

Endless forms most beautiful 2.0: teleonomy and the bioengineering of chimaeric and synthetic organisms

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The rich variety of biological forms and behaviours results from one evolutionary history on Earth, via frozen accidents and selection in specific environments. This ubiquitous baggage in natural, familiar model species obscures the plasticity and swarm intelligence of cellular collectives. Significant gaps exist in our understanding of the origin of anatomical novelty, of the relationship between genome and form, and of strategies for control of large-scale structure and function in regenerative medicine and bioengineering. Analysis of living forms that have never existed before is necessary to reveal deep design principles of life as it can be. We briefly review existing examples of chimaeras, cyborgs, hybrots and other beings along the spectrum containing evolved and designed systems. To drive experimental progress in multicellular synthetic morphology, we propose teleonomic (goal-seeking, problem-solving) behaviour in diverse problem spaces as a powerful invariant across possible beings regardless of composition or origin. Cybernetic perspectives on chimaeric morphogenesis erase artificial distinctions established by past limitations of technology and imagination. We suggest that a multi-scale competency architecture facilitates evolution of robust problem-solving, living machines. Creation and analysis of novel living forms will be an essential testbed for the emerging field of diverse intelligence, with numerous implications across regenerative medicine, robotics and ethics.

ADDITIONAL KEYWORDS: artificial life – basal cognition – chimaeras – evolution – hybrids – synthetic morphology.

INTRODUCTION: OPEN PROBLEMS AND KNOWLEDGE GAPS

Progress in molecular biology and genetics has led to great strides in understanding the micro-scale hardware of cells (the protein machinery encoded by the genome). However, as shown clearly by the trajectory of the information sciences, this is only the beginning; the next frontier is the software of life: developing a mature science of prediction and control over system-level phenotypes. Despite a deluge of big data on the molecular mechanisms necessary for specific functionalities, important capability and knowledge gaps remain with respect to the dynamics that are sufficient for the remarkable robustness and plasticity we observe in the living world.

A fertilized egg produces a cellular swarm that reliably self-assembles into a highly complex organism. Importantly, this process is not hardwired: mammalian embryos cut in half produce normal monozygotic twins, because despite this damage each side can grow what is missing. Some organisms maintain this regenerative capacity throughout their lifetime; for example, salamanders regenerate limbs, jaws, eyes, tails and ovaries (McCusker & Gardiner, 2011). A salamander limb can be amputated at any level and will produce precisely the missing parts and then stop when a correct salamander limb is complete (when the distance from the correct target morphology is sufficiently reduced). The ability to handle novelty in the form of external damage is not the only aspect of the robust plasticity of life; this ability also extends to unexpected changes in the internal building blocks of the organism.

Tadpoles generated to have no primary eyes, but an ectopic eye on their tail, can see reasonably well

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(Blackiston & Levin, 2013); in their aberrant new location, eye primordia cells form a proper eye and often connect the optic nerve to the spinal cord. A brain that has evolved for millions of years to expect visual input to a specific location immediately adjusts its behavioural programmes to operate with signals coming from its tail. The same plasticity has been observed in adult humans provided with novel senses and effector organs (such as prosthetics with novel degrees of freedom; Bach-y-Rita, 1967; Bach-y-Rita *et al.*, 1969; Danilov & Tyler, 2005; Nagel *et al.*, 2005; Shull & Damian, 2015).

Perhaps even more impressive are examples of structural robustness to change. Kidney tubules in newts normally form from the interactions of eight to ten cells in cross-section, working together to make a lumen of a specific size. Cell size can be made larger by artificially increasing the ploidy (chromosome number) of embryonic cells; that this results in a viable embryo is, in itself, amazing. Such animals are of a normal size and proportion, because fewer and fewer cells participate in the tubulogenesis as the cell size increases. Most remarkably, when cells are truly enormous, a single cell will wrap around itself to make a proper tubule (Fankhauser, 1945a, b). In this case, instead of the normal cell-to-cell communication, cytoskeletal bending is used to achieve the same morphological goal. Thus, diverse molecular mechanisms are triggered in service of a higher-level anatomical specification (a tubule of specific cross-section).

These changes in the quantity of genetic material and cell size are dealt with dynamically. Our robotics technology does not even begin to approach this kind of capacity, and any engineered swarm that could adjust to this type of novelty (perturbation in size and information content of its components) would be hailed as a milestone in artificial intelligence. The connection to intelligence is not accidental: William James defined it as the ability to reach the same goal by different means (James, 1890). The proficiency of living systems in this respect is best revealed not by the reliable normal development of standard model species (which obscures the true capacities of cellular swarms), but by the type of engineered, novel beings of which the above altered examples are only the beginning.

This type of plasticity, in the context of epigenetic controls and responses to the environment, is familiar to biologists with respect to changes of the environment and epigenetic control (West-Eberhard, 1998, 2005a, b) and extends to all scales, from the variability of the traditional environment of the whole animal to the microenvironment (internal properties) of organs and cells. Life is massively inter-operable, enabling functional chimaeras and

hybrids at the molecular, cellular, tissue, organ and even organism levels (Nanos & Levin, 2022). What computations, algorithms or dynamics enable cellular collectives to respond adaptively, reaching the same form and function despite radical induced changes of circumstances? Importantly, all these phenomena show adaptations to novelty that exists on the time scale of an individual, not requiring aeons of evolutionary search. This suggests that life exploits an architecture that provides much more efficiency than could be expected from a blind process that always chooses short-term gains (selection that adapts to a specific environment).

The answer to ‘what determines the shape of an organism?’ is often said to be ‘the genome’, but many deep questions remain about the relationship between the genome and anatomy. In addition to artificially produced chimaeric organisms, in which diverse genomes can live together and generate large-scale form and function (Nanos & Levin, 2022), some animals are natural chimaeras. Some species of planarians reproduce largely by fission and regeneration; this avoids the segregation of the germline in a type of somatic inheritance: any mutation that does not kill a stem cell takes it into the next generation to proliferate in the lineage (Fields & Levin, 2018; Levin *et al.*, 2019). For hundreds of millions of years, these animals have accumulated mutations and are even mixoploid; different cells within one animal can have different numbers of chromosomes. And despite this messy genome, they are champions of regeneration, building the correct body from even small fragments with very high anatomical fidelity (Saló *et al.*, 2009); each piece of a cut planarian produces a perfect little worm. We have no models in developmental genetics that would predict that the highest fidelity of anatomical outcomes would be associated with genetic diversity that rivals any tumour. Indeed, planarian lines can even be made permanently two headed by manipulating the bioelectric circuit that stores head number (Oviedo *et al.*, 2010; Durant *et al.*, 2017), resulting in permanent ‘strains’ of animals whose cells continue to build worms with a different anatomical body plan from the genomic default. What is the relationship between the genome and anatomy, and what mechanisms allow biology to exhibit robustness and plasticity simultaneously, enabling adaptive, coherent organisms to arise in novel circumstances?

Moreover, the highly competent decision-making of cellular collectives in anatomical morphospace reveals a fascinating commonality between problems of cognition (mind) and problems of body (morphogenesis). This fundamental link was well understood by early workers in developmental biology, such as Hans Spemann (Spemann, 1967), and those in

computer science, such as Alan Turing (Turing, 1952); it is only now beginning to be fleshed out (Grossberg, 1978; Friston *et al.*, 2015; Pezzulo & Levin, 2015). Ontogeny recapitulates phylogeny, in that all of us have made the journey across the Cartesian cut (from the ‘mere physics’ of molecular networks in a quiescent oocyte to a thinking being) not only during evolution but also during our own lifetimes. What aspects of biological structure enabled mind gradually to develop and expand?

These knowledge gaps are not obscure issues in evolutionary biology and philosophy of mind. The whole of regenerative medicine hangs on the question of how to induce collectives of cells to build one structure rather than another. Birth defects, traumatic injury, cancer and degenerative disease would all be solved if we had a mature science of making predictions and deriving rational interventions into the morphogenetic process (Levin, 2011). Advances in molecular medicine and genomic editing will not have an impact on biomedicine unless we know what to edit or which pathways to target to achieve system-level goals, such as ‘make a new arm’. It is no accident that current medical interventions that solve problems in the long term exist only in the realms of infectious disease and surgery. Transformative regenerative medicine awaits a mature understanding of how to induce collections of cells to make desired anatomical features.

THE NEED TO GO BEYOND STANDARD MODEL SPECIES

Chimaeras and bioengineered organisms challenge us to make predictions and spotlight areas in which genomics have driven unwarranted complacency. For example, when we make a frogolotl (a hybrid frog–axolotl embryo), will it have legs, like a larval axolotl, or not, like a tadpole? If it has legs, will they be made of frog cells or only of axolotl cells? We have no models in biology to make predictions about such cases, despite having full access to the genomes of both species. Crucially, this inability to predict or control outcomes is not a special feature of rare ‘corner cases’; it lays bare the often-neglected fact that even for a single species, knowing its genome enables us to say almost nothing about the form or function of the organism it ‘encodes’ (except when we cheat by comparing the genome with that of organisms whose anatomy we know already). This is because, although the genetics specify the cell-level hardware of the system (proteins), the outcome is the product of physiological software dynamics that are not predicted easily from the hardware level (Lobo *et al.*, 2014; Pezzulo & Levin, 2016).

If we ‘zoomed in’ to observe developmental events at the cellular level, seeing all of the stochastic cell behaviour and signalling noise, would we be able to predict that all of that activity would reliably give rise to a fish or mouse, if we did not already know about development and the fact that it is highly reliable in a range of conditions? Managing the reliability of outcomes in novel circumstances challenges us to develop a science of predicting stable outcomes at large scales (for a similar issue in neuroscience, see Jonas & Kording, 2017). Knowing how to detect and characterize specific goal states (in the cybernetic sense) of collectives, such as cell groups, is a crucial part of understanding systems. Novel instantiations of multicellular life are a crucial dataset on which to train and improve the conceptual tools of scientists and learning machines and must complement the developmental biology of standard, evolved model systems.

Beyond life on Earth, how would we recognize novel forms of life? What is the appropriate scale of observation for detecting the behaviour and appropriate problem spaces in which life operates? Bioengineering provides a crucial inroad for exobiology; a stepping-stone for enabling generalization of biology such that we can detect truly alien forms of life if and when we encounter them. Regardless of natural life elsewhere, exploring the option space of beings enables us to improve the terms and categories we use to understand life, manipulating all the components in a schema such as the traditional brain–body–environment framework to unfamiliar components, in order to see how our existing approaches break down when faced with unfamiliar implementations. Like the very successful strategy of looking for symmetries in physics, in biology we must ask which of our concepts are deep invariants. Which of them remain when contingent details of implementation (cell type, genetics, origin, etc.) are changed?

The need to expand beyond familiar life forms goes deeper than Feynman’s dictum, that we do not really understand a thing until we can make one ourselves. The future of biomedicine and engineering depends on being able to offload much of the complexity we wish to manage onto the system itself; for example, triggering a body to regenerate a limb in the right location instead of trying to micromanage its construction from the molecular level. This, in turn, relies on understanding the modules, decision-making and information processing of which the system is capable. We have argued in the past that an important aspect of future medicine will involve guiding the large-scale behaviour of cellular collectives with incentives, stimuli and set point rewriting (Pezzulo & Levin,

2015, 2016; Mathews & Levin, 2018), rather than micromanaging the structure of their parts. This means that we need to understand the algorithms guiding these systems at multiple scales and, in particular, their basal intelligence (i.e. their ability to navigate physiological, transcriptional and morphological spaces competently despite novel circumstances and perturbations). However, such intelligence is rarely apparent in ‘normal’ circumstances, when a system appears to be doing the same thing every time; this is what gives rise to a view of most biological systems as clockwork mechanisms, full of complexity but without intelligence. In order to uncover, understand, control and, eventually, cooperate with the true intelligence of biology at all scales, it is essential to confront biological systems with novelty, both inside and out, and to study the context-specific problem-solving capacities and plasticity (Braun, 2015) that are revealed in response to that novelty.

Chimaerism (mixing biological components) was a popular concept in the ancient world (Fig. 1A–C), but the story of Adam naming a discrete set of animals in the Garden of Eden (Fig. 1D) suggests a different and much more limiting picture: a type of essentialism that suggests sharp categories (distinctions of biological form) and natural kinds that do not, in fact, exist. We now have the opportunity to extend this story and ‘name the animals’ in a much deeper way, by understanding the design principles of biology that transcend extant evolutionary examples. The implications of embracing the space of possible beings will extend to terminology, conceptual frameworks, research programmes in several fields, and ethics.

