

Semibiotic Persistence

C. Prothmann (1) and K.-P. Zauner (2)

(1)

Massachusetts Institute of Technology

77 Massachusetts Avenue

Cambridge, Massachusetts 02139, USA

ckp@mit.edu

(2)

Electronics and Computer Science

University of Southampton

Highfield, Southampton, SO17 1PQ, UK

kpz@ecs.soton.ac.uk

Abstract

From observation, we find four different strategies to successfully enable structures to persist over extended periods of time. If functionally relevant features are very large compared to the changes that can be effectuated by entropy, the functional structure itself has a high enough probability to erode only slowly over time. If the functionally relevant features are protected from environmental influence by sacrificial layers that absorb the impinging of the environment, deterioration can be avoided or slowed. Loss of functionality can be delayed, even for complex systems, by keeping alternate options for all required components available. Biological systems also apply *information processing* to actively counter the impact of entropy. The latter strategy increases the overall persistence of living systems and enables them to maintain a highly complex functional organisation during their lifetime and over generations. In contrast to the other strategies, information processing has only low material overhead. While at present engineered technology is far from achieving the self-repair of evolved systems, the semibiotic combination of biological components with conventionally engineered systems may open a path to long-term persistence of functional devices in harsh environments. We review nature's strategies for persistence, and consider early steps taken in the laboratory to import such capabilities into engineered architectures.

Keywords

Bio-hybrid architectures, information processing, resistance, resilience

Introduction

Designing systems that are required to function over long periods has been one of the key engineering challenges for the exploration of space and other extreme environments. If we review the history of engineering, the direct knowledge gained from archaeological artefacts is limited to ancient materials and methods. To employ more recent technologies one can, however, draw on general observations about objects that have persisted over extended periods of time and on strategies employed by biological systems. Four general strategies emerge (Fig. 1).

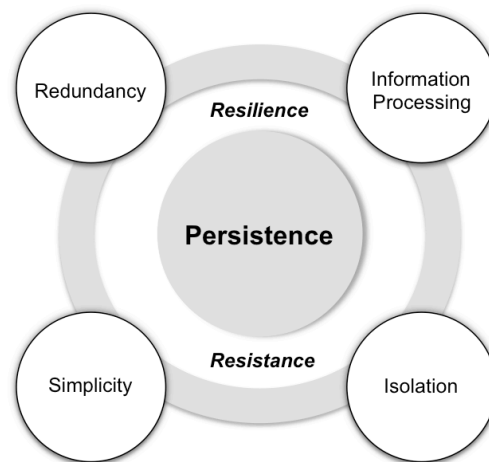


Fig. 1. Engineering principles for persistent structures and systems.

One strategy is *simplicity*: If all functionally relevant features are very large compared to the changes that can be effectuated by the environment, the system will erode only slowly over time. It is then possible to design a system in which the decay over the time period under consideration is negligible with regard to its function. Another strategy is *isolation*: If the functionally relevant features are protected from environmental influence by sacrificial layers that absorb the impinging of the environment, deterioration of the protected core can be avoided over the period of interest. Both *simplicity* and *isolation* are principles that aim to enhance

system resistance. The Temple Mount platform in Jerusalem and the Egyptian Pyramids could serve as examples of, respectively, simplicity and isolation. Arguably, the Chinese Wall requires more active maintenance and would be closer to resilience in Fig. 1, if manual repair is viewed as an integral part of the architecture. *Redundancy* of critical system modules has been applied to many modern engineering challenges, including nuclear reactors and space exploration devices, and is particularly useful if there is only a limited possibility of repair during operation [1–3]. Simplicity, isolation and redundancy are engineering principles, which have been successfully battling with system disturbances, however, only to a certain point. Historical examples of resistance engineering clearly demonstrate that these structures decay and that deterioration can only be counteracted by active restoration from outside of the system. Furthermore, structures and systems with a high level of resistance exhibit a very low overall functional complexity. Maintaining highly complex functional systems requires other strategies to ensure functional integrity. Although redundancy is certainly one option to address this challenge, an exclusive reliance on redundancy is an inefficient solution.

