How an information perspective helps overcome the challenge of biology to physics.

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Abstract

Living systems have long been a puzzle to physics, leading some to claim that new laws of physics are needed to explain them. Separating physical reality into the general (laws) and the particular (location of particles in space and time), it is possible to see that the combination of these amounts to efficient causation, whereby forces are constrained by patterns that constitute embodied information which acts as formal cause. Embodied information can only be produced by correlation with existing patterns, but sets of patterns can be arranged to form reflexive relations in which constraints on force are themselves formed by the pattern that results from action of those same constrained forces. This inevitably produces a higher level of pattern which reflexively reinforces itself. From this, multi-level hierarchies and downward causation by information are seen to be patterns of patterns that constrain forces. Such patterns, when causally cyclical, are closed to efficient causation. But to be autonomous, a system must also have its formative information accumulated by repeated cycles of selection until sufficient is obtained to represent the information content of the whole (which is the essential purpose of information oligomers such as DNA). Living systems are the result of that process and therefore cannot exist unless they are both closed to efficient causation and capable of embodying an independent supply of information sufficient to constitute their causal structure. Understanding this is not beyond the scope of standard physics, but it does recognise the far greater importance of information accumulation in living than in non-living systems and, as a corollary, emphasises the dependence of biological systems on the whole history of life, leading up to the present state of any and all organisms.

Keywords: formal cause, emergence, circular causation, ATP synthase, biological organisation

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1 Introduction

Since Schrödinger (1944) famously mused that “other laws” of physics might be necessary to explain life, several authors have suggested that biology demands new physics to explain how the animate arises from the inanimate (e.g. Rosen, 1991; Walker, 2017). Many still agree with Mayr (1997, p.32) that biology and physics are separate and “autonomous” sciences, perhaps implying that biology cannot be wholly derived from physics, but more likely because they see no need for deriving life from physical laws. Kauffman (2020) concludes that life is beyond the explanatory power of the laws of physics because of its historically contingency. This arises from the particular (the locations in space and time of every particle), but for inanimate physical systems, such contingency is mostly just random noise that can be removed by course graining to leave relatively simple initial and boundary conditions (weather modelling presents a challenge, but is still partially susceptible). Such coarse-graining is inappropriate only when the particular remains important to the trajectory of the whole system for an extended time. When variations are not diffused away by thermal noise, but are reinforced and accumulated into a formative memory (by positive feedback), then the pattern of particles at time t has considerable effect on the pattern at later time $t + T$, which is the problem we have in understanding life (and to a lesser extent, the weather). Here it is argued that understanding the way ‘the particular’ (which will be identified with information) constrains ‘the general’ (especially physical forces), plus the way biological systems preserve information by embodying it in systems that are closed to efficient causation, including the translation from arbitrary ‘code’ to physical force fields, could bridge the gap between physics and biology.

All patterns of matter and energy in space and time are axiomatically equivalent to *embodied information.* The word ‘information’ alone is better reserved for *relational information*, which is information presented by system A about system B, rather than just that embodied in A. Embodied information is that which specifies the form of the object which embodies it, simply by virtue of the embodiment: it equates to the information that would be necessary and sufficient to recreate the pattern that is the *form* of the object (see Floridi (2003, 2005) for detailed explanation). For example a DNA sequence has a form that can be written as a nucleotide string (A.G.T.C...), this pattern being embodied information, which only in the context of ‘reading’ (more generally interaction with another pattern), becomes relational information, i.e., information as we usually understand it (the *Shannon* sense). An *informed system* is one which uses additional information beyond that embodied in its own form; e.g., the genome of an organism, or the operating system of a computer are additional to the metabolic components and the hardware respectively. Closure to efficient causation (hereafter *clef*) describes a closed loop in causal relations, where e.g. A is the efficient cause of B and B is the efficient cause of A (developed in detail by Louie (2009), Sect 6.16). Efficient cause will be defined in section 2.4.

The aim of this work is to root within physics the main organisational systems-biology concepts that have proved useful to understanding life as a process (e.g., in Hofmeyr

(2021)). The method will be to build up an explanation of them using information-based concepts, from the origin of information, through its role in causation and the way different kinds of causation are combined into multi-level causal structures, cyclic organisational systems and the information processing from which autonomy arises.

2 From fundamental physics to a practical model of causation

In this first section, a concept of formal, efficient and material cause is built to become the foundation for considering living systems as causal systems.

2.1 The physical roots

The overarching axiom of this work is that physical reality is the consequence of dynamic patterns of matter and energy in space and time. Philosophically, this places it roughly in the Information Structural Realist camp (attributed to Floridi (2008)), but perhaps with a more committed view on structure than objects (Floridi aimed for minimal commitment to both). Specifically, the present work does not concern human thoughts, minds or any putative reality beyond the natural world with which physics and other sciences deal – see Gillies (2010). The commitment to structure over material comes from the fact that patterns are the source of variety and dynamic behaviours in the natural world, with matter and energy performing the role of a substrate through which patterns act in space and time. The substrate is necessary for the natural world as is the space and time in which it can be arranged. But without particular arrangement, natural reality would be no more than uniformly random—the expected eventual 'heat death' outcome for the universe. It is therefore pattern, i.e., non-uniformity of arrangement, that brings about anything interesting in the universe and the pattern is what we interpret as embodied information. We may remind ourselves that the behaviour of molecules can be completely described by Schrödinger's equation, written here in time-independent, but explicit space with n electrons and nuclei having space coordinates $\underline{\mathbf{x}} = \mathbf{x}_1, \mathbf{x}_2, \cdots \mathbf{x}_n$:

$$\widehat{\mathbf{H}}\ \mathbf{\Psi}(\underline{\mathbf{x}}) = E\ \mathbf{\Psi}(\underline{\mathbf{x}}) \quad \text{where,} \tag{1}$$

$$\widehat{\mathbf{H}} = \sum_{i=1}^{n} \frac{-\hbar}{2m_i}\nabla_i^2 \ + \ \sum_{i=1}^{n}\sum_{j=i+1}^{n} \frac{q_i q_j}{4\pi\epsilon_0\ |\mathbf{x_i} - \mathbf{x_j}|}$$

is the Hamiltonian consisting of the classic kinetic energy (first term with masses m_i) and electrostatic energy (second term, with charges q_i, q_j). This emphasises that the behaviour of the system: a) obeys general constraints of fermion exchange and anti-symmetry ($P\psi = (-)^P\psi$) and b) depends on the *particular* arrangement of particles in space, i.e. particular constraints on the system. This general/particular dichotomy is consistent with the philosophical insight of Howard Pattee (1982; 1995; 2001), who identified an epistemic separation between physical and semantic (symbolic) representations of reality, the two being complementary and both necessary for life. The physical consists of particles, waves and forces; the semantic consists of patterns among these in space and time. Physical laws are definitively universal, whilst patterns are definitively particular and both together inform the structure and behaviour of matter-energy in space-time. Without referring to semantics (and its connotations of cognition), we can simply say that reality results from the particular constraints imposed by patterns on the shape of force fields that obey the general laws of physics.

2.2 The origin of pattern information

Heat ensures that particles of matter are in constant motion. In constantly changing configurations of ensembles, patterns will occasionally appear spontaneously—they will have no significance at all and will disappear as fast as they arrived. Any one of these transitory patterns is no different from any other configuration in random variation. Conversely, information is definitively non-random. In the absence of anything else, only the improbable persistence of a pattern can lead us to suspect the presence of information. That is, no particular momentary pattern is special—even if particles fleetingly configure to form a recognisable object. If, however, they form a configuration that—without intervention—persists, then something must be biasing the probability of configurations. More precisely, in a system of n particles having time-dependent state coordinates for position and velocity $\mathbf{z} = x_i(t), v_i(t)$, $(i = 1...3)$, information is embodied within the system if for at least two particles their time-series $\mathbf{z}(t)$ are correlated. Equivalently, if $d_m(t) = \sum_{m-1}(d_{j,i})$ is the sum of spatial distances $(\mathbf{x}_j - \mathbf{x}_i)$ among a set of $m < n$ particles, then there is information if $\frac{d}{dt}d_m(t) < \bar{D_n}$, where $\bar{D_n}$ is the constant (mean) displacement rate (diffusion rate) of particles in the system of n, i.e., integrating $d_m(t)$ w.r.t. t, the total mutual displacement among the m particles after time T: $d_m(T) < \bar{D_n}T$. Information—as pattern in a natural dynamic system—can therefore be identified with the 'stillness' of the pattern relative to that expected from random displacement. Note this implies that a 'frozen' pattern (temperature = 0°K), embodies information: it holds information at time t about its its configuration at time $t - T$ (though no information about when it froze). This information transmission through time is fundamental to defining an object since the object only exists because it is a persistent pattern and that is only because information about its configuration at the time of observation (t) informs the observer of its configuration at an earlier time ($t-T$). Embodied information of this kind serves to give existence (diachronic identity) to an object for which all the material parts are continually replaced, e.g., a vortex in a fluid.

Patterns can only be persistent if they are reinforced: physical forces must influence the trajectories of the moving particles so that the inequality $d_m(T) < \bar{D_n}.T$ remains true. Physical forces emanate from the particles themselves (in general only from particles). The direction and strength of these forces at the locations of the particles is determined by the positions of the particles relative to one another. Reinforcement thus results from the pattern in the vector sum of forcefields being positively correlated with that of the pattern in particle locations.

One obvious cause of persistent pattern, and probably the first acting in the history of the universe, is gravity. It is self-reinforcing because it concentrates matter in space, creating a pattern that further concentrates the gravitational forces. All force fields are limited in extent only by the light-cone of special relativity, though their effective range is inversely related to the mass of their exchange boson, which is believed to be zero for gravitons and must be zero for photons. What the placement of force-generating bodies does is determine a particular shape of the forcefield (over all space) for a particular configuration, thereby specifying the coordinates of the force-generating particles, in space and time, effectively constraining the forcefield. Any pattern of particle locations is, in turn, influenced by the forces that it constrains. The emergent feedback between displacement and force leads to an attractor (e.g., a black hole, or the equilibrium of a mass-spring system).

Since all forces can be represented by vectors, the constraint is the determination of a particular direction for the force acting between bodies set at particular locations in space and time. Imposing the particular over the general is both a potential source of information (by creating a pattern) and also a consequence of pattern (information) constraining the system. Some have wondered how 'intangible information' can influence physical reality, but if 'patterns of force fields affecting particles' is all we observe and if 'pattern in matter and energy distribution is embodied information', then it is not a mystery. Persistence of a pattern, as opposed to a transient state in random reconfiguration, is achieved only when the pattern exerts a positive feedback to make itself more likely than any other possible configuration.

