



#### PERSPECTIVE

## The world beyond physics: How big is it?

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### Perspective

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# The world beyond physics: How big is it?

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**Abstract** – We discuss the possibility that the complexity of biological systems may lie beyond the predictive capabilities of theoretical physics: in Stuart Kauffman's words, there is a World Beyond Physics (WBP). It is argued that, in view of modern developments of statistical mechanics, the WBP is smaller than one might anticipate from the standpoint of fundamental physical theories.

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Introduction. – Despite their vast differences in history, purpose, methods and procedures, in the last decades physics and biology have taken significant steps towards each other. In particular, modern developments in nonequilibrium thermodynamics and statistical physics have shown increasing bearing on the understanding of the spacetime dynamics and evolution of biological organisms [1]. The main theoretical thrust behind this endeavor is that the astounding progress in theoretical, experimental and computational methods has taken us to a position where we can explore many instances of biological complexity on quantitative grounds. Hence, in an optimistic vein, closing the gap between physics and biology might be basically just a question of time.

On the other end of the spectrum, a few noted scholars maintain that the gap cannot be closed, by a matter of principle, because the "world is not a theorem" [2,3].

In his highly inspired and inspiring book "A World Beyond Physics", Stuart Kauffman provides a series of passionate arguments on the reasons why biology cannot be reduced to physics. In particular, he portrays physics as a discipline dealing with a machine-like world, as opposed to the biosphere of living creatures which shape the laws they depend upon in ways which cannot be pre-stated and encapsulated in equations, rules or algorithms.

In this Perspective, I wish to argue that, while there is hardly any question that biology cannot be reduced to physics (Phil Anderson said it best [4]), the portrait of physics as a science devoted to a machine-looking world does little justice to modern advances of theoretical physics, and most notably to the flourishing branch at the interface between physics, chemistry and biology,

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best known as soft matter and its theoretical underpinning, that is non-equilibrium statistical physics [5].

In light of these developments, we argue that the WBP appears significantly narrower than Kauffman's stimulating picture would have.

The world beyond physics. - Kauffman argues that the complexity of the biosphere cannot be captured by physics because physics cannot anticipate the emergence of structures whose very function is to promote and sustain their own existence (auto-poietic, Chapt. 2, "Function of Function"). Of course, such structures are contained within Newtonian phase-space but they sit in an astronomically narrow corner which is not accessible to Newtonian dynamics: the biological universe is not ergodic. That is why the heart, and for that matter, any other biological organ, would live in a world beyond atoms and beyond physics, Kauffmans' Kantian Whole. The argument is fair and square, save for a couple of key points; first, there is (way) more to modern physics than Newtonian dynamics; second, the ergodicity of Newtonian systems is still an open issue. Before we spell the points out in some detail, let us first dig a bit deeper into the WBP.

*Kantian wholes.* In broad strokes, the hierarchy from physics to biology runs across the following multilevel sequence:

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atoms -> molecules -> macromolecules -> CELLS -> tissues -> organs -> body
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This seven-level sequence encompasses ten decades in space, more than twice in time for a total of about hundred thousands Avogadro's atoms ( $10^{28}$ ), running their show over nearly hundred years on a time-clock ticking every femtosecond, thus covering about 24 decades in the

process. This is the spacetime slice taken by a human being in his lifetime. So, in purely reductionistic terms, the equation of the human body is basically a  $10^{28}$  (quantum) many-body problem. But is this purely reductionistic view operationally viable? The answer is a decided no.

A more sensible and productive way of handling the seven-level hierarchy is to ask how complexity grows as one walks across the various rungs of the ladder. Is it monotonically growing or does it exhibit sharp growth or perhaps even discontinuous jumps which would make biology operationally and perhaps even ontologically disconnected from physics? In principle, it is plausible to posit that the onset of cells marks a boost in complexity, in the same way as the formation of stars marked a quantum leap of complexity in the history of our Universe. This is another and perhaps more appropriate way of reformulating the basic question of this Perspective: how big is the world beyond physics? How far can physics reach into the complexity of the above "Life chain"?