All three principles discussed so far are not well suited for space-travel due to their inefficient use of resources and material. Long-term functionality can be also achieved by actively countering deterioration through using *information processing*. The system-inherent capability of repairing complex functional systems has only been observed in biological systems that use information processing to actively counter the impact of entropy [4–7]. Evolution has optimized biological systems to resist, respond, and recover from environmental disturbances [7, 8]. Organisms exemplify a range of solutions, combining structural resistance, redundancy, and the ability to actively self-repair, to achieve persistence and maintain functionality [7]. Over the past six decades, design principles derived from biological systems have found their way into engineering, material sciences and architecture. Biomimetics [9] has become a growing field that focuses on studying mechanisms, processes and structures of biological systems with the goal of imitating solutions optimized over evolutionary time scales [10]. Biomimicry-inspired applications include biomaterials [10, 11], biomechanics and robotics [12], and architecture [13, 14], as well as algorithms for machine learning [15] and optimization [16]. Practical experience with these application domains has, however, demonstrated that biomimetic approaches - while

in some areas competitive with existing engineering methods - in many instances do not live up to the expectations generated by the performance of organisms. Obstacles that stand in the way of more successful biomimetic architectures arise from two sources. Firstly, the limitations in fabricating specialised materials, such as nature produces in the form of customised macromolecules. And, secondly, from the limited integration density of manufacturing processes compared to the developmental processes available to nature. A case in point is the integration of electronic circuits that has seen exponential advancement over the past half century. Even after its astonishing progress, a connection density comparable to that achieved by natural neuronal networks - where the average number of inputs received by a single neuron in the mouse cortex is around 8000 [17] - is not in sight.

It appears unlikely that in the near term the gap between synthetic and natural materials and functional systems will significantly narrow. As a consequence, it is attractive to make use of the materials and systems available in nature by integrating them with conventionally engineered components and devices into hybrid biosystems [18, 19]. Such semibiotic architectures incorporate biological components into a technical setting to transfer some of the desirable qualities of biosystems to the resulting architecture [20]. In-situ replenishment of complex components that have degraded, dynamic reallocation of material and energy resources, and self-repair following damage are typical examples of what can be achieved in semibiotic architectures - but what is currently out of reach for conventional engineering.

The developments at the interface between engineering and biology are summarized in Fig. 2. Biology, on the one hand, supplies ideas for solutions to engineering problems, giving rise to the field of biomimetic engineering. In this field, the concepts inspired by biology are implemented with conventional fabrication methods and materials. Both, methods and materials fall far short of what nature has available. For example, growth processes and self-assembly allow for biological systems with high interconnection density, and macromolecules with customized functionality enable high integration density in organisms. In contrast, the limitations of the materials and fabrication methods available in engineering hamper biomimetic engineering. However, the interfacing between conventionally engineered systems and biomimetically engineered systems is typically not difficult. Biology, on the other hand, acts as a source of components for hybrid devices developed in the field of semibiotic engineering. Here the key

challenges are the lack of direct control over the autonomously acting biological subsystem and the development of suitable interfaces between biological and conventionally engineered subsystems.

At present, most of the interface development falls on the side of the conventionally engineered subsystems. However, initial steps to reengineer organisms to optimise the interface from the biological side have also been taken [21]. The engineered adaptation of organisms specifically for integration with conventional architectures is becoming increasingly feasible as the field of synthetic biology progresses, and future semibiotic architectures are likely to comprise engineered biosystems rather than components extracted from nature. Before we consider the contribution that information processing can make to the persistence of semibiotic systems, it will be instructive to consider examples of resilience in biological systems.

