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It’s “Goodbye” from me and “Hello” from him

by Freddie Theodoulou, Science Editor

They say that all good things must come to an end and it is with very mixed feelings that I put fingers to keyboard to write my valedictory editorial for The Biochemist. The day job is calling – rather insistently! – and after eight years as Science Editor, it’s high time to hang up my red pen and head back to the lab (well, ok, the office). It’s been an honour and a privilege to take care of our Society’s magazine, a role that has brought wonderful opportunities to meet and work with a host of fine minds and lively personalities. I will miss this enormously and will always feel a tiny thrill when I see a copy of The Biochemist lurking in a Departmental coffee room when I’m out and about.

Although I won’t miss the pressure to knock out 500 coherent words every two months, part of me doesn’t want to go, much like David Tennant as the Tenth Doctor Who, expressing a poignant moment of regret on the brink of regeneration. A little research revealed that The Biochemist turns 30 this year and the regenerating Doctors strike me as an apposite analogy for The Biochemist editors, with each actor bringing fresh perspective and a different character to a long-running series. Although editorial responsibility was originally shared between Society officers, Roy Burdon and Alan Malcolm, the first General Editor proper was Harry Bedford. Harry was succeeded by Frank Burnet and Richard Reece in 1994 and 2002, respectively, and I started in 2010 which I figure makes me the Fourth Doctor (Tom Baker). Now you are all wondering who will be The Biochemist’s Fifth Doctor, and, at risk of overdoing the analogy, I am delighted to announce I will be handing the keys of the TARDIS to Chris Willmott in the New Year. I leave Chris in the very capable hands of our in-house Editor, Helen Albert and the magazine’s Designer, Rowena Weedon; it has been a pleasure working with them.

It just remains to offer my wholehearted thanks to all the people (past and present) who have helped in different ways to create and produce The Biochemist, many of whom have become good friends during my tenure. And all our authors! I continue to be delighted by the willingness of busy and eminent scientists to write for the magazine. No-one gets paid for features and we don’t have an impact factor that can adorn a CV, but I can tell everyone who has given up precious time to write engaging and erudite articles that your efforts have been appreciated enormously by our readers. My gratitude also goes out to Wikipedia (not always one hundred percent correct, but spectacularly convenient and so often my first port of call), the Thesaurus function of Microsoft Office Word, the many people who, wittingly or unwittingly, gave me ideas for things to write, ‘The Duke’ for invaluable contributions to the creative process, but perhaps above all, those of you who were kind enough to say that you enjoyed reading my ramblings. Thank you.
The history of our planet is underpinned by roughly 4 billion years of microbial evolution. From its emergence in a (probably) hot and anoxic environment, microbial life has evolved to colonize every available niche on our planet, including the inside and outside of other organisms. Yet, the emergence and evolution of microbial metabolism remains a major unsolved problem. How have microbes adapted to colonize every available environmental niche, including other organisms? How did they evolve to colonize mammals and our human ancestors? Answers to these questions will allow us to understand the emergence and evolution of life on our planet, inform the search for life elsewhere and, in the making, reveal important insight that will help us fight infections.

A microbial world

There is little doubt today that prokaryotes were the earliest forms of life on our planet. Life as we know it is currently based on energy-conserving reactions that allow the exploitation of naturally occurring redox gradients to perform chemical, mechanical and transport work. Over 30 years of research on the origin of life has led to recognition of the importance of molecular hydrogen, carbon monoxide and naturally occurring electron flows across mineral surfaces as possible early energy sources in protometabolism. Assuming that we have identified the earliest forms of energetic metabolism, we still have to understand how microbial metabolism diversified from relatively few early energy-conserving reactions to almost every redox couple available on earth.

On our planet, microbes influence biogeochemistry, climate and overall planet functioning. They outnumber any other living organism by far, with recent estimates of microbial biomass ranging between 9 and 31×10^29 cells, and control all major biogeochemical cycling of elements. Microorganisms produce about 50% of the oxygen we breathe, and control the emission of important greenhouse gases like nitrous oxide and methane. They are responsible for the re-mineralization of organic matter, effectively recycling living biomass. Over time, they have influenced the overall redox state of the surface of our planet and permanently bioengineered the environment.

While the influence of environmental parameters in forcing the evolution of metabolic traits was recognized a long time ago, the ability of life to influence environmental conditions has been long overlooked. Only in the last decade have we begun to appreciate how the geosphere and biosphere have co-evolved, ultimately resulting in the complex network of metabolic reactions we see today.

Besides controlling biogeochemical cycles, microbes also affect human and animal health. Microorganisms that comprise both beneficial strains and potential pathogens colonize the exposed areas of our bodies and our gastrointestinal tract. Recent studies have highlighted the importance of a balanced microbiome on the functioning of our immune systems, and the gut microbiome has been shown to directly influence brain function via the gut–brain axis. We also know that an increasing number of pathogens are developing significant resistance to current antibiotics, and the threat of infections by multidrug-resistant bacteria is rising quickly.

Understanding how microbes have adapted to colonize every available environmental niche, including the outside and inside of other organisms, may hold the clue to a more efficient fight against microbial diseases. The reconstruction of the evolutionary history of key biochemical functions is critical to understanding this process.

In the broader context of the earth’s microbiome, only very few species of bacteria are capable of causing human diseases. These pathogens evolved the ability to colonize humans in relatively recent times, possibly from environmental relatives that pre-dated humans and mammals. Phylogenetic studies suggest that some of these pathogens might have evolved from ancestors that inhabited geothermal environments. Hence, the microbiology of extreme environments may provide a new angle in understanding the emergence of pathogenesis, the role of adaptation and innovation in colonizing new
environments, and the ecological dynamics within microbial communities. All this information may prove critical in our fight against diseases.

**Extreme environments as a window into the past**

Extreme environments are ubiquitous on our planet and include diverse ecosystems, characterized by a broad range of environmental conditions, e.g. high and low pH, extremes of temperatures, high salinity and pressure, low energy availability and low water activity. In particular, geothermal environments are widely distributed on our planet, both underwater and on continental settings (Figure 1). Given their relationship with volcanic activity and plate tectonics, it is safe to assume that geothermally influenced ecosystems existed throughout the entire 4.5 billion years of history of our planet, and were likely more widespread during the early stage of the evolution of our planet.

Conditions in modern geothermal environments resemble those present on the early Earth and support a broad diversity of microbial species. Therefore, microbes living in these ecosystems probably carry both ancestral metabolic traits inherited from long gone ancestors, as well as more recently acquired traits that reflect their adaptations to Earth’s changing conditions. For instance, extant strict anaerobes inhabiting anoxic geothermal environments inherited the metabolic machinery to conserve energy using redox couples of volcanic origin (e.g. hydrogen and sulfur) and to fix carbon dioxide of magmatic origin. However, it appears that the same organisms also acquired the ability to cope with reactive oxygen species to adapt to the increasing atmospheric oxygen partial pressures that have arisen on earth over the last 700 million years. By contrast, it is reasonable to hypothesize that beneficial and pathogenic microorganisms that today colonize the inside and outside of higher organisms, including ourselves, have evolved recently. Complex animals emerged around 555 million years ago, mammals have been around for about 220 million years and our human ancestors for about 200 thousand years. Thus, geothermal ecosystems may be used as a natural laboratory to understand the evolutionary history of microorganisms that originated in these habitats and later adapted to colonize mammalian hosts.