Kauffman maintains that physics cannot keep up with the untamed rise of biological complexity: the heart exists as a Kantian Whole, an entity that derives its very existence from the function it contributes to sustain: Life. Even more radically: there is no formal system to describe biological evolution because formal set theory cannot account for affordances [6], *i.e.*, the opportunities offered by the environment to the living creatures which co-evolve with it. The issue implies a plunge in deep philosophical arguments far beyond this author's knowledge and ability. It may well be that the degree of contingency (affordances) we are used to in statistical physics, *i.e.*, initial and boundary conditions, various forms of stochasticity, fall short of accounting for the complexity of the different functions that a given organism can deliver. Yet, this does not prove that physical situations dominated by contingencies are outside the realm of formal mathematization. Differently restated, the existence of the heart is obviously compatible with the zillions of atoms that compose it, but the question is: can the equations/algorithms that describe atoms predict its emergence? To begin with, one should recognize that Newton's description is not adequate to answer this question, because its phase-space is far too vast for systematic quantitative explorations. Differently restated, it is not known whether Newtonian trajectories can ever reach those portions of phase-spaces subject to the constraints which control the emergence of the heart from the world of atoms. A similar argument, in a much stronger form, applies to the many-body Schroedinger wave function, which Walter Kohn defined "not a scientifically legitimate concept" beyond some thousands particles, on account of its uncomputability [7].

But other descriptions may offer better insights. For instance, a strong advocate of a rule-driven universe is Stephen Wolfram [8], basing on the "Complex from Simple" (CfS) paradigm: simple rules, indefinitely iterated in time, give rise to fairly complex behavior. Cellular Automata (CA) algorithms stand as a poster child for

this approach. CA are powered by the notion of universality, namely the property by which inessential details are washed out in the process of iterating the rules, while the important ones are reinforced instead. However, with a few noted exceptions, CA fall short of providing a quantitative description of real-life complexity. In fact, it is quite possible that beyond a given level of complexity, Nature may rather obey a more realistic "Complex from Complex" (CfC) paradigm. Some authors note that, unlike physical systems, even the ones most credited as paradigms of complexity, such as spin-glasses [9], complex (adaptive) systems co-evolve with their governing rules [10–12]. The point is interesting, but would take us astray. For the sake of concreteness, we shall focus instead on just two central ideas which do not necessitate co-evolving rules: coarse graining and structure formation. Before plunging into these matters, let us discuss the important notions of weak and strong emergence.

Weak and strong emergence. – The coarse-graining (CG) procedure to be described in the next sections consists in formulating effective equations for collective variables resulting from the aggregation of many microscopic degrees of freedom.

CG is commonly pursued under the basic constraint of *realizability*, *i.e.*, the collective dynamics must be compatible with the underlying micro-dynamics and lack of realizability is regarded as a show stopper for any CG model. This corresponds to the so-called "weak emergence", meaning by this that the emergent interactions are still grounded in the underlying microscopic picture and cannot produce any solution that could not be obtained, *in principle*, by running the microscopic dynamics.

This contrasts with the so-called "strong emergence", whereby one postulates the rise of new "unrealizable" interactions that *cannot* be traced back to the underlying microscopic ones. According to the strong-emergence picture, even if we could solve Newton's equations for an arbitrary number of particles with arbitrary precision and indefinitely long in time (a conceptual as well as practical chimera), we would not been able to tell why X fell in love with Y instead of Z. This requires new functional degrees of freedom which pop out "on the fly" during the evolution of the system and are not contained in Newton's phasespace, no matter how large, see fig. 1. For such systems, phase-space itself becomes a dynamic and growing structure which co-evolves with its inhabitants<sup>1</sup>. This is an overly fascinating idea and possibly even a right one. But complex systems rarely abide by the Keats rule "Beauty is truth and truth is beauty" and in this perspective we shall indeed argue in favor of the more traditional weakemergence picture because of its logical economy: Occam instead of Keats.