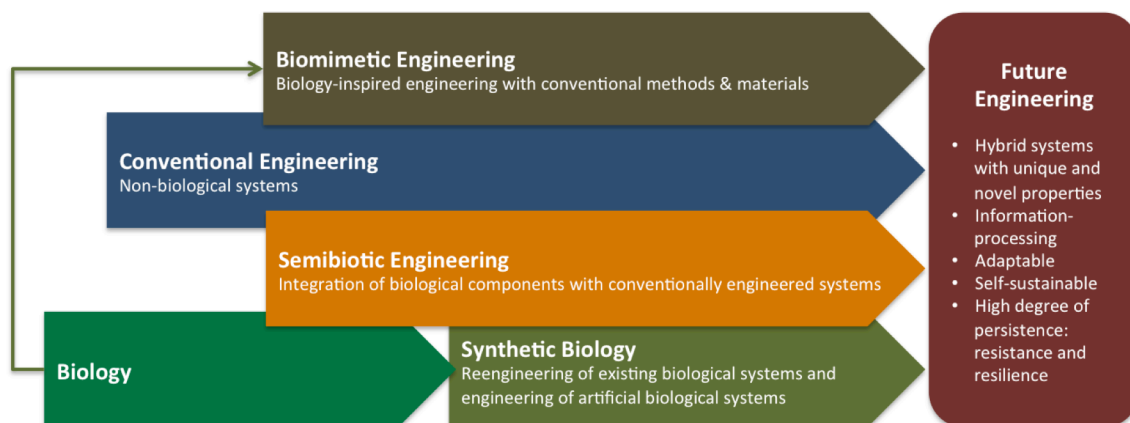


Fig. 2. Engineering approaches.

Persistence Strategies of Biological Systems

Biological systems have developed strategies and mechanisms of persistence - resistance and resilience - on a molecular, cellular and organismic level. All of these strategies differ in their metabolic cost, which has led to the evolution of different mechanisms or combinations of mechanisms employed by individual species [7]. *Information processing*, which is at the core of all life, enables biological systems to maintain their state by mechanisms such as self-repair on all levels of organization [4, 6, 7, 22]. Cells of single and multi-cellular organisms are constantly exposed to exogenous (environmental) as well as endogenous challenges to their structural, functional and informational integrity. Damaging agents, which impair DNA and protein function, include metabolic by-products (such as free radicals), chemicals, and high-energy radiation [23]. DNA, which is the repository of genetic information, is under constant self-repair by a range of mechanisms present in prokaryotic and eukaryotic life forms. DNA repair, which involves multiple and overlapping processes (partial redundancy), relies on proteins that can be inactivated by chemicals or oxidative radicals formed by radiation [24]. Organisms with high radiation tolerance have a highly developed antioxidant system, which actively protects proteins from oxidative damage, efficient DNA repair mechanisms, and processes to recognize and degrade damaged proteins [25]. Components of these processes are further induced after radiation exposure to increase cellular protection and allow for fast recovery from damage [26].

Bacteria such as *Deinococcus radiodurans*, some fungi and animals, including some rotifers and tardigrades, show an extraordinary tolerance to radiation [26–30]. These organisms also demonstrate exceptional robustness towards other extreme environmental conditions and are referred to as extremotolerant or extremophiles, capable of surviving high radiation, desiccation, low temperatures, high pressure, and even vacuum. Tardigrades, which are animals below one millimetre in size and considered phylogenetically related to arthropods [31], are able to survive exposure to the vacuum of space and even solar radiation [32]. Studies carried out with other prokaryotic and eukaryotic organisms indicated that some bacterial spores, some microbial communities, and some forms of lichens have the ability to survive prolonged exposure to space conditions [33, 34].

Many extremophiles are capable of coping with highly challenging environmental conditions in a dormant as well as in a metabolic active state [35]. These life forms possess mechanisms to actively respond to extreme physical environments allowing them to transition into a protective dormant state, such as anhydrobiosis, which is characterized by a very low metabolic rate. The transition back into a metabolically more active state is carefully orchestrated to enable the repair of sustained damage, e.g. DNA repair, before the cells become fully metabolically active. Depending on the environmental extreme, dormant cells are not completely metabolically inactive. Studies of the metabolic rate of organisms in permafrost indicate that microorganisms can retain a very low metabolic rate, which could enable them to actively counteract degradation and repair damage [36, 37]. Extremophiles have evolved an extraordinary ability to limit the impact of environmental disturbances and to actively repair molecular damage at low and active metabolic rate. Several organisms have taken it even a step further and thrive in highly radioactive environments such as nuclear waste or power plants. *Deinococcus radiodurans* exhibits an unmatched level of resilience against multiple physically extreme environments, including high levels of radiation, which seems to be based on having up to 10 copies of its genome (*redundancy*) [38], highly developed mechanisms for actively protecting proteins from radiation-induced oxidation [39], and DNA repair (*information processing*) [40].

