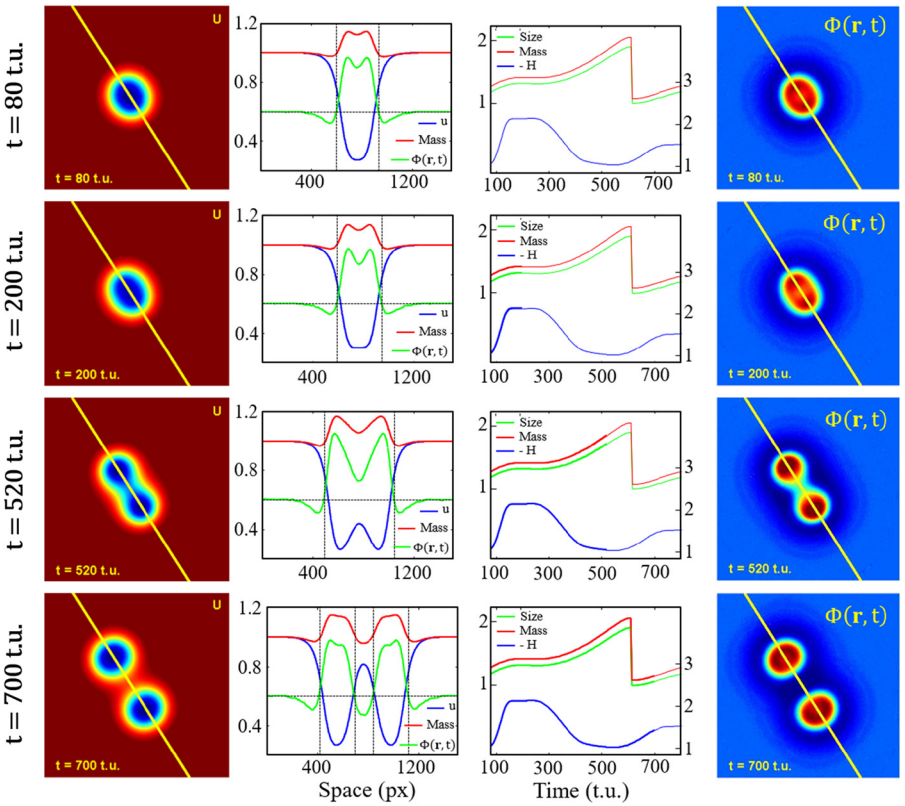

Fig. 4. Evolution of the domain during the division cycle. Left column presents the spatial distribution of the U variable at different instants during the division cycle (red color corresponds with $u = u_o = 1$ while blue corresponds to $u = 0.27$). The yellow line marks the direction along which the cell division takes place. Second column plots a section of the values of u (blue), mass (red) and the values of $\Phi(\mathbf{r}, t) = \sum_{s=u,v,c} D_s \cdot \nabla^2 [s(\mathbf{r}, t)] = D_u \nabla^2 u + D_v \nabla^2 v + D_c \nabla^2 c$ (green) along the yellow line in the previous column (in arbitrary units). The third column presents the evolution of the size (green), mass (red) and minus information entropy (blue) for the whole domain in arbitrary units (only grid points inside the domain boundaries are computed). Fourth column presents a map of $\Phi(\mathbf{r}, t)$ for the whole integration domain at different time steps. Model parameters: $k = 0.064$, $F = 0.035$, $D_u = 0.02$, $D_v = D_c = 0.01$. The integration region was a lattice of 1501x1501 mesh points ($\Delta x = 0.01$, $\Delta t = 0.001$).

species") within the domain can be obtained by multiplying the number of instances of each molecule in the domain by its mass and then adding the result for each of the three participating chemical species. Thus

$$m(\boldsymbol{r}, t) = m_u u(\boldsymbol{r}, t) + m_v v(\boldsymbol{r}, t) + m_c c(\boldsymbol{r}, t) \tag{6}$$

represents that mass. (In our simulations for simplicity we set $m_u = m_v = m_c = 1$ in some arbitrary units.)

