Macroevolution *in Silico*: Scales, Constraints and Universals

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MACROEVOLUTION IN SILICO: SCALES, CONSTRAINTS AND UNIVERSALS

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Large-scale evolution involves several layers of complexity spanning multiple scales, from genes and organisms to whole ecosystems. In this paper we review several models involving the macroevolution of artificial organisms, communities or ecosystems, highlighting their importance and potential role in expanding the modern synthesis. Afterwards, we summarize the key results obtained from our model of artificially evolved ecosystems where individuals are defined as embodied entities within a physical, simulated world where they can evolve different traits and exploit multiple resources. Starting from an initial state where single cells with identical genotypes are present, the system evolves towards complex communities where the feedbacks between population expansion, evolved cell adhesion and the structure of the environment leads to a major innovation resulting from the emergence of ecosystem engineering. The tempo and mode of this process illustrates the relevance in considering a physical embedding as part of the model description, and the feedbacks between different scales within the evolutionary hierarchy. The future steps in modeling macroevolution by means of *in silico* models and how they might contribute to the modern synthesis are outlined.

Keywords: Multicellularity, hierarchical evolution, evodevo, major transitions, digital organisms

The large scale evolution of life appears marked by profound qualitative transitions affecting the structure, dynamics or even the logic of biological systems, from body plans to ecosystem-level features (Benton 1987; Eldredge 1989; Schuster 1995; Carroll 2000, 2001; Gould 2002; Kutschera and Niklas 2004; Nee 2006; Fedonkin et al 2007; Johnson and Stinchcombe, 2007). Such changes can occur at the small scale, when parts of the genetic toolkit experience a rewiring event that promotes the emergence of a novel property. Moreover, macroevolution, as pointed out by Erwin (2000) cannot be seen as an accumulation of small events associated with microevolutionary processes. Several levels of interaction between the evolution of metazoans and their feedback on the environment illustrate the point quite well (Erwin 2011). In particular, the potential for ecosystem engineering triggered by small phenotypic changes in given organisms can lead to large-scale changes in ecosystem organization, sometimes allowing new niches (and thus species) to emerge (Jones et al., 1994). As acknowledged by Kutschera and Niklas (2004), placing macroevolution within the modern synthesis requires embracing multiple biological disciplines and concepts. Among the relevant ingredients in the list, Kutschera and Niklas mention the *in silico* evolution of digital organisms as a complementary approximation between pure theory and field data..

Together with analysis of the fossil record and reconstruction of phylogenetic trees and networks, evolving virtual communities of organisms using simple, appropriate computational models, is a powerful approach towards understanding the emergence of innovations and testing hypotheses. Such models are usually qualitative in their goals and definition (Langton 1995; Adami 1998; Kutschera and Niklas 2004) although they can provide relevant interpretations for statistical patterns of extinction and diversification (Solé et al., 2002; Newman and Palmer 2003). Macroevolutionary patterns are, under these simplified pictures of reality, grounded in the existence of processes that cannot be captured by any simple extrapolation from the species-level picture. The term macroevolution is used here in relation toevolutionary events characterized by qualitative changes in structural, system-level properties. These changes are usually due to the presence of metastable states associated to complex genotype-phenotype mappings. In physics, metastability refers to the presence of long transient times that a given system spends in a given state (which appears steady) before it shifts (usually on a short time scale) to a new state, which can also be itself metastable (Crutchfield, 2003). The reader can easily identify our metastable states and the transitions among them as surrogates of the stasis and punctuation concepts used in evolutionary theory. The nature of metastability and why a transition takes place is of course at the core of the causal origin of punctuations. That necessarily means that the models need to allow for deep qualitative changes and in particular the rise of innovations, but they need also to consider a given range of scales and address well-defined questions. Such choices require simplifications, which often are in sharp contrast with the More importantly, as will be described below, simple models of macroevolution that largely ignore most details (such as biological traits characterizing a given