The persistent configuration that results from reinforcement is the foundation for information, but not sufficient to call it information in a useful sense. A pattern which just persists in isolation is static (frozen) and the most we can say about its causal power is that it causes its own persistence. More interesting, by far, is the effect of one pattern on another, either interacting with it, or creating it *de novo*. The only way one pattern can create another is by 'selecting' it from among random configurations through correlation. This is the way crystal structures grow. Once a self-reinforcing pattern is established in the electrostatic force field around atoms, randomly appearing patterns in the local milieu of free atoms, which just happen to match the crystal structure sufficiently well (i.e., spatially correlate with it) are selected by mutual attraction to become part of it. The selection referred to here is the filtering of configurations, from all randomly occurring configurations, only those that match the existing pattern and this is physically achieved by constraining force field shapes: their particularisation.

2.3 Relational information

When more than one pattern forms it is possible for members of the set of patterns to interact. The physical effect of a pattern in a force field is to constrain the form of any force-carrying configuration that it encounters. The constraint by a single pattern is, by geometric necessity, that of exerting a pattern which reflects its own: selection by correlation, either of self (reinforcement) or selection of correlated patterns from a random milieu, as in crystal growth. The result is that the force-interacting patterns will tend to match with one another—a (muted or partial) reflection of each will form in the other and they will therefore share mutual information. The map of forces observed by atomic force microscopy (from Albrecht et al. (2015, Fig.3)) illustrates the effect of this beautifully.

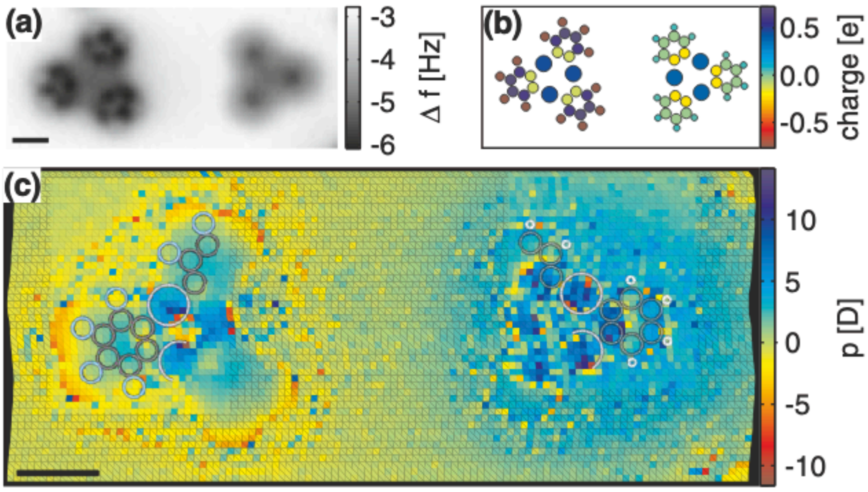

Figure 1: Kelvin probe force microscopy spectral map of electric charge distribution (force field) generated around two molecules which induce a dipole in each other (sharing information). The force distribution and direction is specified by the probability distribution of electrons which is constrained by the particular locations of nuclei, which in turn are constrained by the force mediated interactions among all the electrons and nuclei, reaching a minimum Gibbs free energy configuration. Reproduced from Albrecht et al. (2015, Fig.3), where original caption read: "Highly resolved dipole-distribution map. (a) Δf image recorded at $z = 9.6$Å. (b) Calculated charge distribution deduced from Bader analysis. (c) Dipole-distribution map extracted from $\Delta f(Z, V_i)$ spectra for $F_{12}C_{18}Hg_3$ and $H_{12}C_{18}Hg_3$ (9.6Å $\leq z \leq 10.1$Å; $V_i = -0.2$ and 0.5V)".

Forces induce changes in the patterns that embed shared information, which is then *relational information* because it now involves 'information *about* a thing', not just information embodied in the pattern of a thing. Relational information is a concept more closely resembling the ‘common sense’ idea of information as a transaction among entities (source and receiver). Force fields have an energy level associated with them because the ensemble that they shape (in space) has potential energy. When one pattern changes or reinforces another, it is usually because the change it induces in the other pattern results in a reduction of the combined Gibbs free energy. Schrödinger conceived of an aperiodic solid that could embody the information needed to inform the structure of an organism, but most chemical systems with that property are inherently displaced from equilibrium and costly (in free energy) to make and maintain. One of the essential and special features (for life) of nucleic acids is that they are very close to thermodynamic indifference regarding which nucleotide is bonded to which, i.e., the Gibbs free energy of any pair is equivalent to any other pair. This feature enables nucleic acids to form patterns of arbitrary length (ℓ), embodying 4^{ℓ} bits of information in the sequence. (Note - some pairings are slightly more likely than others in undirected sequence formation). The DNA sequence is embodied information about the organism, but unless it is coupled to a system of patterns that can, via forces, assemble into the organism, it has no effect. We next need the information to be causal.

2.4 The physical basis of causation

Kistler (2021) has laid out the following, very general, criteria for causation:

1. Events F and G are localized in distant spatio-temporal regions (no spatio-temporal overlap).
2. The regions in which F and G are localized are time-like (or light-like) related.
3. The probability of G, given F, is, under certain conditions, higher than the unconditional probability of G.
4. G depends, under certain conditions, counterfactually on F.
5. If F and G are represented by variables f and g, it is possible to intervene on f and interventions on f (obeying the appropriate constraints) are means of modifying g.

In common with most modern philosophy of causation, of the four aspects of cause identified by Aristotle (efficient, material, formal and ultimate cause), Kistler (2021) refers primarily to efficient cause, so we will begin with that.

The change in the shape of the force field of one pattern resulting from an encounter with another is well illustrated (macroscopically) by a footprint in mud or dent in the side of your car if you hit a lamp post. The permanence of this change—and which pattern more substantially changes—is a function of particularities, especially the relative strength of the forces that maintain each pattern and the stability of the patterns under deformation. Colliding billiard balls deform a little on impact and elastically return to their original form, so no information is shared beyond each other’s momentum prior to impact. In the case of a footprint in mud, the mud gains potentially a lot of information from your foot. When two molecules combine into one, they share information about each other's shape and the compound molecule has within it an impression of each separate molecule, not just their original shapes, but each original shape transformed to reflect (partially) the shape of the other.

Many philosophers of science believe there is a physical basis to cause and consider the mechanism behind cause as a transfer of a conserved quantity (energy, momentum or something more exotic like charge or spin) in a material system. This is the concept of transference theory attributed to Salmon (1984) and Dowe (2000) which posits that there must be a spatio-temporally continuous connection between one thing X and another Y involving the transfer of energy, momentum (or other conserved quantity) for X to cause Y. The idea that causation, more particularly *efficient causation*, is realised by the transfer of a conserved quantity and that this transference is necessary and sufficient for (efficient) causation, is robustly defended by Kistler (2021). Surprisingly, it has not yet been explicitly mentioned that the transfer of a conserved physical quantity is the current model of physical force and well represented by the Feynman diagram (Fig. 2) in which sub-atomic particles interact via the transfer of an exchange particle, according with the Standard Model of physics (we can include gravity, still rather speculatively). A good example is the fundamental strong nuclear (colour) force between quarks which swap colour on exchange of a colour/anti-colour gluon (Fig. 2, left). In general, forces arise through the exchange of virtual field quanta: gauge bosons. An example more relevant to biology is the electric force of repulsion between electrons (more generally the quantum electrodynamics of scattering among charged particles), generated by the exchange of photons (Fig. 2, right). This is why the physical basis of causation necessarily involves physical force, behind which there is an exchange of gauge bosons to conserve properties in accordance with Noether's theorem, as described by Feynman diagrams. But this is a sort of raw material for causation, not yet formed into functional shape. That is provided by the particular arrangement in time and space of the interacting particles; their positions determining the strength and direction of the interactions, this being particular and thereby embodying information. The result of exchange particles transferring conserved quantities over particular distances in particular directions is the physical basis, indeed the essence, of *efficient cause*.

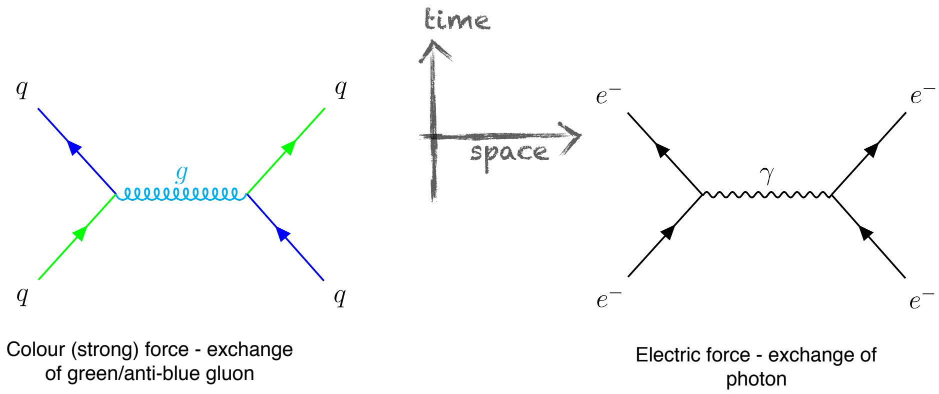

Figure 2: Feynman diagrams representing fundamental forces as the exchange of a gauge boson which conserves properties such as charge and colour. The diagrams respect Noether's theorem (law) and provide a physical explanation for the transference theory of (efficient) causation. The exchange is made obvious in the left diagram representing the strong nuclear force where a blue quark encountering a green quark exchange a green/ anti-blue gluon and thereby swap colours, with the kinematic effect of attraction (not distinguished from repulsion given the generalised space represented in the x-axis). The electrical force between electrons (repelling) comes from the exchange of a photon, which having zero mass, gives an infinite extent to the force field. Note that the process is symmetrical in time (reversible) in both cases (one can reflect the strong force diagram through the vertical and horizontal axes to find an identical diagram).

Let us then define efficient causation as **the action of one force pattern on another, either to change it (transferring information among the patterns), or to reinforce it (maintaining stasis).**

This definition meets all of the criteria set out by Kistler (2021) above, if we accept that 'states' (using the language of physics) can be substituted for 'events'. When, for example monomers come into one another's influence, as patterns in the electrostatic force field they will affect one another's shape and at some point may find a mutually thermodynamically favourable pattern in which they are bonded (every point in this sequence of 'events' can be specified by the states of the particles present in the interaction). Significantly, one pattern does not do this to the other; there is no demarcation between causative agent and recipient. The efficient cause of bond forming is the combination of the particular pattern of the *total* force field and the general causal power of physical force: pattern informing force to produce efficient cause. This cause is not attributable to any single pattern in the interaction, it is strictly a product of all the patterns interacting simultaneously. A reasonable way to conceive this is not as things with individual identity interacting, but rather as a single extended force field with a particular pattern that dynamically evolves towards minimum Gibbs free energy. With this universal perspective, efficient cause seems compatible with the overall symmetry of physics once again, including the probabilistic arrow of time. That is, causation is seen as no more than a sequence of state changes in the universal field which are *in principle* reversible, though the reverse may be very unlikely in practice as free energy may be needed to enact it.