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*Figure 1.* Example of marine and continental geothermal environments. A view of a black smoker in a deep-sea hydrothermal vent along the 9.50°N segment of the East Pacific Rise (top left); a scuba diver swimming through the gas hydrothermal emission of the shallow-water hydrothermal vents off the coast of Milos Island, Greece (top right); and a hot geothermal pool in Yellowstone National Park, USA (bottom). Microorganisms inhabiting ‘relic’ environments resembling early earth, such as geothermal habitats, provide excellent models to reconstruct the emergence and evolution of metabolism.
Extremophiles: modern organisms, ancient trade

While extant extremophiles inhabiting geothermally influenced ecosystems are modern organisms that co-evolved with our planet and had to adapt to changing conditions, they still harbour ancestral metabolic traits. However, the process of reconstructing the emergence and evolution of metabolism is hindered by the difficulties of unequivocally distinguishing new adaptations of older functions from true innovation. Closely related microorganisms whose members inhabit ‘relic’ environments, such as geothermal habitats, as well as ‘recent’ environments, such as the gastrointestinal tract of mammals, provide excellent models to reconstruct how metabolism evolved within the various lineages.

Epsilonproteobacteria are such a group of closely related bacteria, in that they comprise organisms adapted to sulfidic environments (e.g. thermophiles from hydrothermal vents), as well as species that colonize invertebrate and mammalian hosts, including human pathogens (Figure 2). This group of bacteria includes, among numerous environmental strains, the pathogenic Campylobacter spp. and Helicobacter pylori, well-known human pathogens with relatives in all known mammals, as well as the family Nautiliaceae, exclusively harbouring thermophilic strains from geothermal environments. Geothermal processes have always existed on earth, well before oxygen became available as a terminal electron acceptor for respiration and facilitated the subsequent evolution of higher forms of life, all the way to mammals. Therefore, it is reasonable to hypothesize that Epsilonproteobacteria that colonize mammalian hosts, such as the rumen commensal Wolinella, and the human pathogens Campylobacter and Helicobacter spp., have evolved from anaerobic, thermophilic ancestors whose extant relatives are represented by species that inhabit geothermal environments (e.g. Caminibacter, Nautilia, Cetia spp.). Recent phylogenetic studies confirmed this hypothesis and showed that extant thermophilic Epsilonproteobacteria from deep-sea hydrothermal vents represent the most ancient lineages of this class and that their commensal and pathogenic relatives evolved more recently. Therefore, disentangling the evolutionary relationships between hydrothermal vent Epsilonproteobacteria and human pathogens can provide insight into the evolutionary history of microbial adaptation and the origin of pathogenesis.

Recently, our understanding of the ecology, physiology and metabolism of Epsilonproteobacteria has increased rapidly, and the genomes of representative members of this class have been sequenced and are publicly available. Within the Epsilonproteobacteria, it is possible to identify the ‘core’ genome common to all representatives of the group, the ‘shell’ genome, which includes all the genes shared within a subgroup of organisms, and represents common adaptive strategies, and the ‘cloud’ genome, which includes lost or acquired genes. Further, studies of the transcriptome and proteome of the pathogenic Epsilonproteobacteria, Campylobacter jejuni and H. pylori, have shown that when these pathogens establish an infection cycle, they develop biofilms, which are associated with the expression of genes involved in quorum sensing, flagellar motility, adhesion, exopolysaccharide synthesis and protein glycosylation, among others. Deep-sea and shallow-water hydrothermal vent Epsilonproteobacteria also establish biofilms when they colonize the oceanic crust in proximity to vent emissions or when they establish symbiotic relationships with vent invertebrates (Figure 3). The quorum sensing mechanism in pathogenic and commensal Epsilonproteobacteria, which regulated the expression of biofilm-related genes, is conserved in their deep-sea vent relatives. Understanding which portion of the pathogens’ metabolic machinery has been conserved

Figure 2. Phylogenetic tree showing the position of cultured pathogenic and environmental strains of the Epsilonproteobacteria. Two hypothetical patterns of gene flow from thermophilic geothermal strains (top left) to commensal and pathogenic strains (bottom) are shown.
and adapted to new conditions and what portion of their genomes is an acquired trait is fundamental in delineating the evolutionary journey from environmental strains to human pathogens.

**Making of a pathogen**

Numerous key metabolic functions seem to have been repurposed in the Epsilonproteobacteria lineage during the change from inhabiting extreme environments to becoming human pathogens. In the last few years, several studies have focused on the general make-up of the genomes of Epsilonproteobacteria and specific functions such as nitrate reduction, quorum sensing and chemotaxis.

Chemotaxis is a key mechanism that allows bacteria to move in response to a chemical stimulus and is important in the onset of colonization of the gastric epithelium by the pathogenic bacterium, *H. pylori*. Previous studies have identified that the ChePep protein has a key role in controlling chemotaxis in this bacterium. This peptide controls flagellar rotation and is necessary to establish *H. pylori* colonization of the gastric glands. Chemotaxis is found exclusively in Epsilonproteobacteria and is conserved throughout this group. Genetic analysis coupled to differential interference contrast imaging of swimming behaviour and animal infections showed that *H. pylori* ChePep mutants swim abnormally and fail to colonize the gastric glands. Further, complementation of *H. pylori* ChePep mutants with the *ChePep* gene homologues from the deep-sea vent Epsilonproteobacterium, *Caminibacter mediatlanticus*, and from the zoonotic pathogen, *C. jejuni*, showed that ChePep is functionally conserved across the Epsilonproteobacteria. Overall, these findings indicate that the *ChePep* gene is part of the core Epsilonproteobacterial genome and may represent an early evolutionary invention that contributes to the colonization of the host, being either a deep-sea vent invertebrate or a mammalian host.

Quorum sensing is a communication mechanism between cells that depends on their density and the production of signalling molecules, and it is used by bacteria to control gene expression, including virulence genes and functions associated with biofilm formation and host colonization. One quorum sensing system that appears to be widespread across the bacterial domain is based on a furanone derivative known as autoinducer-2 (AI-2), which is synthesized by the LuxS enzyme. In 2015, Pérez-Rodriguez et al. demonstrated that LuxS is conserved in all Epsilonproteobacteria and that the mesophilic strains, including pathogens, shared a common LuxS ancestor nested within the thermophilic lineage. These findings suggest that the epsilonproteobacterial LuxS lineage originated in geothermal environments.

![False color transmission electron micrograph of a pure culture of the mesophilic epsilonproteobacterium, Sulfurovum riftiae isolated from a biofilm growing on the tube of the deep-sea hydrothermal vent tubeworm Riftia pachyptila. The working hypothesis is that deep-sea vent Epsilonproteobacteria, such as *S. riftiae* and its commensal and pathogenic relatives, adopt conserved mechanisms to colonize vent invertebrates, mammals and human hosts, respectively.](image)

Nitrate reduction is a major pathway of respiration in both environmental and pathogenic Epsilonproteobacteria. Thermophilic members of the *Nautiliaceae* couple hydrogen oxidation to the reduction of nitrate to ammonia or to the reduction of elemental sulfur to hydrogen sulfide. This latter pathway appears to be ancient, and is widespread among anaerobic bacteria inhabiting geothermal environments. Nitrate is depleted in hydrothermal fluids, but in modern oceans it is present at millimolar concentrations in deep seawater. Vent microorganisms are exposed to it along redox gradients that form at the interface between fluids and seawater. Similar nitrate concentrations are also common in human body fluids, and nitrate has been shown to be an important signalling molecule during inflammation and at the onset of virulence in several opportunistic human pathogens. The ability to respire nitrate via the periplasmic nitrate reductase (Nap) appears to be conserved within the Epsilonproteobacteria (with the exception of some strains of *Helicobacter*) and probably represent a trait acquired during the evolutionary history of the group.

Comparative analysis of the nap gene clusters of various bacteria revealed that Epsilonproteobacteria lack the NapC subunit, identified as a key component of the electron transport chain during nitrate reductase in *Gammaproteobacteria* (Figure 4). A recently formulated hypothesis posits that the Epsilonproteobacterial nap cluster could be better adapted to the nitrate-limiting conditions of both deep-sea vents and human fluids. However, this hypothesis has not been tested experimentally.