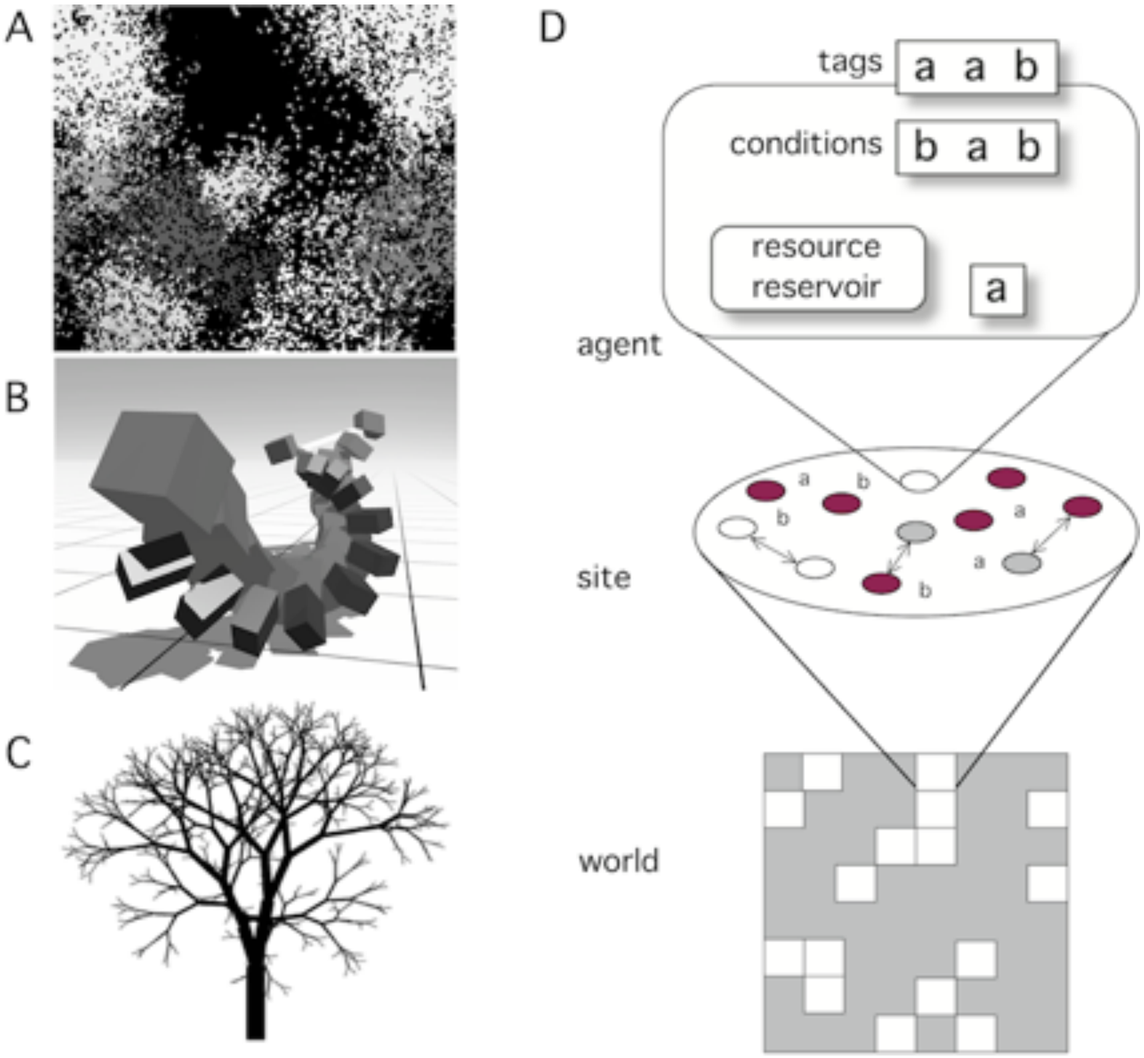


Figure 1. In silico models of evolutionary dynamics beyond the gene-based level involve several key ingredients, such as space (a) in Avida simulations (see text), a physical description of mobile parts (b) used to evolve 3D organisms in a given physical environment under given selection pressures (image by Zach Winkler using Stellar Alchemy package). Within the context of plant development, and structural principles of branching rules (c) along with physical constraints associated to efficiency in gathering light or having mechanical resistance are able to obtain optimal shapes similar to their natural counterparts. Models based on genetic algorithms and a general framework allowing communities of agents to interact, such as Holland's Echo model, allow to consider in a more or less explicit way the presence of hierarchies of organization, as outlined in (d), redrawn from Hraber and Milne, 1997.

species) would seem to be compromised in their explanatory power. At first sight, we would dismiss them for being too naïve. Yet, we have been learning over the last decades that some universal patterns of organization seem to pervade the way complexity rises and falls over time and that includes biological complexity (Kauffman 1993; Solé and Bascompte 2007; Solé 2011). These patterns span multiple scales, from the ups and downs of population-level dynamics (extinction, diversification, recovery) to the emergence of morphological programs. Some levels allow quantitative comparison between model and field data (this is the case of diversity patterns) whereas others can be compared at the logical level. The later would be the case for the emergence of minimal genetic modules allowing morphological innovations to occur and evolve, the emergence of a nested structure involving different interdependent structures or the development of given features such as evolvability or robustness. Here, the exact details of how interactions between genes or cells take place might be less important than the observation of the novelty. The logic structure of interactions among subunits and the potential for generating complex structures is what really matters. More interestingly, models allowing evolution to occur can also allow interactions between organisms and their environment, and the coevolution of such interactions. One example of such scenario will be discussed below.

Here we will briefly consider some examples of in silico models of large-scale evolution, where key innovations are shown to happen. These models (which we will compare) contain relevant ingredients but are also limited in their scope. Some of them consider simplified agents described by a genome but also by a spatial distribution of agents (figure 1a), while others (figure 1b-c) introduce an explicit definition of individual organisms in different detail. For some of these systems (like Echo, figure 1d, see below) the model allows to take into account several levels of complexity in the evolutionary and ecological hierarchy. In our context, hierarchy refers to different levels of organization associated to increasingly larger temporal and spatial scales. Such levels often involve a nested structure, with simple components (chemical reactions, cells or small programs) on the lower level and complex organizations (such as ecosystems or chemical reaction networks) on the higher one. If morphology were taken into account, the nested character of the virtual creatures should reflect a natural sequence of transitions from single-cell individuals to cooperating aggregates and eventually artificial organisms displaying characteristic life cycles. Because of the computational limits of managing embodied creatures, this particularly relevant nested hierarchy (McShea 2001) is often missing from most simulation models of evolution. Nevertheless, each of these approaches address different, although ultimately related, questions. The most important message from them is that, despite their intrinsic simplicity, they are able to display remarkable, sometimes unexpected transitions to novel forms of organization.

The potential for innovation, and the fact that it often produces structures and patterns strongly similar to those found in the large-scale evolution of life, supports a much more fundamental view of the world. This view, based on the physics of complex systems and our perception about the presence of constraints along with universal properties proposes that there are organizing principles that can be applied not just to evolution of living structures, but to any kind of adaptive system able to change. Afterwards, we will present our model approach to macroevolution, at this point centered on early events associated with primitive life forms predating the emergence of true developmental programs and complex life cycles (Solé and Valverde 2012). The model is able to properly illustrate the relevance of considering altogether genetic, ecological and physical components of evolutionary dynamics.

EVOLUTION OF DIGITAL ECOLOGIES

The term universality is well known within physics and pervades our current view of complexity (Solé and Goodwin, 2001; Solé 2011). It refers to the (sometimes surprisingly) robust macroscopic behavior exhibited by simplified models of real systems. This is dramatically illustrated by models of social or economic behavior, where extremely simplified approximations in which humans are replaced by random agents behaving almost as flipping coins and imitating the behavior of each other are often able to reproduce quantitative, nontrivial patterns (Ball 2004). In a very different context, RNA folding dynamics has been studied using string models where only a toy model physics is kept and most molecular complexity is ignored (Schuster et al., 1994; Huynen et al., 1996; van Nimwegen et al, 1999; Fontana and Schuster, 1998) and yet capture the most important aspects of the landscape structure, evolvability and robustness. This example is particularly relevant in our context, since the model illustrates how innovations suddenly emerge and how are they related with landscape structure. If universal dynamical patterns pervade macroevolution, the emergence of novelties would be ultimately understandable. The study of *in silico* complex systems and their space of possible designs has clearly revealed, at least in some cases, that such universals are present. The examples discussed below illustrate the potential of recreating evolutionary trajectories by means of models that necessarily introduce great simplifications. In this section we summarize previous work and the major achievements obtained by using computational models involving agents with different levels of internal complexity, where the evolutionary dynamics take place without an explicit consideration of the organismal structure, its anatomical and physiological properties or developmental programs.