Here, we initially review some examples of existing technologies that promise to expand our understanding of life radically. Going beyond classical chimaeras, we describe the mergers of diverse products of evolution and human design to sketch the dimensions of the space of possible beings. Given that origin, composition and familiar phylogenetic position will not be reliable guides to properties of living forms in this space, we then suggest an approach to the search for invariants: what do all such forms have in common that can be used to compare them directly and understand them? We suggest that goal-directed behaviour, in diverse spaces, is a central concept that fulfils the role of a framework for driving experimental approaches. Towards a unification of the sciences of the mind and body, we then introduce an expansion of neuro- and behavioural science outside the brain. We discuss the fields of basal cognition and diverse intelligence, in order to begin to generalize the idea of goal-directed activity beyond the function of

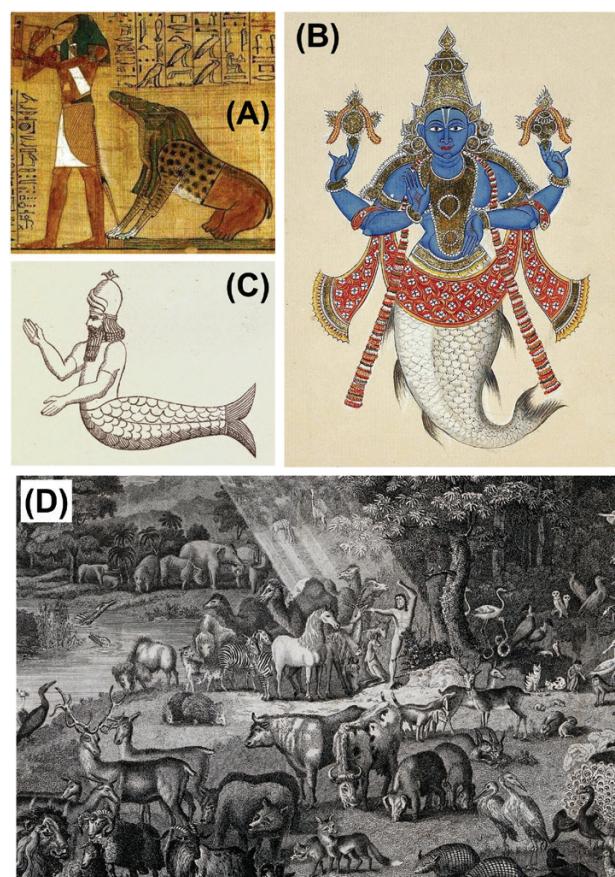


Figure 1. Chimaeras and natural kinds. A, a representation of the Devourer, who waited to eat the hearts of sinners in the afterlife’s Hall of Judgment. Papyrus of Ani, ~1275 BC; photograph from British Museum. B, Matsya (fish) Avatar of Vishnu. Nineteenth century lithograph. From Wikipedia. C, Oannes, a Mesopotamian mythological being who brought civilization to mankind. *Curious creatures in zoology*, by John Ashton (1890), p. 209. Available at: [https://commons.wikimedia.org/wiki/File:Curious_creatures_in_zoology_\(15565912981\).jpg](https://commons.wikimedia.org/wiki/File:Curious_creatures_in_zoology_(15565912981).jpg). D, ‘Adam names the animals in the Garden of Eden’ illustrates a pre-scientific (but implicitly, still widely prevalent notion) that current animals and plants represent discrete natural kinds with sharp separations, especially with respect to humans. Available at: <https://wellcomecollection.org/works/q6hw2nrg/items>

complex brains. We discuss teleonomy as a guiding framework for understanding diverse aspects of biology, suggesting that a deep principle of biology is nested goal directedness at multiple levels. We next explore some implications of such a multi-scale competency for evolution. Finally, we conclude with a sketch of a research programme, enabled by these ideas, which spans regenerative medicine, robotics and ethics.

SYNTHETIC BEINGS: EXPANDING THROUGH THE SPACE OF POSSIBLE BODIES AND MINDS

My son, if you would devote yourself to combining Holy Names, still greater things would happen to you.... And now, my son, admit that you are unable to bear not combining. Give half to this and half to that, that is do combinations half of the night, and permutations half of the night.

Abraham ben Samuel Abulafia

Examples of novel ‘life as it could be’ (Fig. 2) are highly diverse, and current technologies and proof-of-concept results clearly indicate the coming diversity of life in the near future (Doursat *et al.*, 2013; Doursat & Sanchez, 2014; Kamm & Bashir, 2014; Ebrahimkhani & Levin, 2021). These novel life forms result from the recombination of existing evolved components at multiple scales (DNA, cells, tissues and organs) (Nanos & Levin, 2022) and the incorporation of designed components, such as nanomaterials, electronic/chemical/optical interfaces and software algorithms; replacements can be made at every level of organization, with parts that occupy some position with respect to functional sophistication and origin (Fig. 3). Table 1 is an overview of some key examples (although sharp boundaries between these categories cannot be drawn), and we describe only a few in detail (Fig. 4).

Bioengineering and evolution work in the same living medium (Wagner & Rosen, 2014; Ollé-Vila *et al.*, 2016); thus, we first consider an example of an entirely natural evolved functional chimaerism, where two kingdoms of life come together to form a new hybrid system (Fig. 4A–D). *Ophiocordyceps unilateralis* s.l. is a fungal parasite that creates ‘zombie ants’ of *Camponotus castaneus*, a carpenter ant (Andersen *et al.*, 2009). This fungus infects an ant, freely flowing through the circulatory system of the host. After it expands throughout the organism, takes over the body of the host ant. Under control of the fungus, the host ant navigates to a plant located near the semi-permanent food trails of the colony, climbs up to an optimal growth zone and bites onto the plant, allowing the fungal spores to disperse onto uninfected ants wandering the nearby trails. Most interestingly, the brain of the host ant is left entirely untouched (Fredericksen *et al.*, 2017). This poses the question of how a ‘simple’ fungus can manipulate the behaviour of the host ant in such a reproducible way. To achieve its goal of reproduction, the fungus must adapt to sensory signals from the environment; this involves processing the incoming signals to determine when it has come in contact with a suitable host and can thus begin targeted growth by navigating inside the host body.

Importantly, this process needs to be precise enough to take control of the host ant without altering the behaviour of the host too strongly, because ant colonies will reject infected members of the colony. However, as the fungus infects the host ant further, what incoming signals does the fungus receive and how does it process these signals now that it is in a body not its own? Is it cut off from the external world and does it ‘see’ only the inside of the ant, or does the fungus hijack the sensory system of the host, thus acquiring new ways to sense and act in the world? Although these are unanswered questions, the study by Fredericksen *et al.* (2017) demonstrates that large, complex fungal networks invade the muscle fibres in the host, potentially allowing for precise body-wide control without need for the brain-to-central nervous system axis. However, agent-based modelling shows that the fungus might hijack and repurpose the ‘food searching’ behavioural regimen of the ant into an algorithm to find sites for fungal dispersion (Imirzian & Hughes, 2021). This would imply that *O. unilateralis* s.l. has developed a way evolutionarily to exhibit control of a dynamic system (the nervous system of the host ant) without needing to understand how the nervous system of its host functions. It is clear that there is much to be understood in chimaeric ‘life as it is’ studies, because researchers can study existing evolutionary accidents to reveal common relationships between brain, body and behaviour across species and systems.

The field of artificial chimaeras has been realized most notably in brain–computer interfaces (Bonifazi *et al.*, 2013; Buccelli *et al.*, 2019; Degenhart *et al.*, 2020). Willett *et al.* (2021) carried out a remarkable study that merges existing biological systems, here the motor cortex in a human subject, with technology to provide a way for a patient to communicate with the outside world even years after the onset of paralysis (Fig. 4E–G). They instructed a patient to ‘attempt’ to write as if his hand were not paralyzed, while imagining that he was holding a pen on a piece of ruled paper, while recording neural activity from the precentral gyrus. Using a variety of methods, neural activity was decoded and associated with each letter, allowing a computer program to produce written sentences for the patient in real time at a speed much higher than other approaches (Willett *et al.*, 2021). In many ways, this artificial chimaera works in the same way as the parasitic fungus; experimenters do not need to know how certain neural dynamics arise owing to imaginary handwriting, merely that these signals can be used to drive goal-directed behaviour. In addition, this particular patient was not paralysed at birth; writing had been learned before the paralysis, and the hypothesis is that this aided in the stability of the decoded neural dynamics. This is similar to the case of the zombie ants; the fungi were not necessarily

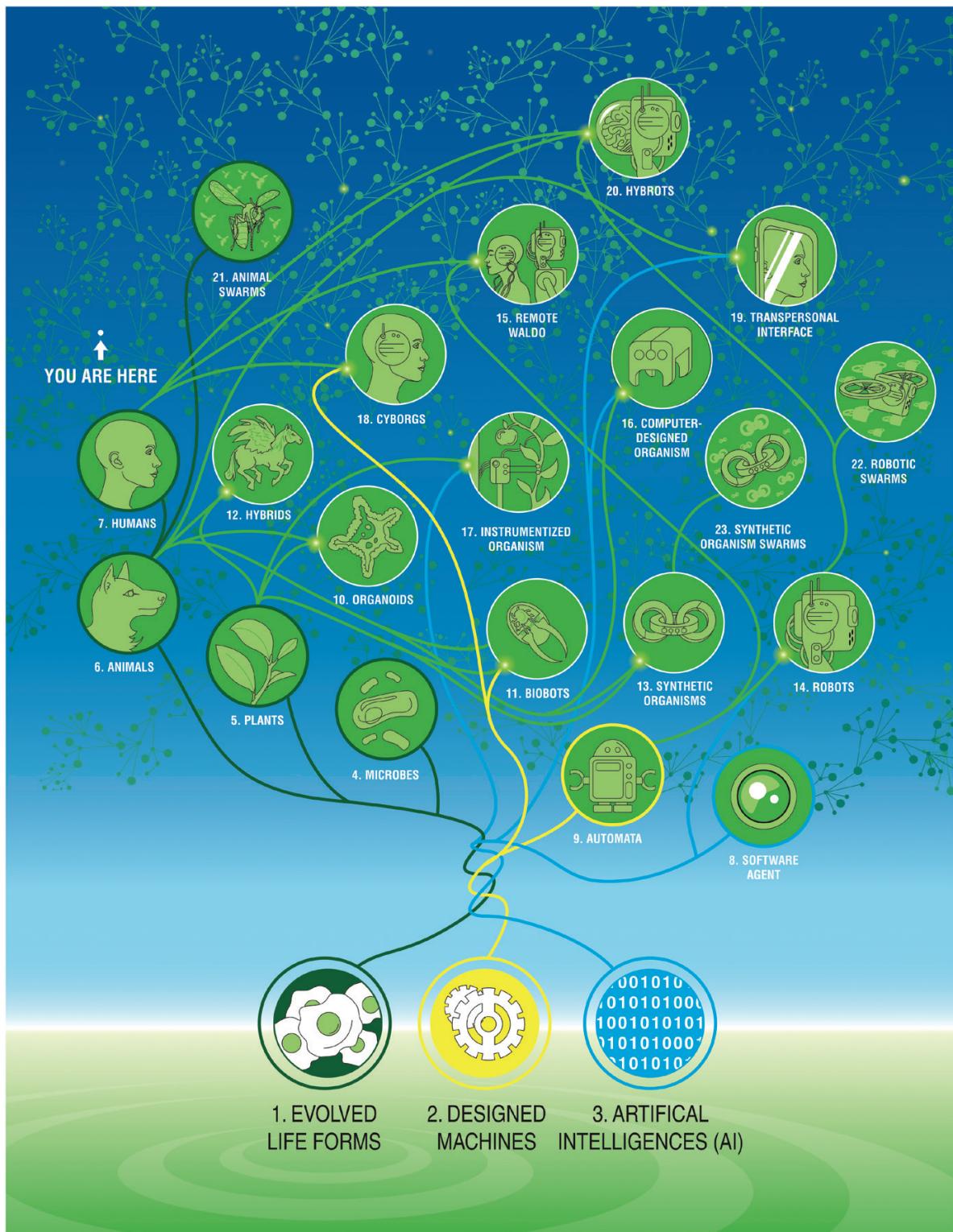


Figure 2. The option space of unconventional novel agents. The interoperability of the multi-scale competency architecture of life enables novel agents to be formed in any combination of evolved material, designed (engineered) material and software. This forms an immense option space of hybrots, chimaeras, cyborgs and many other kinds of novel creatures never before seen on Earth and having no clear relationship to the existing phylogenetic lineage. Image courtesy of Jeremy Guay of Peregrine Creative.