Taken together, these findings highlight the evolutionary link between environmental strains and pathogens, and underline the importance of studying the evolution and adaptation of microbial metabolisms using a broad evolutionary approach. However, growing biases in our sequence databases and a lack of functional information on key metabolic pathways of relevant organisms may hinder our ability to reconstruct the evolutionary history of key biochemical functions.
Making sense of data: a problem of database quality

While there is growing excitement in the field of extremophile molecular biology, and geothermally influenced ecosystems offer an ideal laboratory for the study of the plasticity and evolution of microbial metabolism, the community is facing increasing challenges due to difficulties in annotating gene functions. The size of the sequence database is increasing exponentially, with a large number of new genomes sequenced every year, expanding the diversity of known genes. Currently, during genome annotation, function is assigned to a new gene based on sequence similarity to other genes in the database.

While this approach has proved useful in speeding up the annotation of newly sequenced genomes, it is prone to error. There is a growing need for biochemical and biophysical studies on a wider set of microbial proteins from a broader range of bacteria. To properly define gene function, one needs to obtain information on the enzyme the gene encodes, including, among other parameters, substrate specificity and affinity and reaction kinetics. Such biochemical characteristics will help to constrain microbial physiology and function and reconstruct the evolutionary history of key biochemical pathways.

There are several reasons associated with the slow progress in annotating gene functions in microorganisms from geothermal environments. First, omics-based
surveys of microorganisms inhabiting geothermal environments often advance at a faster pace than the isolation of representative microorganisms necessary for physiological, biochemical and genetic studies. Second, in most cases, a genetic system that allows the generation of knockout mutants in these bacteria has not been developed. Third, the production of large quantities of purified enzymes for biochemical studies is often a limiting step with anaerobic bacteria.

These are exciting times in which the boundaries between medical microbiology and environmental microbiology are becoming blurred, and there are plenty of opportunities to unearth fundamental mechanisms that will allow us to better understand the emergence and evolution of microbial metabolism, as well as how microbes adapted to colonize every available niche on our planet. To capitalize on these opportunities, we will need a better integration of disciplines spanning from geology to biochemistry.

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Donato Giovannelli is a microbial ecologist working on the microbiology of extreme environments at the Earth-Life Science Institute in Tokyo and Rutgers University, USA. Donato’s research focus is on the co-evolution of the biosphere and the geosphere and how life influences planetary-scale processes. By combining field work in remote locations, such as deep-sea and shallow-water hydrothermal vents, continental volcanoes and hot springs, with traditional microbiology and cutting-edge molecular tools, Donato is attempting to reconstruct a blueprint of the evolution of metabolism on earth, and better understand the interplay between life and our planet. For more information about Donato’s research, visit his website: donatogiovannelli.wordpress.com. Email: giovannelli@elsi.jp.

Costantino Vetriani is a professor in the Department of Biochemistry and Microbiology and Institute of Earth, Ocean and Atmospheric Sciences, and the director of the Microbiology Undergraduate Program at Rutgers University. Research in his laboratory focuses on the physiology, ecology and evolutionary history of microorganisms that inhabit marine geothermal environments. Since 1996, Costa Vetriani has participated, either as a research or chief scientist, in over 20 deep-sea expeditions in the Pacific and Atlantic Oceans and in the Mediterranean Sea, and dove in the Deep-Submergence Vehicle Alvin many times. For more information about Costa Vetriani’s research, visit the Deep-Sea Microbiology Lab website: marine.rutgers.edu/deep-seamicrobiology. Email: vetriani@marine.rutgers.edu.

## References


## Additional reading

Life in space isn’t easy, even if you are green

Richard Barker and Simon Gilroy (University of Wisconsin, USA)

In order for terrestrial life to expand beyond the confines of our earthbound existence to bodies such as the moon or Mars it will have to tackle a barrage of stresses, some that it has encountered and adapted to over millions of years of evolution, but some that it will meet for the very first time. Whether reliable, sustainable biology-based (bio-regenerative) life support systems can be developed for long-duration spaceflight and extraterrestrial colonies has therefore become an important area of research. These systems would almost certainly centre on plants and microbes and so questions of how such organisms respond to reduced gravity and radiation become critical. Current research, using approaches ranging from gene expression and protein profiling to detailed growth analyses, suggests spaceflight triggers complex stress responses in these organisms, but that biology has a remarkable ability to cope with the life of a space alien.

To quote Konstantin Tsiolkovsky (1857–1935; one of the fathers of spaceflight): “The earth is the cradle of humanity, but mankind cannot stay in the cradle forever”. We are at an exciting point in our journey to the stars. The International Space Station is providing us with a long-term presence in low earth orbit where we can experiment on what it means to inhabit space. In parallel, space agencies and commercial spaceflight providers are setting their sights on a manned presence on the moon, Mars and the spaces in between. If there is one constant that has shaped the evolutionary history of all organisms, it is gravity; 1G is 1G and always has been. All organisms have evolved with this all-pervasive and unchanging force and so have had no evolutionary pressure to develop adaptations to changes in its level. Yet, in the 1950s, biology entered upon a grand adventure, space. Spaceflight has taken animals, plants and microbes to an environment outside the boundaries that have shaped their evolution. The ‘weightless’ world of spaceflight triggers a myriad of changes in organisms from the cellular to the physiological. Even colonization of the moon or Mars will require life to thrive at ~17 or 38% of 1xG. Couple these effects with the other unique elements of leaving Tsiolkovsky’s protective ‘cradle’, such as exposure to background galactic cosmic radiation, and one could justifiably ask whether biology can make the transition from its terrestrial roots. The answer to this question is that we are still at the very beginning of understanding how the space environment interacts with biological systems.

Increased access to experimentation in space is now beginning to uncover exactly what these new environments trigger in organisms ranging from humans and mice to plants and microbes. The effects on these latter two kingdoms are of particular interest as the mission distances being contemplated are immense and regular access to resupply ships from earth becomes less and less tenable as our sights move from our local surroundings to places such as Mars. Thus, not only will spacefarers have to endure the stresses of their alien environment, they will also have to be self-sufficient for all the nutritional requirements their metabolism demands.

Plants and space

Almost as soon as biological specimens were launched into space, plants were passengers on the rockets and plants have remained a major focus of space research to address two goals. Firstly, spaceflight provides a unique laboratory with which to dissect the role of gravity in modulating biological processes and to conduct weightless experiments that are impossible to perform on earth. In this case, investigating plant physiology, growth and development in space has been driven by curiosity, using this environment to dissect the most fundamental aspects of how plants work. The second driver for putting plants into space is more practical. Plants provide a wide range of services on earth, not least of which are delivering our food and oxygen and purifying our water. Therefore, another major goal for plant space researchers is understanding how to incorporate plants into life support systems that could sustain astronauts long-term missions, so-called bio-regenerative life support. A further bonus to this role in sustaining the food, air and water supply of growing plants during spaceflight that has only just begun to be appreciated, is psychological support. Plants provide a living, growing link to the earth and a break from the highly engineered environments of the space vehicle. The key question that arises from these potential uses in bio-regenerative systems is how do plants respond to growing in space and could they be relied upon to provide critical elements of life support?
Plants do complete their life cycle in spaceflight. For example, in 2000, Mary Musgrave reported seed-to-seed growth of *Brassica rapa* over a 122-day mission on-board the Mir space station, although seed quality was compromised in the spaceflight plants. In addition, the lack of pollinators and the weightless environment of the spaceflight meant that the flowers had to be hand pollinated by the astronauts. The conclusion from many experiments is that plants do grow in space but the question remains, how well and reliably do they perform?