The first attempts to simulate the evolution of complex ecosystems, composed of individuals with the potential to evolve, started with the rise of computers after the second World War (Dyson, 1998; 2012). The first simulation experiments of macroevolution within computers were performed by Nils Barricelli who used ENIAC, the first computer to be used in scientific research (Baricelli 1961, 1962). His work had little impact, probably because of his original viewpoints and the still unknown potential of computational methods, particularly among biologists. Barricelli's work was encouraged by the early contribution of mathematician John von Neumann, who develped the first abstract model of a self-replicating machine (von Neumann,, 1966; Sipper 1998; Freitas and merkle 2004; see also Solé 2009). Von Neumann contribution actually provides a perfect illustration of the potential explanatory power of even abstract theoretical models of living systems. In trying to define what type of machine would be able to replicate itself, and years ahead of molecular biology and our knowledge of DNA structure and function, von Neumann's result was a system that contained an internal description of itself (as it occurs with DNA) which needs to be replicated along with the rest of the machinery, which we easily identify with polymerases and other components of real cells, This machine was operating in an environment full of energy and the required building blocks and thus the so called “kinematic model” did not involve ecological factors nor limiting resources. Barricelli made a step in this direction by considering populations of interacting digital organisms described in terms of small programs.Those ideas remained frozen until Thomas Ray, an ecologist working on biodiversity in rainforest ecosystems, explored similar questions using much faster and more efficient computers. Driven by the question of how such great numbers of species emerge and persist in complex ecosystems, Ray ended up building a simulation model based on a set of computer programs competing for the RAM memory of the computer and having the potential to self-replicate and -more importantly- do it with small mistakes (Ray 1991). The computer programs did not inhabit a real space. Instead, they were stored in available memory positions and every program could interact with any other one.

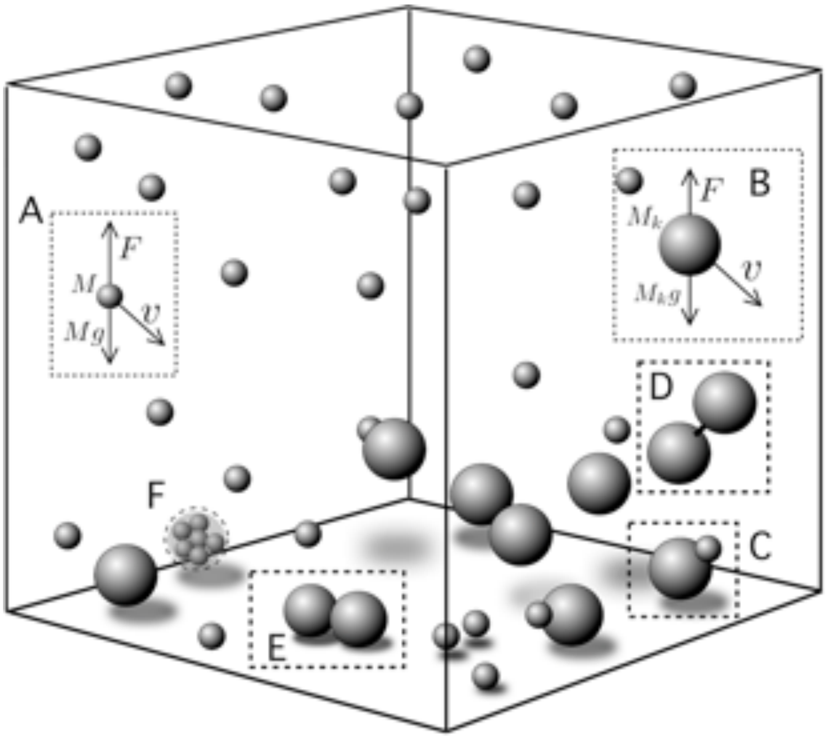


Figure 2. Basic scheme of the components of the CHIMERA model (Solé and Valverde, 2012). The system is confined within a rigid cube. Nutrient particles fall from the top layer (a) experiencing physical forces. Cells also experience the same forces, as described by Newton's laws (b). Additionally, cells (c) and particles get degraded. Cells can interact with the boundaries of the system (e) as well as between them (f). Cells increase in mass everytime they collide with a nutrient particle (g) if they have the right internal metabolism. A detailed explanation of the rules is given in (Solé and valverde 2012).

Under the memory constraints imposed by finite computer resources, the so-called Tierra model was able to show how some evolutionary innovations can spontaneously develop. In particular, some major transitions took place as soon as programs started to compete. An early event was a genome reduction innovation, related to the fact that shorter programs can replicate faster than larger ones. This occurs when parts of the coded program can be removed with no consequences. In that respect, redundant pieces of code could be deleted with no harm. Later on, shorter programs emerged, unable to replicate themselves. In other words, parasites came to (digital) life. Hyperparasites, i. e. programs able to replicate using pieces of code carried out by parasites, came later, and some programs developed the capacity for exchanging parts of their codes, mainly as a response to escape from parasites (see Hamilton et al. 1990; see also Hillis 1990) thus define an innovation that we can label as a primitive version of sex (Ray 1991, 1994, 1998). Eventually, groups of slow-replicating programs were able to replicate faster by cooperating among them.

Tierra's approach was followed by several versions, among them the artificial life platform Avida (Adami and Brown, 1994; Adami 1998; Adami 2006) that included a spatially extended definition of the system. The local nature of interactions makes it possible to observe spatial segregation of individuals (see figure 1a). This system also allows for exploration of questions related to macroevolutionary theory (Chow et al 2004; Yedid and Bell, 2002). The local range of interactions is actually very important, since it provides a great source for diversification tied to limited competition (Solé and Bascompte 2007). The described spatial dynamics, a genome-level description of individuals including epistatic interactions (Lenski et al. 2003) and the possibility of defining a core metabolism based on the internal logic (Adami 2006) makes Avida particularly suitable for in silico experiments of evolution. Interestingly, evolutionary paths are very often punctuated. Such a dynamical regime has been interpreted in terms of a tendency to increased instability (Adami 1999), although a much more general scenario might actually be at work involving neutral landscapes.