We may ask what efficient cause results from the action of force without constraint by information. Force unconstrained means a forcefield generated by randomly located particles; force vectors among them are random (in direction and magnitude) and the usual source of such random force vectors that may impinge on an established pattern is kinetic energy transfer from randomly moving particles, i.e., heat. The effect of heat on, e.g., proteins or DNA is well known; generally it increases the degrees of freedom of the system being heated and randomises its configuration upon cooling: destroying pattern and with it, destroying information and function. Efficient cause necessarily involves forces together with the particular (information) that constrains their vectors of action. We will now identify that information constraint as the Aristotelean notion of *formal cause.*

2.4.1 Formal cause

Formal cause is classically the 'template' or design (i.e., information) responsible for a particular outcome of efficient cause. It comes in two distinct kinds. The first may be called the *general conditions*, roughly encompassing 'the laws of physics', with at the deepest level, Noether's theorem (every differentiable symmetry of the action of a physical system has a corresponding conservation law). From this arise the gauge theories and the Standard Model, along with fundamentals such as the 'principle of least action'. Conservation applies in time to total energy; in space to linear momentum; in rotation to angular momentum and probability is conserved as all possibilities sum to one. The second kind of formal cause may be termed *particular conditions* and concerns the consequences of the particular location of particles in space and time and their particular kind (from among all the possible fundamental particles). General formal conditions are strictly single valued (no degrees of freedom) but particular formal conditions are uniformly probable, subject only to the general conditions (e.g., particles are not allowed to occupy the same space-time coordinates). The appearance of a hierarchy among formal conditions is a consequence of their different degrees of freedom. General conditions constrain particular conditions and both constrain the action of forces to yield efficient cause from the combination of force and formal cause. General conditions are universal both in space and time, so have no memory and are symmetrical in time. This contrasts with particular conditions because at any time t they are necessarily founded on initial conditions at some time t_0 so there is a memory and a direction in time. This dependence on initial conditions is one of the great differences between biology (where history is crucial) and physics (where initial conditions perform the auxiliary role of specifying a particular case)—a point recognised by Pattee (1969, 2001).

2.4.2 Material cause

Material cause (that which results from the nature of the substance) can now be seen as a consequence of force field patterns at the atomic scale. It gives water its fluid, solvent, electrostatic and other special properties that are necessary for biochemistry. It also gives steel its strength and hardness (and the temperature dependence of these). Material is governed by formal cause which is the particular spatial arrangement of atoms making particular the pattern of the force field that holds the atoms in place. Traditional material cause, deriving from the composition of substances either acting or being acted upon by efficient cause can be replaced by a 'micro-formal' cause, since it is formal cause at the atomic scale. In every case, the interatomic forces are determined by the atomic species (each with its own electrostatic force field) together with their configuration: force constrained by particular form. This effectively unites material and formal cause, both of which generate efficient cause via forcefields.

2.4.3 Biological manifestations of efficient and material cause

Physical forces all either cause acceleration or its prevention and all have an orientation (direction) in space. In the absence of constraints the vector sum of forces acting on each member of an assembly of particles is random and accordingly has no (ensemble) effect, other than pressure (Fig. 3 A).

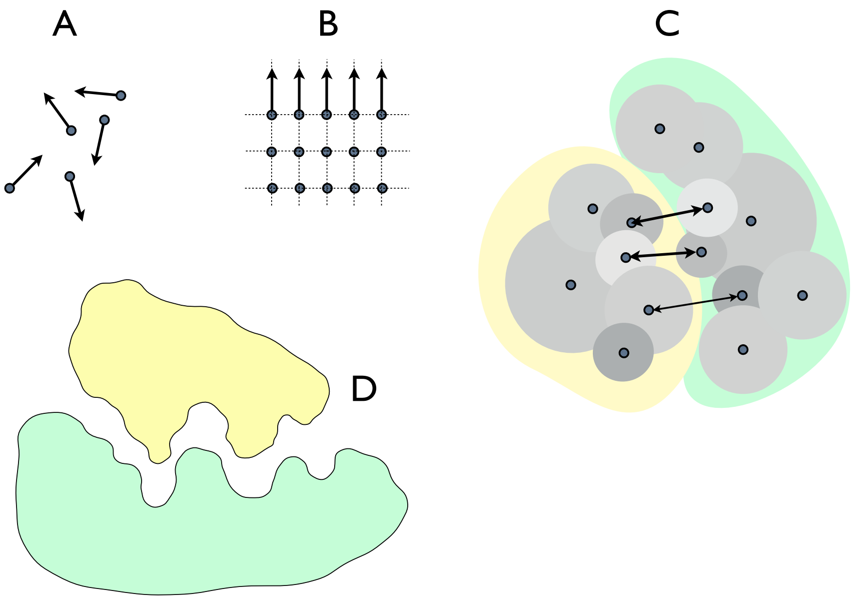

Figure 3: The informational building blocks of biological function. A) random forces are B) constrained by form (in this case a crystalline lattice), resulting in coherent directed forces. C) More information rich forms, as in these bio-molecules, where correlation of patterns in local force fields lead to binding (compare to Fig. 1). D) Correlating patterns of an enzyme and its substrate are the basis of induced fit or lock and key mechanisms with function such as molecular fabrication and cell-signalling, including conformational change. In cases B-D, we may think of the electric forcefield pattern as a whole, with individual molecules as concentrations of force that correlate and share shape information about one another, both reflecting this in their bound shapes. (Adapted and updated from Farnsworth (2021)).

Constraints acting on forces reduce the range of directions in which forces can act among an assembly of particles. The positioning of the constituent parts of a system is embodied information which can now be termed *form*. When particles are positioned in a form that is not random, then the form has a coherent spatial structure, i.e., its parts share mutual information (Fig. 3 B) and this shared information is the basis for *effective* information (Szostak, 2003). It is effective because it constrains forces such that it transfers to them its coherence: the directions of the forces are correlated by the mutual information of the form. The result is that forces, no longer random and merely producing pressure, act with coherence so that they are available to perform work and hence functions. For example, the cylinder and piston of a steam engine is a form which constrains the kinetic force of steam molecules to act in a coherent direction producing a functional motion against the piston (work); equivalently, mitochondria make use of a constrained flow of protons between inner and outer membranes to produce functional motion. Coherent action enables work to be done and is equivalent to the process we call Aristotle's efficient cause: the action that brings about a transformation (or resists it). Hence **efficient cause can be interpreted as the constraint of physical forces by form**: force acting under formative constraint gives efficient cause.

The basic element of efficient cause for biology is the physical configuration of atoms within biologically relevant molecules which, as forms, both constrain and are constrained by intermolecular forces to act in coherent ways. The effects of these coherent interactions include binding (Fig. 3 C) and electrostatic repelling such as in hydrophobic interactions along with their consequences such as conformational changes: indeed the whole repertoire of biochemical interactions that together produce, e.g., protein folding. Of particular importance in biology, the mutual recognition (correlation) of molecular shapes provides the basis for supra-molecular 'codes' (Barbieri, 2015) and the communications systems they enable, involving chemical receptors and their ligands, vividly described as 'lock and key' (Fig. 3 D) and the machinery of transcription and translation, well illustrated by the set of t-RNAs with their anticodon at one end and amino-acid docking site at the other. Networks of such reversible and specific molecular interactions enable information processing at higher levels of organisation (Section 3.1), but we should not forget that underlying even the most abstract and sophisticated biological information processing (e.g., your understanding of this sentence now) is the information sharing by correlation among molecular forms organised into functional networks.

2.4.4 Relation to interpretations of efficient cause in biology

In the relational biology of Robert Rosen (1991) and its further development by Aloisius Louie (2009; 2013; 2017) the Aristotelean causes are related to each other through category-theoretical mappings. The efficient cause f and material cause A of effect B are related in the mapping $f : A \rightarrow B$. Rosen used graph-theoretic diagrams of such mappings to construct his so-called replicative metabolism-repair or (M,R)-system representation of the functional organisation of the cell (Fig. 4A).

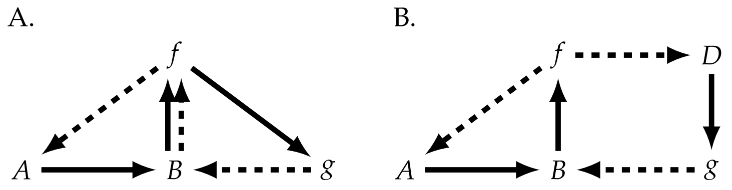

Figure 4: (A) Rosen's (1991) replicative metabolism-repair or (M,R)-system. Solid arrows represent material causation (e.g. chemical transformations) and dashed arrows show efficient causation (e.g., catalysis). We can interpret material causation as the configuration of matter *plus* the matter itself and efficient causation as the information embodied in form *plus* the electrical (chemical) forces that this information constrains to enact the material transformations. (B) Hofmeyr's (2021) fabrication-assembly (F,A)-system, an alternative representation of the causal structure of a living cell that realises its biochemical structure (which the (M,R)-system does not).

With regard to the incorporation of formal cause into such mappings, Rosen (1989) suggested

$$\begin{aligned} f:\ & A \times I \to B \\ & (a,i) \mapsto b = f(a,i) \end{aligned} \tag{2}$$

where $i \in I$ is the formal cause of B. This was also the form underlying the purported paradox Rosen (1959) claimed to have found in Von Neumann and Burks's (1966) description of the universal constructor. However, Hofmeyr (2007) argued that i should be regarded as acting together with efficient cause f and not with A, and so rewrote this as (his Eq. 4):

$$\begin{aligned} (f,i):\ & A \to B \\ & a \mapsto b = (f,i)(a), \end{aligned} \tag{3}$$

which shows information as the formal cause that, together with efficient cause, forms the operator of the mapping (note, (f,i) is an element of $\{f\} \times I$, the combination denoting i *informs* f, where i and f are members of sets I and $\{f\}$ respectively). In this case, efficient cause is closer to the concept of force constrained by form, so that (f,i) matches the definition of efficient cause proposed in the present work. Hofmeyr (2018) developed this further to resolve mappings where formal and efficient cause are either combined into a single entity (informed efficient cause) by a "choice mapping" that selects a particular f_i from a set of possible mappings, or act together as separate entities (f,i). Incidently, incorporating information in this way eliminates the "Rosen paradox" in the universal constructor (Hofmeyr, 2018).