Using this counting strategy other physical quantities and state functions can also be calculated. For example, we can introduce some pertinent probability distribution functions (pdf's) for a given domain (i) defined in terms of the ratios of concentrations as

$$p_u^{(i)}(t) = \frac{\sum_{\boldsymbol{r} \in Domain(i)} u(\mathbf{r}, t)}{\sum_{\boldsymbol{r} \in Domain(i)} (u(\mathbf{r}, t) + v(\mathbf{r}, t) + c(\mathbf{r}, t))} \tag{7a}$$

$$p_v^{(i)}(t) = \frac{\sum_{\boldsymbol{r} \in Domain(i)} v(\mathbf{r}, t)}{\sum_{\boldsymbol{r} \in Domain(i)} (u(\mathbf{r}, t) + v(\mathbf{r}, t) + c(\mathbf{r}, t))} \tag{7b}$$

$$p_c^{(i)}(t) = \frac{\sum_{\boldsymbol{r} \in Domain(i)} c(\mathbf{r}, t)}{\sum_{\boldsymbol{r} \in Domain(i)} (u(\mathbf{r}, t) + v(\mathbf{r}, t) + c(\mathbf{r}, t))} \tag{7c}$$

These functions of course inherit the time and parametric dependences present in the concentrations whose space-time evolution is described by the equations (4a), (4b) and (4c). The initial information in the model is in the values of

the couplings (reaction constants, feed rates, etc.), in the structure of the chemical kinetics and in the initial conditions which then lead to a negentropy (negative entropy) whose value changes as the system ages. In the above, the super index i stands for each of the domains present in the simulations. The Gibbs-Shannon entropy in each domain (i) at a time t after it was formed is given by (note that k_B in this expression will be set to 1 in the arbitrary units of our simulations)

$$H_m^{(i)}(t) = -k_B \sum_{s=u,v,c} p_s^{(i)}(t)\, ln p_s^{(i)}(t) \tag{8}$$

The negative of this entropy may then be interpreted as a measure of the information [96] in the domain. In the following, we will interpret its time evolution as the evolution of information within the domain.

5. Predictions, observations and some results

We can now discuss some qualitative "phenomenological" predictions for Eqs. (4) that can be extracted from the result of the simulations by using the above counting-based measurements. We will discuss the Cell Division Cycle, a primitive form of Adaptation, the presence of Chemotaxis and the induction of typical Population Dynamics behaviors.

(a) Prediction of the overall features of a Cell Division Cycle.

In Fig. 4 we show the evolution of a domain with parameters in the "cell-like" region of parameter space. The signature for a "cell-like" domain is the presence of low values of the U-variable (as in the blue areas) and, correspondingly, large values of the autocatalytic substance V. In the left column of this figure time in arbitrary units increases by scrolling from top to bottom panels. The plots in the second column represent for a typical domain in blue (a) the spatial profile of U along the sagittal yellow line drawn in the leftmost column, (b) in red the "mass" of the domain and, in green, (c), the quantity defined in Eq. (5). The third column shows the evolution of mass (red), size (in green) and (in blue) the negative of the Gibbs-Shannon entropy for that domain. The fourth column shows a map of $\Phi(\mathbf{r}, t)$ in Eq. (5) for the complete integration domain at selected different time steps for each row.

The first row of Fig. 4 shows the state of the system at t = 80 t.u. (arbitrary time units) after the system started its autonomous evolution. The initial perturbation of U by V has a small asymmetry, the diffusive component (in green) vanishes within the boundary (in yellow in the left image) containing V.

We see that size and mass grow smoothly with time (second row, t = 200 t.u.). The Gibbs-Shannon entropy, however, has stopped growing and clearly entered a plateau regime. After some time has elapsed it starts falling (third row, t = 540 t.u.), at which point the increases in size and mass have accelerated. The diffusive transport (tracked by the green line in the center column) is decreasing at the center of the domain which is now beginning to split into two domains.

The split happens as mass and size double sometime between 520 and 700 t.u., while the entropy falls and gently begins to recover as the net diffusive transport has gone through zero from above in the center of the domain.

Fig. 4 column 3 shows the evolution of domain size and its computed informational entropy. Remarkably, the features of these curves turn out to be qualitatively analogous to what is observed for the quantities they represent in real living systems during their CDC. In the idealized natural CDC (see Fig. 1-3 of Ref. [57] from which Fig. 5a below is adapted), the size of a cell's mass and the total mass of its DNA (which we take to be proportional to the total amount of information accessible to the cell) are plotted as a function of time. Fig. 5b displays the evolution of these quantities as calculated from the simulation. The similarity between the idealized natural CDC shown in Fig. 5a and the one computed and represented using the above interpretation in Fig. 5b, is striking. And more so in view of the simplicity of Eqns. (4a)-(4c) and the generality of the hypotheses behind them.