Punctuated patterns of change have also been reported from models of ecosystem evolution based on a more abstract conception of genomes, such as Echo model (Holland 1992, Hraber and Milne 1997, Smith and Bedau 2000). It was originally designed as a model for evolving general complex adaptive systems. The term ”“adaptive” refers to a system composed by many parts (individuals, cells, organisms etc) displaying adaptation, meaning the potential of processing external information and modifying their behavior accordingly. This capacity for adaptation is often referred to as *agency* and those individuals of components capable of adaption are named *agents*. In Echo, individuals have haploid genomes and, like Avida, are located on a two-dimensional lattice (fig. 1d, bottom). Each individual contains a rather abstract definition of its properties as well as a given storage capacity, defining its interaction with available resources. Because Echo was defined in such general terms, it was possible to use it for modeling general problems, such as the emergence of strategies in theoretical game frameworks. Perhaps for this reason, its comparison with biology is more difficult (Hraber and Milne, 1997; Smith and Bedau 2000). In particular, the specific ways in which agents interact or the difficulties of properly defining a species limits its potential to address interesting questions concerning macroevolutionary changes. In this context, we should mention that most models of artificial evolution incorporate a vague definition of species and the cloud of “genomes” associated to the existing pool of strings should be seen more as a quasispecies (Eigen and Shuster, 1977). Those models incorporating programs coding for genome functionality and introducing matching allow to more properly identify clusters of closely related genomes that can be considered properly defined species.

Although a critical view to the original Tierra work (Gould 2002) suggested that some results should be expected (and are thus not truly novel), further work in this field has confirmed the existence of sudden transitions as a rather generic feature. The main lesson from these models is that punctuated change and the emergence of novelty seem to be intrinsic properties of complex systems. These models certainly lack a number of other interesting properties, which are especially important when comparing them to macroevolutionary patterns seen in the fossil record. As we will discuss below, an important part of what might be missing in this type of model is the presence of embodiment (a physical description of individuals within a given external context), and a description of the environment that allows agents to interact with it and eventually modify its properties.

EVOLVING MORPHOLOGIES

Concerning the embodiment problem, considerable efforts have been made in developing evolutionary models of organisms having a well-defined spatial structure (beyond the genotype) and, when possible, a physical description close to some phenotypic representation (Eggenberger 1998; Doursat 2008, Newman and Bhat 2008, Prusinkiewicz and Lindenmayer 1990). An early attempt to this direction was provided by Karl Sims (1994a) who examined how physically defined creatures evolved, including in their description a genotype in terms of a directed graph, which was used to define a neural-like control of mobile parts and a set of connected blocks. Such pieces can move and define the basic physical modules, only constrained by the physics and the presence of other neighboring elements. Using artificial selection operating at the level of efficient movement (how far can you displace in a given time scale) it was shown that, once a given optimization problem was defined, evolved creatures with more or less repeatable features were obtained. In Figure 1b we show one of these creatures, evolved by means of a standard evolutionary algorithm. This creature has been generated in a 3D liquid medium where most optimal organisms have to develop an efficient movement. An interesting observation emerging from these experiments is that some evolved forms remind us of some well-known forms of locomotion displayed by real metazoans. These include fish and snake-like movements. However, we also notice a large number of evolved structures to little resemblance with real life forms. This might be an inevitable result of the limitations associated with the model or might actually involve something deeper: the artificial constraints imposed by the shapes chosen to generate the building blocks. Since the geometry of the blocks is rather artificial and include considerable rigidity, some important limitations to the potential degrees of freedom should be expected.

Evolved creatures like the ones described above are certainly appealing and have been useful in initiating a more ambitious (but still little explored) agenda of evolutionary dynamics. However, the current state-of-the-art model is rather limited for a number of reasons. One limitation already mentioned is that imposed by the building blocks used in these simulations. Another one is the limitations in computer time associated with modeling populations of creatures, which is highly prohibitive. Moreover, individuals move and evolve in space, and no other selection process, except for their performance in moving on their medium, is at work. Since no constraints are operating at the level of finite resources, but especially in terms of the feedbacks with the environment, little is obtained in terms of interesting adaptations. Improvements included using pairwise competition between a reduced number of creatures (Sims 1994b). Some simple modifications, including the role played by substrate adhesion or even its composition (many interesting innovations can be described in terms of how organisms dealt with sediments and bioturbation) would provide a better, and perhaps richer, view. Additionally, much larger populations and a more relaxed definition of the physical blocks should help in comparing the resulting communities with those examples from the fossil record, suggesting a major role for competition. Finally, there is an obvious limitation related with the way the organismal form is generated (see Erwin 2011 and references therein). The whole structure does not result from a developmental process. Instead, the absence of a true developmental program forces a predefined (though complex) mapping between the basic genotype description and the phenotype.

Introducing the developmental rules that shape the organism is a key ingredient in validating macroevolution models in silico. It seems clear that without connecting development and evolution, a large part of the whole picture will simply fall apart. But the introduction of developmental processes, even at a simplified level, is one of the most difficult tasks faced by computational models. Not surprisingly, such an ingredient has been largely ignored by most model approaches to macroevolution. Two successful counterexamples are the Niklas approach to the landscape of ancient vascular plants (Niklas 1994; Niklas 1997 and references cited) and related approximations (Prusinkiewicz and Lindenmayer, 1990) where branching patterns and the underlying morphogenetic constraints are implicitly included. By using an explicit form of fitness function, Niklas was able to define a morphospace of potential plant forms where each axis was associated with a well-defined selective trait. Light capture, mechanical resistance and seed production where (roughly speaking) the basic axes. Starting from a given initial condition representing a primitive, very simple form, an evolutionary algorithm based on adaptive walks (Kauffman and Levin, 1987) allowed for exploration of such space by introducing small modifications of existing structures. These mutations are accepted only when there is an increase in fitness, and in this way we obtain different trajectories depending on the number and nature of the imposed selective constraints. The resulting shapes are remarkably similar to those expected with efficient structures in different habitats and also while looking at the evolutionary time scale.

A different, and very promising avenue considers the role of "generic" physical mechanisms of morphogenesis that are not the result of complex regulatory processes. Instead, physical forces including gravity, adhesion or diffusion are considered (Newman and Comper, 1990). The interplay between these mechanisms allow for spontaneous pattern formation through segregation of cell types. Some of these generic, pattern-forming mechanisms predate the early history of multicellular life forms, along with others controlled by genetic circuits (Forgacs and Newman 2005). Using some of these generic mechanisms, an evolutionary model of form can be constructed. This was made in (Hogeweg 2000a, 200b), where the mechanisms of morphogenesis, defined over populations of multicellular artificial organisms, are evolved. Hogeweg's approach considers the growth of a simulated embryo, including a gene network description, adhesion among cells, cell division and death, cell migration and differentiation. Adhesion is introduced using very simplified but effective physical models (Graner and Glazier, 1992; Glazier and Graner 1993; Sawill and Hogeweg 1997; Podgorski et al, 2007) and is one of the main players influencing the evolutionary dynamics of these virtual metazoans and their potential for diversification, consistent with the role played by development in the context of morphological radiations (Eble 2003). As pointed out by Hogeweg (2000b) differential cell adhesion (consistent with its in metazoan evolution) is regulated by the gene network affecting cell movement, division, growth and death and communication between cells through cell-cell interactions. The model leads to a rich variety of forms. Although no developmental program was present, the choice of the potential phenotype and a properly defined fitness function shows that approximation to the evolution of biological form can be successful provided that the right variables are chosen.