Hofmeyr (2021) provides an even clearer account of the different configurations of formal cause, used for his model of the cell with the causal structure of Fig. 4B, which is functionally equivalent to the replicative (M,R)-system, but with a structure that matches the realised biochemical system, thereby solving a longstanding problem in relating the (M,R)-system to known cellular organisation. He distinguishes three modes of formal cause either acting on (or combining with) efficient cause or acting on material cause in a material transformation $A \rightarrow B$ (Fig 5). All three can be interpreted in the present terms: form as pattern, embodying information, combined with physical forces to give efficient cause.

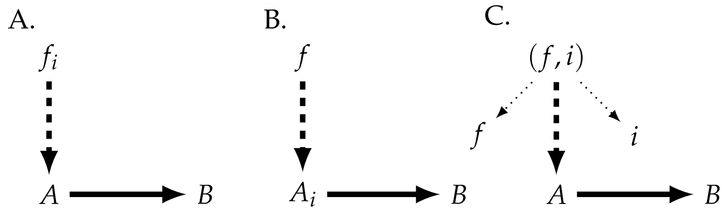

Figure 5: *Formal cause in graph-theoretic diagrams of mappings.* (A) Formal cause i associates with efficient cause f by parameterisation to f_i (a single entity). (B) Formal cause i is intrinsic to material cause A, a propensity of A to transform into B. (C) Formal cause i combines with efficient cause f to form the pair (f, i), which is an element of the Cartesian product $\{f\} \times i$. The dotted arrows are projection maps that allow f and i to appear as distinct entities in the diagram. Adapted from Hofmeyr (2021).

In the first (Fig. 5A), there is a specific formal cause i for B such that the efficient cause is constrained by the formal cause uniquely identified with B: $f_i : A \rightarrow B$, i.e. the formal cause is particularised by the form of B, analogous to a particular socket in a mechanics socket set. The catalytic action of aminoacyl-tRNA synthetase is an example since each of the set is specific to a particular tRNA amino-acid pairing. This is a case of a particular form acting via its forcefield in a particular way on some other form. The formal cause is mediated through correlation among the patterns and the efficient cause is then the effect of this constraining the combination of forces involved. Any particular aminoacyl-tRNA synthetase can only match a particular tRNA with a particular amino acid: all determined by the forms involved constraining forcefields as shown (in abstract) by Figure 3.D. We can say that f_i is to be found in the form of a catalyst that is particular to B.

In the second mode (Fig. 5B), formal cause is an intrinsic property of the material cause (note that this is not equivalent to eqn 2, where $i \in I$ is a physical entity separate from B). This can be explained in terms of an uncatalysed reversible reaction $A \rightleftharpoons B$, where "the formal cause of B would be the intrinsic propensity of A to transform into B, while that of A would be the intrinsic propensity of B to transform into A; in a sense the formal cause of B can be thought of as a model of B inherent in A, and *vice versa*" (Hofmeyr, 2021). Here the pattern of the molecule A correlates with (carries information about) that of B such that when thermodynamically conducive ($\Delta G < 0$), the forward reaction takes place and *vice versa*. For example, the carboxyl group at one end of an amino acid implicitly embodies information about the amino group at the other end by correlating with it, and *vice versa*, enabling them to form the peptide bonds that join them (the mutual information of these patterns is in the shapes of their electrostatic force fields as explained in Section 2.2, analogous to jigsaw pieces that fit together because their shapes correlate). In this mode, formal cause is the constraint of electrostatic forces emanating from each molecule by the forms of the reacting molecules themselves.

The third mode (Fig. 5C), is more complicated. Here, the entities to be associated with formal cause i and efficient cause f can be physically separated (Hofmeyr calls them 'freestanding'). But it is only when they physically associate with each other that they can actually function as formal and efficient causes—their combination is represented by the Cartesian product of the sets to which they belong ($\{f\} \times I$). This is described by saying the efficient cause is informed by the formal cause: the latter is what to do and the former, how it is done. Hofmeyr's example of this is the combination of an mRNA molecule (freestanding formal cause) with a ribosome (efficient cause) to produce a polypeptide. In this case, the pattern of the mRNA is considered to exert its influence independently of its force field, but more precisely, it is irrespective of the magnitude of the forcefield, so that only the information matters. This is because, to a reasonable approximation, the physical interaction between each nucleotide and the ribosome is constrained to differ in only one way depending only on which of A, G, C or U it is, so the only information exchange is that of the sequence. In information terms, individual nucleotides bring no unique information, only their class information (that of A, G, C and U). In the context of the ribosome (plus aminoacyl-tRNA synthetase and other helping molecules) nucleotides act as quaternary switches making a 3-bit combination lock of the codon to permit the ligation of a single amino acid onto the growing polypeptide chain. The whole translation apparatus constrains the nucleotide forcefields to this unitary effect, in a sense by preempting (or accounting for) any other efficient cause they could enact otherwise. Their very specific embrace within the ribosome neutralises every aspect of their forcefield but one—that which identifies them as A, G, C or U. This is classic machine behaviour in which an apparatus (complex of forms) is arranged to constrain the effect of a class of objects (e.g., the letters of a mechanical type-writer which are constrained by the form of the typewriter to strike a single point and leave an impression of a fixed face). The freestanding efficient cause in this mode is the form-constrained forcefield exerted by the apparatus (ribosome complex) on the interactions between the amino acid and the polypeptide to which it is attached. The classic machine metaphor (and example) is that of a Jacquard loom where the tape serves as formal cause providing additional constraint to a much larger and stronger set of constraints set by the form of the loom, where the puny force difference between tape and its holes is negligible in magnitude, effectively leaving only the information. To say that mRNA is formal cause and ribosome is efficient cause is a reasonable approximation, just as it would be to call the tape of a Jacquard loom 'pure information'. Rendering the force magnitude negligible with an apparatus, effectively stripping it from efficient cause to leave only information (freestanding formal cause) is of great importance to biological systems as we shall see in Section 3.4. Consistent with the definition of efficient cause given early in this section, it is clear that, even in this mode of causation, to act as an efficient cause, forces cannot stand free from their associated formal cause: without formative constraint we are left with randomness; merely heat.

3 Organising causes with patterns to make wholes with agency

Organisms are patterns of patterns interacting through efficient causes that are organised into networks by yet higher level patterns. Here, we build up an idea of how this informational scheme emerges to result in the organism.

3.1 Nested levels of phenomena and emergence

Patterns of patterns, like the mosaic artwork of Anna Halm Schudel, show us how the arrangement of patterns, each having individual properties, can produce apparently novel effects at the larger scale that could never be identified at the smaller scale. This is because the arrangement at the larger scale embodies information that does not belong to the component patterns. This contrasts with a jigsaw puzzle where the shape of all the pieces determines their places in the whole, so all the information effective in the larger pattern is already embodied within its components. In a jigsaw puzzle, the larger pattern is the result of particular formal constraints imposed by the component parts, but in the art mosaic, formal - particular - constraints are additionally embodied at the scale of the larger pattern. Because a large scale pattern can always be broken down into variations at the small scale (e.g., any shape can be digitised or spectrally decomposed with a Fourier transform), the mosaic picture is not, in itself, an example of emergence. Emergence refers to properties and behaviours, not patterns and the main indication for emergence is the appearance of properties and behaviours that could not even be conceived of using lower-level descriptions. For that reason, an emergent-level *effective theory* is needed (Ellis, 2020), in which case the properties - and the levels attributed to them - are considered irreducible. One of the recurring themes of biological challenges to physics is the appearance of a hierarchy of irreducible levels (see e.g. Polanyi (1968)), though in physics, such hierarchies have been invoked in accounts of various phenomena (reviewed in Gibb et al. 2019), especially following Anderson's (1972) observations.

Taking a biological example, suppose the large scale pattern were a functional molecular machine such as the ATP synthase complex (F_0F_1–ATPase), composed of amino acid sequences (the small-scale patterns). Could we - even in principle - deduce from the amino acids, its ability to add a phosphate to ADP, making ATP? Standing in the way of that are a) the particular sequences of amino acids in the polypeptides, b) the way they are folded into functional proteins, c) the way these are assembled into the machine and d) the way the machine operates dynamically (like a little dynamo). At least folding and the dynamo behaviour are new concepts that are necessarily associated with higher levels of organisation than the amino acids and (because of the thermodynamic equivalence of amino acid sequences) unlike jigsaw pieces, the order in which they are joined is not strictly determined by their individual properties (therefore not predictable from knowledge of them as individuals components). This example, typical of biological systems, shows the appearance of properties that can only be attributed to a larger scale pattern because they are not already fully specified in the smaller scale constituent patterns. In general, "Emergent properties are irreducible to the microstructure from which they emerge" El-Hani and Emmeche (2000), citing Blitz (1992, p.175) and Kim (1996, p.227-229). That is, if the properties of a system do not supervene on the properties of its components, then it has an emergent property. Accordingly, strong supervenience is usually taken as a definitive negation of emergence, following Kim's (1984) definition of strong supervenience (also quoted by El-Hani and Emmeche (2000)):

"(SS) [A set of properties] A strongly supervenes on [a set of properties] B just in case, necessarily, for each x and each property F in A, if x has F, then there is a property G in B such that x has G and, necessarily, if any y has G, it has F."

Put more simply, "A-properties supervene on B-properties if and only if a difference in A-properties *requires* a difference in B-properties" (McLaughlin and Bennett, 2021). Hence, if a property of a biological system does not depend *solely* on the properties of its molecular parts, then it is an emergent property and we would have to conclude that the biological system was irreducible in respect to that property. This seeming violation of the reductionist paradigm can arise because properties at one level are the consequence of properties of its lower level components *together with* the arrangement of those components (the higher level embodied information). Properties and arrangements, being ontologically different entities, cannot be reduced together to a single description at the lowest level. This is not in conflict with the total forcefield-pattern concept of Section 2.2 because this irreducibility refers to emergent phenomena, not the patterns (these points are elaborated in the Appendix and a more comprehensive analysis of the separation of property emergence from system emergence is provided in Ellis (2020)).