Melanised fungi, which have been reported in places such as the Chernobyl nuclear reactor, not only survive when exposed to ionizing radiation, they have also been described to show increased growth and are therefore referred to as radiotrophic fungi. The molecular mechanisms that promote increased cell growth are still being elucidated, though data indicates that some melanised fungi are able to effectively protect themselves from ionizing radiation (*isolation*) and repair radiation-induced damage (*information processing*) while enhancing their growth rate [28, 41, 42]. Some authors hypothesise that these fungi are able to utilize radiation as an additional energy source [41].

Biological systems have developed astounding molecular and cellular mechanisms to ensure survival in harsh environments. Although organisms exhibit a certain level of redundancy and employ protective measures, e.g. melanin in case of the radiotrophic fungi (*isolation*), to increase their environmental resistance, self-repair of cellular functions (*information processing*)

is a key mechanism for achieving resilience.

Slime moulds are organisms that undergo a complex life cycle including a single-cellular/mono-nucleated, a unicellular/multi-nucleated (plasmodium), and a multi-cellular differentiation stage ending in a fruiting body carrying spores [43]. The plasmodium of *Physarum polycephalum* can reach a size measured in square meters and is basically one very large cell with millions of nuclei [44, 45]. The mechanical fragmentation of the plasmodium leads to smaller microplasmodia, which are capable of either fusing back to a macroplasmodia or individually undergoing the full lifecycle of *Physarum polycephalum* (*redundancy*) [46]. True multicellular organisms with complex bodies have also developed mechanisms to maintain and restore their overall structural integrity and function. Complex organisms establish their morphological features, including different cell types, tissues and organs, as a result of a development process [47]. Injuries to tissues and body structure trigger response mechanisms that contain the damage and aim to compensate for the loss of structure and function. Repair may lead to some structural but only limited functional recovery, unless compensatory growth is possible. Regeneration is a self-repair process that leads to the reconstitution of most, if not all, of the lost structures and functions. Plants and many animal species display regenerative processes [48]. Animal regeneration has been most extensively studied in invertebrates such as hydra and in vertebrates such as various amphibians. Stem cells that are capable of differentiating into various tissues are key to regeneration and have been identified in animals ranging from primitive sponges to mammals [48].

Sponges represent an interesting example for investigating the relationships between structural resistance, organizational complexity, regenerative self-repair, and overall persistence. Interestingly, sponges, which were in the past mainly harvested for their skeletons, have become of interest for biomimetic engineering due to composite-like biomaterials of their skeletons, which might guide the development of novel biomimetic materials [49]. Recently, the structural design of sponges also served as an inspiration for innovative architecture of skyscrapers [50]. Sponges are sessile, mostly filter-feeding aquatic organisms that represent one of the earliest multicellular forms of animals [51]. The body plan of sponges consists of an outer and an inner layer of cells with the mesohyl that functions as an endoskeleton in between.

Instead of tissues in the classical sense, sponges have a cellular grade organization consisting of specialised and unspecialised cells supported by an endoskeleton with mineral and organic components. Sponges grow in a variety of shapes, ranging in size from less than a centimetre to giants measured in meters [52]. Pores and a canal system - through which water is actively circulated by the movement of the flagella of the choanocytes to ensure the supply of oxygen and food - characterize the basic body plan of sponges (Fig. 3). The morphology of sponge species can differ and range from cup shape, branching, or tubular to globular and encrusting forms [53, 54].