Finally, let me emphasize that the strong emergence portrayed above is stronger than the one discussed for instance in [13], in which it is assumed that the collective

 $<sup>^1\</sup>mathrm{I}$  owe this clarification to Marina Cortes and Andrew Liddle.

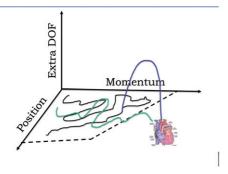


Fig. 1: Weak and strong emergence. According to the WBP idea, the "heart corner", albeit part of Newtonian phase-space, cannot be reached by any Newtonian trajectory, no matter how long in time (black thin curve), because the biological universe is non-ergodic. According to the weak-emergence scenario discussed in this paper, Newtonian degrees of freedom "coalesce" to form coarse-grained variables undergoing collective motion. Such collective motion permits to explore phase-space much faster than Newtonian mechanics, but since it is realizable, by definition, it cannot reach any region of phase-space which would not be accessible to Newtonian trajectories as well. According to the strong-emergence picture, the heart can only be reached by taking a jump along extra-dimensions beyond Newtonian phase-space, described by novel degrees of freedom which arise "on the fly" and cannot be prestated (horse-shoe segment in blue).

degrees of freedom react back on the microscopic ones (downward causation) but are still microscopically realizable. The coarse-graining picture described in the sequel is compatible with such "weak" form of strong emergence, as detailed in the closing section of the paper.

**Coarse graining.** – Coarse graining (CG) is the act of turning from a microscopic to a higher level of description, in our case a mesoscopic or macroscopic one. By "meso" we mean an intermediate level between the microworld of atoms and the macroworld of (classical) continuum fields. Somehow, between discrete molecules and fluid density, pressure, temperature and so on. A world where probability takes the central stage. The genuinely new interactions which govern the CG procedure are often called *emergent*, since they literally emerge from the underlying microscopic interactions by some form of statistical averaging. Although they do not enjoy the same status of the fundamental three, electro-weak, strong and gravity, they are much more effective in exploring the complex interface between physics and biology [4,5,14].

The key is that once one shifts focus from individual to collective motion, which is precisely what statistical physics does, genuinely new interactions arise, which are well positioned to narrow down the gap between physics and biology because they can converge to the regions of phase-space relevant to biological evolution much faster than Newtonian dynamics could ever possibly do. The claim here is that no co-evolving landscape is needed.

After such general premise, let us illustrate CG in some more detail. The state of a classical (non-quantum) many-body system consisting of n individual units (atoms for convenience) is described by a set of n Newtonian equations of motion:

$$\frac{\mathrm{d}r_i}{\mathrm{d}t} = v_i,\tag{1}$$

$$m_i \frac{\mathrm{d}v_i}{\mathrm{d}t} = \sum_{j>i} f(r_i, r_j), \quad i = 1, n, \tag{2}$$

where n is a large number, say of the order of the Avogadro number,  $N_{av} \sim 10^{23}$ . The key ingredient are the interatomic two-body (for simplicity) forces  $f(r_i, r_j)$  which, albeit known from the fundamental point of view (say electrostatics or gravity), give rise to an enormous variety of dynamical behaviours just due to the fact that they are many and nonlinear. A glass of water contains an Avogadro number of molecules....

Most importantly, the rich variety of solutions depends critically on the boundary and initial conditions, a crucial issue to which we shall return shortly. Since the manybody Newton's equations are far too many to solve, one naturally seeks for cogent simplifications which would not only retain the essential physics, but actually *distill* it out of the multitude of the possible microsolutions, thus cutting away the unvisited regions of phase-space (nonergodicity) but also visit the accessible ones which would remain unexplored by the microscopic dynamics for lack of time.