In our calculations this process of cell-like division is autonomously and periodically repeated with consecutive cell divisions. Figure S5 shows the result of a simulation where a single initial cell divides up to 40 times. We further point out that the actual values of size and mass in the "cell-like" domain change with time due to a competition for resources among neighboring "cell-like" domains. It is also interesting to note that the addition of some noise in the simulations (at least for the noise considered in our simulations) does not affect the observed general features (see Fig. S6 for more details).

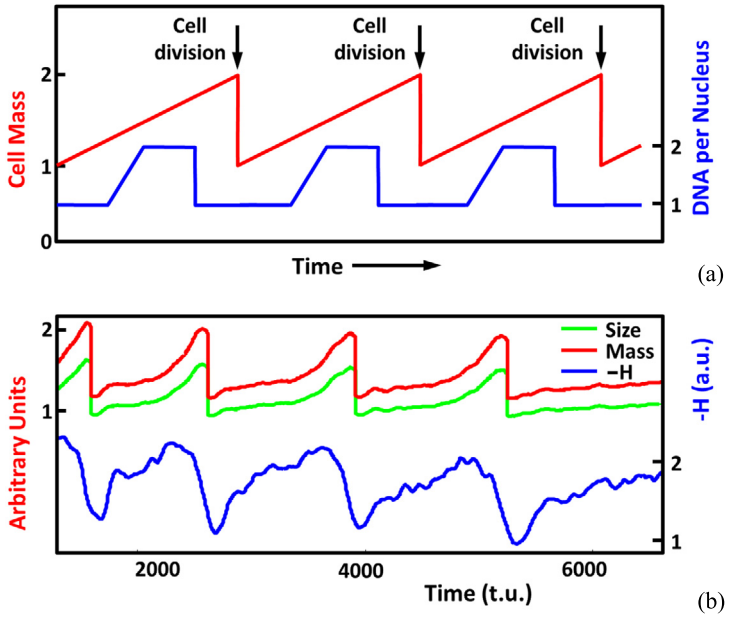

Fig. 5. (a) Idealized scheme of the Cell-Division-Cycle with three cycles represented. Adapted from Ref. [14] (b) Equivalent cycle measured with the sCARD model (Model parameters: K = 0.065, F = 0.04, Du = 0.02, Dv = Dc = 0.01. Additive noise is considered only in the u variable with a zero mean value and a standard deviation of 0.20. The integration domain was a lattice of 501x501 mesh points, $\Delta x = 0.05$, $\Delta t = 0.01$).