Returning to the case of ATP synthase, the highest-level pattern translates the flow of protons across a membrane into rotation of a large molecular complex and it is this rotation, not the pattern, that is the emergent phenomenon (see Fig. 6 with accompanying explanation). As stated in Section 2.2, a pattern can only contribute to cause (other than self-reinforcement) in relation to another pattern and we see that the ATP synthase is an interconnected set of patterns at multiple levels, interacting with one another through their influence on one another's force fields, i.e. through efficient causes. In general, we can attribute to any assembly at level L: $({}^{L}\mathbf{A})$, a set of *potential* efficient causes ${}^{L}\mathbf{G}$, i.e. those possible effects that the assembly's force field may have on any other assembly. Whenever ${}^{L}\mathbf{A}$ interacts with any other ${}^{M}\mathbf{B}$ of level M, the set of efficient causes that can actually occur is selected from the mutual interaction of forcefield patterns (since efficient cause is a relational phenomenon). However, there is in this no restriction that M must be equal to L. If it is equal, we would call the interaction between the two assemblies 'same-level' causation; if $M > L$, we would say 'upward causation' and if $M < L$, it would be 'downward causation'.

3.2 Downward causation

The idea of downward causation remains controversial as several philosophers of science continue to reject it (especially following Kim (1998)). Notably, Craver and Bechtel

(2007) argue that "the conception of causation as a physical connection between two things does not accommodate interlevel causes between mechanisms and their components because mechanisms and their components are distinct events, objects, or processes." In the present terminology, Craver and Bechtel (2007) are asking if cause involves the transfer of exchange particles (force), then how can this be between a composite (higher level) and one of its constituent parts? The answer is that it is not, instead, the vector sum of forces from all the members of the composite (combined) acts on (transferring exchange particles with) each and every one of the constituent members (recalling the whole-forcefield concept of causation from Section 2.4). But cause is more than these forces, it is also the constraint by pattern information upon them and the pattern, in the case of downward causation, is the form of the composite whole (the macro-level). There is no principle to restrict relationships among patterns formed at different levels because relationships in pattern are just geometry. As we saw in the previous section, a pattern of patterns is in fact a single pattern with a low frequency peak in autocorrelation (mutual information), indicating the higher level order. In material (molecular configurations) it is also a set of spatially localised minima in free energy (the individual molecules that form the composite whole). Craver and Bechtel (2007) contend that any part of a whole is, by being a part, never able to spatiotemporally intersect with the whole. This is because "if a conserved quantity is possessed by one of the components (say a mass or charge), that conserved quantity is also part of the whole." My answer is that forcefields of the individual parts (e.g. atoms) are indeed constituents of the whole, but the combined pattern they make as a whole belongs to the whole and not to the parts.

What is really happening in downward causation is that the forcefield generated by a part (e.g., constituent molecule) interacts with the pattern of the combined forcefield of the whole (including its own) in a way that produces an energy minimising pattern for the part (within the whole) that differs from that of the part in isolation. This is exactly what happens in the case of the ATP synthase complex where the active site is seen to distort (conformational change) in response to the force applied by the asymmetrically shaped armature protein (γ subunit), which rotates as a consequence of dynamics occurring at the next higher organisational level (Ma et al., 2002) (see MRC Mitochondrial Biology Unit (2020) for instructive animations). The higher level pattern of the rotating γ subunit constrains the directions of inter-atomic forces in the active site of the β subunits, producing the efficient cause of conformation change in these active sites, which in turn alternately grasp and release the small molecules of the ADP/ATP/Pi cycle. It works because the energy minimising spatial configuration of the active site changes with its forcefield context (i.e., as the pattern of the whole changes). In the language of emergence: a change in the properties of the micro level (the active site) is induced by the change in the properties of the macro-level (whole ATP synthase complex), which is emergent from the micro-level of molecular shapes. Heuristically, we might say that at the inter-atomic scale of the active site, functional changes take place that can only be conceived of with knowledge of the higher-scale pattern, which 'reaches down' to distort those inter-atomic distances. More deeply, we see that it is the patterns (information) that are ontologically important in determining the causal relation among levels, it is not the forces they constrain. The macro-level of the whole ATP synthase complex embodies macro-level information in its structure (the high level pattern), this information changes as the micro-level proton flow pushes the rotor proteins (dynamic pattern), which in turn apply a force on the stator proteins which change in direction and magnitude as the rotor turns (macro-level dynamic) resulting in a micro-level change of pattern (the distortion of the active site with its effect of alternately binding and releasing ADP/ATP). So here we see downward causation as the effect of a dynamic macro-pattern imposing a change on a constituent micro-pattern, resulting in efficient cause directed from the micro-level (proton flow) to the macro-level (protein complexes) and back down to the micro-level (the active site). The macro-level pattern organises the action of forces from the proton flow to the active site and that is essentially its function. Finally, note that none of this is strictly synchronous action, though at the speed of light over such small distances, it appears so.

By regarding efficient cause as the informed constraint of forces, clearly delineating the separate constituents—information and force—we can have a simple mechanism-based understanding of downward causation. It can be illustrated in a very simple and graphic way by soap bubbles on the surface of water: alone they are hemispherical (energy minimising), but when formed together as a group, they adhere and distort into an approximately hexagonal shape, characteristic of space and energy minimising packing. The shape of level L structures is determined by the configuration (embodied information) of level $L + 1$. This is a case of downward causation involving change in the constituent parts of the whole. It is not one of the philosophically trivial kind (Craver and Bechtel, 2007; Kistler, 2009) in which either a) separate systems described at different levels are causally linked (e.g., when a person (one system) pulls a rubber band (the other system), atoms are displaced in the band) or b) causal links are essentially constitutive (e.g., when a wheel turns, its constituent atoms also move). Kistler (2009) recasts downward causation as a process of constraint by $L + 1$ on L in response to the rejection of downward causation by Craver and Bechtel (2007) and that is consistent with the mechanistic concept (presented hearin) of $L+1$ information constraining forces that act in level L. In other words: **downward causation is efficient cause that is informed by information embodied at the higher level of pattern**.

3.3 Closure to efficient causation

The term closure to efficient causation refers to a property of hierarchical cycles, following Rosen (1985), in which the hierarchy refers to the containment of one efficient cause within another. This can be understood using the relational biology language of category theory: for any two mappings (morphisms) $f \in H(A, B)$ and $g \in H(C,\ H(A, B))$, each representing efficient causes (as in any of Fig 5), we see that g takes elements in the set C of material causes (more precisely, patterns) and maps them to a codomain which is a set of mappings (i.e. another set of efficient causes), specifically the member f which transforms members of A to members of B. Concretely, this is achieved when an efficient cause transforms a pattern in matter into one that then has the ability to effect another efficient cause (i.e. the pattern is reconfigured by the first efficient cause so that it constrains forces such that another efficient cause results). This is distinctly different from a mere concatenation of efficient causes, such as $C \xrightarrow{g} A \xrightarrow{f} B$, where g and f transform a pattern in C into a pattern in B via an intermediate pattern in A: the point is that A is a set of patterns, not of efficient causes, so $C \xrightarrow{g} A \xrightarrow{f} B$ is termed 'sequential', rather than 'hierarchical' (see Louie (2009); Louie and Poli (2011) for more detail) . Closure refers to the case when the output end of a system of connected mappings is equivalent to the input end, forming a loop (a cycle). The loop is a hierarchical cycle only if every efficient cause required for it is contained within another efficient cause that is part of the loop. This is equivalent to requiring the loop to have no exogenous efficient causes, which means that for a hierarchical cycle, every causal part of the cycle is itself caused by the cycle: hence it is a *clef* system. For example, if $f \in H(A, B)$, $g \in H(C,\ H(A, B))$ and $k \in H(D,\ H(C,\ H(A, B)))$ and also $B \equiv H(D, H(C, H(A, B)))$, then the system of efficient causes $\{f, g, k\}$ is a *clef* system. (Louie and Poli, 2011, Section 2.5) point out that "Both the hierarchy of containment and the cycle are essential attributes of this closure" and also that the "accounting (and tracking) of *all* efficient causes in an entailment system is crucial in our understanding of hierarchical cycles, one needs to preserve every [efficient cause]". In practice, closure and hierarchy together impose a very strong requirement on a system.

Using our example, the ATP synthase complex may supply ATP-energy to a proton pump crossing the same membrane and this pump may maintain the trans-membrane proton gradient which drives the ATP synthase complex. One might think that here a set of patterns produce an efficient cause which results in the transformation of another set of patterns to produce an efficient cause that transforms the first set of patterns such that it produces the first efficient cause and so on, in a cycle, but that is not enough to claim that we have a *clef* system before us. Those familiar with relational biology might say that this system is a sequential cycle, i.e. closed to material cause. But if material cause is micro-formal cause and formal cause, without forces, is unable to achieve change, then that is strictly impossible. In this system, there are forces and they are constrained by patterns, so we do have efficient causes. But analysis shows that not all the efficient causes involved are contained hierarchically by efficient causes within the cycle (Fig. 6), since efficient causes such as R_H and F_γ stand out as 'bristles' of exogenous origin around the cycle.

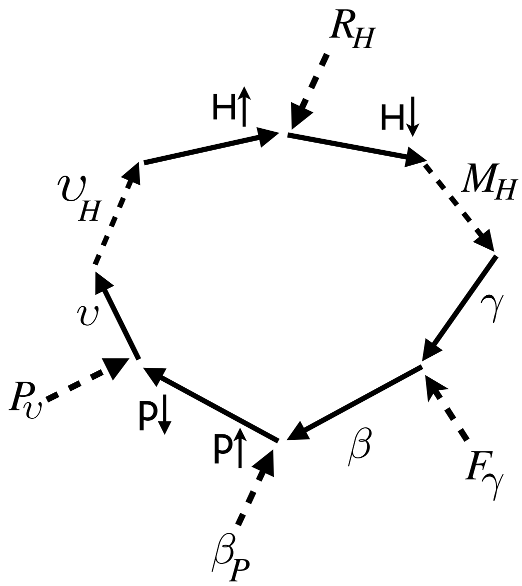

Figure 6: Causal analysis of the ATP synthase / proton pump system showing efficient causes (dashed arrows) are both part of the cycle and exogenous to it, so the system is not closed to efficient causation. Starting with protons (H) in the high energy state (H ↑) (concentrated e.g. in the inter-membrane space of a mitochondrion), they then relax (material cause denoted by the solid arrow) under electrostatic and kinetic forces, but are constrained to flow through the proton channel in the ATP synthase, by its pattern (efficient cause R_H). Since this pattern was not caused by any part of the cycle, it is exogenous. The constrained flow creates the proton motive force that is efficient cause M_H for rotating the γ-subunit (the symbol γ represents this rotation which is a change in formal pattern, hence a material cause). That rotation changes the direction of the force applied by the γ-subunit to the β-subunit, but the force itself is produced and constrained by the *pre-existing* pattern of atoms in the γ-subunit, which all move together as one. Because its formal cause is pre-existing, the efficient cause (F_γ) of the γ-subunit force is exogenous to the cycle. F_γ causes a conformation change (material cause) to the pre-existing pattern of the β-subunit, to which phosphorylation is coupled, represented by β_P, resulting in ATP (P ↑). Hydrolysis-coupled conformation change in the proton pump υ returns ATP to ADP+P_i (P ↓) only because of the pre-existing pattern of the proton pump, hence the material cause υ depends on exogenous efficient cause P_υ. However, like the proton motive force M_H, the proton pump exerts efficient cause υ_H - constraining forces - upon the protons, driving them back into the H ↑ state.