A most drastic and yet highly informative mesoscale approximation of Newtonian mechanics is the so-called Langevin equation, in which the ensemble of n Newtonian atoms is lumped into just one single "meso-particle", representing the average particle interacting with all other molecules through effective one-body forces. In general, each meso-particle represents a collection of  $\mathcal{B}$  molecules where the "blocking factor"  $\mathcal{B}$  provides a quantitative measure of the degree of coarse graining, see fig. 2. In this many-body mesoscale representation, each mesoparticle obeys the following set of generalized Langevin equations, known as Dissipative Particle Dynamics (DPD) [15,16]:

$$\frac{\mathrm{d}R_I}{\mathrm{d}t} = V_I, \tag{3}$$

$$I_I \frac{\mathrm{d}V_I}{\mathrm{d}t} = \sum_{i=1}^N (F_{II}^C + F_{II}^D + F_{II}^R) \quad I_i J = 1, \quad N = n/\mathcal{B},$$

$$M_I \frac{\mathrm{d}r_I}{\mathrm{d}t} = \sum_{J>I} (F_{IJ}^C + F_{IJ}^D + F_{IJ}^R) \quad I, J = 1, \ N = n/\mathcal{B}.$$
(4)

In the above  $R_I$  is the position of the *I*-th mesoparticle of mass  $M_I = \sum_{i \in I} m_i$  and  $V_I$  is its velocity. The mesoscale force consists of three components, labelled by C, D and R for conservative, dissipative and random, respectively, acting on the *I*-th mesoparticle as a result of the direct interaction with the *J*-th one.

By its very nature, compression of information brings to light new interactions which would remain hidden in

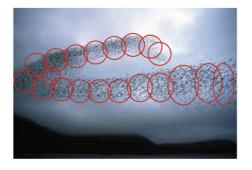


Fig. 2: The notion of collective variable (mesoparticles). A swarm of thousands birds displays collective motion which takes birds to regions of space that would remain inaccessible to each bird in isolation (useful to avoid predatory attacks). This collective motion is best described in terms of a few "mesoparticles" (red circles), each of which represents the dynamics of a large group of "correlated birds".

the forest of Newtonian details. Incidentally, nonlinearity is key since coarse graining does not commute with nonlinearity, and the new interactions arise precisely from this lack of commutativity. A few comments are in order. First, we note that the DPD equations still bear a strong resemblance to Newton equations, yet, with the following *three* crucial twists:

1) Conservative forces. The mesoscale force

$$F_{IJ}^C \equiv F^C(R_I, R_J)$$

is generally different from its micro-counterpart  $f(r_i, r_j)$ and usually more complicated. In the most fortunate instances, such difference boils down to a rescaling of the interaction parameters (renormalization), in which case the conservative force is called "minimal". It should be borne in mind that renormalization is a fortunate circumstance and by no means the rule. Hence, the specific form of  $F^C$ is mostly based on informed heuristics. To be noted that while the mass of the mesoparticles scales like  $\mathcal{B}$ , the mesoforces scale at most like  $\mathcal{B}^{2/3}$  because the internal forces within the particle cancel out by Newton's third law. As a result, the acceleration scales like  $\mathcal{B}^{-1/3}$ , meaning that a given distance can be covered by a larger timestep, scaling like  $\mathcal{B}^{1/6}$ . This is a weak dependence, but with  $\mathcal{B} \sim 10^9$ –  $10^{12}$ , it implies a nearly two-order boost in the timespan of the trajectory at a given number of time steps. Two orders of magnitude are significant, but astronomically short of accounting for the prodigious speedups displayed by fundamental biological processes, such as protein folding. To this purpose, the mesoscale forces ought to display highly non-trivial remappings of Newtonian forces, such as the emergence of free-energy funnels [17,18], leading to an exponential acceleration of the CG dynamics, which is how biologically relevant regions of phase-space may become accessible.

2) Dissipative forces. The second term on the RHS is brand new, as it reflects a mechanism, dissipation, with no counterpart in the Newtonian world (non-minimal

coupling). Dissipation is the result of the interaction of the mesoparticles with their environment (reservoir), to which they irreversibly loose their momentum and energy. A popular choice is the simple linear expression

$$F_{IJ}^D = -\gamma (V_I - V_J) e_{IJ},$$

where  $e_{IJ}$  denotes the unit vector along the direction joining particle I to particle J. The role of dissipative forces is again crucial, for they assure the convergence to the proper attractors.