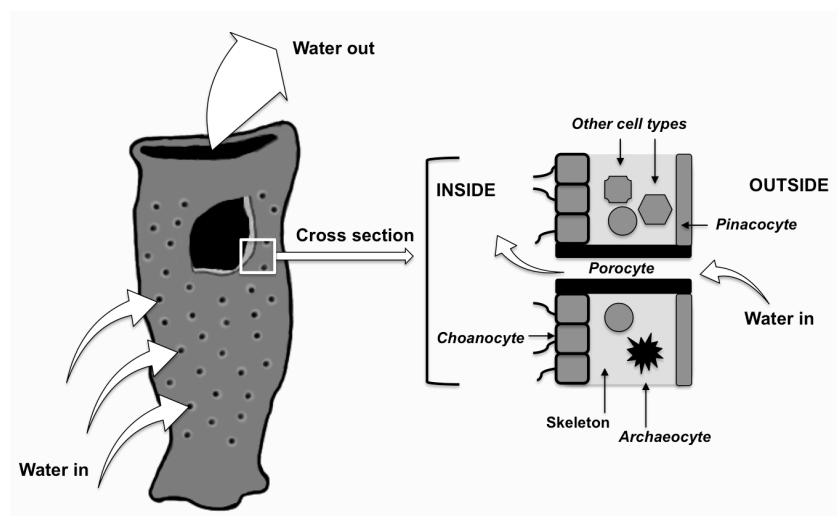


Fig. 3. Basic sponge anatomy with cross section, adapted from [54].

Although sponges have no nervous system or muscle tissue, they are capable of coordination and reacting to environmental changes. Sponges can control their feeding circulation by mechanisms that involve electrical impulses in response to sediments in their filtration system [55]. Further, they have been reported to undergo contractions to remove waste from their body system, which shows that sponges have some sensory capacity and the ability to coordinate movements [56]. Despite the fact that sponges are considered sessile, except for their larvae, some sponge species have demonstrated the ability to move or crawl short distances [57, 58]. Marine sponges contain complex microbial communities and interact with microorganisms such as bacteria and fungi on multiple levels [59]. One of the well-studied symbiotic relationships is

the metabolic interaction with photosynthetic cyanobacteria [60]. Microorganisms can contribute more than 35% of sponge biomass [61] and are suggested to assist in a variety of host functions, including nutrition, chemical host defence [62], and antifouling response [63] - and might also contribute to the structural rigidity of some sponges [64]. Different species of sponges vary in the morphology and composition of their skeletal structure, making them more or less prone to damage from environmental disturbances (*isolation*) [65]. The structural simplicity of sponges is exemplified by the lack of tissue, a limited number of cell types, and a highly flexible cellular level of organization. Sponges have extraordinary reconstitutive abilities as shown by the formation of functional sponges from dissociated sponge cells (*redundancy and information processing*) [66]. The regenerative faculty of sponges is attributed to the presumably totipotent archaeocytes and possibly choanocytes in some sponge species [67]. Molecular markers indicate that archaeocytes resemble stem cells, which would explain the exceptional ability of sponges to reconstitute and recover from injuries [68]. Sponge species differ in their strategies for improving their overall persistence by applying a species-distinctive balance between their ability to resist damage and the ability to recover from damage [65]. This has been documented in a large study that compared the extent of hurricane damage sustained by sponges and their ability to recover after 5 weeks [65]. The study indicates that sponges with strong resistance based on sturdy skeletons were on average better protected against damage. However, when these sponges sustained significant damage, they had a more limited ability to recover. As a consequence, more sponges with sturdy skeletons perished after the storm, which led the authors to conclude that there is an inverse relationship and trade-off between the ability to resist damage and the ability to recover from damage. The giant barrel sponges of the species *Xestospongia muta*, which shows a balanced mix between damage resistance and recovery, are assumed to be the longest-lived animals known, with a life-span exceeding more than 2,000 years [65, 69].

Information processing lies at the core of living systems and enables the self-sustainability of life by responding to internal and external changes on a molecular, cellular, organismal and even ecological level to ensure propagation and persistence [4-6, 22, 70]. Evolutionary selection has optimized biological systems to develop and employ diverse mechanisms for persistence, including self-repair up to the point of full regeneration. Although most organisms come with a

similar basic set of persistence mechanisms, which are critical for the sustainability and perpetuation of life, they can exhibit varying degrees of resistance and resilience approaches to improve overall persistence [7]. The ability of self-repair, however, remains the central trait for achieving long-term sustainability and persistence, even in extreme environments. Next we will turn to the question of how resilience, and especially the information processing aspect of it, can guide the design of persistent semibiotic systems for the exploration of extreme environments such as space.

Towards Semibiotic Persistence

The long-term survival strategies described in the previous section are so far not replicable in engineered systems. Semibiotic engineering, however, provides a pathway for importing capabilities of biological systems, such as self-repair, into subsystems of purpose-built architectures. To clarify the mechanism of biological persistence, it will be useful to take an abstract perspective on the role of self-repair in biological systems.