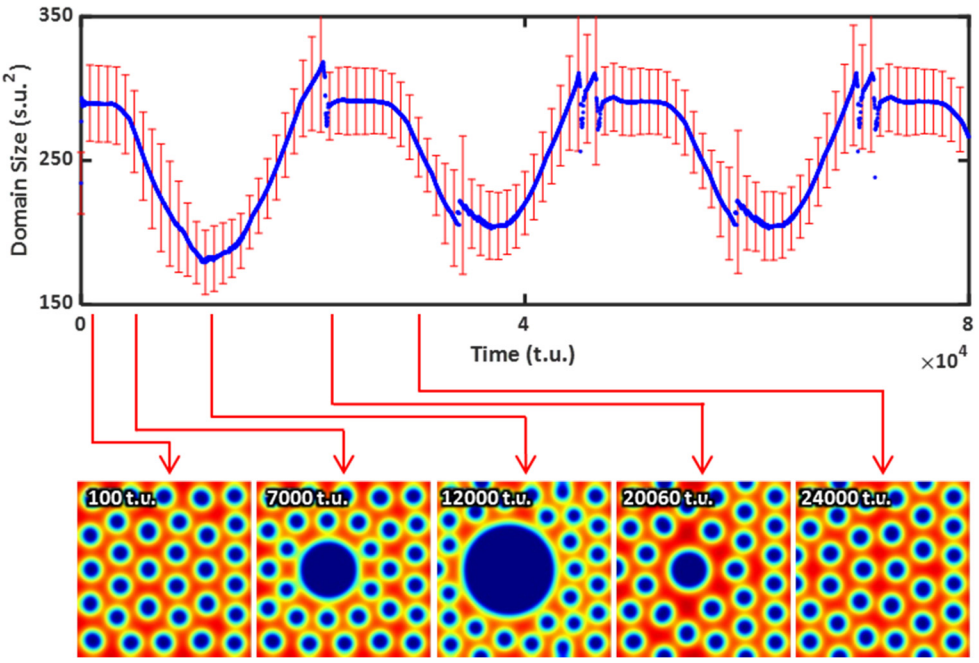

Fig. 6. Adaptation to changing boundary conditions. The central spot is forced to increase its size periodically which induces the other domains to adapt their sizes to the changing environmental conditions. Parameters used k = 0.064, F = 0.035, $D_u = 0.02$, $D_v = D_c = 0.01$ (no noise), $\Delta t = 0.01$, $\Delta x = 0.05$, grid size 501x501. Forcing period = 25000 t.u.

(b) Presence of a primitive form of adaptation.

Simulations in the "cell-like" regime show adaptation as conditions change at both the individual domain and population levels. In Fig. 6a we show the evolution of the average size of the ("cell-like") domains as the integration region

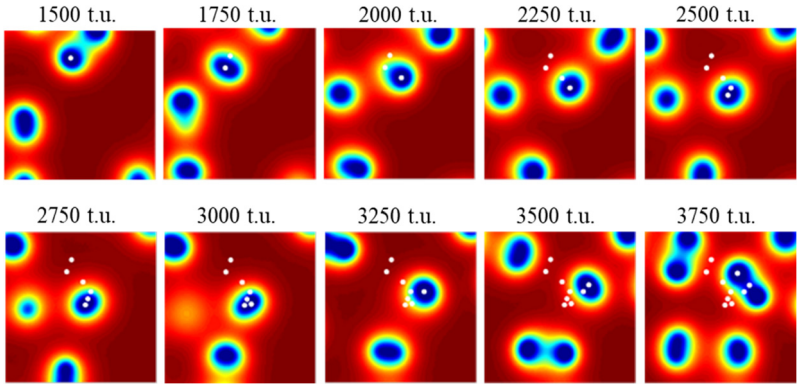

Fig. 7. Chemotaxis. Domains move towards less populated areas thus gaining more access to resources. White dots mark consecutive positions of a particular domain. Model parameters: k = 0.058; F = 0.01570, $D_u = 1.06$, $D_v = 0.5 = D_c = 0.5$, integration size 1001x1001, $\Delta t = 0.05$, $\Delta x = 0.5$.

is periodically reduced and increased. Note that the cells also reduce their size when the medium becomes smaller and resources become scarcer. This can be understood as a direct consequence of the Turing mechanism which indicates that for a given set of parameters there exists a range of wavelengths compatible with Turing's conditions. Applied to our situation, this means that different domain sizes are possible for the same values of the model parameters. We also see that reducing the integration region forces the "cell-like" domains to adapt by changing ("mutating") to another size still compatible with the Turing instability but more suitable to persist as a Turing structure in the changing conditions. This result from the model fits within the notion of adaptation as some form of persistence [97].

(c) Observation of chemotaxis.

The plots in Fig. 7 show that chemotaxis also takes place in the solutions to the model belonging to the "cell-like" type. In this sequence of plots, we follow the evolution of a single "cell" which shows how its position changes with time. Furthermore, a detailed inspection of the plots shows that a "cell-like" domain tends to move towards less densely populated areas. We can interpret this as a primitive form of chemotaxis which has also been previously reported in related numerical systems [82]. Note that the actual size of the "cell" also changes depending on the number of surrounding cells (as reported in Lenski's [98] evolution experiments).

(d) Emergence of an effective population dynamics.

The above cell division cycle repeats many times for each member of a population and therefore reflects on the population size. In some simulations, after a few consecutive CDCs, some members of the population of domains disappear. That is, they "die". However, depending on the choice of parameters for the kinetics in Eqns. (4) and the statistical details of the noise, it is possible for the system to access dynamical situations where the population of domains is in a long-term homeostatic state with its environment. (An example of this behavior is shown in an SI movie and several plots are included in Fig. S7, [74], [99].)