One of the most important results coming from Hogeweg's work is the existence of a neutral landscape of possible phenotypes that pervades the punctuated nature of transitions (Hogeweg 2000b; see also Fontana and Schuster, 1998). Long periods of stasis are characterized by slow increases in fitness as small variations in phenotype are achieved. Selection for diverse gene expression patterns is used (see also Solé et al., 2003). Such choice can be justified by the well-known trend. The number of cell types is a good measure of complexity, which is known to increase through metazoan evolution (Carroll, 2001, 2005; Valentine et al., 1994). Increases in cell type number provide a high potential for further evolution of anatomical and functional complexity, essentially through division of labor and the formation of specialized tissues (Maynard-Smith and Szathmary, 1995). Since the imposed selection pressure is rather generic, no special constraints are posed on the way genes (here defined as a Boolean network, see Kauffman 1993) interact and influence cell arrangements; no particular, predefined architectures and developmental plans are favored. The model is able to evolve complex forms, and in the process of evolving them, different remarkable changes take place. Complex shapes and some familiar ways of obtaining them (such as tissue engulfing) appeared and complex interactions between apoptosis or migration emerged. As pointed out in (Hogeweg 2000a), morphogenesis itself emerges as a byproduct of optimization for cell diversity. It is worth noting that other works involving cell type richness as a fitness function favour the explosion of pattern forming motifs as soon as a threshold of genetic complexity is reached (Solé et al., 2003).

The richness of relevant results obtained from the previous models is something we cannot ignore. Simple models are able to reproduce some key traits of evolutionary dynamics. Some models suggest that artificial and real evolutionary patterns share important commonalities. A missing ingredient, is the potential for feedbacks between developmental processes and the ecological scale. Such feedbacks, if present, can trigger major transitions. The next section presents: a simple example of a model ecosystem where cellular interactions, the evolution of adhesion properties and a physical description of cells and their interactions unleash a large-scale evolutionary change.

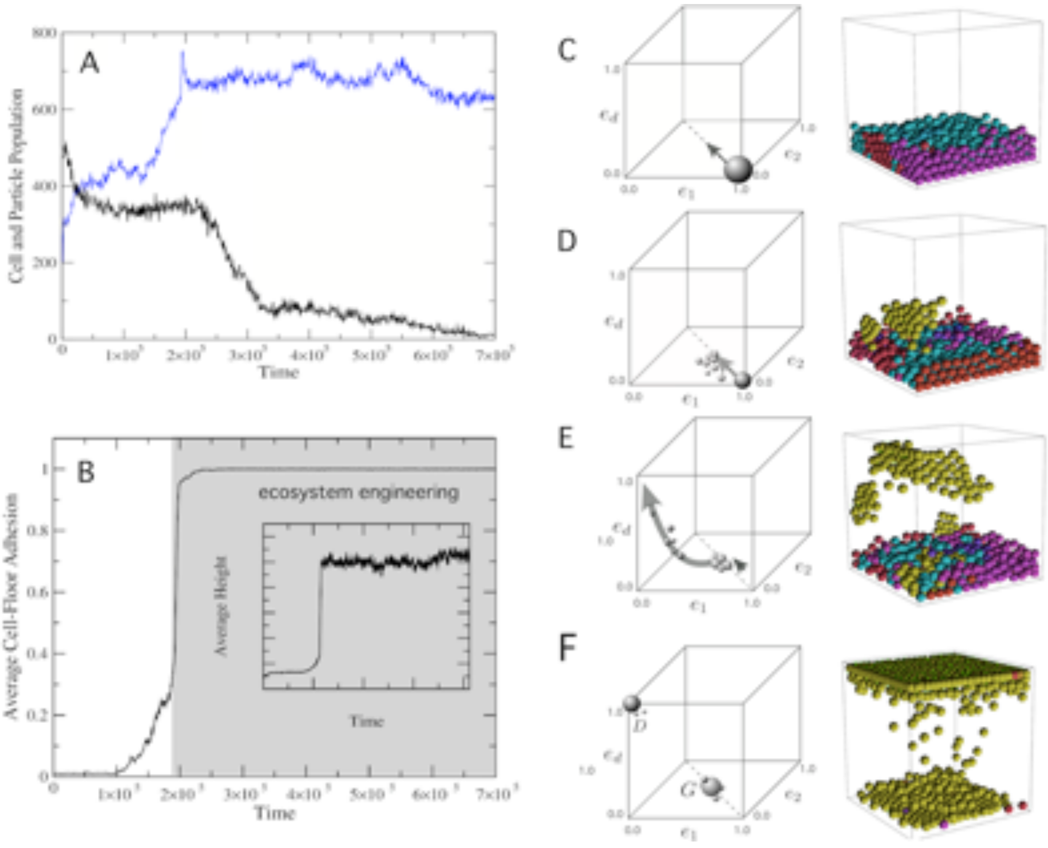


Figure 3. Emergence of a major innovation at the ecosystem-level in the CHIMERA model. The population dynamics (a) of cells and nutrients is coupled with the development of cell aggregates and the interaction between cells and their environment (b). A summary of some of the events is displayed in (c-f) where both the trajectories in efficient space (left column) and the actual distribution of cells in the system (right) are shown. After a transient, the whole community structure gets inverted and the nutrient flows completely modified. As a consequence, a new community structure emerges.

EMBODIED EVOLUTION OF NOVELTIES

The previous models teach us something important. Even under rather limited assumptions, some of the key innovations that mark the large-scale pattern of evolution seem to emerge. If we introduce the appropriate ingredients associated with the emergence of forms, whether or not tied to a genetic network, some major innovations to arise. In this context, embodiment seems important in two relevant ways. Embodiment provides (if properly defined) a selection level that can be made explicit and well connected with an external environment where selection pressures take place. On the other hand, embodiment results from the process of development responsible for the construction of the body (Forgacs and Newman 2005). An evolved organism has a size and shape that largely results from both internal rules of construction along with constraints imposed by the external world.