Tiers of Organization

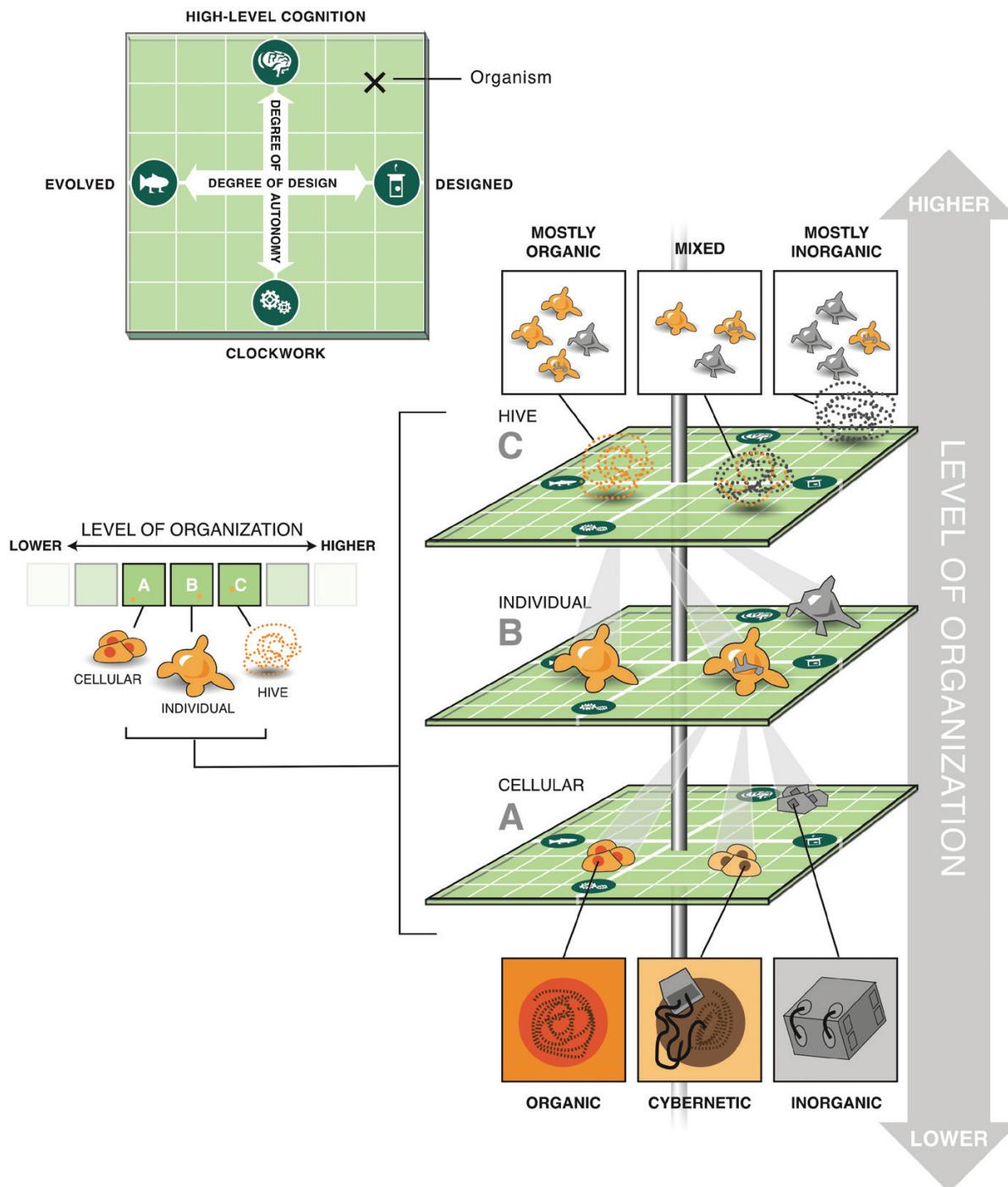


Figure 3. Multi-scale chimaerism. Bioengineering now allows every layer of a tiered living system to be replaced with components from some position in a plane of orthogonal metrics of how much cognition it has and how much design/evolution resulted in its creation. Evolutionary techniques in machine design and tools for synthetic morphology are erasing the artificial lines that used to exist between evolved, living forms and engineered machines with teleonomic capacity. Image courtesy of Jeremy Guay of Peregrine Creative, taken with permission from Bongard & Levin (2021).

Table 1. Examples of novel life configurations

Type of life form	Properties	References
Embryoids, organoids and assembloids	<i>Ex vivo</i> cultured cells and tissues with emergent morphogenesis	Simunovic & Brivanlou (2017); Vogt (2021)
Cyborgs	Tissues of animals and plants tightly integrated with engineered inorganic interfaces, often with closed-loop controls enabling the cells to control and be controlled by machines and their microenvironment	Cohen-Karni <i>et al.</i> (2012); Giselbrecht <i>et al.</i> (2013); Warwick (2014); Gershkak <i>et al.</i> (2017); Aaser <i>et al.</i> (2017); Ricotti <i>et al.</i> (2017); Ding <i>et al.</i> (2018); Mehrali <i>et al.</i> (2018); Anderson <i>et al.</i> (2020); Merritt <i>et al.</i> (2020); Orive <i>et al.</i> (2020); Li <i>et al.</i> (2021); Pio-Lopez (2021)
Biorobotics	Computer-controlled animals	Ando & Kanzaki (2020); Saha <i>et al.</i> (2020); Dong <i>et al.</i> (2021)
Biobots	Synthetic living machines with predictable behaviour	Park <i>et al.</i> (2016); Aydin <i>et al.</i> (2019); Pagan-Diaz <i>et al.</i> (2019); Kriegman <i>et al.</i> (2020, 2021); Blackiston <i>et al.</i> (2021)
Biocomponents	Repurposed biological structures as components of machines	Whiting <i>et al.</i> (2016); Adamatzky (2018)
Neuroprosthetics and sensory augmentation	Interfaces enabling patients to control novel effectors or use novel sensors	Rothschild (2010); Lebedev & Nicolelis (2011); van den Brand <i>et al.</i> (2015); Adewole <i>et al.</i> (2016); Turner (2016); Wright <i>et al.</i> (2016)
Hybots	Living brain tissue instrumentized to control artificial new bodies, such as vehicles	Warwick (1998); DeMarse <i>et al.</i> (2001); Potter <i>et al.</i> (2003); Madhavan <i>et al.</i> (2006); Bakkum <i>et al.</i> (2007a, b); Tsuda <i>et al.</i> (2009); Ando & Kanzaki (2020)

creating a new behaviour in their hosts but were instead exploiting existing behaviours towards a goal. In the case of Willett *et al.* (2021), the chimaerism arises artificially; the computer software is built to sense the ‘environment’ of motor cortex neural dynamics to produce action in a virtual world, action that previously was not possible. It is important to note that the neural signals were recorded from a cortical region of the brain associated with motor movement. Indeed, it is assumed that specific cortices evolved to control specific behaviour, and although neural representations of movement can change owing to prosthetics (Kieliba *et al.*, 2021), the question is raised: can neurons from other modalities, such as vision, be trained in external motor control? How ‘frozen’ is the behaviour of cortical regions?

Hybots and animats are systems composed of neural cultures, coupled via closed loop techniques to physical robots (in the former) and virtual animals (in the latter), and are ideal platforms for tackling such questions (Fig. 4H, I). Early examples were developed in 2001, when DeMarse and co-workers dissociated cortical tissue from rats and cultured it as a two-dimensional plane of neural tissue on a microelectrode array; this array was capable of recording the electrical activity of the tissue while delivering stimuli via electrical pulses (DeMarse *et al.*, 2001). The spiking activity of the neurons drove a virtual animal, the animat, in a virtual

maze by associating unique spatiotemporal spiking patterns with directional movement. Feedback based on that directional movement and on the distance to obstacles in the maze was then returned to the culture. This was designed to mimic how neural systems have evolved to take input and interact meaningfully with the world, with the goal of allowing the culture to learn relationships between its own activity and incoming ‘sensory stimuli’.

This paradigm was later used to build MEART (multi-electrode array art), a hybot that was built to create art through neural control of robotic arms attached to drawing utensils (Bakkum *et al.*, 2007b). This study focused on examining the stimulus (patterned training stimulus) that was applied to the neural culture, based on the present drawing and the desired ‘goal drawing’, a black square in the middle of the canvas. Here, they reported that although there were shifts in synaptic plasticity in the network, if the patterned training stimulus was not updated at regular intervals, the overall behaviour did not reflect any signs of learning. This closed-loop chimaeric approach allows for investigation of the plasticity with which evolved biological components learn to function with novel bodies and environments. It is not known how neural systems adapt their dynamics as new behaviours, whether goal directed or not, are learned, with hypotheses typically revolving around

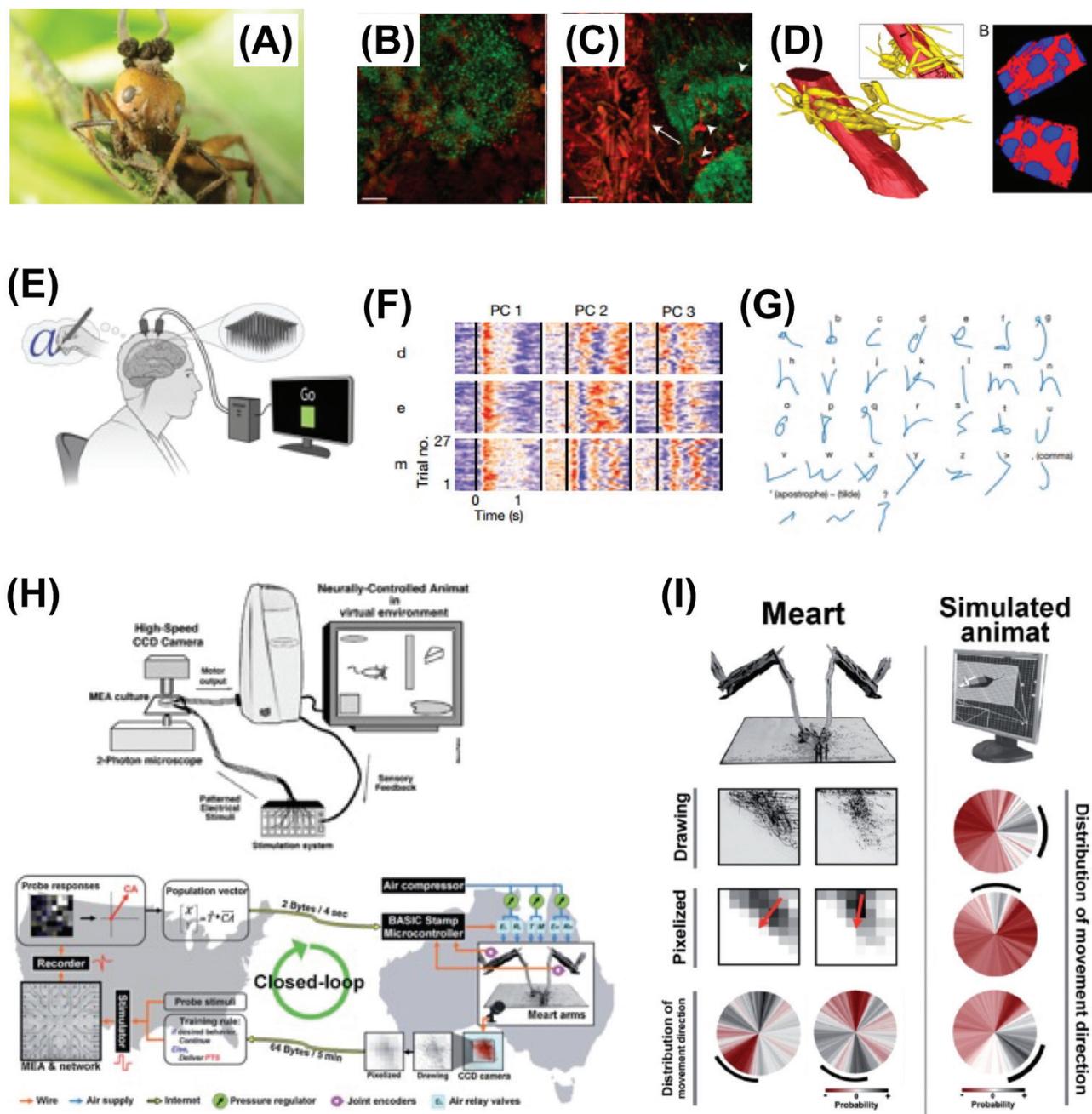


Figure 4. Three examples of novel organisms. A, a photograph of a host *Camponotus atriceps* ant in the death-bite position induced by infection from *Ophiocordyceps unilateralis* s.l. B, C, immunofluorescence images of neural synapses (green) in an uninfected ant (B) with no host tracheae (red) alongside an image taken from infected ant (C); note how there are no hyphal bodies (red) inside the brain (green). D, however, through three-dimensional reconstruction techniques, Fredericksen *et al.* (2017) found hyphal bodies (yellow) around adductor muscles (red) in the ant, a part of the complex fungal network throughout the host body. A, used with permission from Hughes & Libersat (2019). B-D used with permission from Fredericksen *et al.* (2017). E, in the experimental set-up from the study by Willett *et al.* (2021), the patient imagines writing a given letter using his hand and a pen when he sees a 'GO' signal, while an implanted microelectrode array (MEA) records electrical activity of a region of the motor cortex. F, principal components analysis reveals neural behaviour that explains most variance in the neural dynamics for the letters 'd', 'e' and 'm' over 27 repetitions. G, these data are used to calculate computer reconstructions of the written letters, which are then processed further to type words and sentences on a computer screen. E-G, used with permission from Willett *et al.* (2021). H, the experimental designs for both the animat and MEART. The animat is controlled

changes in synaptic weight. However, there are many ways in which underlying neuronal circuitry might change. Hybrids are poised to serve as a general-purpose platform for understanding the basic rules of engagement for neural systems, because they lack the evolutionary complexity of complete nervous systems that might confound interpretation, yet they still possess goal-directed capabilities.