**‘Omics’ and spaceflight**

To help answer the question of how consistently productive plants are in spaceflight environments, we have an increasingly rich set of gene expression and protein profiling data from multiple space agencies and researchers for a range of plants grown in space including: Arabidopsis, rice, mizuna and even the fern Ceratopteris. NASA has also recently developed the GeneLab public data repository (Genelab.NASA.gov) which pulls many of these data sets together (along with many others on species ranging from mice and bacteria, to fruit flies and nematodes), providing an increasingly data-rich set of resources to mine for the molecular fingerprints of spaceflight responses.

Some common themes are emerging from analyses of the plant spaceflight gene expression and protein profiling. There is a disruption of cell wall-related events that may well reflect the reduced mechanical loading from growth in a weightless environment. Thus, changes in the expression of wall-modifying enzymes are a common feature of gene expression analyses from Arabidopsis samples grown in space. Members of the peroxidase family were highlighted by Kwon and co-workers in 2015 as being down-regulated by spaceflight and alterations in transcript levels of these enzymes are also seen in many other spaceflight gene expression studies. Markers of oxidative stress are also regularly observed to be up-regulated across species as varied as rice, Arabidopsis and mizuna. Interestingly, in a spaceflight experiment where Arabidopsis cell cultures were flown on the Space Shuttle, up-regulation of molecular chaperones such as heat-shock proteins was noted. These proteins are thought to protect and repair cellular machinery from damage, so their increase likely reflects response to the cellular-level stresses that these conditions are triggering. Similar chaperone-related responses are seen at the whole seedling level, but the finding that these changes occur in cell cultures implies that this response is to an effect of spaceflight on some common cellular process rather than disruption of the directional gravity-sensing system that operates at the whole-organism level.

The story that emerges from these analyses is that a range of stress-signalling pathways are triggered by spaceflight. The major open question is how far these reflect adaptive responses to components of the spaceflight environment versus induction of inappropriate or random signalling networks in response to conditions that biology has never previously encountered.

**Gravity: more than just up and down**

The ‘weightless’ environment of spaceflight does disrupt many biological processes that rely upon directional sensing – yes, astronauts get disoriented and experience motion sickness when first flying in space and yes, plants lose their directional growth entrained to gravity (gravitropism) such that roots no longer grow down and shoots no longer grow up. This latter effect has been used as a tool to look for responses masked by the overwhelming directional cue of gravity on earth. Research by the Kiss laboratory has revealed how plants growing in space exhibit directional growth towards red light (red light phototropism) that is never visible on earth as the far stronger gravity response masks this light-driven effect.

However, gravity provides biology with much more than simply a sense of up and down. For example, on earth, gravity drives buoyancy-driven convection, i.e. warmer gases expand, are less dense and so rise due to their buoyancy, pulling in gases from below.

Spaceflight exposes terrestrial biology to a series of stresses including altered levels of gravity and increased radiation dosages that are outside life’s evolutionary history. A range of technologies profiling patterns of gene expression (microarray, RNAseq) and protein levels (proteomics) are now being used to try to understand how organisms respond to this situation. Analysis of the model plant *Arabidopsis thaliana* grown in space is providing a window into the complex interplay of stresses that likely shape how biology acts in response to this alien environment. Radiation dosages are shown for the surface of the Earth, the trip to Mars and the range of exposures recorded for the Apollo astronauts during their moon missions.
In a weightless environment, buoyancy does not occur and so such convective mixing of gases is lost. On earth, temperature gradients are ubiquitous and so convective gas mixing is the norm. On the Space Station, without convection, steep gradients in gases build up and rapidly respiring tissues can deplete the oxygen around them. With no convective mixing, O2 resupply is then limited to the rate of diffusion, severely restricting the O2 supply. This effect is thought to lead to the generation of hypoxic zones around metabolically active regions of organisms, such as around rapidly respiring plant roots, which in turn negatively impacts growth and development.

**Radiation: the great unknown**

There is one further factor that contributes to ‘space syndrome’ once biology leaves the cradle of the earth’s atmosphere and the protection of the planet’s magnetosphere – radiation. Indeed, radiation damage has the potential to severely impede a sustained presence of terrestrial organisms away from their evolutionary home. The earth’s magnetic field and the blanket of the atmosphere shields the biosphere from more than 99% of the harmful radiation produced by the sun and background galactic cosmic radiation. The average daily amount of radiation received by humans at the earth’s surface is around 10 microsieverts, with most of this dose coming from geologic sources such as radon gas. In space, the radiation environment is much more pervasive and energetic. Galactic cosmic rays are produced by distant ancient supernovae and permeate space. Indeed, the Apollo astronauts reported seeing bright flashes of light every few minutes during their missions beyond the earth’s protection and eventually these were determined to be from cosmic rays travelling through their eyes. Joining this background of galactic cosmic radiation are solar energetic particles, the ‘solar wind’, comprised of components such as protons fired from the sun during a coronal mass ejection event or as a result of distant stellar flares. How large is the radiation dose once leaving the earth’s protective magnetosphere? While en route to Mars in 2012, the Curiosity rover’s radiation meter was activated and recorded the radiation dosage of a true trip to the red planet. The journey delivered 0.33 sieverts, or about 90 years of background radiation on the earth’s surface in a 253-day trip. Upon arrival, a Mars-bound astronaut would further have to cope with the fact that this planet has no magnetic field and solar winds stripped the atmosphere away millions of years ago, leaving a remnant of about 1% that of the earth. Thus, any organisms that are capable of making the journey would need to find shelter from the inevitable elevated radiation at the planet’s surface. These realizations have spurred ideas including building Mars stations within the protection afforded by deep sheltered trenches on the Martian surface, such as Valles Marineris or the Hellas Planitia.

The key question now is how does this long-term radiation dosage from solar and galactic cosmic radiation affect biology? Once again, we are only just beginning to answer this question. The earth offers us so much radiation protection that performing the requisite long-duration experiments exposing biology to solar and galactic cosmic radiation for months to years have simply proven impossible. However, short-duration exposure experiments have been performed at facilities like the Space Radiation Laboratory at Brookhaven National Lab and so we do have some data on radiation responses to compare with spaccflight effects. The gene
expression data for Arabidopsis plants grown on the International Space Station show some changes expected for radiation response, but does not precisely mimic the patterns seen in the radiation experiments performed on earth. Confounding factors here may be that the low earth orbit of the Space Station is still within a large part of the protection afforded by the earth’s magnetosphere, reducing exposure. In addition, it is unknown how closely the acute exposures provided in experiments on earth can mimic the biological effects of the prolonged lower level doses inherent in spaceflight. Whether radiation exposure will be just a technological hurdle to overcome or will become a permanent stress that life in space will have to somehow accommodate remains a critical question for our future away from the Earth.

**Future perspectives**

Humanity has long had Mars in its collective imagination and for centuries science fiction writers and scientific visionaries have postulated what might be found there and how the journey could be achieved. The flight to Mars will send explorers many millions of miles further than any other human has ever travelled. Research conducted on the International Space Station is now revealing many of the physiological consequences associated with such a trip but we are far from understanding just how terrestrial biology is affected by leaving the earth’s protection. Over many millions of years, evolution has tailored organisms to thrive in the conditions of Tsiovkovsky’s cradle. The challenge now is to understand whether we will have to somehow bring the conditions of earth with us wherever we travel or whether given enough biological insight and appropriate technology (both engineering- and biology-based) that the spaceflight environment will not be so alien after all.

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**Further Reading**

Terrestrial life has evolved several general mechanisms for dealing with water loss. Larger organisms, such as mammals, avoid loss by reducing their surface area to volume ratio, having waterproof coverings and reducing water losses involved in essential processes such as respiration or excretion. Another method to avoid water loss in a variable environment is to migrate to better environments when times get hard, for example to burrow deeper into the mud to avoid the drying up of a river bed, or following the seasons across a savannah landscape. A third method is to go into stasis when times are hard, and to remain in stasis until times get better.