3) Fluctuating forces. The third term is also nonminimal, as it reflects another mechanism which does not exist at the microscopic level: statistical noise, due again to the erratic interaction of the mesoparticle with its fluctuating environment,

$$F_{IJ}^R = \sigma \xi_{IJ} e_{IJ},$$

where  $\xi_{IJ}$  is a random number in [0, 1] and  $\sigma$  measures the strength of the fluctuations, *i.e.*, the temperature of the system. Note that fluctuation and dissipation are two faces of the same medal, linked by the so-called fluctuation-dissipation theorem, which fixes  $\gamma$  as a function of  $\sigma$  and vice versa. Random forces are essential to escape local minima in the (free) energy landscape.

Both dissipative and fluctuating forces may carry nonlinear and non-local dependencies in space and time (non-Markovian processes), because the motion of the particle affects the environment, so that the next particle may find a different one as compared to its forerunner. Since the environment is much larger than the particle, it is expected to regain its equilibrium on a much shorter timescale than the one of particle motion. Whenever such assumption fails, memory effects (in space and time) take stage. That is how long-range correlations emerge from local microscopic interactions, a profound hallmark of complexity.

Emergent interactions are no less fundamental than the microscale interactions they derive from. In fact, with reference to their own level of description, they are actually *more* fundamental. The point where they "lose" fundamental status is different, and namely the fact that while Newton's equations are self-consistent, n equations for the n degrees freedom, at the mesoscale level self-consistency is lost and must be forced back in by a procedure which is bound to lose information. A process known as *closure*.

In other words, the act of formally deriving the equation of motion for the mesoscale coordinates  $R_I$  and  $V_I$ , inevitably generates additional variables (correlations), which in turn obey additional equations, along an open hierarchy which only closes once N = n collective variables are included. At this point coarse graining reduces to a "mere" change of coordinates, which may be useful on its own, but defeats the very spirit of the ordeal, namely cut down the amount of information to be processed by retaining what is essential and discarding the unessential (the usual "baby in the tub" problem). There are no exact procedures to accomplish the "perfect" CG, except for very special instances, which means that CG invariably comes at the price of some irreversible loss of information. This is precisely where CG picks up its "artistic" component: maximize the return on investment by relinquishing unnecessary information without mangling the essential physics. This is a powerful strategy for Nature to search the tiny corners of phase-space "where things work" (the heart). It is often emphasized that living systems are powerful information processors, less noted perhaps that they are also and perhaps primarily, fairly efficient CG machines [17].

As to the ergodicity of Newtonian trajectories, rigorous results are exceptionally hard to obtain [19,20] and computers can help, but only to a point, because of the infamous time-gap problem. Tracing months-long trajectories (the time it takes for the heart to form) by ticking at a femtosecond scale, means simulating of the order of  $10^{21}$ steps. Not only is this far beyond the capabilities of any foreseeable computer. Some authors maintain that even if such computer were with us, they would not help much because of dynamic instabilities as combined with roundoff errors due to the floating point representation of real numbers [21]. One may observe that the above hindrances have not prevented the correct calculation of transport coefficients, nor did they hamper the predictions of climate models, as recognized by the 2021 Nobel Prize in Physics, but the point remains an interesting and important one.

The key issue, though, is the capability of correlations to fast-drive the systems towards the "hidden" regions of phase-space where biological functions can flourish, while ignoring the overwhelming majority of phase-space in which such functions stand no chance.