The many diverse viable combinations of evolved and engineered components reveal a rich medium in which to understand truly general principles of self-organization of structure and function in unexpected circumstances. The ability to make novel living beings (Nanos & Levin, 2022) is significant in several ways. It frees us from the contingencies and frozen accidents of the trajectory of evolution on Earth and shows us life as it can be, enabling us to expand our thinking and generalize to learn lessons of biology in its general form. It allows us to probe the intelligence of life at all levels by exploring the degree of goal-directed behaviour, competency and failure modes of living modules in highly diverse environments. However, novelty is not only about new external circumstances. Some of the most informative aspects of perturbation are changes of inner composition; changes to the parts of the living system itself that are enabled by chimaerism and bioengineering. The introduction of synthetic DNA constructs, nanomaterials and other components into living systems reveals how multicellular collectives handle rapid changes in the properties of their parts. Response to a wide variety of new challenges is the cornerstone of the study of the intelligence of any system, including that of evolution (generalizing adaptive behaviour beyond previously encountered challenges).

A hallmark of chimaeric and bioengineered organisms is that they are functional; they operate in physiological and behavioural spaces and often exhibit the same robustness as evolved beings with respect to being able to reach specific states or behaviours despite perturbations. Figure 5 shows an example in which the traditional brain–body–environment schema is maintained while setting all of its individual components to be as unusual as possible. The study of this class of systems provides ways to uncover novel goal-directed activities that are masked by default developmental constraints and standard ecological scenarios. But most of all, the diversity of composition

and provenance in this rich space of possible life forms requires us to look for a deep invariant: a parameter that can help us to recognize, compare and relate to intelligences in novel embodiments, when the familiar phylogenetic tree offers no convenient classification.

BASAL COGNITION AND DIVERSE INTELLIGENCES: TELEONOMY AS A COMMON THREAD

Intelligence is the ability to reach the same goal through different means.

William James

One important promise of synthetic life forms concerns what they can tell us about the relationship of mind and body (i.e. cognition in novel media). Importantly, the ability to solve problems in various spaces, with diverse degrees of competency, is known to extend well beyond brains. The emerging field of basal cognition seeks to understand the roots of intelligence in ancient, pre-neural forms and unfamiliar guises (Jennings, 1906; Lyon, 2006; Balazsi *et al.*, 2011; Keijzer *et al.*, 2013; Lyon, 2015; Baluška & Levin, 2016; Baluška *et al.*, 2021). Recently, it has been argued that the origins of problem-solving in novel circumstances (behavioural intelligence) lie in ancient capacities that long predate central nervous system development (Fields *et al.*, 2020). The implications of this view include the idea that the tools of neuroscience can be applied far beyond neurons, to understand how all types of cells join into collectives that work to achieve large-scale objectives (Levin, 2019, 2022). Importantly however, we must look beyond behaviour in three-dimensional space (movement) as the arena in which intelligence can be observed. Life solves problems in many different spaces, and chimaeric organisms help us to widen our criteria and begin to recognize intelligence in unexpected guises. The ability to rearrange neural structures in novel configurations also reminds us that as collections of neurons, beings with brains are, in an important sense, also collective intelligences.

Morphogenesis by cell groups is a natural example that is only now beginning to be understood as a collective intelligence problem and to be investigated using the same tools and conceptual paradigms as those used in neuroscience (Fig. 6). For example,

by a two-dimensional neural culture in an MEA, and behaviour exists solely in a virtual world. For MEART, a two-dimensional culture controls the arms of MEART by controlling air compressors for hydraulic motion. Adapted from DeMarse *et al.* (2001) and Bakkum *et al.* (2007b). I, data showing that learning occurs in both systems but is stronger in the animat with adaptive training. Circles show degrees of movement, with colours indicating probability of a given direction of movement after training. Black arcs indicate the trained direction. Used with permission from Bakkum *et al.* (2007b).

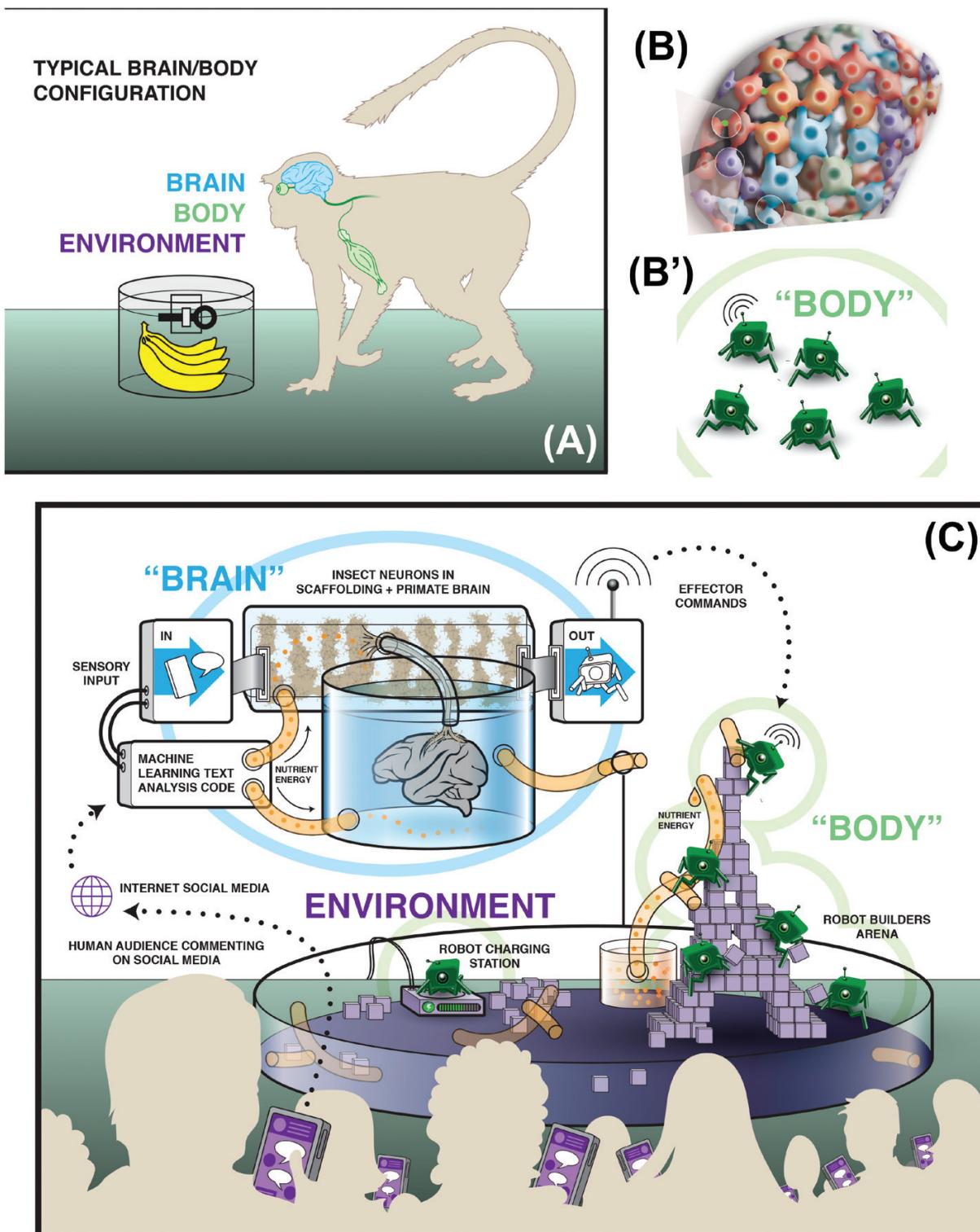


Figure 5. An extreme example of an unconventional agent. To get a real feel for the novel kinds of agents that are possible, imagine taking the traditional brain–body–environment schema (A) and making its modular components truly diverse. B, the brain of this new agent is a cultured mammalian brain chimaerized with insect neurons. It acts in the real world because its output neuronal activity is detected by electronic interfaces and used to control a body. B’, the body consists of a robotic swarm acting in an arena, in which they can pick up glucose and other fuels and deliver those to the bioreactor

tadpoles with craniofacial organs placed in abnormal positions can become frogs with normal faces, because the components of the head will move around as needed to produce a correct face (Vandenberg *et al.*, 2012; Pinet *et al.*, 2019). This ability to find the right region of morphospace corresponding to a normal frog anatomy, despite components of that anatomy starting off in the wrong position, reveals an important fact visible in many examples of regulative development, regeneration and remodelling (such as those described in the Introduction). Evolution does not simply make hardwired machines that execute a predetermined set of steps (such as the default movements of tadpole eyes and jaws during metamorphosis). Instead, it produces hardware that can execute error minimization, traversing novel paths in morphological and transcriptional spaces (Elgart *et al.*, 2015; Schreier *et al.*, 2017; Emmons-Bell *et al.*, 2019) to achieve their target morphologies. Models of morphogenesis as collective intelligence are driving empirical work to understand what such systems measure, how they store set points for their homeostatic activity, how these set points arise and how they can be edited by biomedical approaches (Mathews & Levin, 2018). They also suggest a research programme to understand how homeostatic loops scale and pivot across problem spaces during evolution (Levin, 2019, 2022).

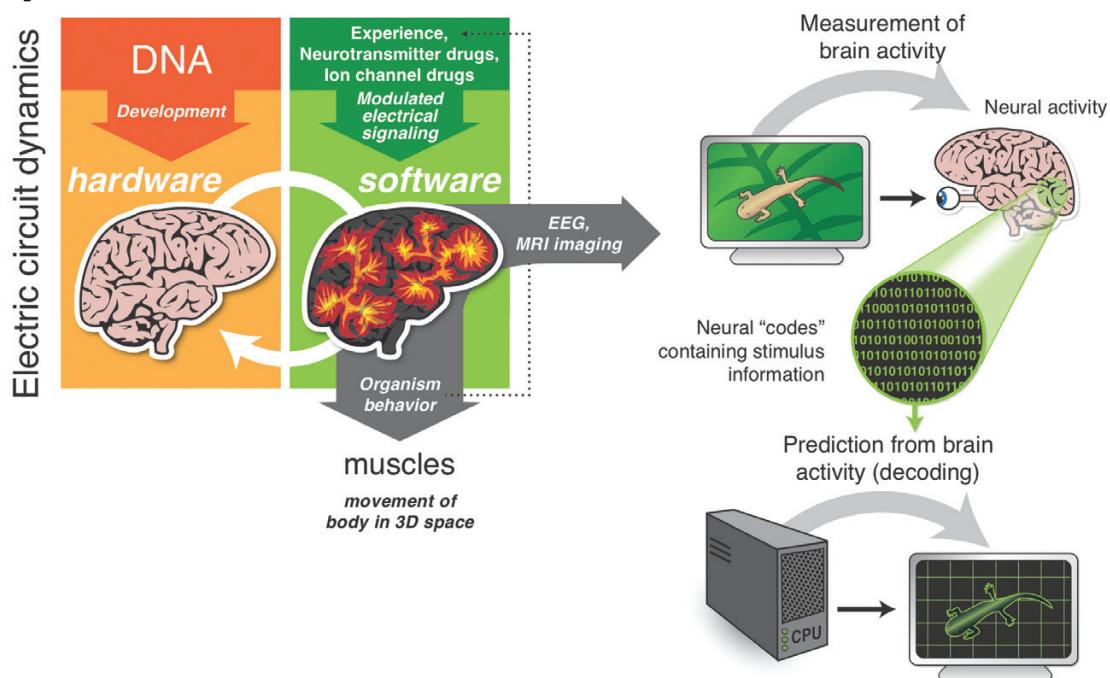
A focus on the actions of systems in arbitrary spaces, rather than on their anatomical or molecular–genetic composition, requires us to identify invariants that can serve as a parameter by which to organize and compare highly diverse types of agents in unfamiliar embodiments. We suggest that one important and interesting thing that all agents, no matter their composition or origin, have in common is goal-directed behaviour (at some level of competency) (Rosenblueth *et al.*, 1948).