Many organisms follow an extreme version of this third option, and are able to survive complete loss of all their body water. When free water becomes available again, they rehydrate, and resume their lives. This process is called anhydrobiosis – life without water. Anhydrobiosis is found in bacteria, many ‘protozoa’, in fungi and in plants. Mosses and lichens on a desert rock, or on a British garden wall on a sunny day, can dry to a crisp and still come back to life when the rains come (rarely in the desert, frequently in the British summer).

**Dried-up animals?**

Among animals, anhydrobiosis is quite common. Many members of the meiofauna – animals with body lengths less than a millimetre that live in the water films surrounding soil grains and on plants and lichens – are frequently challenged by drying of their local environment. Because they are very small, and lack the ability to escape, being able to survive a temporary loss of water is an effective strategy. Unlike larger animals, which can retain water within shells, cuticles or other coverings, meiofauna cannot both respire and prevent total water loss. Thus a zoo of animals can be revived from bone-dry moss by the simple addition of rainwater (See Box). The animals that make-up terrestrial meiofauna are not often seen unless one goes hunting for them. They include nematodes (roundworms), rotifers (wheel animals) and tardigrades (moss piglets or water bears). In each group, many species are able to undergo anhydrobiosis. Our research has focused on the tardigrades. Not all tardigrades can undergo anhydrobiosis. Marine species, and species living in freshwater, are unable to perform this trick, and it is likely that many soil tardigrades are also not anhydrobiotic. However, many species are. When challenged by drying conditions (low relative humidity) they stop feeding and moving, and slowly contract as all their body water evaporates. At the completion of drying out, essentially all their body water has gone, and they form ‘tuns’ – contracted barrel-shaped specks. These tuns can be stored dry for years. The current record is held by some freeze-dried Antarctic tardigrades revived 30 years after they were collected and preserved as part of a herbarium moss specimen. Some species – slow anhydrobionts – need hours of warning that dry times are coming (a period of reduced humidity), while others – rapid anhydrobionts – can be dried in 30 minutes, without problems. Rehydration in both groups is rapid. A tun transforms into a walking tardigrade in half an hour. We have mainly studied two tardigrade species, *Ramazzottius varieornatus* and *Hypsibius dujardini*. These are relatively closely related (they are both members of the Hypsibiidae) but *R. varieornatus* is a rapid anhydrobiot, while *H. dujardini* needs a physiological warning. We have generated genome sequence data for both, and explored the dynamics of transcription during anhydrobiosis, identifying the likely players in the process.

**How do they do it?**

So how do tardigrades (and other anhydrobionts) achieve this remarkable feat? If we take mammalian cells, or other small animals and dry them up, they do not survive. Water loss leads to three major, catastrophic effects in normal living cells. Membranes rely on the interaction between amphipathic lipids and water for their stability: in the absence of water, membranes collapse and fuse. Proteins rely on water for stability and function, and many water molecules are coordinated with each protein, keeping
it in solution; in the absence of water, proteins denature and precipitate. Lastly, water is the solvent for most small molecules and salts in the cell: loss of water results in extreme and damaging effective concentrations of ions and other metabolites. To survive drying out, tardigrades must avoid these three lethal effects.

Our, and others’, analyses of slow anhydrobiont tardigrades entering anhydrobiosis indicates that this triggers expression of a set of genes with revealing features. Some of these genes are members of known heat-shock protein (HSP) families. Many HSPs in other organisms are induced under stressful conditions, but some are constitutively expressed. In general, HSPs serve as chaperones, assisting in the correct folding of newly expressed proteins or in the refolding of damaged proteins. They prevent misfolded or unfolded proteins from interacting with other, functioning parts of the cell machinery and permit recovery from damage. It is likely that the tardigrade HSPs are performing the same function. In a similar vein, a second set of stress-induced protein genes is also found to be up-regulated in drying tardigrades. These antioxidant and detoxification enzymes have roles in protecting proteins from attack by oxyradicals and other noieties generated as a result of, for example, breakdown in the compartmentalization of metabolism in the cell. Surprisingly, both our species have lost some peroxisomal and hypoxia pathways found near-universally in other animals, a loss we attribute to the need to avoid catastrophic recruitment of apoptotic damage processes during anhydrobiosis.

The third group of genes, up-regulated upon entering anhydrobiosis, express small proteins that have no clear domain similarities to other proteins, but share a particular structural property: they are predicted to be natively disordered. Natively disordered proteins are ones that do not appear to have any favoured, stable, three-dimensional structure. They are poorly crystallizable, if at all, and under nuclear magnetic resonance spectroscopy display few stable intramolecular interactions. Natively disordered proteins have also been described in other anhydrobiotic organisms, such as plant seeds (where anhydrins are abundant), in nematodes and in rotifers. While these natively disordered

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Tardigrade hunting

To catch your own tardigrades and other anhydrobiotic animals you need a clump or tuft of moss (one centimetre in diameter) from a richly covered wall or roof, some still spring water, two dessert spoons, a small Petri dish or watch glass and a microscope. A good binocular ‘dissection’ microscope is best, but a simple compound scope works fine – it is just harder to find the animals in the small field of view.

Take the button of moss and place it in one of the spoons. Pour on a full spoonful of still water. Leave for 30 minutes or more if the moss was dry when you got it. Force the water out of the moss and into the Petri dish by squeezing the two spoons together. Let the sediment settle in the Petri dish before looking at the dish under the microscope. Illuminate from below, if possible slightly obliquely.

Under medium power (so the field of view is about a centimetre) slowly scan across the dish, focusing on the sediment, sand grains and moss leaves on the bottom. You are looking for movement – signs of animal life. When you see something moving, stop. Focus up and down, and change the lighting. If you can, zoom in.

After a while, once you have got your eye in, you will identify a menagerie of life in your miniscule world. Nematodes are long, see-through worms, thrashing about, often with their tails attached to the surface of the dish or a sand grain. Rotifers move by looping like caterpillars, and feed by attaching their tails and unfurling their ‘wheel organs’, coronae of cilia that waft food into their mouths. Single-celled ciliates, some as big as the rotifers, swim around bumping into things and occasionally settling to feed.

Then you will spot a tardigrade, clinging onto a leaf or clawing vainly to get traction on the bottom of the dish. They are between ~1 mm and 0.2 mm when adults, have eight stumpy legs, and often paired eyespots on their heads. Each leg ends in claws, which allow the animals to grip and traverse their miniature world.

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Image: A tardigrade, a rotifer and a nematode from a moss clump on a drystone wall in the eastern Cairngorms of Scotland. Close-ups of the tardigrade head, the rotifer containing a large egg and the nematode’s tail. The tardigrade is 0.3 mm long.
Extremes

proteins from different phyla and kingdoms are not orthologous (i.e. they do not derive from a single common ancestor) they share certain properties, such as a sub-repetitive sequence with abundant representation of alanine and valine amino acids, and adoption of an amphiphilic alpha-helical structure upon water loss. These proteins are extremely abundant in dried up tardigrades.

What are these disordered proteins doing? It is likely that they are replacing the water molecules lost to evaporation. Proteins are not volatile, and polar side groups in the anhydribs and the tardigrade anhydrobiosis proteins are well placed to replace the structural water molecules that coat cell membranes and perform essential structural roles in maintaining enzyme and other protein integrity. Excitingly, the rapid anhydrobiosis species constitutively express high levels of just these proteins, explaining their lack of requirement for preconditioning.

A dry tardigrade is a supertardigrade

Water is a dangerous molecule on which to base life. It is liquid over a small temperature range, and most biochemistry is possible only in a small fraction of this range. Freezing kills cells and organisms as ice crystals puncture membranes and force proteins and metabolites into concentrated salt-rich phases. Heat kills organisms as proteins denature and membranes solubilize. However, once water is excluded, and the cells' machinery is stabilized by non-volatile proteins, these temperature barriers are opened.