If disturbances from the environment impinge on a simple functional system, it will degrade over time (Fig. 4). Entropy from the environment drives changes in the system. Because the system in this case is assumed to be simple, many of these changes will not move the system out of the subset of states in which it remains functional. Over time, the system will reach states in which it is only marginally functional and from which further impact from the environment can push it into a set of states of degraded functionality. For simple systems, the latter set is typically large and it will on average take significant time until the accumulation of damage leads to the destruction of the system. Entropy acts on the system without direction and consequently the transition probabilities among the sets of states - and accordingly the lifetime of the system - are determined by the relative size of the sets of states that correspond to a functional, degraded, and destroyed system. The dominant transitions for a simple system are illustrated in Fig. 4. Any transition backwards is exceedingly unlikely, because the set of functional states is much smaller than the set of degraded states, and this in turn is far smaller than the set of states commensurate with the system being destroyed. The vast size of the latter is symbolised by its

dashed boundary in the figure. Transition pathways with negligible probability, such as the backwards transitions and the direct transition from functional states to destroyed, are not shown in this and the following transition graphs.

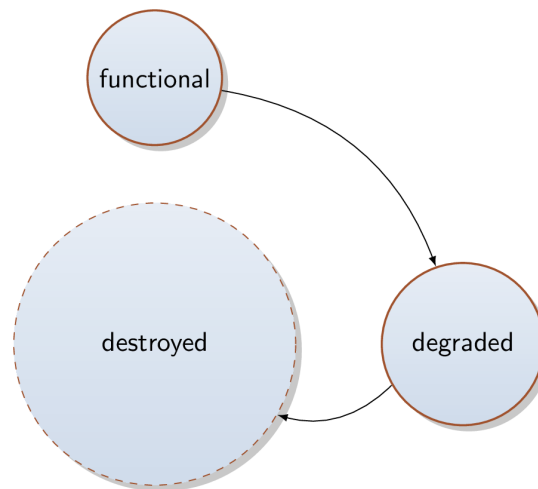


Fig. 4. Simple System

If we consider, in contrast to the simple system, the situation for a complex non-biological system (Fig. 5), we find that more detailed requirements for the organisation and functionality of the system restrict the set of possible system configurations, which are functional. Similarly, the interdependencies in a complex system restrict the set of states that exhibit degraded functionality rather than no functionality. As a result, the entropy from the environment impinging on the system is likely to degrade the system or may even destroy it directly if critical components or links are affected. The more sophisticated requirements for a complex system also result in a much more rapid transition from a degraded state to the full destruction of the system. The complex system is brittle in the sense that it deteriorates more rapidly along the path indicated by thick arrows - a consequence of the relatively small sets of states that are compatible with the requirements of the system. It is possible to reduce the transition probabilities along this path to some degree by introducing redundancy, a measure that in effect increases the sets of functional and of degraded states. In contemplating the complex system (Fig. 5), we have in essence equated complexity with a small number of functional and

degraded states. With the transition probability among these state sets being a direct consequence of their relative size, it may appear at first sight as if shielding from the environment is the only path to achieve a long lifetime for a complex system. However, the transition probability towards destruction is only determined directly by the relative size of the state sets if the transitions among states occur at random. That this does not necessarily have to be the case is exploited by organisms. All forms of life are highly complex systems but survive the impinging of environmental entropy over extended periods and do so by going beyond shielding or *isolation*. Crucial to this ability is the use of *information processing* in order to direct transitions from degraded states to functional states.

