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News & views

Evolution

A foundational view of the physics of evolution

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How can physics underlie the emergence of biology's complex functionality? A powerful interface between physics and biology that describes the processes of evolution by natural selection provides a compelling answer.

Everything we see around us, including ourselves, emerges out of physical interactions between fundamental particles. But because physics does not have any concept of function, it cannot distinguish the emergent functional features that are central to biology[1] from random fluctuations. The complex structures of proteins, all of which have emerged to perform specific biological functions, are a case in point[2,3]. In addition, the laws of physics are timeless and eternal, unaffected by historical events, so cannot be used to describe how the past evolution of species affects their present and future. Writing in *Nature*, Sharma *et al.*[4] present what they call assembly theory as a way to fill this gap, providing a framework to unify descriptions of evolutionary selection across physics and biology.

The existence of living beings that are well adapted to their environment is explained by Charles Darwin's theory of natural selection. At a macro level, natural selection states that species evolve by initially random variants being selected for survival over many generations through their relative reproductive success[5]. But attempts to describe this process quantitatively, for example through Hamilton's Rule and the Price equation[6], just describe outcomes and do not relate to the underlying physics. The same is true of Fisher's fundamental theorem of natural selection[7] and of mathematical formulations of population genetics.

Assembly theory fills this gap in an innovative way by quantifying the degree of evolution and selection in an ensemble of objects. Conventionally, an object is defined by the material particles from which it is made. Assembly theory instead defines an object through its possible formation histories in an 'assembly space' in which objects are made by joining elementary building blocks together recursively to form new structures.

The assembly universe is the space that contains all of the conceivable pathways for assembling any object from the same building blocks. But the parts of this space that are actually accessible are limited, first by the laws of physics, and second by historical contingency: new things can be built only on the basis of what is already there, further constraining what is possible.

The authors build a quantity they call 'assembly' from two variables: copy number, meaning the number of copies of an object in an ensemble; and assembly index, the minimum number of steps needed to produce an object. These combine to give an equation that determines the amount of selection that was necessary to produce an ensemble of objects. The authors' key contention is that a transition from no selection to selection – such as happened when inanimate matter became animate – changes the pathways taken in assembly space in a mathematically definable way embodied in this equation. In essence, an object with a high assembly index that has a high copy number is evidence of selection. Two timescales determine the dynamics of the assembly process: the rate at which new, unique objects are formed, and the rate at which those objects are copied after they exist. If the relationship between these two timescales is such that resources are available for making more copies of existing objects, then selection can occur.

The assembly index of a molecule could possibly be determined experimentally, which would allow a check on theoretical calculations. Sharma *et al.*[4] give examples of assembly pathways for molecular processes, including the joint assembly space for polymeric chains and processes catalysed by enzymes, as well

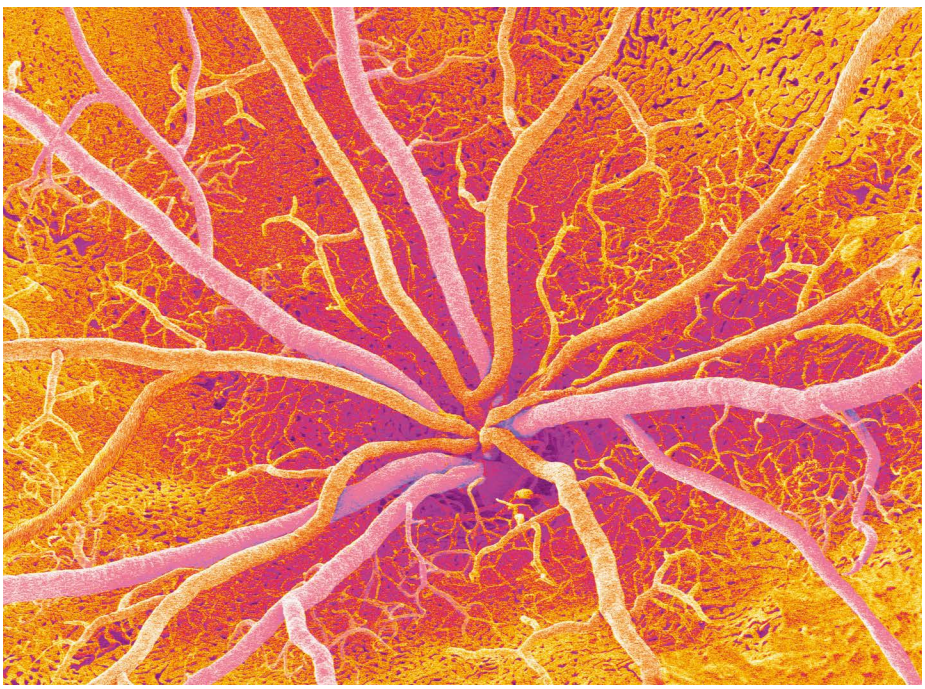

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Figure 1 | The mystery of function. The system of blood vessels within a human body – here in the retina of the eye – evolved to allow the heart to pump oxygen to every cell and so keep people alive. Physics as currently formulated cannot explain why such a complex structure with specific functionality exists – a gap that the assembly theory of Sharma *et al.*[4] could help to close.

as spaces in which selection has generated ensembles of high complexity.