Anhydrobiont tardigrades have superpowers. They are also cryobionts – they can be frozen with no adverse effect on recovery as there is no water to form ice crystals. They can be heated to above the boiling point of water, as there is no water to lose. They are resistant to pressure changes, as one of the major effects of low atmospheric pressure is loss of water vapour. Dried tuns can be blown like specks of dust into the upper atmosphere and distributed globally, immune to the lack of air pressure and the low temperatures. Biological systems are damaged by radiation, often through the interaction between high energy particles and cellular water, creating oxyradicals that attack DNA and proteins. In the absence of water, anhydrobiotic tardigrades are also resistant to radiation at levels that kill hydrated ones in minutes. R. varieornatus improves its radiation resistance by expressing a protein that traffics to the nucleus and protects the chromosomal DNA. When expressed in human cells this protein reduced the DNA damage caused by X-rays by 50%.

Immune to heat and cold, surviving in the vacuum of near space and resistant to radiation, it has been suggested that the tardigrade tun could be the spore of life's diaspora to other planets. Could they even have been transported here from another planet? Sadly for this attractive science fiction meme, the DNA of tardigrades clearly and unequivocally identifies them as earth animals, related to arthropods (insects and relatives) and nematodes. As not all tardigrades have anhydrobiotic abilities, and the ones that do are nested within non-anhydrobionts, including many marine species, it seems most parsimonious that tardigrades evolved their anhydrobiotic abilities independently here on earth. Tardigrades' ability to survive in (near-earth) space has been tested in European Space Agency experiments on the International Space Station, which showed that they can survive space vacuum and cosmic radiation, but not well, and not for long.

Making tardigrades useful

Tardigrades are near the bottom of lists of organisms that threaten our well-being: they do not cause disease in humans or our farmed species. Similarly, apart from claims of a role in ecosystem functioning, they do not
provide benefits: we do not eat them, or derive life-saving drugs from them – yet. Their main current contribution to human life appears to be that they are ‘cute’. However, the biology of anhydrobiosis offers tantalizing leads for exploitation. If the mechanisms that tardigrades use to survive dehydration could be isolated and deployed elsewhere, their obscurity could be a thing of the past.

Preserving cells and tissues is an important part of modern medicine and agriculture. Important germplasm and cells are frozen away, at expense and sometimes with low recovery rates, and under the ever-present risk of system failure, freezer meltdown and loss. What if cells could be dried and rehydrated at will, simply by infusing them with one of the natively disordered proteins tardigrades have evolved? Personalized tissue banks could be developed and stored cheaply, assuring availability of matched tissues for grafting or therapy. The R. variornatus protein that protects cells against radiation could be targeted to healthy cells surrounding an invasive tumour and the tumour lethally irradiated while the healthy cells survive. A cell bank could be kept securely on a shelf in a lab or medical facility, shipped around the world and deployed where needed. Cellular and live vaccines currently need a chain of (working) fridges and freezers between the production plant and the communities in low- and middle-income countries where they are needed most. Shipping a vaccine costs more than producing it. If the vaccine was dried, stably preserved in a tardigrade anhydrin, it could be posted to the village clinic, kept there ready for use in outbreaks at low cost and high reliability. Tardigrade genes promise to become interesting biotechnology tools.

**Life after death**

One last thought. Life is defined as the presence of biochemical activity, the processing of metabolites into other metabolites with the production and consumption of ATP as its core currency. Life involves the maintenance of ion gradients and thus electrical charge across lipid membranes. Life involves the processing of nutrients into reproductive propagules that carry the genetic material of the parent forward in time.

As a tun, a ‘living’ tardigrade is indistinguishable from a ‘dead’ one. No biochemistry is happening. There is no calorific output, and no enzyme-driven transformations are taking place. No food is being consumed and no waste produced. Its chemical and isotope signatures will indicate that it is likely the product of a living process, but it is not possible to distinguish a tun from a dead tardigrade, or from dead organic matter. Like Schrödinger’s mistreated cat, it is only possible to tell if a tun is alive by rehydrating it, at which point it is no longer a tun. Neither dead nor alive, it exists in a third state of possibility.

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**Further reading**

Salt has been historically used for preventing decay and preserving food, as many microbes are unable to survive under high salinities. Despite this, several organisms – also known as halophiles (from the Greek “salt-loving”) – are specifically adapted and thrive under such conditions. The study of their biodiversity provides us important new biomolecules and biotechnological applications, which are vital resources for the Bioeconomy. Equally important, research on halophiles offers new insights on Life’s resilience, and its possible existence outside our planet.

**White gold**

Salt is the only rock that is directly consumed by humans and part of our regular diets. It is essential to life and is a substantial part of our bodies and cells. The production and trade of salt has generated wealth, fuelled wars and supported empires. It has been used as currency, associated with the first taxes and linked to social unrest. Some historians even place it at the forefront of the movements that led to the French Revolution, Gandhi’s march for India’s independence and the toppling of China’s Imperial Government. Salt’s preserving properties have long been known and have been used for the preservation of vegetables, meat, fish and raw hides, and even for preserving human and animal bodies (in a process currently known as mummification). The biochemical challenges presented by high salt conditions have nevertheless not prevented organisms from surviving and even thriving in these extreme environments.

**Hypersaline environments**

Several natural environments across the globe are enriched in salt and considered hypersaline (i.e. salinity is higher than standard seawater: 3.5%). Typical examples of such environments include shallow coastal areas such as salterns and coastal lagoons, salt flats, as well as a variety of isolated salt lakes and bigger water bodies (e.g. Great Salt Lake, Dead Sea). Less obvious salty environments include pickled food, some typical fermented products used in oriental cuisine, as well as the surfaces of salt-excreting desert or coastal shrubs, human or animal skin, and other places exposed to periodical drying. Among the least-studied hypersaline environments are subterranean brines, evaporite deposits and brine-filled deep-sea basins. Their exploration has been frequently hampered by their remoteness, and technical and sampling impediments, the on-going increase in the number of sampling expeditions, and use of new techniques and equipment is quickly changing our perspective.

**Halophiles and their diversity**

Despite the historical use of salt for preservation and preventing microbial growth, an incredibly wide range of organisms are known to live and thrive in high salinity environments.
salinities. These organisms are collectively referred to as halophiles. Archaea are traditionally perceived as the typical inhabitants of hypersaline environments. Halophilic Archaea (mostly members of euryarchaeal class Halobacteria) are very successful, and thrive under extremely high salinities all the way up to saturation. Members of this group are particularly diverse and are known for their unusual morphologies (Figure 1).

Despite this clear archaeal dominance, halophiles are present in all three domains of the Tree of Life: Bacteria, Archaea and Eukarya. Bacteria in hypersaline environments are more relevant and abundant than originally anticipated. The discovery of the abundant genus *Salinibacter* was a clear turning point, but was followed by the identification of several other groups that are equally successful and abundant. *Salinibacter* was originally mistaken for a member of the Archaea, as it shares several common features with members of this group. Fittingly, a large percentage of its genes have archaeal origin, and were introduced via horizontal gene transfer.

Halophilic eukaryotes tend to be less diverse, but include the very well-known *Dunaliella salina* (a green micro alga) and *Artemia salina* (a species of brine shrimp, popularly known as Sea-Monkeys).

**Applications of halophiles**

Mankind has been making use of halophiles for at least 5000 years. The typical reddish hues observed in saltern crystallizer ponds around the world (Figure 2) are mostly due to carotenoid pigments of halophilic microbes thriving in such environments. The reddening of the brines increases light absorption, speeding up the process of water evaporation and salt production.