These exogenous efficient causes represent the necessary effect of pre-existing patterns, without which the system would not function. In the system, pre-existing patterns are varied by constrained forces with causal effect: conformation changes in the β-subunit and proton pump; rotation in the γ-subunit and translation for the protons. But pre-existing patterns are not created by efficient causes belonging to the system. Each variation of pattern in the loop can be considered as a material transformation (change of form) and because material transformations have a physical cause, forces must be engaged (and appropriately constrained), so underlying the material transformations, we must find efficient causes. Despite the material transformations composing a loop, constituting closure to material cause by underlying micro-efficient causes, the loop is not a *clef*-system because additional exogenous efficient causes are also necessary. Enclosure of efficient causation definitively entails all the necessary efficient causes in the loop, they must all be endogenous and we do not see that here.

Significantly no example of a *clef*-system can be provided at this molecular level of detail yet: the minimal known case of a *clef*-sytem is that of the whole living cell for which the model provided in Hofmeyr (2021) is the most detailed current causal examination. That is because requiring all efficient causes to be endogenous restricts *clef* to mean that all the components of the system cause one another to be: the efficient causes amount to the fabrication and assembly of the parts that are in turn responsible for the causes. Here, *clef* is not a claim that molecules make themselves, but rather that the system composed of them makes copies whilst retaining the organisation of them, materially different molecules replace their predecessors in order to maintain the organisational integrity: the embodied information is maintained by diachronic, not synchronic causation. Indeed, most of the functionally crucial molecules are fabricated and assembled by the function of the whole system that includes a previous generation of them. But one more ingredient is needed to achieve this, as we shall see next using a more general description.

Describing a cell as closed to efficient causation was shown in Hofmeyr (2018) to be consistent with Von Neumann's constructor theory of self-reproduction (Von Neumann and Burks, 1966), which represents reproduction as $(P + Q + R) + \phi(X)$ where P is a 'fabricator', $\phi(X)$ is the 'blueprint' (information content) of machine X, Q is a 'blueprint copier' and R a controller. Hence, there needs to be a reproduction machine plus information about what to reproduce and both have to be duplicated for self reproduction. Cellular life conforms to this arrangement by encoding $I = \phi(P + Q + R)$ in the form of DNA which acts as formal cause, leaving the information embodied by $P + Q + R$ to inform efficient cause. The distinction between digital (algorithmic) and analogue information referred to by Walker and Davies (2013) and Walker (2017) is this same distinction between information embodied for purely formal cause and for efficient cause. Hofmeyr (2021) resolves construction into two distinct parts: *fabrication* being the building of biomolecules, particularly polypeptides and polynucleotides, and *assembly* (following it) being the folding of polypeptides into functional forms and the organisation of these into a functional spatial pattern. With the representation of ontological causal structure (Fig. 4 b), a model of the cell was constructed that explicitly includes formal and efficient causes combined into a *clef* system, with $I = \phi(X)$ explicitly identified with DNA and P, Q, R matching known biochemical subsystems: Hofmeyr's (2021) fabrication-assembly (F, A) model. Expanding (Fig. 4 b) to identify all the main metabolic, anabolic and informational flows Hofmeyr (2021) shows that the cell must use an independently embodied source of information to achieve closure to efficient causation, making it an *informed system* (defined in the Introduction). The causal role of this information is purely formal, it does not exert efficient cause in and of itself, instead it has to be re-embodied into forms that do exert efficient cause and this transfer of information from one embodiment to another is the process of transcription and translation, which necessarily entails biological coding (Barbieri, 2015). Specifically, since $I = \phi(P+Q+R)$ is formal cause, it needs to be (literally) transformed to become a source of efficient cause and that is accounted for in the (F, A) model of Hofmeyr (2021) by explicitly including the causal role of ribosomes and their related molecules.

But why is this additional information necessary at all? To inform the efficient cause, information in $P + Q + R$ must be embodied so as to constrain the forces that result in fabrication, copying and control. But to act as $I = \phi(P+Q+R)$, it needs to be in a form that produces no appreciable efficient cause (just like the tape of the Jacquard loom). It is not possible for the same pattern to act in both ways simultaneously. Logically, it seems self-evident that a thing cannot be both the basis for efficient cause and constrained not to produce efficient cause at the same time and place. In other words the formal (nucleic acid-based) $I = \phi(P+Q+R)$ is kept from exerting direct efficient cause by encrypting it and this encryption simultaneously protects it from (all but very select) efficient causes in $P+Q+R$. The separation of roles for this information is universal across life and Von Neumann himself may have seen the necessity for it (based on his theory of complicated autonomata). In Burk's account of the 1948 Illinois lectures (Von Neumann and Burks, 1966) there is a hint of this "... it is preferable to proceed, not from original to copy, but from verbal description to copy" (p.84). That 'preference' is increased by the way Von Neumann's replicator works, the copying machine Q has to make two copies of $\phi(X)$ (p.85). Significantly, Von Neumann refers to $\phi(X)$ as a 'memory' and in his cellular implementation (a forerunner of Conway's Game of Life), he requires a particular cellular automaton to be 'embedded' as an initial condition (p. 108), effectively constituting the memory and reflecting the historical contingency that characterises life. Burk comments on the (sadly incomplete) work: the 'strongest' solution for the self-reproduction problem required "a complete description of the secondary [daughter system], expressed by the linear array of cells **L**, to be attached to the primary [parent]" (p. 118). I am unaware of a proof of this, but perhaps demonstrating that a replicator is an *inference device*, as defined by Wolpert (2008) would provide one. More practically, the search for a ribozyme capable of self-replication (Tjhung et al., 2020; Khatib and Raslan, 2021) demonstrates the difficulty of simultaneously using information to effect self-construction and to be the blueprint for that process. A whole ribosome is far simpler than an organism and Hofmeyr (2021) correctly points out that even the ribosome cannot self-replicate. Even if that were possible, it would leave no room for error correction, which has been a major stumbling block to the creation of synthetic ribozymes.

Obviously nucleic acids embody additional information, but they are not the sole source of information to the cell. Another insight of Hofmeyr (2021) was recognition of the intracellular milieu as a functional component of the *clef* system, responsible for e.g., protein folding. This milieu has to be maintained within tight biochemical parameters, for which a closed-loop control network of transducers and actuators (e.g., ion pumps) is necessary. A share of both the milieu (cytosol) and the membrane, with all its transmembrane components embedded, is physically transferred to the daughter cells. All closed-loop control systems need set-points which are internally embodied information (formal cause) representing the *goal*—a special point in an objective function (e.g., osmotic potential). Set-points for homeostasis are ubiquitous among the networks of cellular biochemical pathways, but we still do not know how, in general, they are embodied or encoded (Reed et al., 2017). It is likely that they are, at least in part, trasferred along with the material components of cytosol and membrane. Set-points are another example of information embodied to function as pure (stand-alone) formal cause and seem to be unique to life (Farnsworth, 2017).

3.4 Ultimate cause, goals and functions

The set-point represents a goal in an objective function (e.g., osmotic potential) and with that a *purpose* for control is established. Homeostasis is apparently unique to life and certainly implies an intention or goal. Once we have a goal-seeking purpose, we can define *function* as working to achieve that goal. Functional information is that which contributes to the functioning of the whole and in the case of organisms, that corresponds with the *master function* (Auletta et al., 2008) of the organism, which is established by evolution as maximising life-time reproduction success (biological fitness) (Farnsworth, 2017). Function does not imply teleology if defined as a *process* enacted by a system **A** at emergent level L which influences one or more processes of a system **B** at level $L+1$, of which **A** is a component part (Farnsworth et al., 2017). But once we identify a master function for the whole system, teleology is unavoidable (Mossio and Bich, 2017). Homeostasis is necessary because the functioning of the whole requires the living system to be within a particular range (sub-set) of states, though its environment may change. It also implies a means of detecting the changing environment, without being determined by it in a linear chain of efficient causation (as would be the case for a non-*clef* system). This requires isolation from exogenous causation, but not from the information embodied by exogenous forces. The stripping of force from exogenous efficient causes, leaving only the formal causes (information) is achieved by the plasma membrane of the cell plus its many embedded transducers (Farnsworth, 2018). Again we see the incorporation (literally) of patterns that separate the formal information from the force, resolving efficient cause into its fundamental components.

3.4.1 Transduction and causal isolation

The action of a transducer, which detects patterns of forces on one side of a barrier and relates them as information in signals on the other side is approximately performing this stripping of formal cause from efficient cause that was described in terms of a Jacquard loom in Section 2.4.4. In first messenger–second messenger signalling, transmembrane molecules can change the way information is embodied and in so doing totally change the nature, arrangement and magnitude of the forces that accompany its embodiment. For example when a retinal molecule absorbs a single photon, it extends to its *trans* conformation from the flexed *cis* conformation, producing a distortion in the shape of the much larger opsin protein (a G-protein coupled receptor) that holds it. This conformational strain triggers a second messenger signal via a complicated cascade, part of which sees an active site in the rhodopsin molecule bind to a G-protein and by doing so, activates it. The internal chemical signal, not a photon, is available for amplification via a chemical chain reaction, and in the case of the retinal photo-isomerisation, the signal eventually triggers the release of neurotransmitters from where a nervous system can amplify by mutual excitation of neurones; clearly the photon itself has been replaced with a signal representing the arrival of a photon. Even more clearly, when physical pressure is applied to a cell, especially one adapted to detect physical forces, mechanosensory systems embedded in the membrane, based on gated ion channels, transform the physical force into a chemical signal (Gillespie and Walker, 2001). The information (e.g., vibration frequency) is retained by the transducer, but its efficient cause is stripped of its force by the transducer/membrane complex, leaving a signal, again embodied in signalling molecules, or ionic concentrations. Once this happens, there is no longer an inevitable causal link between the external agent (physical force) and internal response, instead a causal branching point has been created Ellis and Kopel (2019). Branching points are forks in causal relations under the control of an additional efficient cause, which switches from one causal branch to the other (in effect both efficient causes are necessary to determine the effect). For example ion channels may open upon reaching a threshold of strain in the membrane and this threshold may be determined by internal control using a set-point, so that the effect of the strain could become functional at the whole system level.