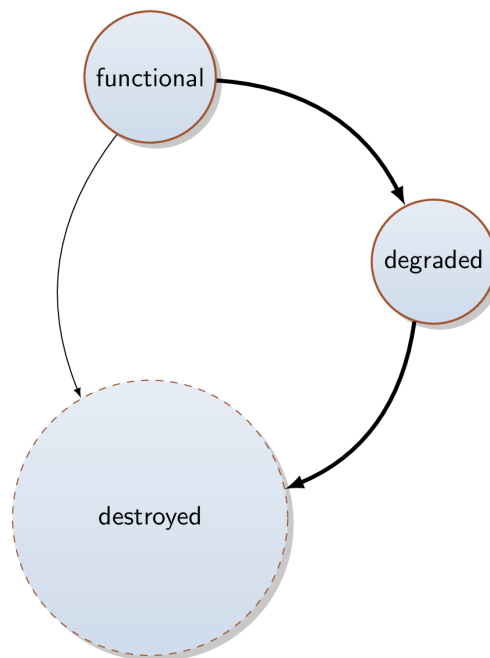


Fig. 5. Complex System

This scenario is depicted in Fig. 6. Biological systems are always complex systems and therefore the underlying situation is as in Fig. 5. The specialised requirements for a living state make state changes resulting in degraded functionality and further decay to destruction very

likely. But there is a new path that takes degraded systems back to a functional state.

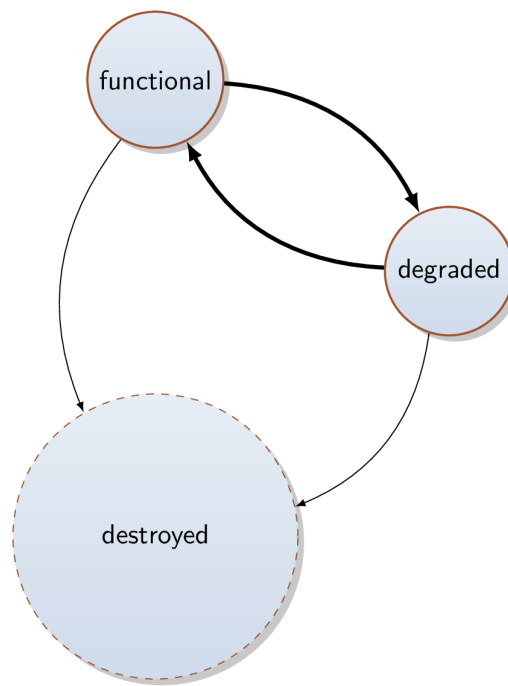


Fig. 6. Biological System.

If the transition probability along this new path would be determined by the relative size of the state sets, this path would not exist. Instead, it is actively driven in the unlikely reverse direction. The driving force could be free-energy minimization, as in the case of molecular self-assembly, or provided through other energy sources. The effect of the new transition path is a reduced probability for a degraded system to be destroyed and a reduced time for the system to be in a degraded state. This requires the expenditure of energy to work against entropy and information processing to determine the direction of the preferred transitions. If the deviation from normal operation is slight, the active biasing of the transitions back to the fully functional state can be viewed as dynamic control or stabilisation. If it is severe, it will give rise to self-repair. In either case, information processing is key to preventing the complex organisation that underlies all life forms from deteriorating rapidly. As a consequence, life as a robust phenomenon cannot exist without information processing. This information processing is starkly different from conventional

computing and tightly coupled to the physical properties of the underlying material substrate that implements it. The course of computation is determined by free-energy minimisation rather than by enforcing - from a materials perspective, arbitrary - mathematical constraints. Whereas a computer follows a carefully arranged sequence of state transitions, natural information processing can be better pictured as a process of crystallisation. The consequence is twofold. Firstly, nature's information processing is very energy efficient, because it does not need to be driven through a prescribed sequence of state changes. Secondly, in the present context even more importantly, it is more robust as it does not require the careful preparation of a starting state, because of the availability of a very large set of potential starting states, all of which are lead by energy minimisation to the solution [71].

Prototypical Semibiotic Systems

At present, it is not possible to reproduce the fine-grained, robust, and energy efficient information processing that enables organisms to maintain their alive state with man-made technology. However, a number of laboratory prototypes have shown that one method of maintaining highly complex structures in engineered architectures is the integration of living cells as functional components into the system. By doing so, it is possible to import the self-repair capability of the living cell at least for the most complex part of the architecture. For example, a cell can be used as a living biosensor that - in contrast to a conventionally engineered device - can replenish its receptors upon contamination or degradation and thus stay functional over a long period of time [21, 72]. Other prototypes have used living cells as mechanical actuators. Prokaryotic [73, 74] and eukaryotic cells [75] have been employed to pump fluids in microfluidic set-ups.