**Structure formation.** – The ability of growing coherent structures by exchanging mass, energy and information with the surrounding environment is one of the main hallmarks of living systems. The standard mathematical paradigm for structure formation is the reaction-diffusion model pioneered by the epoch-making Turing's paper [22] back in the 1950s. Mathematically this is described by a set of coupled reaction-diffusion equations of the form

$$\partial_t c_s = D_{ss'} \Delta c_{s'} + \mathcal{R}_s(c), \tag{5}$$

where  $c_s$  is the concentration of species s,  $D_{ss'}$  the corresponding diffusion matrix and  $\mathcal{R}_s$  is the rate of production/consumption of species s due to chemical reaction with the other species. Details change from system to system and they matter a lot, but the basic mechanism is fairly general; chemistry is local and nonlinear, while diffusion is linear and non-local. Taken together, they manage to transfer energy, mass and momentum across scales thus giving rise to a rich variety of non-equilibrium pattern formation phenomena. In particular, chemistry selects the critical size above which structures can grow and survive against dissipation, laying the foundations for morphogenesis.

Dissipative structures and beyond. The key insight is that the coupling between non-linear local chemistry and linear non-local diffusion, gives rise to organized patterns in spacetime which owe their stability (order) to the entropy they manage to dump to the environment [23]. To quote Prigogine, "entropy is the price of structure" [24,25].

This insight extends to a broad variety of nonlinear systems far from equilibrium, a paradigmatic example in point being Rayleigh-Benard cells, namely the coherent rolls which develop upon heating from below a fluid confined between two plates kept at constant temperature, once a critical temperature difference between the lower (hot) and upper (cold) plates is exceeded.

Prigogine's passionate attempts to elevate dissipative structures to the status of a paradigm of living systems, did not meet with much consensus among his peers. One of the reasons, as observed by Anderson, was the lack of a theory of dissipative structures far from equilibrium. Indeed, Prigogine's principle of maximum entropy production builds heavily on Onsager's reciprocity, which only holds near equilibrium. Modern developments in nonequilibrium statmech, particularly the fluctuation theorems by Crook, Jarzsynski and Gallavotti-Cohen [26-28] considerably extend the scope for quantitative analysis of systems far from equilibrium. For instance, England recently suggested "dissipative adaption" as a general paradigm by which living systems adapt to time-varying external drives by maximizing dissipation and quotes a number of self-assembling phenomena as a practical manifestation of such "principle" [29,30]. England's grand picture is very elegant but again, whether such elegance captures the actual behavior of real-life living systems remains open for grabs.

Interestingly, Kauffman notes that one reason why DS fail to attain the level of complexity of living organisms is the fact that biological systems spend useful work (free energy) to build up their own boundary conditions, the cell being a prime example in point.

By contrast, dissipative structures are subject to fixed boundary conditions, hence they can only generate more structures of different sizes and energy, but no qualitatively new structures at a higher level of the complexity ladder. This is a truly insightful remark which, in my view, could stimulate genuinely new work in modern statmech. This takes us to the next and final item: soft flowing reactive matter.

**Soft flowing reactive matter.** – Systems that spend work to build their own boundary conditions and co-evolve jointly together are a commonplace in soft matter. Consider for instance the formation of supramolecular structures, such as membranes, micelles and others, from the mesoscale dynamics of the system. In these models, one specifies suitable effective interactions which drive the formation of such supramolecular structures due to the combined effect of many nonlinear physical mechanisms, like surface tension (capillary forces), near-contact interactions of various sorts [31–34] and dissipation. Once these structures are formed, their motion affects the dynamics of the surrounding species, thereby realizing a set of co-evolving boundary conditions. This is how soft reactive matter implements the downward causal branch invoked by the "weak" form of strong emergence. The driving engine behind this scenario is the peculiar ability of nonlinear interactions to transfer mass, energy and information across scales, from small to large (coalescence) and back (breakup). This multiscale coupling is the physical mechanism implementing downward causality.