A more general set of questions should be considered in order to fill the chasm between these two well-defined scenarios. These questions pervade some of the key problems associated with expanding the modern synthesis. In particular, how the interaction of physical context, cell-cell adhesion properties, and ecological and genetic factors favor the emergence of cell aggregates? How does the environment modify or influence the evolution of cell diversity and cell-cell interactions? Is there a role for spatial embodiment in favoring the emergence of innovations? Here such a pre-body plan scenario and its potential for generating complexity is explored by allowing a physically embodied model of a cellular community to freely evolve. As will be shown below, a simple model of physically interacting cells with adhesion properties starting from a set of independent, genetically identical cells exploiting a single energy resource (from a repertoire) evolves in time towards a spatially segregated community involving a trophic chain. The ecological network includes both a population of generalists feeding on all food sources available along with a population of specialized detritivores. The transition from the original monomorphic population to the spatially organized aggregate with ecological structure takes place through the emergence of an innovation grounded in evolving adhesion between cells and walls as well as cell-cell adhesion. In spite of its simplicity, it fairly well illustrates the value of this type of model to explore the potential for niche creation and innovation of even simple embodied evolution models. The creation of new niches is actually an important aspect of innovation, since they naturally define new context where novelty can arise.

All the models described above lack several components that seem to be required in order to obtain satisfactory results. Phenotypic features decoupled from environmental clues might fail to properly address the nature of innovations. Some forms are likely to appear because there is no true selection pressure and potential sources of convergence might actually correspond to limited potential repertoires. Here we consider a new model approach that intends to include within the same framework several key ingredients spanning different scales. In our modeling approach, the so-called CHIMERA model, evolution takes place within a spatially confined environment where physical forces play a role as external constraints. Organisms are also spatially embedded structures and their embodiment is relevant as it provides the proper link with the external world and the biotic scenario where other organisms inhabit.

Our starting point here is a population of single-cell organisms, where each cell in the initial population is identical. The spatial domain is a cube with floor and walls, with a vertical gravitational field and external fluctuations of a given intensity. In figure 1 we display a basic scheme of the system considered here along with the different components of the physical interactions that are taken into account. This framework is somewhat related to recent experimental designs using yeast strains of cells in order to explore in vivo scenarios for the emergence of multicellularity under the action of gravity and selection for size of aggregates (Ratcliff et al., 2011). It was shown that, under the selective pressure associated to selecting the largest aggregates that formed in the experimental design, aggregates of a given average size and internal differentiation were selected.

Specific physical rules are introduced in order to simulate cell-cell collisions. Particles are produced constantly at the top of the box, falling under the simulated gravity and degrading at a constant rate. Initially, we introduce a cell population able to exploit only one of these food sources with maximal efficiency. The technical details (particularly the implementation of the Newtonian physics used to move cells and particles as well as managing their interactions) are described in (Solé and Valverde 2012), but a summary of the key rules can be made as follows:

1. Movement: both particles and cells experience a gravitational field as well as a fluctuating velocity field associated with a turbulence-like changing environment. Particles are removed from the system with some probability. The total number of different types of particles is constant (we have used two, four and six types with similar results).
2. Each cell carries a given set of internal parameters and variables: they have a given size and mass and they have a list of possible particle types that they can take and the efficiency of the grazing for each particle type.
3. Cells can attach to the surface of the walls with some probability. When they do, adhesion forces are equivalent to a physical, elastic string connecting cell and wall surface. Another adhesion probability (and another type of spring) is used to make cell-cell adhesion. At the beginning none of these adhesion features are present.
4. If a cell (which has a given size) interacts (collides) with a given particle, it ingests this particle when the efficiency for metabolizing that type of particle is non-zero. The value of the efficiency gives the probability of ingestion. If taken, the mass of the particle gets transformed into mass of the cell.
5. There is a maximum cell size allowed. Once reached, the cell splits into two daughter cells with the same size. There is a minimum cell size allowed: if cell mass drops below this value, it dies and disintegrates into a number of detritus particles proportional to its original size. Detritus particles are also allowed to be part of the nutrient intake of cells (initially, the efficiency of detritus consumption is zero).
6. Each time a cell divides, mutations can occur in the daughter cell. A new type of particle can become accessible with small efficiency (and the previous efficiencies are reduced) and thus the new cell is more generalist. Alternatively, the existing efficiencies might experience changes (always keeping the trade-offs associated with specialization versus generalism). Similarly, adhesion to the medium or to other cells can cause mutations. In this way, the potential to form cell aggregates increases and cells can also climb the walls, offering a larger area for capturing particles.

The model is simple and only captures a basic physical interaction framework along with simple rules of mutation, growth and death. Selection of different phenotypes is thus affected by the way cells are able to improve their grazing efficiency. But in spite of this simplicity, the model is able to evolve towards a rather unexpected organization. In figure 3 we illustrate some of the key events that occur in a typical simulation run. In (a) we show the overall pattern of population change (in terms of numbers of cells and particles). As can be seen, the population grows until it stabilizes around 700 cells. The change in the number of particles in the environment (lower curve in (a)) is much more complex. At the beginning, particle population decays (as expected) and stabilizes for a while, then starts to drop and keeps decaying. If we also follow the evolution of adhesion probability to the walls, we can see (figure 2b) that a rapid increase starts at some point and grows in an accelerated way until its maximum is achieved. The plot of the average position of cells along the vertical axis (figure 3b, inset) illustrates this qualitative change: initially all cells are at the bottom but, with increased cell-wall adhesion they start to occupy higher positions until a whole inversion of the cell population occurs.

Figures 3c-f illustrate what has taken place. Each plot shows an idealized picture of an efficiency space (left column) with two efficiencies e_1 and e_2 associated with incoming particles and a third one e_d associated to processing detritus particles. The right column shows the actual location of cells with a color-coded probability of cell-floor attachment. The flow of particles has been removed for clarity. As the evolutionary experiment proceeds, a better way of capturing particles is reached by increasing the overall surface they can offer to the flow. This is achieved by an increase in the probability of cell-wall attachment, but also by an increase in the cell-cell adhesion. The later allows cell aggregates to prevent cells from falling to the bottom. As this occurs, the generalist aggregates become able to graze on all kinds of particles with moderate efficiency. However, as soon as some particles hit the roof, they actually interact with the direct source of particles and start attaching to the upper boundary of our spatial domain, eventually growing there and strongly reducing the downstream particle flow. This defines a major change in the community organization, and it actually creates a new niche: dead cells are transformed into detritus and the bottom layer gets enriched with them. As time proceeds, so does the emergence of a new group of cells that become specialists: a detritivore layer appears and a stable food web with three layers has been created. Given the fluctuating nature of detritus particles, a strong cell-floor adhesion is no longer useful and this parameter evolves to small values.