**Food industry**

Other examples of ancient applications of halophiles include the production of fish sauce, soy sauce and other traditional fermented foods commonly found in South East Asia. More modern applications in the food industry include the production of natural additives and colourants (e.g. polyunsaturated fatty acids and β-carotene), or exopolysaccharides. Some of these compounds are further used in other sectors including the pharmaceutical, cosmetic, paint, paper and textile industries.

**Compatible solutes**

The protective properties of this heterogeneous family of compounds, produced and accumulated by
some halophiles to cope with life under high salinity, can be applied to a variety of other biomolecules. They are extensively used in biotechnology (as protectants of enzymes, proteins, DNA, membranes and even as whole-cell stabilizers), and several of them can only be produced via biotechnological methods.

**Bacteriorhodopsin**

Some of the most innovative applications of halophiles are linked with bacteriorhodopsin. This molecule is a component of the photosynthetic system of several halophilic archaea, naturally occurring in a two-dimensional crystalline structure. Its chemical and thermal stability, together with its photosensitivity and photocyclicity, clearly surpass any current synthetic materials, making it an attractive source of applications, including holography, artificial retinas, neural networks, optical computing and new types of memories.

**Bioplastics**

Several halophiles are known to produce and accumulate different types of polyhydroxyalkanoates (PHAs), most frequently in the form of poly-β-hydroxybutyrate (PHB). Several of these compounds are seen as a viable, sustainable alternative to oil-derived plastics, with additional advantages such as biodegradability, resistance to water and biocompatibility. The production of such bioplastics by certain species of halophiles is seen as especially promising due to the potential for large-scale growth in abandoned salterns and low risk of contamination. An additional factor is the reduced cost of production, as some species can use cheap substrates such as agricultural waste, and an inexpensive extraction process, since cellular lysis and release can be easily induced by placing the cells in water.

**Other applications**

Additional examples of the wide range of applications of halophiles include the production of several types

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**High salinity environments in the UK**

The most common high salinity environments are usually associated with coastal areas that are exposed to high solar incidence and temperatures. Despite the fact that the UK does not fit this type of setting, we have several locations known for their higher salinities, mostly focused around the NW and NE of England, as well as Northern Ireland (Figure 3).

The most notorious of these areas is probably the Cheshire Salt District, particularly in the areas around Northwich, Middlewich and Nantwich (the suffix -wich is usually associated with salt production). Indeed, this area has been involved in the production of salt since before Roman times, although modern commercial activity seems mostly restricted to extraction of salt at the Winsford salt mine (one of the biggest in Europe), and production of brine at the Holsford brine fields. The district is also known for the presence of several brine springs, brine fields and salt flashes (Figure 4), which are poorly documented and remain chronically underexplored.

**Figure 3:** Distribution of salt-bearing strata and principal salt-producing sites in the UK (Reproduced with permission of the British Geological Survey © NERC 2017)

**Figure 4:** The Anderton Brine Springs are one example of an underexplored hypersaline environment in the Cheshire Salt District

Additional noteworthy hypersaline areas in the UK include Boulby mine (located in North Yorkshire and hosting the Boulby International Subsurface Astrobiology Laboratory) and Droitwich (Worcestershire).
of enzymes, as well as gas vesicles for bioengineering, highly resistant liposomes for the cosmetic industry and antimicrobial compounds (halocins). Halophiles are also increasingly used for bioremediation of contaminated soils and waters, the recovery of saline soils for farming and the enhancement of oil recovery.

**Long-term viability of halophiles: implications for astrobiology**

The exploration of the microbiology of rock salt and ancient salt deposits has led to the isolation of halophilic microbes, fuelling a heated debate on their long-term survival. A large body of evidence seems to support that halophilic archaea are particularly well suited for long-term preservation in the fluid inclusions present in such rocks and further studies have analysed the effects of entombing mixed cultures in controlled crystallization experiments. Related to this, considerable interest has been raised regarding the implications on the exploration of salt deposits beyond Earth.

The cross-disciplinary field of astrobiology, which focuses on looking for evidence of life outside our planet, has taken a particular interest in high salinity environments and their microbes. Indeed, there is significant evidence for the presence of salty oceans in several icy moons of the outer solar system (e.g. Europa and Enceladus) and of brines in the subsoil of Mars. The identification and exploration of hypersaline environments on our own planet provides us with helpful terrestrial analogues that will facilitate future studies of these extraterrestrial brines. Likewise, the study of halophiles, from their biodiversity, to their resilience and their adaptations to extreme conditions provides vital information for the search of potential microbial inhabitants in such locations.

Another trending, vital area of halophile research in astrobiology is planetary protection. This field aims to prevent interplanetary contamination of other bodies of our solar system with biomolecules or viable microbes from earth (forward contamination), or of potential extraterrestrial microbes being transferred to our biosphere (back contamination). The transport of such contaminants in space probes would lead to false positive results when looking for evidence of life on other planets. Furthermore, the transport of halophiles in particular, could have devastating consequences for these extraterrestrial ecosystems, and their potential microbial inhabitants.

**Future directions**

The exploration of hypersaline environments and their inhabitants is a diverse and thriving field of research. Such studies provide a valuable source of new microbes and new biomolecules, which are relevant for a very wide range of fields, from microbial ecology and biodiversity, to biotechnology and even astrobiology. Further efforts to identify and study unexplored new hypersaline locations in the UK and across the globe contribute to the discovery of new microbes and applications, and will lead to important new insights into the diversity and resilience of life.

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**Additional reading**

- Antunes, A., Simões, M.F., Grötzinger, S.W., Eppinger, J., Bragança, J. and Bajic, V. B. (2017) Bioprospecting Archaea: focus on extreme halophiles. In Bioprospecting (pp. 81–112), Springer International Publishing
Forty years ago, scientists discovered an animal at the bottom of the ocean that changed forever how we view life on this planet. Abundant, thriving animals were not expected in the deep sea, due to the very low levels of organic carbon that sink down from above. The giant tubeworm *Riftia pachyptila* pays little attention to this problem, having renounced its mouth and digestive system during the course of evolution. Instead, this animal relies on a partnership with internal bacteria that act as a built-in source of nourishment and, in exchange, *Riftia* performs unparalleled physiological feats.

### Extraordinary physiology

Deep-sea hydrothermal vents are home to a variety of invertebrate species, many of which host chemosynthetic bacteria in unusual symbiotic arrangements. *Riftia pachyptila* is probably the most successful invertebrate host living at the vents along the East Pacific Rise. These gigantic, gutless worms must meet the metabolic needs of their symbionts. The bacteria are housed inside their cells, snuggled between mitochondria and a nucleus, within a novel organ called the trophosome (literally meaning ‘feeding tissue’) not observed in any other animal lineage. Unlike other animals, *Riftia* must take up and transport carbon dioxide (CO$_2$) and hydrogen sulfide (HS-) to their symbionts. Typical animals respire CO$_2$, having produced this waste product from the oxidation of organic carbon – like humans breathing out CO$_2$ after eating scrambled eggs for breakfast. Further, HS- is an incredibly toxic molecule that can (and often does) cause death when present in very low concentrations in much larger animals, such as humans. On top of this, the primary metabolism of the internal symbionts—sulfide-driven chemosynthesis – i.e. conversion of CO$_2$ into organic carbon using energy from the oxidation of reduced sulfide compounds – results in the massive production of protons (H$^+$). This would normally drive the internal pH of these worms to fatally acidic conditions, were it not for their souped-up ability to efficiently get rid of these ions. All things considered, being a host to intracellular chemosynthetic symbionts is an intimate relationship that, while critical to survival, requires physiological compromise and a great deal

A large clump of red-headed *Riftia pachyptila* tubeworms, two miles deep in the Gulf of California, soaking up the sulfide emanating from nearby hydrothermal vents. © Monterey Bay Aquarium Research Institute
of effort by this unusual, yet incredibly successful, deep-sea worm.