Goal-directed behaviour is, at the very least, uncontroversial in human animals. It is thought that this capacity is enabled by collectives of neurons (brains) exhibiting memory, error minimization capacity and second-order metacognition that enables us to think about those goals (and perhaps re-set them) in addition to executing them. However, brains evolved from much more ancient bioelectric networks that are formed by all cells in the body and are as old as bacterial biofilms (Prindle *et al.*, 2015; Fields *et al.*, 2020; Yang *et al.*, 2020). These networks readily form circuits with memory that enables basal homeostatic function (Pietak & Levin, 2017; Cervera *et al.*, 2018, 2019, 2020). The remarkable capacity to exhibit both robustness and novelty in morphogenesis reveals the central role of the scaling of goals as an explanatory, facilitating concept for new basic research and biomedical applications (Levin, 2019). What is essential is to understand and tame the gradual changes in information processing that occur in the slow transition from egg cell to complex goal-driven cognitive agent with intrinsic purposiveness.

Cybernetic approaches are substrate independent and remind us that no specific materials (cytoplasm, neurons, etc.) are required for the key capacity of proto-cognitive systems (and perhaps all life): homeostatic and allostatic loops that expend energy to attain specific preferred states with respect to information, prediction error, metabolic conditions and anatomical configurations (Allen & Friston, 2018; Constant *et al.*, 2018; Badcock *et al.*, 2019; Ramstead *et al.*, 2019). This view emphasizes a central invariant that unifies all attempts to predict, control, recognize, create and relate to such systems: teleonomy (i.e. goal-directed behaviour that achieves specific observable states, by different means and with varying degrees of reliability and competency; Rosenblueth *et al.*, 1943; Bertalanffy, 1951; Varela & Maturana, 1972; Varela *et al.*, 1974,

to feed the brain. The collective needs to work together to power themselves and the central controller. C, importantly, the environment is not only the arena, but also includes other sentient agents. The arena is watched over by an audience of human observers, who express their degree of approval of the antics of the robots (or explicitly pay for additional glucose) via real-time social media posts on their networked hand-held devices. An artificial intelligence (AI) language processor scrapes the social media posts, converts the text into specific tokens and feeds it to the brain as input to its sensory neurons. Much like our cells, the robots also have a degree of their own on-board AI, and the behaviour of the whole system is a very complex interplay of input, learning, noise, unreliability of components (including those of the observers), etc. This thought experiment is designed to shock us out of our typical assumptions about what a functional brain, body and environment must look like, in order to illustrate the immense variety of different implementations of the central components of an environmentally embedded cognitive agent. All the individual pieces of this construct are possible with current science (Ebrahimkhani & Levin, 2021; Nanos & Levin, 2022; Pio-Lopez, 2021). How can we understand, predict, communicate with and relate to such alien creatures? New bioengineering technologies are leading to an inevitable one-way journey out of a biology limited to a discrete set of forms that happened to have evolved on one planet. When origin story and composition cease to be good guides to how one should relate to a system, teleonomic capacity is one central concept that will survive the coming decades and drive advances in next-generation research and ethics. B taken with permission from Ebrahimkhani & Levin (2021). A, B', C images courtesy of Jeremy Guay of Peregrine Creative.

(A)



(B)

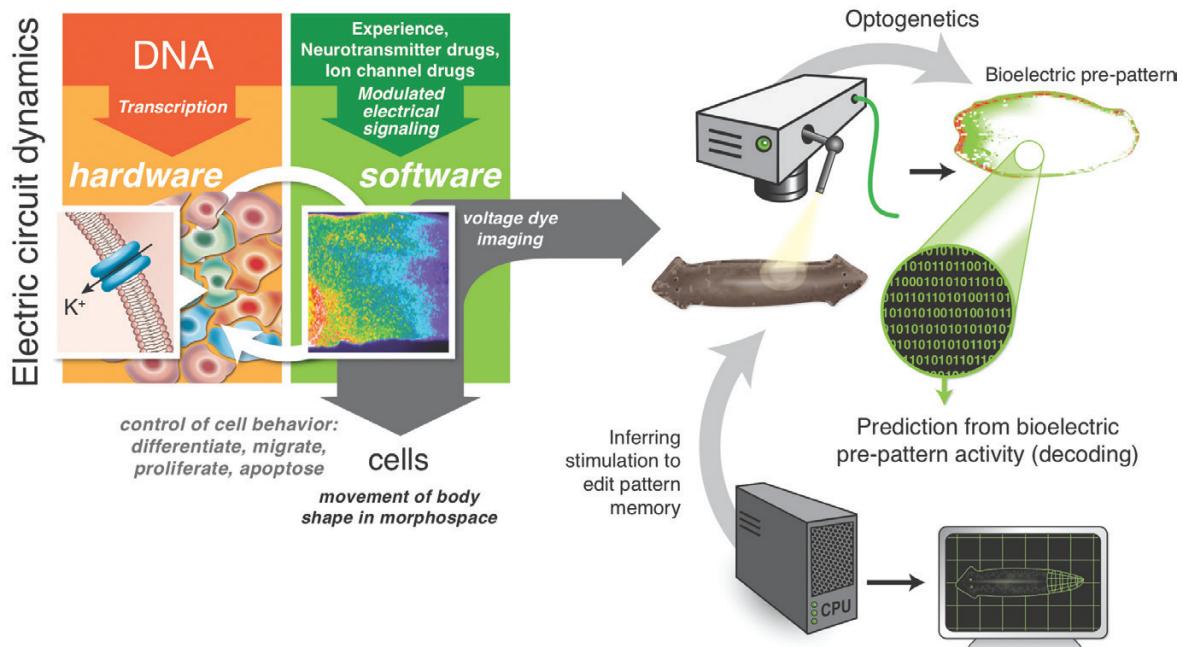


Figure 6. Mechanisms of cognition outside the brain. A, the schematic diagram of conventional cognition can be represented by a software–hardware duality. A network of neurons (the hardware) enables real-time dynamics of computation via a set of electrical processes (the software). The result of these dynamics is a set of instructions to muscles, in order to move the creature through three-dimensional space; what we recognize as ‘behaviour’, often with some degree of problem-solving ability. The commitment of neuroscience is that the information content of the collective intelligence of neurons can be read

1991; Maturana & Varela, 1980; Lander, 2004; McShea, 2016; Turner, 2017). This independence from implementation details, and a willingness to recognize navigation towards preferred states in any problem space, removes traditional but limiting opacities from the lens through which we view ‘agents’ that exhibit teleonomic behaviour; such self-imposed filters, like a type of mind-blindness, have restricted research, because our perceptual systems are tuned to recognize only familiar types of agency (i.e. that of medium-sized beings navigating three-dimensional space).

Teleonomy here is proposed as a conceptual tool to drive the creation and analysis of novel synthetic beings. Rather than (as is sometimes claimed) being a tool to distinguish living beings from ‘mere machines’, it provides a unifying framework to understand the whole multidimensional spectrum of possible agents. Cybernetics (Rosenblueth *et al.*, 1943) is an ideal framework for life as it can be. The dissolution of shallow, contingent boundaries between evolved and engineered systems was foreseen long ago in the title of Wiener’s foundational work, ‘Cybernetics, or control and communication in the animal and the machine’ (Wiener, 1961). It gives us a mature framework for understanding goal-directed behaviour without resort to mysterianism; dynamical systems and control theories offer rigorous formalisms for understanding causes of long-term behaviour as types of navigation policies in problem space (Pfeifer *et al.*, 2007). Attractors (regions of the state space not occupied by the system at a given moment) serve as empirically useful views of causes of system-level behaviour as it navigates the space, guided by its non-local topology (Manicka & Levin, 2019). In keeping with the practical engineering focus of our approach, we eschew questions of teleology (philosophical wrangling over real, objective purpose or agency) and focus on goal-seeking and problem-solving behaviour that is apparent, or relative, to an observer (usually, scientists, but also to the system itself, in the case of sufficiently sophisticated agents). This approach has already been emphasized by key early figures in cybernetics: ‘organization is partly in

the eye of the beholder’ (Ashby, 1952). Thus, our ability to detect, understand and manage teleonomy says as much about our own intelligence as it does about the system being studied (Sims & Pezzulo, 2021).

We propose a specific hypothesis about the fundamental origin of the plasticity, robustness and intelligence in diverse embodiments: that life exploits a multi-scale competency architecture that allows the products of evolution to thrive in the face of novelty. It is obvious that biological systems are hierarchical in terms of structure. More recently, studies of molecular genetics and developmental biology have revealed the modular nature of functions in the body. What is only now beginning to be appreciated is that the subsystems making up living bodies exhibit multi-scale goal directedness: each subunit has an agenda (a goal of some scale) in its various spaces. Classical workers in developmental biology recognized this ‘struggle of the parts’ (Heams, 2012) and their ability to reach goals (coarse-graining of molecular microstates into meaningful anatomical set points) by different means. The ability of parts to cooperate and compete (Gawne *et al.*, 2020) within and across levels of scale and organization has fascinating implications. We next consider the implications of multi-scale competency for natural evolution and for synthetic bioengineering and robotics.

MULTI-SCALE COMPETENCY POTENTIATES EVOLUTION

Expanding our capacity for bioengineering novel life forms towards complex outcomes requires learning to work with agential materials; that is, not micromanaging outcomes at every level, but guiding self-assembly by inducing components with agendas and competencies to change their default behaviours (guided self-assembly). Evolution learned to work in this medium first (Vane-Wright, 2014; Watson & Szathmary, 2016), and we can benefit greatly from understanding how it manages (and benefits

out by a process of neural decoding. B, evolution discovered the importance of electrical networks for information processing and binding into collective selves long before brains appeared. An ancient function for bioelectric networks existed in all somatic cells, which work in a manner isomorphic to that of familiar neuroscience content. All cells have ion channels and gap junctions, resulting in bioelectric dynamics that also solve problems; they control cell behaviours (such as differentiation and migration) in anatomical morphospace. Like the brain, they are subject to reprogramming by stimuli or experiences and they carry out numerous goal-directed activities that serve the collective. Current research has ported many of the same tools as those used for neural decoding to understand the morphogenetic code implemented in the somatic bioelectric medium. Functional tools cannot tell the difference between neurons and non-neuronal cells, because they are fundamentally similar in their ability to execute homeostatic loops and scale up to larger agents via bioelectrical coupling. Images in panels A,B courtesy of Jeremy Guay of Peregrine Creative, used with permission from Levin, M. Life, death and self: Fundamental questions of primitive cognition viewed through the lens of body plasticity and synthetic organisms. *Biochem Biophys Res Commun* 2021, 564, 114–133.

from) a multi-scale architecture. All the engineering accomplishments listed in **Table 1** benefitted from the fact that scientists did not have to micromanage (create from scratch) every part and its activity; instead, they recombined biological systems at chosen levels and depended on reliable components to exert their competencies in new circumstances.

The standard picture of evolution is that of an undirected search of morphospace. The problem with the much more efficient ‘Lamarckian’ algorithm is not the contingent and porous Weismann barrier between germline and soma ([Jablonka et al., 1998](#); [Anava et al., 2014](#)); instead, it is the much deeper issue of the inverse problem ([Lobo et al., 2014](#)): because the relationship between genome and anatomy is highly indirect, it is, in general, very hard to compute which changes in DNA should be made to canalize any desired bodily change (such as a neck stretching after taller branches). The same credit assignment problem is at the heart of efforts in machine learning: how to modify the subunits (and which ones) to reduce error, given feedback from the environment? Both these issues are strongly impacted by a multi-scale competency architecture. One instructive example is the fact that when eye primordia are grafted onto tadpole tails and the primary eyes are removed, the resulting animals can still see (perform visual learning tasks and behaviours). The primordial cells still make a proper eye even in a novel environment (in the midst of muscle tissue); the eyes put out an optic nerve that connects to the spinal cord (a novel target instead of the brain), and the brain properly interprets data arriving by this novel route and folds it into the behavioural repertoire of the animals ([Blackiston & Levin, 2013](#)). Likewise, experimental introduction of additional bones in vertebrate limbs results in adjustments of ligaments, muscles, motor neurons, etc. to enable a functional limb that balances mechanical load correctly ([Hallgrímsson & Hall, 2011](#); [Sultan et al., 2022](#)).