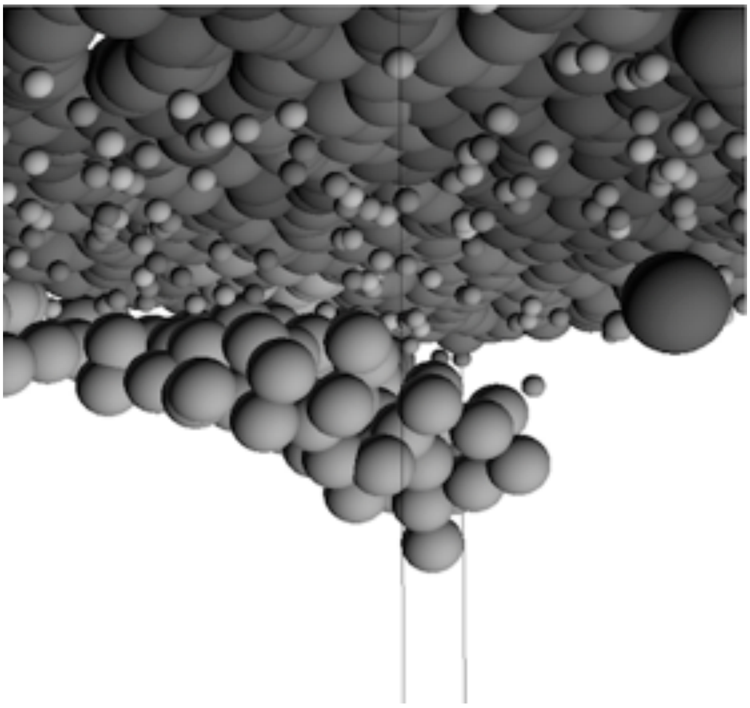


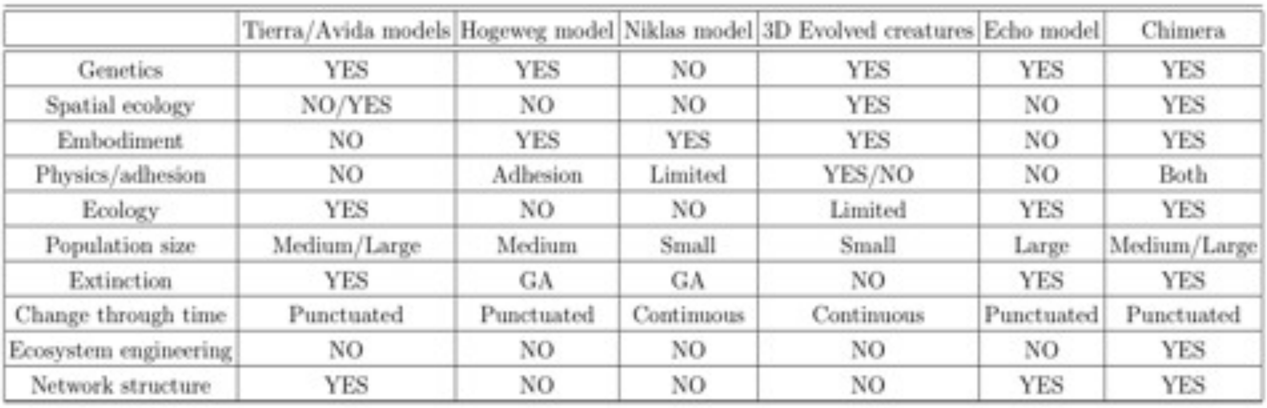
Figure 4. Multicellular aggregates with characteristic size and exhibiting compact shapes are obtained when we allow more complex physical interactions among cells to occur. Here we show an example of such aggregate, which appears on the top of our 3D medium. Such aggregates remain cohesive and attached for very long times, and often involve cooperation among cells.

The previous result is interesting in several ways. On the one hand, it illustrates the potential for generating a higher-level organization where cell aggregates do not strictly cooperate in terms of sharing resources, but they do cooperate in maintaining the coherence through the innovation process. The ”“discovery” of the source of nutrients can be interpreted in terms of an innovation that allows the emergent system to act in terms of ecosystem engineering: the new organization provides an opportunity for further change and speciation. As adhesion levels increase, cell aggregates are favored. It is this increased adhesion, which slowly favors the grazing, that eventually triggers the ecological transformation. Once the new top-floor community is organized as a large cell aggregate, flows are transformed and along with the detritivore niche, a cell-level attribute (adhesion parameters) is modified. We can see here that the feedbacks between different levels are strong and required in order to understand how the transition from a generalist-dominated community to a structured community displaying new niches can occur. At a simple level, we can also see that the hierarchy cannot be easily broken into upper and lower layers without missing important information.

DISCUSSION

In silico models of evolutionary change should be natural components to consider in our exploration of macroevolutionary patterns. Previous models might have been limited in offering a solid ground for understanding real processes. Nevertheless, they offer, along with experimental dynamics using microbial populations (Lenski and Travisano 1994; Elena et al., 1996; Elena and Lenski 2003), what no other approach can: an opportunity to recreate the past and explore how complexity can emerge over time. The previous example is an illustration of how evolutionary complexity can emerge from a rather simple set of rules, provided that we give an opportunity for developmental and ecological processes to interact. Our artificial creatures are autogenic engineers (Jones 1994): they change their environment mainly via their own physical structures. The success of our model might be due to the complete set of key components that we allow to interact freely. By using space, diverse ecosystems can be built through spatial segregation of subpopulations. By allowing simple components of pattern formation or aggregate generation, it is possible to introduce simple forms of cooperative dynamics. By embedding the virtual creatures within an ecosystem where physics plays a role, we allow for selection pressures. Previous models have been very useful in providing insight into relevant questions concerning the origins of evolutionary innovation, but their answers are necessarily limited, and new modeling approaches will be required if we want them to help in defining a new synthesis. The variety of ingredients incorporated by mainstream modeling approaches is considerable (Table 1).