Self-catalytic DPD. Self-catalytic advection-diffusionreaction networks provide a rich source of structure formation, hopefully beyond the level of Turing patterns and dissipative structures, hence they may reach farther towards the goal of explaining structure formation at the level of the organs. I mean systems of DPD-like equations, augmented with self-catalytic reactions of the form:  $A + B \rightarrow C$ ;  $C + D \rightarrow E$ ;  $E + F \rightarrow A$ . Note that none of the three elementary steps above is auto-catalytic, but the set of the three together is, because at the end of the loop, A returns to A. This kind of reactions are conducive to a key property of living systems, *i.e.*, the ability to replicate and eventually reproduce. The spatial interactions are then in charge of securing that such replication/reproduction effects take place only where and when needed. Much work has been done on auto-catalytic networks, but I am not aware of any merger with mesoscale reactive particle dynamics (being itself a dynamic network). Once mesoparticles are equipped with suitable interactions supporting surface tension and other forms of dispersion forces, along with dissipation and suitable self-catalytic reactions, such combination might take us one step forward towards the emergence of functional structures.

Formally, they look as a series of reactive DPDs, one for each chemical species:

$$\frac{\mathrm{d}R_{I,s}}{\mathrm{d}t} = V_{I,s},\tag{6}$$

$$\frac{\mathrm{d}(M_{I,s}V_{I,s})}{\mathrm{d}t} = \sum_{J>I,s'>s} F_{IJ}^{C,ss'} + F_{IJ}^{D,ss'} + F_{IJ}^{R,ss'}, \quad (7)$$

$$\frac{\mathrm{d}M_{I,s}}{\mathrm{d}t} = \mathcal{R}_{I,s} \quad I = 1, \ N \ s = 1, N_S.$$
(8)

Can such reactive DPDs ever reach the complexity of biological organs, such as the heart or the eye, *i.e.*, *physiological complexity*? I, for one, would be inclined towards a sharp no, but I think it is fair to concede that until we figure out in quantitative detail what kind of structures can emerge from the above equations, the question remains open. Interesting work along these lines is just beginning to appear, see fig. 3 [35].

Summary and outlook. – In this Perspective I have tried to argue that modern statmech has developed a

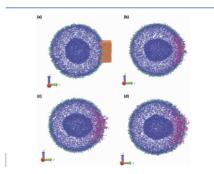


Fig. 3: Reactive DPD simulation of a shape-changing vesicle under the effect of adsorption of solvophobic monomers (brown particles) at the outer region of the membrane. The chemical reactions at the outer membrane convert the solvophobic monomers into solvophilic ones, with a consequent hange in the shape of the vescicle. Figure taken from [35].

number of remarkable ideas which shed new light into mechanisms at the roots of biological complexity. They can account for replication, non-ergodicity, memory, nonlocality, self-catalysis, co-evolving boundary conditions, and other fundamental mechanisms typical of living systems, not explicitly apparent from Newtonian physics.

Is it enough to predict the emergence of the heart? Is there room for "functional purpose" in our equations and algorithms? Steven Weinberg famously sentenced the Universe as pointless: "the more the Universe becomes comprehensible, the more it appears pointless" [36]. No room for purpose in the world of Lagrangians. To which another towering figure, Freeman Dyson, retorted that "no Universe with intelligence can be pointless" [37]. I stand by Dyson, on a blind date: there is more to physics than Lagrangians. The emergence of the cell first and of the brain later, mark two subsequent boosts of complexity which have changed the course of the natural world in ways that may indeed stand beyond reach of computable pre-stated equations, rules and algorithms. This is a fascinating and welcome speculation in many respects (who likes to be computable?). Yet, until we know what levels of complexity can be effectively attained by the systems I have tried to describe in this Perspective, this question remains up for grabs.

**Personal disclaimer.** – Whenever science investigates the functioning of living systems, it gets inevitably in close touch with religion, a close encounter which for many spells inevitable conflict. I am not among these: in my view, science and religion address different instances of human quest and they should proceed independently, with great mutual respect. The fact that physics may one day explain evolutionary properties of matter, including the emergence of complex functional units like organs, does by no means rule out the existence of a Superior Being. Quite on the contrary, it would point to a plan that comes with both hardware and software, which only makes it more subtle, elegant and worth admiration and gratitude. Georges Lemaitre says it best [38]: "the whole story of the world need not have been written down in the first quantum like a song on the disc of a phonograph. The whole matter of the world must have been present at the beginning, but the story it has to tell may be written step by step".

\* \* \*

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