The time evolution of the number of "cell-like" domains, $N(t)$, during a typical simulation is shown in Fig. 8. We find that the population size generated by the model can be put into correspondence with solutions of the Lotka-Volterra evolutionary population equation $\frac{dN}{dt} = rN\left(1 - \frac{N}{N_o}\right)$ where r is the growth rate and N_o represents the "carrying capacity" for the population of "cell-like" domains (see for example [100]). That is, the sCARD model gives rise to populations of domains whose collective dynamical behavior is consistent with a logistic evolution in a population dynamics context.

Finally, we also tested the effect of changes in the model parameters and noise amplitudes which led to the results shown in SI, Fig S8 and S9. We also see that variation of the control parameter k induces a Hopf bifurcation which in this context means that the population or total number of cell-like domains (after a critical value for k is reached) does not reach a stationary value. Instead, it fluctuates with time (see SI, Fig. S10) around some sigmoidal maximum.

This manifestation of collective behavior can be extended to accommodate different populations of "cell-like" domains competing for resources in the same medium [101]. For example, a simple way to introduce another population

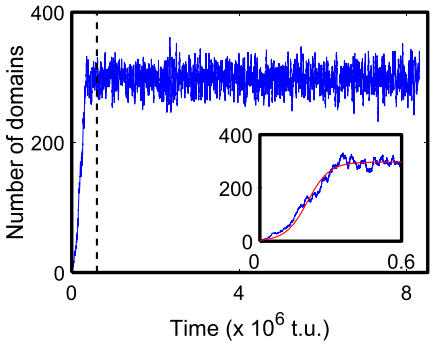

Fig. 8. Evolution of the number of cell-like domains in a typical simulation with homeostatic behavior (k = 0.058, F = 0.0174). Inset is a zoom of the larger graph (area before the dashed line). Red line is the fit of the data to the logistic equation (r = 22 and N_o = 297.3). (Model parameters $D_u = 1.06$, $D_v = D_c = 0.5$, additive noise with standard deviation 0.01 in u-variable, $\Delta t = 0.05$, $\Delta x = 0.5$ and integration region 1001x1001).

of cell-like domains competing for the same (shared) resources is by considering the extension of Eq. (4a, b, c) to the following set of kinetic equations,

$$\begin{aligned} &\text{Reservoir} \xrightarrow{F} \text{U}; \\ &\text{U} + 2\text{V} \xrightarrow{\lambda_1} 3\text{V}; \qquad \text{V} \xrightarrow{k_1} \text{C} \\ &\text{U} + 2\text{W} \xrightarrow{\lambda_2} 3\text{W}; \qquad \text{W} \xrightarrow{k_2} \text{C} \end{aligned} \tag{9}$$

where W is a second autocatalytic species whose dynamics is controlled by model parameters λ_2 and k_2. (Of course, this describes only one of many straightforward ways to generate dynamics among different interacting populations.)

Simulations of Eqs. (9) produce two types of "cell-like" domains co-evolving in the system. They are characterized respectively by a large value of the V-variable or the W-variable (see SI, Fig. S11). Not surprisingly, different values of the parameters produce different behaviors, although in all the cases that we have considered here the asymptotic final state turns out to be eventually made up of one type of the domains and the complete extinction of the other type (see SI, Fig. S11 for details). Both types of populations coexist only when $\lambda_1 = \lambda_2$ and $k_1 = k_2$. Fig. 9 shows the variation with time in this particular case of the number of cell-like domains of each type. Note that for the given value of k both populations oscillate with time but, given enough time, the oscillations synchronize in phase or antiphase, which indicates the presence of induced non-trivial collective interactions between the two populations.

6. Discussion and conclusions

Remarkably, in spite of their variety and complexity, all living systems on Earth share a reduced number of fundamental physical properties which are expressed with biochemistry. They are out of equilibrium chemical systems which (i) handle information, (ii) metabolize, (iii) self-reproduce and (iv) evolve in the presence of noisy (stochastic) environments. These properties can be separately represented mathematically at a high level of abstraction in the form of reaction-diffusion chemical kinetics and they are unified by out-of-equilibrium chemistry, in the form of biochemistry, during the execution of the Cell Division Cycle of extant living systems.