3.4.2 All together - the living cell

Now we can see a living cell as a *clef* system which also embodies the information needed to inform its self-construction (both fabrication and assembly), and homeostatic control, following the causal architecture described in Hofmeyr (2021). It is a large set of efficient causes acting across levels; a dynamic pattern in a very complicated (mainly electrostatic) forcefield. It is not only *clef*, but by using its physical boundary with embedded transducers, along with embodied control information (set-points), it also achieves cybernetic autonomy (transforming from cause-effect to signal-response) via a nested hierarchy of homeostatic systems. This hierarchy of signal-response systems physically forms the basis of decision making that leads from the most basic homeostasis up to action valuation systems (Farnsworth, 2017, 2018). The very idea of decision making implies autonomy, options and criteria to measure them by (Noble and Noble, 2018). Embodied information serving as set points provides the criteria as goals in physiological objective functions (variables). This embodiment of formal cybernetic information is a prerequisite for ultimate cause (Farnsworth, 2017), that most controversial of Aristotle's four, which seems unique to life (Mossio and Bich, 2017). It pre-supposes *purpose* which is necessarily subjective and cannot be defined without reference to an agency to which it belongs. This, with its teleological implications, may be permitted only in the case of organisms because they alone among natural systems have the properties of causal agents (Bich and Damiano, 2012; Friston, 2013; Froese et al., 2007; Kauffman and Clayton, 2006; Varela, 1979). Two attributes are necessary and apparently sufficient for this causal agency: first that systems be *clef* and second that they possess autonomous information that formally acts as at least one set-point for homeostasis. Living cells include hundreds of set-point based homeostatic systems which interact with the formal information of the genome, these together constituting a computer that runs the cellular operating system Auletta et al. (2008), enabling the cell to respond to its environment and execute fitness enhancing actions.

4 Discussion

The ideas presented here can be summarised as follows. Form is the arrangement of particles in space and time. Associated with every particle is a forcefield of characteristic shape and whenever two or more particles are sufficiently close to significantly interact, it is because their forcefields sum over space to produce a new combined shape. If this shape persists in time, it is because the configuration of the particles (pattern) is thermodynamically favourable compared to alternatives ($\Delta G < 0$) and the pattern then embodies information. The pattern, in turn, constrains the vectors of forces among the particles (by making specific the direction and magnitude of exchange particle transfers among them). Formal cause is this constraint of forces by pattern (information). Efficient cause is the physical effect of formal cause and the alternative of unconstrained physical force (absence of formal cause) manifests as heat. Material cause is atomic-level efficient cause. Multiple levels of organisation arise from the spatial distribution of mutual information (spatial autocorrelation) in the overall pattern. It is the patterns, not the forces they constrain, that determines the causal relation among organisational levels. As a consequence, there is no impediment to inter-level causation. Emergent phenomena arise when a higher level pattern informs efficient cause. An important example of that is the emergence of downward causation, whereby small scale patterns are varied by the larger scale (e.g. the rotating armature protein inducing conformational change in the active site of the β-subunit of ATP synthase). Circular efficient causation (*clef*) is diachronic not synchronic and involves a special case of downward causation in which higher level patterns organise lower level patterns to result in the fabrication and assembly of copies of themselves. Systems possessing this property must also be informed systems, meaning they must incorporate an additional source of formal cause over and above that which informs their efficient causes (i.e., they need a memory). Above all, these properties make the living cell uniquely potent as a physical system. Finally, ultimate cause can only apply to a *clef* system and requires autonomous formal cause (at least one set-point) to establish a goal, from which purpose and function can be defined and without which ultimate cause makes no sense.

Throughout this informationist account, the concept of organisation by constraints within living systems is crucial. It was developed by Juarrero (1999) in response to a perceived inadequacy of conventional theory to account for emergence. She distinguished between context-free (effectively external) constraints and context-dependent (self-organising) constraints which act as a form of downward causation; significantly calling the action of an object "informationally dependent and constrained behaviour" (Juarrero, 2000, p.30). Context-dependent constraints were later differentiated into first and second order, the former enabling emergence from joint probabilities (correlation) among interacting parts; the latter implicating the symmetry breaking that leads to reinforcement of pattern, non-linearity and dependence upon the history of the system (Juarrero, 2009). This was inspired by the probability theory approach towards e.g. complex ecological systems, especially exemplified by Ulanowicz (2019). We see here the beginnings of a coherent theory recognising the mutual dependence of state-space probabilities among system components and the connection of that (not yet equivalence) with information. Montévil and Mossio (2015) reiterate the idea of self-control by constraints in an effort to specify efficient cause in biological systems, taking their inspiration from the 'work-constraint cycle' concept of Kauffman (2000). For Montévil and Mossio (2015), constraint closely matches the idea of efficient cause developed by Rosen (1973, 1985). This was resolved into formal and efficient causes, for which information has an explicit role in the fabrication-assembly model of the cell developed by Hofmeyr (2021). The work presented here strengthens that by explicitly identifying information as the particular constraint on physical force that acts as the basis for all causation and by showing how information embodied in lower-level patterns (e.g. molecules) is manipulated by higher level patterns in organisms to effect autonomous agency. This emphasises that life is quintessentially an emergent phenomenon - strictly not accessible from the study of component parts alone.

The reductionist approach has been so successful that it has misguided us towards believing that the small scale is the only real one and that all processes are in fact processes at that scale. Understanding that everything, except elementary subatomic particles, exists because of information embodied in the particular arrangement of those particles, enables us to see it the other way round. Certainly, all causes can be traced back to the constraint of physical forces acting among all the particles present, these constraints being the geometric configuration of the particles in space and time. But realising this can give us a radically integrative view telling us that material objects composed in a hierarchy of levels of organisation and interacting with one another via physical forces are in fact all parts of one pattern of elementary particles with symmetry breaking occurring at multiple spatial scales, from which we identify the levels. For each fundamental force, the pattern creates a single forcefield: the vector sum of forces emanating from all the particles and influencing the movement and position of them all. Rather than the smallest level being the fundamental basis of reality, it seems the largest level, the one where the forcefield is a unitary whole with a particular (and typically changing) pattern, is the source of the reality that we experience. In this context, organisms are special because, as patterns within the whole, they possess both closed loops of efficient causation (albeit diachronic) and also the information, embodied as part of their pattern, that informs the fabrication of the patterns from which they are composed and by which they are self-regulated. The form of an organism is necessarily (but selectively) closed by a material boundary (one or more cell membranes) and necessarily contains a template-memory that has accumulated, presumably through evolution (we do not yet know how) and arranged so that it creates copies of its own pattern, leading both to self-maintenance and also to self-replication. Organisms are self-informed dynamic patterns within the whole (a considerable advance on e.g. vortices), having the properties of autonomy derived from their internalised information that gives them a goal and the autonomy to pursue it, but they are ultimately a part of the whole. In this way, life is not separate from the universe, instead, it is the greatest known elaboration of the information structure of the universe.

The concepts proposed here are far from the full answer to overcoming the challenge of biology to physics, but the resolution of efficient cause into force and formal cause (information), with all its consequences, seems to provide a sufficiently fresh perspective to stimulate further progress. There are several unanswered questions, notably it remains a mystery how the information needed for autonomous operation of a living cell was accumulated in the first place. More detailed problems such as the mechanisms of protein folding and the way the protein parts of molecular machines are correctly assembled and the whole inventory of parts is managed by the cell, remain to be answered by further research.

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Appendix - the irreducibility of hierarchies of biological function

The following is a simple analysis of emergence using the concepts introduced in Section 2.2 of the paper.

For any level L in an organisational hierarchy of pattern, let ${}^{L}\mathbf{A}$ be an assembly of n_L components (lower-level assemblies) $\{{}^{L-1}\mathbf{A}_1 \;\cdots\; {}^{L-1}\mathbf{A}_{n_L}\}$, configured in space as a pattern of patterns ${}^{L}\mathbf{C} = \{{}^{L-1}\mathbf{C}_1 \;\cdots\; {}^{L-1}\mathbf{C}_{n_L}\}$. For the first level assemblies, we have ${}^{1}\mathbf{A} = \{e_1 \cdots e_n\}$, where e_i are fundamental particles, each with an associated force-field f_i and these are configured in space by ${}^{1}\mathbf{C} = \{\mathbf{z}_1 \cdots \mathbf{z}_n\}$, where each $\mathbf{z}_i$ is the set of relative coordinates of particle e_i (for relative, take any one particle as the origin and measure coordinates from there). Every pattern constrains forces in the sense stated in Section 2.4, irrespective of its level: every ${}^{1}\mathbf{C}$ constrains the forces emanating from the particles it places in space and any higher e.g. ${}^{2}\mathbf{C}$ adds further constraints by virtue of specifying the relative position of each member ${}^{1}\mathbf{A}$ within ${}^{2}\mathbf{A}$, following the principle set out in Section 2.4. For example if ${}^{1}\mathbf{A}$ was a water molecule and ${}^{2}\mathbf{A}$ an ice crystal, the arrangement of molecules in ice would be ${}^{2}\mathbf{C}$).

For strong emergence (Chalmers, 2006), it is necessary to show that the properties of ${}^{L}\mathbf{A}$ do not supervene on the properties of its member parts ${}^{L-1}\mathbf{A} = \{{}^{L-1}\mathbf{A}_1 \cdots {}^{L-1}\mathbf{A}_{n_L}\}$, thus implying that a change in properties of ${}^{L}\mathbf{A}$ can be brought about without changing any of those of its component parts ${}^{L-1}\mathbf{A}$. Clearly, the level-L pattern ${}^{L}\mathbf{C}$ can change without changing any of its component parts $\{{}^{L-1}\mathbf{C}_1 \cdots {}^{L-1}\mathbf{C}_{n_L}\}$, simply by rearranging those parts, noting that ${}^{L}\mathbf{C}$ specifies a *particular* arrangement of the ${}^{L-1}\mathbf{C}$ patterns. But we still need to establish whether a change in level-L pattern alone can result in a change in level-L properties.