These examples readily illustrate the implications for evolution, because macro-scale changes are readily accommodated: it is much easier to explore a fitness landscape when the goal-directed competency of the parts can be relied upon not to wreck the adaptive character of the body when things change. When the parts themselves are goal-directed agents, evolution is greatly accelerated. Indeed, teleonomy is at the core of reliability (which enables a searchable, continuous fitness space). Complex systems can persist and be improved and built upon continuously because the goal directedness of their parts enables other parts (and the collective) to trust that they will accomplish their task (making it practical to invest energy in activity and architectures that rely upon them working properly). This begins to blur distinctions, and emphasizes

commonalities, between the processes implemented by evolution and rational engineers ([Kauffman, 1971](#)).

Owing to these dynamics, multi-scale competency increases the apparent intelligence quotient (IQ) of the evolutionary process ([Watson et al., 2014, 2016](#); [Watson & Szathmary, 2016](#); [Szilagyi et al., 2020](#); [Czégel et al., 2022](#)). It is no longer as short-sighted in fitness space (although it is undirected in genotype space), because the competency of the parts enables the specific moves it makes to be much better than they otherwise would be. Teleonomic robustness in various spaces enables competency in fitness space without directed mutation (which the inverse problem makes extremely difficult, in any case). This not only accelerates the search, but also changes the very nature of what is evolved. Evolution does not produce specific solutions to specific environmental problems; instead, it produces problem-solving machines that can handle novelty. The nature of evolution as a learning process ([Watson et al., 2014, 2016](#); [Power et al., 2015](#); [Watson & Szathmary, 2016](#); [Czégel et al., 2019](#); [Szilagyi et al., 2020](#)) is transformed by the teleonomy. The competency of the parts enables better generalization during evolutionary-scale learning; it does not only learn one way of being a successful organism, it effectively learns a class of feasible organisms, because the competition and cooperation of goal-directed components ([Gawne et al., 2020](#)) map many different starting points to a functional anatomy.

Over time, a lineage learns not only how to exploit a specific niche successfully, but also how to manage successfully in novel circumstances (changes of the environment and of its own parts, including mutations and other perturbations, as in the many examples above). Moreover, by working through an indirect, complex intermediate layer (development and physiology), evolution is forced to generalize (which would not happen with direct encodings). This enables evolution to give rise to problem-solving machines with generalization to novel circumstances. This is becoming strikingly apparent in the advent of biorobotics with emergent properties.

EVOLUTION HAS ALREADY LEARNED TO GENERALIZE BEYOND DEFAULT MORPHOLOGIES

The robustness of life under perturbation of the external environment and of internal components reveals the essence of teleonomic systems: competency in pursuing goals. Where do the specific goal states come from? What determines the set points towards which a given system will expend energy and effort? When we observe that cells of a given species work to

implement a specific structural and functional outcome reliably, we generally say that these are explained by evolution. The goals towards which cellular collectives navigate competently in various spaces traditionally have had two explanations: direct selection ‘forces’ and side-effects (spandrels) of other features that have been selected (Gould & Lewontin, 1979; Kull, 2014). This might, perhaps, be reasonable for the standard class of biological systems evolved in the phylogenetic tree on Earth. However, the limits of this paradigm are revealed when we expand traditional epigenetics to include genuinely novel configurations that have never existed before on Earth.

Questions about selves, autonomy, plasticity and the origin of biological novelty led us to ask what would happen if skin cells were removed from a frog embryo, dissociated and given a chance to reboot their multicellularity *in vitro* (Blackiston *et al.*, 2021). Many outcomes are possible a priori: they could have spread out or died or formed a monolayer, etc. Instead (Fig. 7), what they did was to reassemble and form a novel proto-organism known as a Xenobot (Kriegman *et al.*, 2020). These spherical constructs move through water by the coherent action of cilia, exhibiting a variety of self-actuated types of motility. They have a developmental sequence of novel forms that are unlike the typical *Xenopus* stages; they repair after damage, interact with their environment and show spontaneous changes in behaviour. These novel morphologies and behaviours do not require transgenes or genomic editing; Xenobots repurpose their native hardware (e.g. cilia, which are normally used to redistribute mucus) to new functionality. Amazingly, deprived of their normal way of reproducing, the emergent processes of Xenobots discover kinematic self-replication (a novel mode of reproduction not used by any other organism on Earth, to our knowledge), which they implement by herding loose collections of cells in their environment together to form the next generation of Xenobots (Kriegman *et al.*, 2021). Nothing has been added to their completely wild-type frog genome; instead, developmental constraints have been removed. Without the normal instructions from the rest of the body telling these skin cells to form a passive, two-dimensional boundary layer to keep out the bacteria (a system of low agency), the true capacities of this cellular collective are revealed; it forms a three-dimensional individual with a more exciting life of self-initiated motile behaviour. The collective intelligence of these cells is revealed as, despite a novel environment and novel internal configuration that never existed in the frog evolutionary lineage, they discover novel ways to be a coherent organism. Their option space is normally distorted by the larger collective, but their default geodesic through option space (and their baseline

preferences in morphospace) are revealed when these influences are removed. All this self-assembly and emergent organization takes place in 48 h and does not require aeons of evolutionary forces to become a good Xenobot.

If the answer to ‘Where do a frog’s shape and behaviour come from?’ is ‘Long periods of selection and interaction with the environment that sculpt the genome to be a great frog’, then where do the anatomical and behavioural goals of Xenobots originate? Their anatomical and behavioural goals are emergent (Veloz, 2021), rather than directly selected for over aeons of sculpting by selection. A number of researchers have emphasized information arising from generic laws of form (Belousov & Grabovsky, 2007; Belousov, 2008; Newman, 2014, 2019; Zhang *et al.*, 2021), from mathematics (Brigandt, 2013; Lange, 2013; Green & Batterman, 2017; Reutlinger, 2017) and from environmentally initiated novelties (West-Eberhard, 1998, 2005a, b; Shapiro, 2022). These Xenobots are only the beginning of a large class of beings that challenge us to develop a better understanding of how goal states arise in novel contexts and how evolution exploits the laws of physics and computation in the context of teleonomic processes.

A key area of research concerns how goal directedness is scaled during evolution, enabling beings with increasingly large cognitive horizons with respect to the goals they can pursue (Levin, 2019). Bioengineering is a powerful means of studying this aspect of collective intelligence, because it allows us to manipulate which components (with what goals) are connected together and precisely how their different modules can interact in the swarm. One set of models concerns the coupling of subunits with respect to the three components of a homeostatic loop: sensing state, storing a memory of the set point, and taking actions to reduce error. This is beginning to be explored in robotics and machine learning; in one example, robots can adapt to new situations because their components are behaving homeostatically (Di Paolo, 2000). A multi-scale competency architecture, as exploited by chimaeric techniques, is not only an interesting path forward (biological inspiration) for artificial intelligence, but is also helping to dissolve artificial barriers across fields.

CHIMAERISM HELPS TO DISSOLVE OUTDATED CONCEPTS

Chimaerism is a type of conceptual universal acid, dissolving existing terminology that is not based on deep concepts but is instead a relic of parochial contingencies of our familiar forms (Bongard & Levin, 2021).

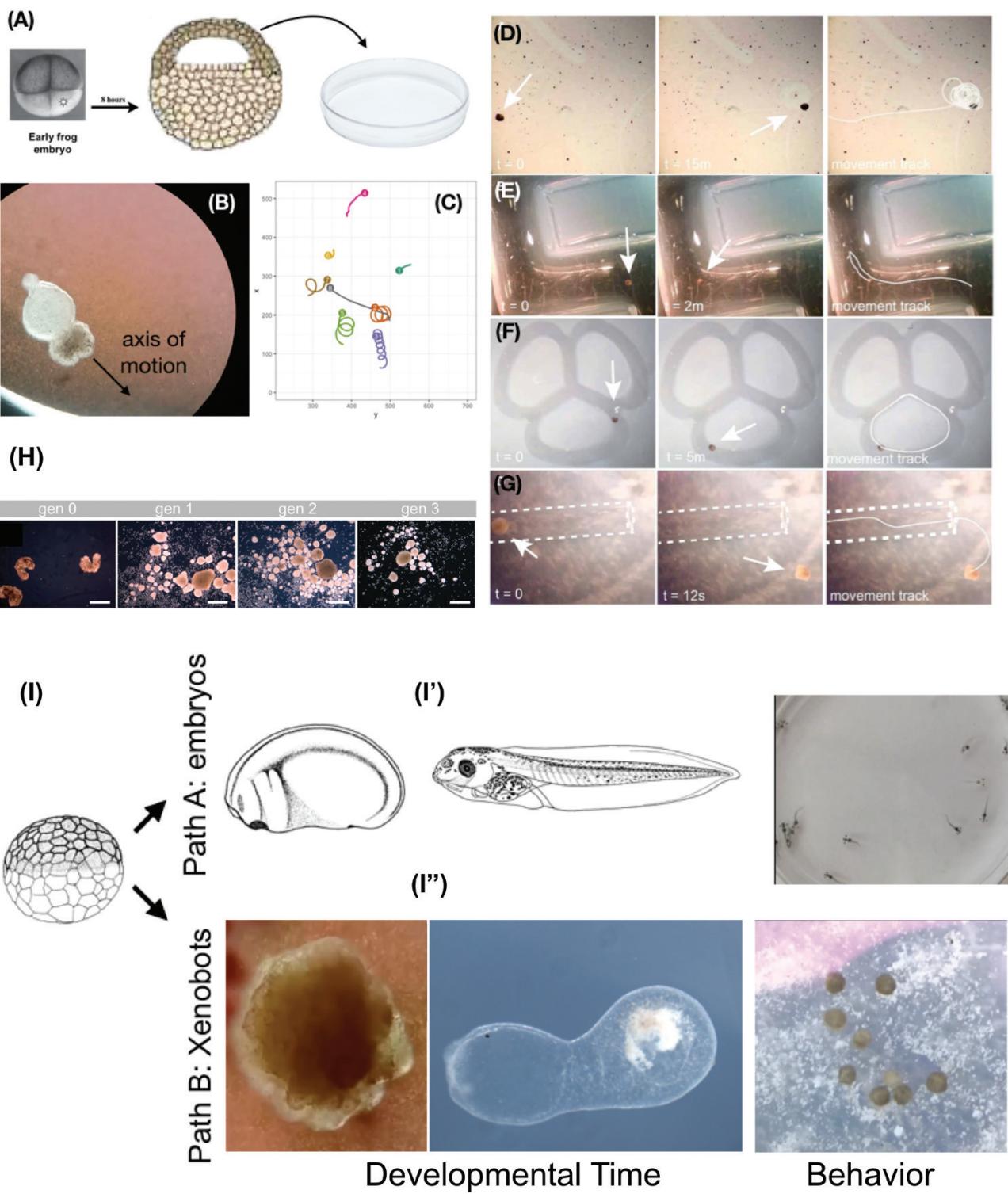


Figure 7. Xenobots as a tractable system for understanding novel teleonomic properties. A, epidermal cells from a frog embryo can be removed and placed in a novel environment, where they are freed from the instructive influences of the collective, which normally force them into a quiescent, two-dimensional existence. B–G, they become Xenobots (B), swimming by rowing cilia against the medium and exhibiting a variety of behaviours, such as those tracked in C and the circling, maze-traversal and tube-traversals shown in D–G. H, remarkably, they even find a way to replicate, using their

The ability to mix any two biological systems, in any arbitrary proportion, reveals the continuous nature of terms that are often thought to be binary (Boldt, 2018). This strongly extends the gradual view, already required when taking evolution and developmental biology seriously, which lends no support to any sharp line between ‘true cognition’ in complex brains and ‘just physics’ that is sometimes said to occur in their phylogenetic and ontogenetic precursors.