After reviewing how one can use chemical kinetics to represent each of the above basic properties, we argue that a suitable kinetics for a minimal unified (i.e. integrated) representation of the above properties is provided by three coupled stochastic cubic autocatalytic reaction-diffusion equations governing the interaction and space-time evolution of three abstract "substances": the living system's internal matter (V), its food (U) and the degraded material it produces (C). A coupling of the Turing and Hopf instabilities built into these equations is essential in order to produce a model jointly expressing all the above properties. The Turing instability provides the capacity to compartmentalize a domain in space and time at some characteristic length scale while the Hopf instability provides a clock for the system. Working together, they enable the representation of programmed self-reproduction in the model. This system of equations has a few free parameters, including a feed rate, an autocatalytic coupling and a rate to account for chem-

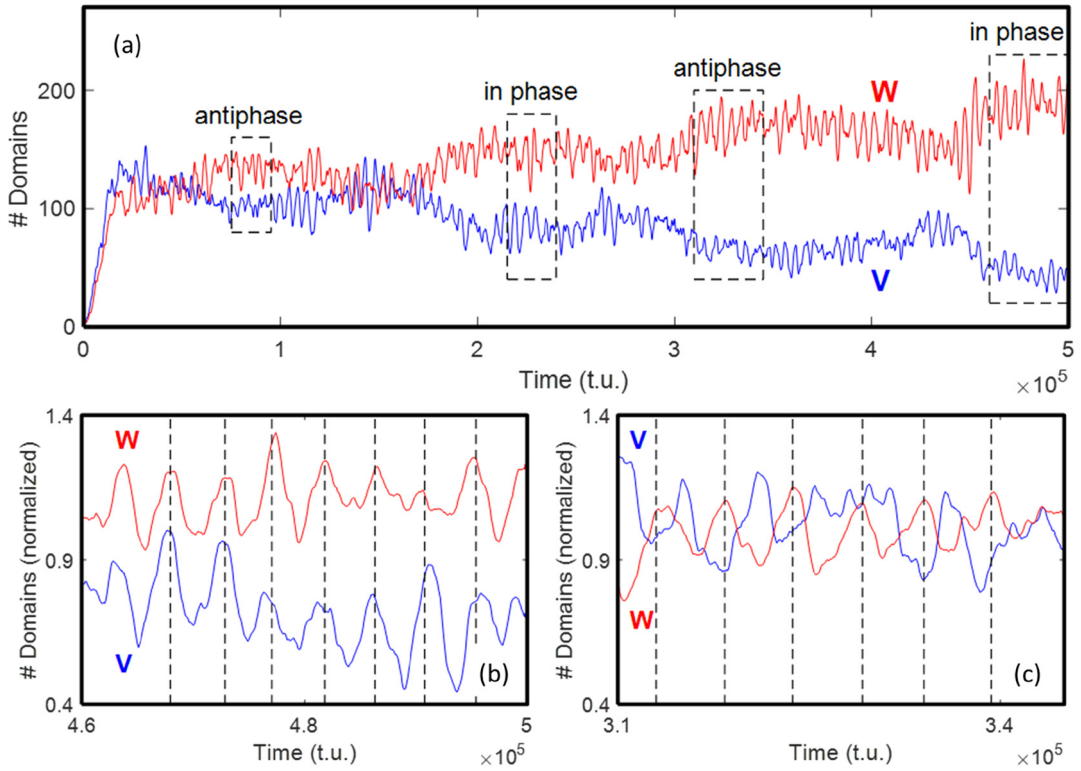

Fig. 9. Competition of two different populations of cell-like domains equally adapted to the environment. (a) Evolution of the number of domains of V type (in blue) and W (in red) with time. In some cases, the two populations oscillate synchronized in phase (b) while antiphase synchronization is observed in different regions (c). (Model parameters for Eqs. (4a), (4b), (4c): F = 0.0178, $k_1 = 0.059$, $k_2 = 0.059$, $\lambda_1 = 1$, $\lambda_2 = 1$, $D_u = 1.06$, $D_v = 0.5$, $D_w = 0.5$, $D_c = 0.5$, size of the integration domain 1501x1501, $\Delta t = 0.05$, $\Delta x = 0.5$.)

ical degradation, plus diffusion constants, masses for the three meta-chemicals and the parameters characterizing the statistics of the noise.