Early steps to interface living cells as information processors have also been taken. A number of groups have interfaced neurons on chips (cf., e.g. [76]), but it is also possible to connect to more robust cells. The plasmodia of *Physarum polycephalum* discussed above can be integrated into electronic circuits and interfaced either optically [20] or with impedance

measurements [77]. An interesting aspect of integrating plasmodia enclosed in microfluidic chips with electronic circuits (Fig. 7) is that they can be stored for several months in a dormant (sclerotia) state and activated within 1.5 h upon water contact. Plasmodia and sclerotia have a very large number of redundant copies of their genetic information and can therefore withstand significant damage between periods of self-repair. It is conceivable that in the future such devices could be employed to withstand periods of high radiation without requirement for heavy shielding, by relying on the combination of the genetic redundancy provided by millions of nuclei in combination with self-repair. These prototypes point towards the development of bio-hybrid devices with components that are alive. Such future living devices are attractive in the context of space technology, because of their potential to enable self-repair and self-reconfiguration, as well as efficiency with regard to both material and energy [78].

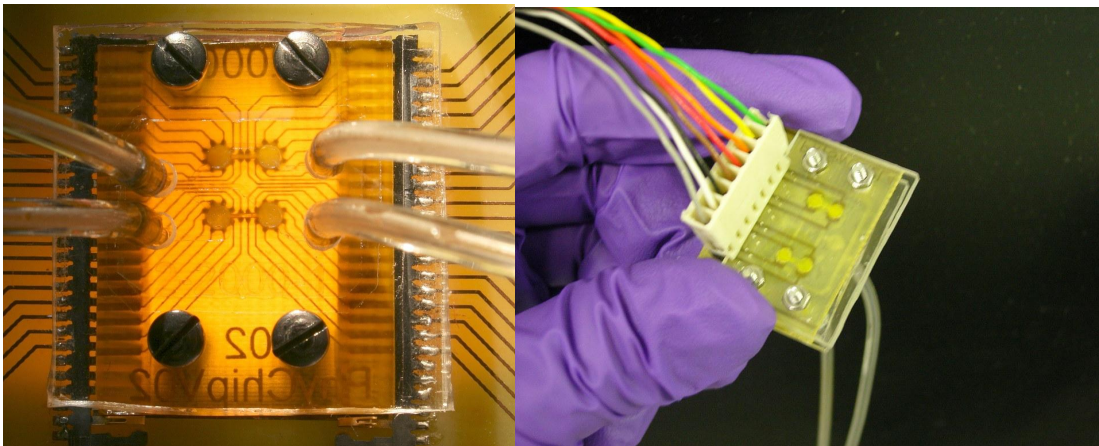


Fig. 7. *Physarum polycephalum* on microfluidic chips for integration with electronic circuit.

Conclusions

Biological systems achieve persistence through a combination of resistance and resilience mechanisms - however, with a greater reliance on the latter by exploiting both redundancy and information processing. The combination of both is a necessity, since information and the ability of information processing are required for directing self-repair and other persistence measures. Organisms evolved and apply varying degrees of resistance and resilience mechanisms depending on the extremity of environmental disturbances. While redundancy is commonly applied for mission-critical components in engineered persistence, the low-level physical information processing required for self-repair is not easily duplicated in conventionally engineered systems. A potential solution to the challenge of building light, persistent devices of high complexity may be provided by semibiotic architectures that defer the burden of maintaining the most complex components to biological systems. Such a strategy can be viewed as an intermediate solution that is closer to realisation than completely artificial systems capable of self-repair. This solution has its own challenges, such as the risk of contamination and in case of living components, the potential of evolving away from the functionality required by the host architecture. Among the challenges of making semibiotic persistence a useful technology is the requirement to integrate biological components with conventional engineering. There is rapid progress in the development and miniaturization of suitable interfaces, but it will also be necessary to develop design strategies capable of coping with autonomous components that cannot be characterized by rigid specifications. In fact, the need to adapt the prescriptive control of present engineering approaches to architectural designs that are more suitable for living matter, may be the largest obstacle to overcome on the path to semibiotic persistence.

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