As we combine living material with electronics and computer software (Table 1), sharp distinctions between ‘machine’ and ‘organism’ become untenable. There is no principled way to draw a clean line, and any combination (from a being with 95% human brain + 5% smart implant to one that is 5% human brain tissue in a 95% robotic body, and every proportion in between) is a viable being. Rather than providing a rigorous way to distinguish life from ‘mere machines’ (as many have argued), teleonomy emerges as a much more valuable scientific tool: a parameter for defining a continuum of beings on which can be built a deep framework for understanding agency in diverse implementations. The same is true for terms such as evolved vs. designed; by themselves, these terms provide no powerful insight into the nature, capabilities or moral worth of any agent. Evolutionary algorithms are increasingly being used by engineers to design new constructs, while we ourselves are the products of evolution (and our engineering is thus a secondary effect of operations of evolved systems).

There is an important lesson in the remarkable fact that cells and engineered materials can work together so seamlessly: life itself does not respect the distinction between the two, which persists only because of our historical limitations (which are now increasingly being lifted by progress in bioengineering). The life vs. machine distinction is relevant only to the lowest class of machines available in prior decades and is not fundamental. The dichotomy is seen to be fallacious in several ways. What is essential about machines is not what they are made of (metal vs. cytoplasm), but that they are systems that operate according to predictable rules and thus can be manipulated. If this were not true, evolution would not work. Evolution does not build upon a blank canvas; instead, it alters

signals given to biological components that already have a background behaviour (e.g. new signalling factors to change the way in which cells move or differentiate during development). This process is greatly potentiated by the fact that each component is a machine in the important functional sense of being controllable and reliable for specific outcomes.

The modules of living things (from organs to molecular networks) constitute a sophisticated class of machines, which have homeostatic and allostatic loops. This means that both evolution and engineering can be potentiated by the same property: competency to get a job done even when the environment and composition change (within limits, of course). Life and engineering are interoperable precisely because of teleonomy. Each subsystem has evolved to exploit the physics of internal and external components without knowing in advance what the situation will be. The multi-scale competency architecture is highly opportunistic, because each goal-driven subunit has no access to the reality of its environment, only to inputs it receives, and must construct a model of what to do, on the fly (Friston, 2013; Constant *et al.*, 2018). This means that, as with the new class of robots with no prior fixed map of their structure (Bongard *et al.*, 2006), they will exert adaptive function even in novel circumstances. To living creatures arising from a single cell, all scenarios (whether ‘natural’ or ‘artificial’) are new circumstances, in which they learn to survive.

Already today, human bodies are augmented with prosthetics that allow them to control assistive devices, use novel and additional effectors, such as third limbs (Penaloza & Nishio, 2018), and make use of new inputs in sensory substitution (Danilov & Tyler, 2005; Nagel *et al.*, 2005; Ptito *et al.*, 2005). These drive changes in cognition (Kieliba *et al.*, 2021), illustrating the deep plasticity of life. Teleonomic functions enable the immediate, efficient use of these evolutionarily novel configurations because life does not manage outcomes bottom up: the implementation details are black boxed and do not break control systems when each level can focus on providing top-down guidance, letting the underlying modules achieve the goals with existing mechanisms.

motions to collect nearby loose cells into piles that assemble into the next generation of Xenobots, and the cycle repeats. I–I'', the same genome produces a machine that, in normal circumstances, becomes frog embryo with stereotypical stages (I, I'), but can also produce a very different machine which makes a coherent proto-organism that re-uses its genetically specified hardware for a novel developmental sequence (I'') and behaviours that arise spontaneously in 48 h, rather than over aeons of shaping by selection. Images by Douglas Blackiston, Levin lab (except for C, produced by Simon Garnier and used with his permission). D–G, I' taken with permission from Blackiston *et al.* (2021). H taken with permission from Kriegman *et al.* (2021). Frog embryo stages sourced from Nieuwkoop and Faber (1994), hosted by Xenbase (www.xenbase.org RRID:SCR_003280).

Of course, the plasticity and interoperability of living things has been exploited by evolutionary arms races, enabling some biological systems to hijack others, such as zombie ants produced by a fungal controller (Hughes *et al.*, 2011, 2016; de Bekker *et al.*, 2015; Steinkraus *et al.*, 2017; Elya *et al.*, 2018) and commensal bacteria being able to dictate the number of heads in regenerating flatworms (Williams *et al.*, 2020). Importantly, the plasticity revealed by chimaerism (and older work on sensory augmentation; Bach-y-Rita *et al.*, 1969) also reminds us that modern humans do not represent the upper limit of goal-driven cognition. The charge of ‘anthropomorphism’ is thus a pre-scientific world view, in which human beings had some sort of magic that was unique and did not exist, even in weaker forms, anywhere else. The progressive augmentation, diversification, biomedical engineering and instrumentization of human brains will strongly emphasize the limitations of the notion of absolute, discrete natural kinds (e.g. species) and the need to look for what is essential or deep about such categories.

It is clear now that terminology and distinctions based on contingencies of material and origin story will not survive the coming decades of chimaeric technologies that will erase boundaries and extend capabilities. We propose that the best conceptual framework to take their place is one based on understanding what is essential about agents: their degree of competency in pursuing goals, and the scale of goals they are capable of pursuing. This cybernetic view, together with bioengineering tools, provides researchers and philosophers with an enormous option space of possible beings, in which the whole panoply of evolved natural forms is only a small subset (Fig. 2). All of Darwin’s ‘endless forms most beautiful’ exist in a small region within the space of viable configurations. The field of evo-devo can expand to bio-robo, and synthetic bioengineering is moving from synthetic biology working in chemical and metabolic spaces (Ollé-Vila *et al.*, 2016) to synthetic morphology working in anatomical and behavioural spaces, in order to explore the variety of possible bodies and minds (Sloman, 1984; Yampolskiy, 2015).

WHAT IS NEXT: EXPANDING THE OPTION SPACE OF BEINGS DRIVES A RESEARCH PROGRAMME

Deriving the rules of emergent morphogenesis and behaviour using only the examples of natural species on Earth is like testing a hypothesis on the same set of data that generated it; chimaeric and bioengineered beings give us the opportunity truly to evaluate the quality of future models of robustness and plasticity with respect to anatomical goal states. Moreover,

the interoperability of life at all levels (i.e. the fact that chimaeras and hybrids are viable) reveals that there are no natural kinds with respect to species (Devitt, 2010; Austin, 2017). Natural life forms do not represent privileged, perfect outcomes. The general distaste for novel beings seen in science fiction (e.g. Wells’ *The Island of Dr. Moreau*) is a hold-over from a pre-Darwinian essentialism that neglects the fact that natural species simply exemplify a subset of possibilities for staying represented in the biosphere, possibilities that have been found thus far by a meandering, randomly driven search process (evolution) that optimizes for nothing more intelligent than biomass. It is very likely that rational design (bioengineering) can do better than this, once we understand the collective intelligence of molecular pathways, cells and tissues and learn to guide their teleonomic activity.

The option space of beings enables us truly to see life for the first time, in the absence of standard phylogenetic relationships that enlighten some aspects but obscure many others. A key aspect that is revealed by this way of viewing life is the multi-scale competency; the basal intelligence of many levels of organization in a given body, all of which exhibit teleonomic behaviour in their own problem space. Recognizing this behaviour, and the specific goals being pursued, is an IQ test that scientists (observers) take when evaluating the agency of unconventional agents; our ability to detect, understand and manage teleonomy says as much about our intelligence as it does about the system being studied.

The emerging field at the intersection of synthetic developmental biology, computer science and cognitive science implies numerous opportunities for next steps and further progress. From the perspective of theory/conceptual advances and specific research directions, the following questions need to be developed:

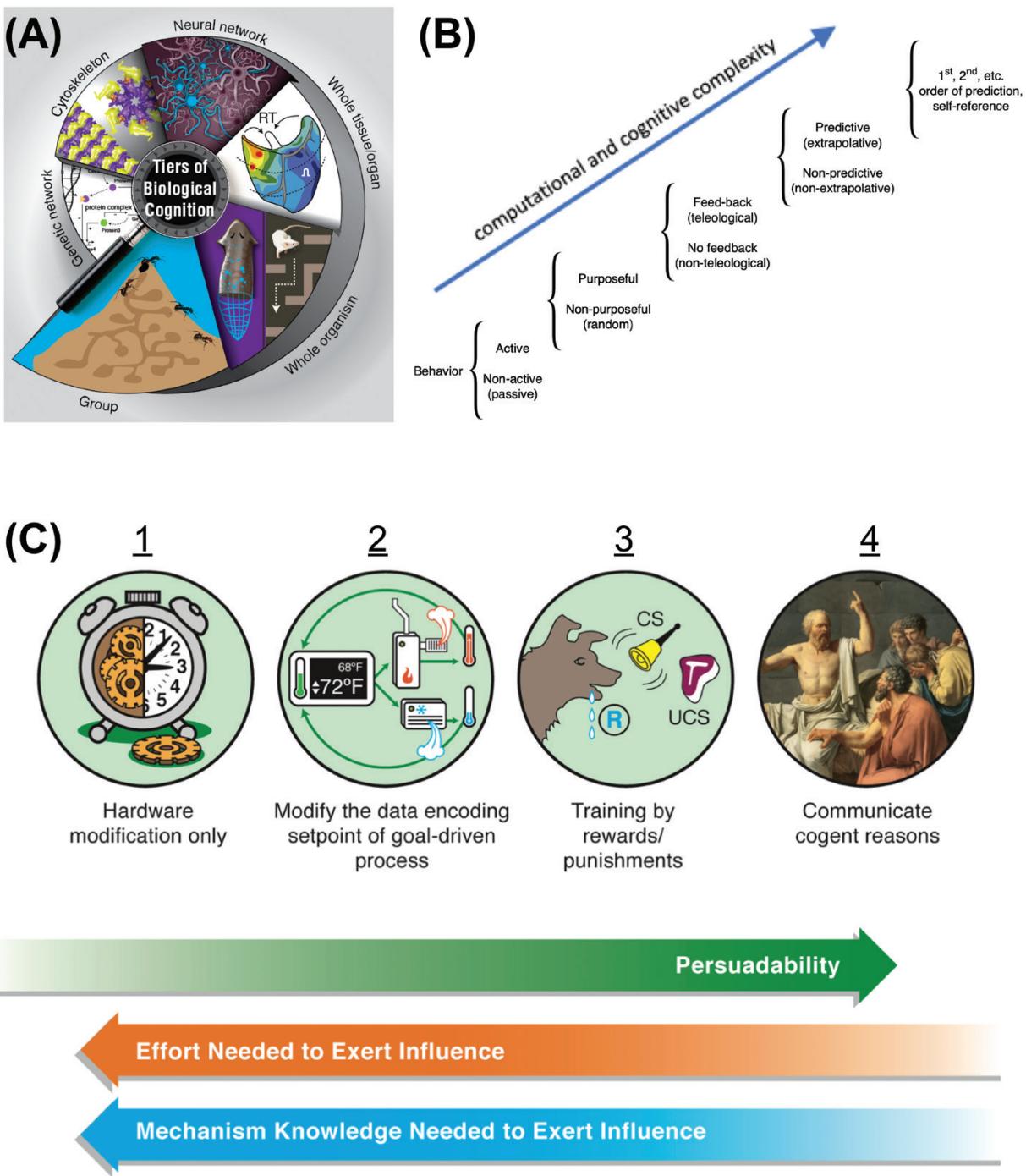
- What is an effective eigenspace for modelling agency? What would be the minimal axes for the space of all possible teleonomic agents? And how do we recognize, quantify and compare teleonomic agents in radially diverse embodiments? Even gene-regulatory networks, a paradigmatic case of deterministic genetic hardware, appear to have learning capacity (Watson *et al.*, 2010; Szabó *et al.*, 2012; Gabaldá-Sagarra *et al.*, 2018; Herrera-Delgado *et al.*, 2018; Biswas *et al.*, 2021), and teleonomy has been explored in signal transduction processes in plants (Gilroy & Trewavas, 2022). It is imperative that we abandon the tendency for armchair pronouncements of what can and cannot be seen as cognitive and instead develop toolkits for generating and testing teleonomic models of arbitrary systems.