Inspired by the extended space-time structure of living systems, we represent a simple living system as a dynamical (time-dependent) lattice on each of whose nodes there exists one instance of the above system of equations. Extensive numerical simulations of this system show that for some ranges of values of the model-parameters, the abstract properties of life are represented in solutions to the equations. These "boot-up" (autopoietically) from an otherwise homogeneous system seeded with appropriate initial conditions in a nurturing medium and subject to additive stochastic perturbations. They manifest as discrete domains we call "cell-like". For the ranges of parameters where "cell-like" behavior holds we can identify physical "observables" associated with these domains. The observables, which are straightforwardly measured and extracted from the simulations, can be used to study general features of living systems predicted by the model. In particular, it is possible to measure the mass of the "cell-like" domains as well as their informational (Gibbs-Shannon) entropy. These data generate for the "cell like" domains the equivalent of an idealization of the generic cell division cycle. We also explored model predictions for adaptation, chemotaxis, and the population behavior of the "cell-like" domains which in computer experiments were found to follow the time evolution predicted for Lotka-Volterra populations. The latter implies that the "cell-like" domains "communicate" among themselves.

This model presents a conceptual view of living systems somewhat akin to the one for chemical reactions and networks using [102] chemical kinetics. In chemistry, the overall reaction is underlain by a reaction mechanism often consisting of many other shorter time scale reactions and species which collectively enable the overall reaction [103]. The process of going from larger to smaller scales is the inverse of what in condensed matter physics is called "coarse-graining" [86], [104]. Coarse graining presents the observed large scale properties of a system as resulting from the contributions to its large scale physics (or chemistry) from degrees of freedom (or chemical species) active at intermediate scales "shorter/faster" than the ones being observed and measured at the larger scale [105]. The contri-

butions from these degrees of freedom are said to be "integrated out" from the large scales and manifest in the values and dimensions of the parameters, such as reaction constants, observed at the large scales. In principle, these can be estimated from the physics of the degrees of freedom observed at the longer scales by using the renormalization group [86], complemented by (mathematically and physically) "informed" guesses due to the semi-group nature of the renormalization group and dictated by the coherence between the short and long scale dynamics in appropriate limits [106], [107], [108]. Well known in theoretical high energy physics, this process is intimately connected with the "effective decoupling" of the shorter scales degrees of freedom [105], [106]. In other words, degrees of freedom that do not explicitly appear in the dynamics at the larger scales but which are the source (or are related to the cause) of the behavior seen at the larger scales. (Put succinctly, this approach to represent a system, common in unification efforts in high energy particle physics, is conceptually analogous to describing a plane as a flying machine but without giving details about the multiple internal systems that implement the necessary engineering.)

Although the work discussed and reviewed here is a very modest attempt to represent life in a concise, integrated and minimalistic fashion, it is interesting that while the model starts with a brief list of requirements, each of which containing some form of non-linear behaviors, their collective unification enhances their non-linear and dissipative aspects into those equivalent to a form of non-equilibrium autonomous self-assemblage. This makes the emerging numerical phenomenology very rich. Based on its predictions, the model does a reasonable qualitative job in the description of a hypothetical minimal living system as a general out of equilibrium chemical system without needing to make at this level any commitment to any particular form of known chemistry. It is biochemistry agnostic, and contains descriptions of chemotaxis, communication and population behaviors. Extension of the methods presented here can lead to the numerical exploration of the emergence of collective behavior and evolutionary transitions. The description of the environments can also be used to explore the relationship between signatures of life and the fitness landscape on which the chemical evolution occurs. Of course, many questions remain, including the extension from 2D+time to 3D+time dimensions, the connection with actual models/instances for their chemical expression, the connection and differences between this approach and other attempts to describe life "simply", including cellular automata, Ganti's chemoton and its chemical structure, Adami's artificial life, the extension of self-reproduction to other modes such as spore-reproduction and many other problems that could be tackled making use of the rather simplified, but minimal model presented here. And last, but by no means least, finding and classifying the many possible specific translations of the model to actual chemistry.

Finally, we believe that the approach to model living systems followed here contains seeds for the extension of some of the most successful methods of theoretical condensed matter physics to some of the most complex manifestation of condensed matter: living systems.

CRediT authorship contribution statement

Both authors contributed equally to this work.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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