The large-scale development of evolution is a single-experiment event. Such an event, as it happens with our own universe, starts with an explosion (Marshall 2006). Reconstructing the pace of past events has been a successful enterprise (Fedonkin 2007; Erwin et al 2011). Moreover, evo-devo provides a unique way of understanding the potential sources of morphological innovation at the organism level and how they might have participated some of the major transitions. However, there are several layers of complexity that might require other theoretical and computational approaches, able to connect different scales.



	Tierra/Avida models	Hogeweg model	Niklas model	3D Evolved creatures	Echo model	Chimera
Genetics	YES	YES	NO	YES	YES	YES
Spatial ecology	NO/YES	NO	NO	YES	NO	YES
Embodiment	NO	YES	YES	YES	NO	YES
Physics/adhesion	NO	Adhesion	Limited	YES/NO	NO	Both
Ecology	YES	NO	NO	Limited	YES	YES
Population size	Medium/Large	Medium	Small	Small	Large	Medium/Large
Extinction	YES	GA	GA	NO	YES	YES
Change through time	Punctuated	Punctuated	Continuous	Continuous	Punctuated	Punctuated
Ecosystem engineering	NO	NO	NO	NO	NO	YES
Network structure	YES	NO	NO	NO	YES	YES

Table 1. A comparative list of features exhibited by the in silico models of evolution discussed in the text. Here we have used a list of relevant features and listed their presence or absence. The table reveals a wide diversity of combinations, often related to the particular scope of the problems being addressed. The last feature (network structure) refers to the presence or absence of a food web organization and thus an explicit ecology.

Some basic conclusions have to be extracted from the previous analysis, with important consequences for future models of macroevolution:

1. Despite their differences, several important trends seem to be shared by most *in silico* models. The presence of punctuated equilibrium seems to be the most obvious one. This result appears consistent with the suggested universality of neutral landscapes where complex systems evolve (Schuster et al., 1994; Huynen et al., 1996; van Nimwegen et al, 1999; Fontana and Schuster, 1998; Wilke 2001; see also Macia and Solé 2009; Raman and Wagner 2012). Such universality is grounded in the assumption that these systems share a fitness landscape percolated by large domains of neutrality. The landscape itself is stable, since it is assumed that genome complexity or how organisms feedback with their environment can be neglected. This assumption can be taken as a good approximation under some circumstances, but certainly not when dealing with complex organisms on very long time scales. A more general framework is needed.
2. Embodiment has been ignored by most modeling efforts due to its costly implementation. This method, however, provides the right interface between the environment and organismal structure. As such, embodiment defines an essential piece of the genotype-phenotype mapping. Small improvements introduce further physical realism, such as directed interactions (and not just distance dependent, radial ones) enable a bigger potential to develop more complex structures. In figure 4 we show an example of the CHIMERA model after such improvement was made. Cohesive aggregates of some given average size are formed, defining a new level of organization.
3. Most models ignore an essential but complex part of the organism: the generative plan for creation from a process of development. Decoupling development from evolution is problematic. The strong links existing between evolution and development ask for a serious attempt to connect them also in silico. In the present version of CHIMERA discussed here there is a linear mapping between the underlying genotype carrying as associated phenotype the set of numbers characterizing the individual's efficiency. Future versions will introduce an explicit regulatory network and thus the potential for epistatic interactions which can evolve in time. Such networks

might also help defining the requirements for minimal genetic toolkits able to facilitate the emergence of multicellular systems.

4. Typically, models of large-scale evolution decouple individuals (agents, organisms) from their environment except for their presence/absence from a given spatial location. Organisms gather resources whose only impact is to provide the appropriate energy to sustain individuals. In this way, ecosystem-engineering events will not be present and an important component of macroevolutionary dynamics will be missing. Such coupling, which is bidirectional and cannot be broken in most cases, leads to a causal loop where two levels become dependent on each other. In our example, the requirement for efficient grazing favours an increase in adhesion rates which is further enhanced as aggregates of closely packed cells form on the boundaries of the system. Such aggregates are actually a primitive form of cooperation based on physical rules of attachment. The continuous set of changes (which we can think of in terms of a simple genome where each gene carries specific information) ends up suddenly when the evolved adhesion and growing aggregates trigger a major transition which actually modifies the vertical organization of the whole ecology. None of the two series of events (increased adhesion and reorganization of nutrient flows) could be understood separately from each other.
5. Properly designed experiments using virtual communities of organisms evolving in a given ecological and physical context allow us to test potential theories associated with the relevance of ecological interactions on the emergence of novelties. In silico models considering ecological levels of organization should be used in order to analyze the effects of extinctions and their subsequent recovery patterns, which have been explored in recent years using different approximations, particularly at the level of paleocommunity food webs (Solé et al, 2002, 2010; Roopnarine 2006). Although the problem has been also modeled using the Avida platform (Yedid et al 2012) by simulating external shocks on virtual communities of evolved, embodied creatures can provide a better source of insight, connecting multiple scales of the evolutionary hierarchy. In particular, it can help understanding the interplay between evolving developmental programs after mass extinction and their role in shaping new ecosystems.

The existence of universal trends in large scale evolution might seem a rather bold idea. In the end, the paths followed by evolutionary trajectories are tangled and seem unique. Even so, convergent dynamics might be widespread (Conway Morris, 2003). Such convergence is in itself a major component of evolution. Convergence is also a mark of universality and the common laws pervading the physics of adhesion or diffusion are likely to constrain potential pattern forming mechanisms. Disparate systems often display very common traits (particularly in their large scale patterns) associated with universal properties of the underlying dynamics. Such an idea has been used in macroevolution within the context of adaptive walks on rugged landscapes (Kauffman 1989; 1983). Although this early work provided a great insight into the qualitative nature of innovation, it assumed that landscapes are static and that evolutionary changes are defined by climbing up on such fixed landscapes, as originally proposed by Sewall Wright. This picture might be satisfactory under some conditions, but is unable to capture macroevolutionary transitions associated to ecosystem engineering and other key features.

Finally, we should mention that there is no perfect model for all scales. Models are useful as far as they can answer a well-posed question (usually at some given scale) or help to formulate questions in a well-defined way (Crutchfield and Schuster 2003). But in some cases, as it occurs with our example of embodied evolution, different scales become tangled. Because different levels contribute to macroevolutionary dynamics, from changes in the gene network wiring within cells to the impact of a given species acting as ecosystem engineer, simulating these processes requires a so called multiscale modeling approach, so that the actual interactions among levels, if any, can be characterized and understood. Such an approach is being successfully used in many disciplines, including biology (Schnell et al 2007) and macroevolution appears to be a great candidate to follow the same path.

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