The authors state that assembly theory neatly unifies physics (the processes that make assembly possible) with biological selection (the effects that determine what is actually realized), thus enabling the incorporation of novelty generation and selection into the physics of complex objects.

Other researchers have adopted similar approaches to bridge this divide. For instance, in January, a 'theory of the adjacent possible' was published[8] that shares many features with assembly theory: a focus on possibility spaces, and the constraints imposed on the near-future outcomes of a development process by the objects that already exist. But, similarly to those earlier attempts to quantify evolution, this description does not relate to the underlying physics.

Perhaps a closer approach is 'constructor theory'[9], which considers how self-reproduction is compatible with the laws of physics, reformulating the laws as statements about which object transformations are possible and impossible, and why. Its similarities with assembly theory include carrying out transformations recursively through so-called constructors. It does not, however, characterize the resultant assembly paths or quantify selection, even though the theory is compatible with evolutionary selective processes.

Assembly theory is potentially a profound approach to evolution and its foundation in physics. The theory as initially stated is very general, and could well have applications in other spheres. It might, for example, provide a route to detecting alien life on other planets, by identifying specific molecules with high assembly indices as 'biosignatures' – a project that some of the authors have been deeply involved in[10].

Technologies also follow processes of evolutionary development on the basis of what is already available at that time[11]. This is mentioned in the paper, but not developed in detail. It would be worth investigating whether assembly theory could characterize such selection, in effect quantifying the degree of innovation. Implied in such applications is the vexed issue of agency — the ability of living things to control their own actions and decide what to do next. This underlies the existence of all technology, but it is an ability that, again, is hard to explain in terms of conventional formulations of physics. Assembly theory does not address this as such, but a key point is that after intelligent action becomes possible, the kinds of assembly path that are possible change fundamentally.

The authors develop the idea's application to biological processes in depth only at the molecular scale. A key issue is whether it can usefully be extended to explain the workings of other levels in the biological hierarchy of emergence — organelles, cells, tissues, organs, organisms, populations of organisms, ecosystems and, ultimately, the entire biosphere.

In this hierarchy, function emerges at the level of organelles and above[12]. In humans, for example, gene regulatory networks control the synthesis of proteins at the cellular level to maintain the body and allow growth; neural networks in our brains process environmental cues to predict outcomes and determine our behaviour; the heart pumps oxygen to all cells in the body to keep us alive (Fig. 1), and so on. Higher levels of organization emerge from lower levels by evolutionary processes that act on long timescales (the structure of the heart comes from genes that were selected to produce that structure), developmental processes on intermediate timescales (those genes are read in such a way that an embryo develops a heart) and functional processes that act on short timescales (the cells in the heart function in such a way that the heart pumps blood).

But causation also works in the downward direction. Higher levels set boundary conditions and time-dependent constraints on lower levels, for example in controlling gene expression according to physiological needs. However, they also shape processes that create, modify and delete lower-level elements (such as processes that determine cell type according to position in a developing embryo).

Causal closure — the ability to explain why things happen as they do — takes place only when all levels linked in this way are considered. The downward processes do not alter the physical laws underlying the whole in any way, but they do shape specific outcomes. For example, how electrons flow in nerve axons in the brain depends on what an individual is seeing in the world around them at a given time.

Evolution by natural selection applies in a coherent way at every level from macromolecules upwards, including metabolic and gene regulatory networks and physiological systems, to the level of whole organisms. This evolution is shaped in a downwards direction by what happens at the levels of populations and ecosystems, which, in turn, are subject to selection, and at the level of the entire biosphere.

Assembly theory can describe all this in principle, because it is such a general framework. But organisms become what they are through complex, context-dependent developmental processes. The emergent nature of these processes is key to survival and hence to evolutionary outcomes. The important question is to what extent concepts such as assembly index, copy number and pathways through assembly space can usefully be applied in practice to such complex contexts, such as how gene regulatory networks function to control protein synthesis.

Perhaps the roundworm (*Caenorhabditis elegans*) could be used to explore this more; its genome is fully known[13]. Each and every adult roundworm has precisely the same number of cells (apart from sex cells), and the history of every one of these cells is known, providing a basis for an assembly-theory analysis. It would seem ideal for taking the project further.

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