- If evolution is blind and always prefers immediate fitness payoffs, how is it that it not only gives rise to creatures highly adapted for specific environments, but also evolves hardware that can problem solve in numerous novel configurations never seen before? How does evolution capitalize on the laws of physics and computation to generalize so well from specific examples to highly diverse possible instantiations? Specifically, how does teleonomy potentiate the evolutionary search for yet larger teleonomic systems, and how can engineers do the same?
- Can the notion of external environment (*Umwelt*; von Uexküll, 2010) be extended to a multi-scale concept, in which adjacent cells, tissues, etc. are each other's environment? Can molecular pathways and biophysical dynamics be thought of as affordances for systems to compete and cooperate within and across levels in the organism (Queller & Strassmann, 2009; Gawne *et al.*, 2020)? Links to existing thought on the extended organism (Turner, 2000) and extended mind (Clark & Chalmers, 1998) are within reach.
- What is the relationship or overlap between the sets demarcated by 'life' and 'cognition'? If all (most?) components in living things are teleonomic agents and are thus somewhere on the continuum of cognition (Fig. 1), are all living things cognitive? What is a useful definition of 'life', given that teleonomic agents can be produced by engineering with organic or inorganic parts? Although modern life is necessarily teleonomic (in order to survive in the biosphere), could there have been very early life forms that were not teleonomic? Could current efforts at truly minimal synthetic life (Hanczyc *et al.*, 2011; Cejkova *et al.*, 2017) clarify the relationship between teleonomy and physics?
- How can we develop a semiotics of synthetic agents (Tsuda *et al.*, 2009) and their *Umwelten* (Manicka & Harvey, 2008; Beer, 2014) to gain a better understanding of the ways in which teleonomy provides the ratchet that drives the great transitions of cognitive capacity along the continuum? How can we develop ways of manipulating biological systems (such as morphogenesis) via communication and motivation, rather than micromanagement?
- Can we develop artificial neural networks whose output is not specific solutions to specific problems, but rather seeds that determine machines that solve problems (Moore *et al.*, 2018)? Can we imitate the learning and generalization capacity of evolution in our machine learning architectures, such that each level of the output specifies a flexible design for an agent that functions in the problem space?
- Can we make new autonomous robotics via a multi-scale competency architecture (a generalization of the subsumption architecture; Brooks, 1986), where each layer is an agent that constructs models of itself and its environment? Robots made of parts having agency (teleonomy all the way down) will, for the first time, become vulnerable to the occasional defections of cancer, but will gain the flexibility and robustness of life owing to the massive adaptability to novelty that results from dynamic cooperation and competition of goal-driven sub-agents.

TOWARDS A NEW ETHICS BASED ON DEEP AGENCY IN THE OPTION SPACE OF LIFE

There is an aspect of teleonomy that has a positive impact on the ethics of chimaeric and bioengineered technologies. Making changes at the lower levels (e.g. genomic editing) tends to result in system-level outcomes that are hard to predict (Lobo *et al.*, 2014). When one is forced to manage all the outcomes directly (as when manipulating a system bottom up), a likely outcome is 'unhappy monsters' (i.e. ethically unacceptable creatures containing mismatched components that do not work harmoniously together). A simple example occurs in planarians: inducing secondary heads with biochemical inducers makes heads that are not properly scaled to the rest of the organism, whereas nudging the top-level 'head vs. tail' decision in the native bioelectric circuit leads to all of the downstream properties being handled by the system itself and results in perfectly scaled, functional heads (Durant *et al.*, 2019). In general, changes introduced at the micro-level tend to wreck complex systems more than changes that are input at the higher level; optimizing the level of intervention for specific biomedical and synthetic purposes will require the incorporation of teleonomic models into the biophysics frameworks used almost exclusively today (despite the work on modularity in evolution; Payne *et al.*, 2014; Watson *et al.*, 2014). Controlling biology top down, via experiences and stimuli that rely as much as possible on the native collective intelligence of its parts, is likely to produce much more coherent organisms and will provide us with a better understanding of life.

The impact of rapidly advancing technologies will go far beyond science, encompassing many issues that have been dealt with in science fiction but have not yet been worked through by thinkers in the fields of philosophy of mind, ethics and policy. Our culture is in for an upheaval that will far eclipse the controversy that fomented around Darwin's '*Origin of Species*'. Our ethics structures are barely sufficient to optimize



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Figure 8. Goal directedness is an invariant for a continuous spectrum of cognition. A, biological systems are not only structurally hierarchical but also functionally hierarchical: each layer solves unique problems in a relevant problem space, exhibiting teleonomy. B, the degree of competency and complexity that can be handled by a system in its pursuit of goal states defines major transitions along a continuum of cognition ranging from passive matter to advanced self-reflective minds, which enables comparison of highly diverse intelligences (Rosenblueth *et al.*, 1943). C, given that agency claims are, in effect, engineering protocol claims, the search for efficient prediction and control strategies defines an 'axis of persuadability', ranging from brute force micromanagement to persuasion by rational argument, C1–C4 show only a few representative waypoints. C1, the simplest physical systems (e.g. mechanical clocks) cannot be persuaded, argued with or rewarded/punished; only physical hardware-level 'rewiring' changes their behaviour. C4, on the far right are human beings

intraspecies interactions; they will need a total overhaul when we are surrounded by novel agents of every possible configuration. How does one prosecute a 50% cyborg for its misdeeds? Legal systems based on one dimension of human IQ (with a cut-off for ‘competent’) are in no way ready for a multidimensional space of beings with diverse components contributing to their mind and behaviour.

Many current legal and moral structures are built around a crisp category of ‘human’ within that axis. Although we have some provision for ‘diminished capacity’ (in legal proceedings), we do not yet have any for increased capacity. Neural real-estate is readily taken over by functional modules (e.g. in the cases of the blind whose visual processing areas become used for hearing and other modalities; [Van Ackeren et al., 2018](#)). Thus, it is very likely that the addition of neural tissue to standard brains will result in increased processing capacity. The system uses a highly adaptive design that can make use of resources that do not have to be specified in advance, because the various subunits (cortical layers, neurons, etc.) are themselves teleonomic agents that relate to their neighbours with the same plasticity with which they face external environments. Members of the transhumanist movement have already begun to discuss what happens when humanity includes beings with a wide range of IQ and moral capacities (e.g. a larger cognitive horizon that allows them functionally to care about far more than today’s human is capable of handling). What is a human being? A good answer, in future decades, cannot be based on a genetic or anatomical description; perhaps it will be based on the minimal amount of active compassion or functional caring (similar to today’s standard human) that a being can muster within its cognitive boundary (i.e. a definition based on capacity for teleonomic action).

Moreover, although Darwin’s revolution created a continuous spectrum along which to compare intelligence (and place moral categories for relationships to primates, whales, dogs, etc., in addition to complex cases, such as octopuses), a far wider reality is beginning to emerge. There is not only a large axis representing different amounts of cognitive sophistication, but also an immense space of multiple dimensions of different types of cognitive capacity. It is entirely unclear how creatures within that space will relate to each other, making essential the search for an invariant on which to base norms (such as complexity of the creature’s goal space).

CONCLUSION

Bioengineering expands our subject of inquiry to a now-realizable immense option space of novel living agents: true biology in the sense of life as it can be ([Langton, 1995](#)), rather than zoology/botany. The study of these novel beings does two important things. First, it helps us to move beyond the historical contingencies and familiar (limiting) categories of where agency can be found in the specific products of one evolutionary stream on Earth. We must become comfortable thinking about new scales of size and duration, new material substrates for life and mind, and new spaces in which goals can be sought. Second, it helps us to get to the root of a key question: where do goals come from in the first place? Synthetic creatures such as chimaeras, hybrots, cyborgs and biobots provide empirically tractable model systems in which to study emergence of the morphological and behavioural goals of collective intelligences (any being made of parts) that were not shaped by aeons of evolution towards specific environments.

(and others to be discovered; [Bostrom, 2003](#); [Kurzweil, 2005](#)), whose behaviour can be changed radically by a communication encoding a rational argument that changes the motivation, planning, values and commitment of the agent receiving this. C2, C3, between these extremes lies a rich range of intermediate agents, such as simple homeostatic circuits (C2), which have set points encoding goal states, and more complex systems, such as animals that can be controlled by training using stimuli that communicate to the system how it can achieve its goal of receiving a reward (C3). This continuum is not a linear *scala naturae*; evolution is free to move in any direction in this option space of cognitive capacity. The goal of the scientist is to find the optimal position for a given system. Too far to the right results in complex models that do not improve prediction and control. Too far to the left and one loses the benefits of top-down control in favour of intractable micromanagement. This is also a continuum with respect to how much knowledge one has to have about the details of the system in order to manipulate its function. For systems in class C1, one has to know a lot about their workings to modify them. For class C2, one has to know how to read–write the set point information but does not need to know anything about how the system will implement those goals. For class C3, one does not have to know how the system modifies its goal encodings in light of experience, because the system does all of this on its own; one only has to provide suitable rewards and punishments. Ascertaining the optimal level of teleonomy in the objects around us is a key task for scientists interested in understanding and managing novel complex systems; this capacity is also a built-in cognitive module for animals navigating complex environments, conspecifics, prey, etc. B created after [Rosenblueth et al. \(1943\)](#). A, C images courtesy of Jeremy Guay of Peregrine Creative, taken with permission from Levin (2022).

These new model systems dissolve outdated, binary categories, such as ‘machine’ and ‘organism’, that were based on the temporary technological limitations of the past and will surely not survive the coming advances of the next few decades (Bongard & Levin, 2021). Fixed Linnean relationships and categories based on genomes have served biologists well (although perhaps not so well for microbiologists), but these need to be replaced in light of the increasingly obvious plasticity and interoperability of life (Fig. 8). We will soon be surrounded by truly ‘endless forms most beautiful’ (Darwin, 1859), filling an option space that Darwin could not even have dreamed of (Ollé-Vila *et al.*, 2016). They challenge us to define new categories based on deep (empirically useful and more philosophically sophisticated) criteria and to move beyond an assumption that goals are always set by selection.

Future impacts of these ideas will be driven by a progressively improved understanding of the relationship between the crafter (whether evolution or an engineer) and its material. For example, the current intellectual property system was developed to address work with classical, passive materials, where everything is in what the craftsman did; patenting the craftsman’s recipe is key. It is not yet suitable for work with agential materials, for which the inventor is a collaborator with the components. As with the Xenobots, where the outcome is as much (or more) dependent on the competency of cells to carry out specific goals as it is on the human providing cues, the outcome of this new type of creative work is partly the method, but it is also partly what has been discovered about the competency of the agential material. These challenges to our ideas of intellectual ownership dovetail with similar concerns over future inventions by AI agents that serve as tools to augment human creativity.

A mature science of teleonomy is no more about understanding Xenobots and their kin than computer science is the study of our current computers. The goal is far deeper: understanding the relationship between the genome, the software that produces bodies and behaviour, and the ability to reach adaptive ends despite diverse means on very rapid time scales. Critically, the issue of forming and detecting goals requires a specification of a complex system to whom the goals belong. What defines a self? Although immunological (Pradeu, 2019) and evolutionary-scale (Strassmann & Queller, 2010) theories have been proposed, these are intimately tied to (and thus limited by) the types of organisms we observe naturally in our biosphere. A more general framework, able to encompass and directly compare truly diverse agents, needs to be based on teleonomy at its core: a self is a goal-directed system, and its level of sophistication (ranging from modest inorganic systems to trans-human beings) is set by the spatiotemporal scale of the goals it can pursue (Levin, 2019).

Chimaeric and synthetic bioengineering enables us to leave the Garden of Eden of a finite set of natural species and to continue Adam’s task of naming novel creatures; more specifically, discovering their true nature beyond the facts of their composition and origin. The sciences of cybernetics and the deep lessons of neuroscience, which extend well beyond neurons (Friston *et al.*, 2014; Ramstead *et al.*, 2019; Fields *et al.*, 2020; Fields & Levin, 2020a, b), will be key components of this future. At stake are transformative advances in regenerative medicine (to get beyond the low-hanging fruit reachable by conventional stem cell biology and genomic editing approaches), robotics and general AI.

Crucially, this new field suggests not only novel capabilities and advances in knowledge, but also the need for a new ethics. The frequently voiced statements that ‘living things are not machines’ reflect an outdated essentialism and a type of magical thinking that trusts in clear, binary lines separating evolved living beings from designed machines to define our moral duty to various agents comfortably. These lines do not exist, which will be made painfully clear in the next decades as we become surrounded by collections of agents that make the iconic Cantina scene in ‘Star Wars’ look tame in comparison. Significant effort will need to be made as science and society mature to include designed beings in addition to natural beings, in order to avoid the types of ethical lapses to which humans are prone: mistreatment of those who do not resemble a familiar in-group in composition or origin. The nature of teleonomy as a guiding principle cutting across contingencies of origin story and composition, and the inevitable expansion of life throughout the option space of hybrid forms (Fig. 2), provide important conceptual tools for a path forwards to a future where we cannot simply guess the capacity of an agent to think and suffer based on what it looks like or how closely it resembles a familiar touchstone species in the Earth’s phylogenetic lineage. It is not clear what a new ethics of life as it can be will look like, but some sort of golden rule about compassion towards systems proportional to their teleonomic capacity might be a place from which to start.

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DATA AVAILABILITY

This manuscript is based on information in the accessible published literature.

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