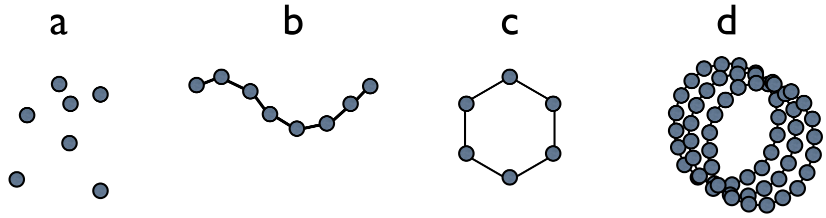

Figure 7: Emergent properties of levels of pattern: level-1 elementary particles (a) have only their own properties, e.g. charge and spin. A level-2 pattern such as a string (b) has new properties, e.g. length. A level-3 pattern made with the string, e.g. a ring (c) can have a diameter and shape (hexagonal in this case). A string can also be coiled to make a tube, as in the tobacco mosaic virus (d): the coiling is a level-3 pattern and has new properties such as diameter and flexibility. If it were to be pinched to form a figure of eight cross-section, it could branch and from this a ramiform level-4 pattern could be built, making e.g. an arterial tree.

Let us associate with every ${}^{L}\mathbf{C}$, a set of properties, ${}^{L}\mathbf{P}$, for example geometric properties such as those of a string of particles (Fig. 7.b) and those of the string formed into a ring (Fig. 7.c), or a cylinder formed from a spiral of the string (as in the tobacco mosaic virus, Fig. 7.d). Note that in forming a string, we change the spatial dimensionality of the assembly and further change it when forming the ring and spiral. These are examples of symmetry breaking, whereby the pattern no longer appears the same when viewed from any angle. Symmetry breaking was strongly identified with emergence by Anderson (1972) and has since been an important part of its explanation in physics (e.g Ellis, 2020). The precise meaning of 'properties' remains somewhat obscure, so let us assume that (other than for fundamental particles) properties are what we recognise in higher level patterns as enabling efficient causes that could not be attributed solely to the lower level patterns (this is consistent with the definition in Baas and Emmeche (1997), used by El-Hani and Emmeche (2000), though they did not explicitly refer to efficient causes). For example, the strength of a material depends on how its atoms are arranged (level-1 pattern) and a tube formed from a spiral enables the containment and direction of fluid flow; these potentialities arising from 'tube-properties' (Fig. 7.d), which are what we recognise of the level-2 pattern. That is, properties of level-L are *observed*, recognised and ascribed; they exist specifically because of the level-L pattern, hence they depend on information embodied by the level-L pattern and in fact, according to El-Hani and Emmeche (2000), they arise from the constraining of the relations among the parts, in space-time, such that "the pattern of constraints realizes and thus, explains ${}^L\mathbf{P}$" (they used a plain P notation). Given this, we can identify the properties of the particles making up a string as ${}^1\mathbf{P}_1$, those of the string itself as ${}^2\mathbf{P}_1$ and those of the ring as ${}^3\mathbf{P}_1$ and the spiral cylinder as ${}^3\mathbf{P}_2$ to compose a hierarchy of patterns, with particles at level-1, the string at level-2 and the ring and cylinder each at level-3.

Since the above definition of a property entails efficient causes, we also need to associate a repertoire of *potential* efficient causes, ${}^L\mathbf{G}$ with its pattern ${}^L\mathbf{C}$, which is no problem since by constraining forces, the pattern can produce these, according to Section 2.4 (note there is no necessary relation between the number of components in ${}^L\mathbf{C}$, the number of properties in ${}^L\mathbf{P}$ or the number of potential efficient causes in ${}^L\mathbf{G}$).

The constrained forces depend on all the particles in the level-L assembly ${}^L\mathbf{A}$ and the level-1 ways they are configured ${}^1\mathbf{C} = \{{}^1\mathbf{C}_1 \cdots {}^1\mathbf{C}_{n_1}\}$ and the level-2 ways ${}^2\mathbf{C} = \{{}^2\mathbf{C} \cdots {}^2\mathbf{C}_{n_2}\}$, and so on up to ${}^L\mathbf{C}$ (which has only one member). Other than the particles (and their forcefields), that means ${}^L\mathbf{G}$ depends on the patterns at all the levels and we can summarise that (without repetition of patterns that are the same) by $\{{}^1\mathbf{C} \cup {}^2\mathbf{C} \cdots \cup {}^L\mathbf{C}\}$. This, though, is just a decomposition of the total pattern and is no more than an information-efficient (compressed) way to describe it, equivalent to a description entirely at the first level of fundamental particles.

If that was all ${}^L\mathbf{P}$ depended on, then it could be completely described in terms of the total pattern that specifies the coordinates of every fundamental particle. This description necessarily includes information about the larger scale patterns, but to show strong emergence, we would need to identify a block on reducing all the necessary conditions for ${}^L\mathbf{P}$ to the lowest level. This block arises from the definition of properties as depending on both lower level causes and same-level pattern - two ontologically different things existing at two different levels of organisation.

Specifically, the properties ${}^L\mathbf{P}$ of ${}^L\mathbf{A}$ depend on both the properties ${}^{L-1}\mathbf{P}$ of the assemblies within ${}^L\mathbf{A}$ and also on the way they are configured by the pattern ${}^L\mathbf{C}$. For example, the properties of a ring (${}^3\mathbf{P}$) depend on those of the string from which it is assembled (e.g. its length) and *also* the geometric shape of the ring (circular or hexagonal, etc.), which are specified by the ring's pattern (${}^3\mathbf{C}$) and do not exist (even as concepts) at the lower levels, even though the possibilities for ${}^3\mathbf{C}$ are brought into existence by the string (which is a level-2 assembly: ${}^2\mathbf{A}$). The properties of each of the ${}^{L-1}\mathbf{A}$ in turn depend on ${}^{L-2}\mathbf{A}$ composing ${}^{L-1}\mathbf{A}$, all the way down to ${}^1\mathbf{A}$. To illustrate: the ring might be a string joined in a tight circle composed of six molecules of type

A and B, (strung together as A-B-A-B-A-B which is the pattern ${}^{2}\mathbf{C}$). Suppose each of A and B has the property ${}^{1}P_A$ and ${}^{1}P_B$, respectively, of a particular surface charge distribution (one for A and one for B), determined by the properties of the atoms from which it is composed and the way they are arranged in the molecules: $\{{}^{1}\mathbf{C}_A\ ,\ {}^{1}\mathbf{C}_B\}$. By this alternating charge, (a ${}^{2}\mathbf{P}$ property of the string) the ring acquires the property ${}^{3}\mathbf{P}$ needed for it to produce the efficient cause of a molecular motor in the context of a yet higher level (4) of pattern in atoms. It obtained this level-3 property from level-2 properties in conjunction with its ${}^{3}\mathbf{C}$. The level-2 properties were obtained, in turn, from level 1 properties in conjunction with the level-2 pattern of alternating molecules.

Thus, it is clear that properties arise from a conjunction of ontologically different entities: lower level properties together with patterns. This means that they are not reducible to a single low-level description (as the hierarchy of patterns $\{{}^{1}\mathbf{C} \cup {}^{2}\mathbf{C} \cdots \cup {}^{L}\mathbf{C}\}$ was). For this reason, we can conclude that strong emergence is a natural (physical) consequence of organisational levels having properties that depend on the information embodied at their (same) level, as well as the properties of their component parts. In plain language: **because properties at one level are the consequence of properties of its lower level components *together with* the arrangement of those components, they cannot be reduced to a single lowest-level description**. The properties uniquely associated with each level give rise to the 'new concepts' referred to in some other accounts of emergence and the irreducibility of levels results from having to combine ontologically different things to form each of them. This also explains why property emergence is always associated with causality, rather than mere patterns, though of course it depends on assuming that properties themselves are more than mere patterns. Indeed, many refer to them as emergent phenomena.

The analysis just given exposes the problem of subjectivity (dependence on an observer) that lies at the heart of current attempts to account for property emergence (see e.g. Blundell (2017)). Essentially the problem is that properties cannot be rigorously defined without including the view-point of an observer because they are the result of observation. We are left unsatisfied because, as scientists we want there to be a natural objective meaning for emergence before we are willing to fully accept the idea of it into main-stream science, which is an objective account of natural systems. What happens if we let go of properties and instead focus on only those things that are certainly objective? We may see that what is important about the component assemblies $\{{}^{L-1}\mathbf{A}_1\ \cdots\ {}^{L-1}\mathbf{A}_{n_L}\}$ of ${}^{L}\mathbf{A}$ in the formation of efficient cause is their repertoire of efficient causes $\{{}^{L-1}\mathbf{G}_1\ \cdots\ {}^{L-1}\mathbf{G}_{n_L}\}$. These can be organised into one or more higher level efficient cause by the level-L pattern ${}^{L}\mathbf{C}$. It does not matter exactly what the ${}^{L-1}\mathbf{A}_i$ are, it is their potential effects that matter; in principle, different assemblies may enact the set of efficient causes, so they are multiply realisable and we may more precisely refer to equivalence classes of ${}^{L-1}\mathbf{G}_i$. If more than one level-$(L-1)$ assembly can produce the same ${}^{L-1}\mathbf{G}_i$, then more than one ${}^{L-1}\mathbf{C}_i$ can be responsible for its production, that is, at least in principle, there is a set $\{{}^{L-1}\mathbf{C}_{i,1} \cdots {}^{L-1}\mathbf{C}_{i,J}\}$ which, constraining their particle forcefields, results in ${}^{L-1}\mathbf{G}_i$. This leaves us in the same position of needing to combine ontologically different objects at each level to form the efficient causes: this time it is functional equivalence classes combined with patterns. The effect is the same: we cannot reduce the combination to a lowest level description.

Satisfyingly, this prohibition on decomposition becomes stronger when the system is a biological one, for which the relevant efficient causes (of all potential efficient causes in ${}^{L}\mathbf{G}$) are those which confer biological function. In this case, every level-L function ${}^{L}\mathbf{F}$, is the result of ${}^{L}\mathbf{C}$ organising components that have biological function sets $\{{}^{L-1}\mathbf{F}_1 \ \cdots \ {}^{L-1}\mathbf{F}_{n_L}\}$ (consistent with the Farnsworth et al. (2017) definition of biological function). These sets are functional equivalence classes (Farnsworth et al., 2013); certainly an ontologically different entity from the embodied information ${}^{L}\mathbf{C}$, so the combination of them with ${}^{L}\mathbf{C}$ cannot, even in principle, be decomposed into a level-1 description. The result is the possibility of strong emergence of biological functions. Not only that, but the organising information ${}^{L}\mathbf{C}$ has the effect of selecting from $\{{}^{L-1}\mathbf{G}_1 \ \cdots \ {}^{L-1}\mathbf{G}_{n_L}\}$ those potential efficient causes that are functional in the sense that they contribute towards ${}^{L}\mathbf{F}$. Thus in living systems, the nested hierarchy of organisational levels is also a nested set of selection processes, each selecting function from the potential efficient causes of the assemblies in the level below it. Since the functional repertoire of each level is a real and essential feature of that level and dependent on this selection, every level is irreducible.

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