**Life in the abyss**

By the 1930s, early accounts of life in the deep sea (based mainly on eyewitness accounts by Dr William Beebe, a pioneer submersible diver) dispelled the notion that the deep sea was an extreme, inhospitable, wasteland, virtually devoid of life. Nothing, however, prepared scientists for the revelation made on-board the *R/V Lulu* in February 1977, off the Galapagos Islands. In 2500 metres of water, they saw thriving, dense, animal communities that rivalled tropical rainforests in biomass – despite the absence of light, deep at the bottom of the ocean. The discovery of life near these underwater volcanoes ('hydrothermal vents', as they are called), fuelled almost entirely by chemicals gushing from superheated fluids, forever changed our idea of the outer limits of life on this planet.

**Enabled by a secret partner**

When dense populations of worms and bivalves were first reported from deep-sea camera tows along the Galapagos Spreading Center, they were described as filter-feeding organisms, subsisting by gathering up the very little organic carbon that remains suspended in seawater at a depth of 1.5 miles. The fact that these worms had no mouth or digestive system must have cast doubt on these initial assumptions. But, it was not until groundbreaking examinations by two research teams ultimately uncovered the secret to the success of these unusual animals – a symbiotic merger with chemoautotrophic bacteria. One research group (at Scripps Institution of Oceanography) took an enzymatic approach and tested *Riftia* tissues for enzymes found only in metabolic pathways of autotrophic organisms (ex. bacteria and plants), including ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCo) and adenosine phosphosulfate reductase. High activities of these and other enzymes suggested the presence of a second organism, an autotrophic bacterium, within the tissues of the enigmatic deep-sea worms. Simultaneously, a research team at Harvard University used electron microscopy to observe bacteria, packed like sardines within the unusual trophosome tissue of *Riftia*. These unprecedented findings put to rest the idea that somehow *Riftia* could sustain very large populations based solely on the uptake of small particulate carbon, and kicked off a scientific revolution of sorts, unveiling the powerful and pervasive nature of bacterial partnerships with marine invertebrates.

A worm that acts like a plant

Autotrophy is a term given to an organism that creates its own organic carbon from inorganic carbon (the literal translation of autotrophy is ‘to generate one’s own food’). Numerous studies in the 1990s confirmed that the bacterial symbionts of *Riftia* require so much CO₂ to support not only their own organic carbon production, but also that of their fast-growing worm host. The animal as a whole exhibits net CO₂ uptake from the surrounding seawater, thus behaving like a plant. *Riftia* worms accomplish this CO₂ uptake by virtue of precision
pH control (they maintain a blood pH differential 1 pH unit above the slightly acidic environment, equivalent to 10-fold more hydrogen ions) and an enzyme known as carbonic anhydrase, that catalyses the interconversion of CO₂ and bicarbonate ions in seawater, thereby facilitating movement of inorganic carbon into the animals. Based on recent genomic and proteomic analyses, we now know that the *Riftia* symbionts are also able to use two different pathways for the conversion of CO₂ into organic carbon: the well-known Calvin–Benson cycle and a reverse version of the citric acid cycle, known as the reductive tricarboxylic acid cycle. Why the bacterial symbionts of *Riftia* have such carbon fixation versatility is not known, but scientists suspect this may be a way to respond to rapid environmental changes, including sulfide availability, and to accommodate enzymatic sensitivities to compounds such as oxygen.

A towering assemblage of *Riftia pachyptila* tubeworms, some of which no longer appear to be alive (at left), likely due to changes in the flow of life-giving hydrothermal fluids. © Monterey Bay Aquarium Research Institute

The manipulator arm of the R.O.V Doc Ricketts prepares to sample a piece of the billowing hydrothermal chimney, nearby small clumps of *Riftia pachyptila* tubeworms. © Monterey Bay Aquarium Research Institute
Human-like haemoglobins allow sulfide transport

In addition to CO$_2$, the bacterial symbionts must also be supplied with ample amounts of HS$^-$ in order to produce enough ATP to fuel the expensive fixation of carbon. These worms actually take up the charged form of HS$^-$ via surface transport proteins. As mentioned, sulfide is not only an excellent energy source, it is incredibly toxic, swiftly poisoning many metabolic pathways, including aerobic respiration. *Riftia* accomplishes this proverbial dance with death by using haemoglobin much like our own, to bind and transport sulfide. Haemoglobin is a type of respiratory pigment (i.e. a coloured protein involved in gas exchange) found in many animal lineages, and some plants. It is thought that this molecule originally evolved to bind and detoxify gases, including oxygen, but was co-opted as a taxicab for oxygen delivery to the tissues of active, larger animals. Haemoglobin is also very attracted to HS$^-$, in addition to oxygen, which is partly the reason for sulfide toxicity in animals. *Riftia* possesses not one, but three different haemoglobin molecules that travel within circulatory vessels, moving sulfide from the surface of the feathery anterior plume to the bacteria-containing trophosome. Once at the location of the symbionts, deep inside the animal, a molecular hand-off occurs; the haemoglobin releases both the oxygen and sulfide it carries. The symbionts then use these two compounds together to generate ATP via substrate level phosphorylation and via traditional oxidative phosphorylation through an electron transport chain. In this way, toxic sulfide is kept bound for its entire residence time inside of the animal and is never free to poison either partner.

Internal ion balance is critical

The maintenance of a proper internal pH is critical for all living organisms. However, in the case of *Riftia*, it is paramount, given that this makes possible the uptake, unusual for an animal, of both CO$_2$ and sulfide. In experiments on-board the research ship, worms are collected from the seafloor by submersible pressurization to *Riftia’s* optimal pressure – 3000 psi (i.e. pounds per square inch; imagine the equivalent of 10 baby elephants sitting on every square inch of your body). Exposure of these experimental worms to chemical inhibitors of specific ion transport processes revealed H$^+$-ATPases as the dedicated mechanism by which *Riftia* counteract the build-up of acidic end-products of symbiont metabolism (they maintain an alkaline internal pH of 7.0–7.4, versus the surrounding environment, of pH 6.0). Total ATPase activities measured in *Riftia*, in response to the internal production of protons by their beneficial symbionts, are three times higher than those observed in other marine worms, thus making them champions of the acid-base balance Olympics.

More mysteries await

*Riftia* provided the first ever demonstration of a symbiosis between a marine invertebrate and chemoautotrophic bacteria. However, shortly after this discovery, numerous other chemosynthetic symbioses were revealed in both the deep-sea and shallow water sulfide-rich habitats, including seagrass beds, mangroves, estuaries and sewage outfalls. These novel symbioses were considered exceptional within the animal kingdom until the advent of molecular tools that allowed the rapid assessment of bacteria associated with all kinds of habitats and organisms, including other animals, plants and even some protozoans (single-cell eukaryotes). Even today, novel bacterial symbioses are being discovered at a rapid pace – symbionts that can use hydrogen as an energy source, in addition to HS$^-$; marine bivalves that have sulfide-utilizing autotrophic symbionts, as opposed to their typical wood-degrading heterotrophic symbionts; and even a recent discovery of symbioses in both mussels and sponges based on short-chain alkanes as energy sources. What began as a niche field of research now provides fundamental knowledge about the crucial cooperation among organisms, including bacteria and humans. Without a doubt, the discovery of giant tubeworms at the bottom of the ocean is one of the greatest discoveries of the 20th century.

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Dr Shana Goffredi is an Associate Professor of Biology at Occidental College. Her research interests mainly concern beneficial symbiotic partnerships between bacteria and marine invertebrates. For 20 years, she has been exploring the deep ocean. She focuses on the physiology and biochemistry of deep-sea symbiotic systems, within the context of ecological questions and how environmental influences dramatically affect their functioning. At Occidental College, she teaches courses on zoology, microbial diversity and symbiosis. Dr Goffredi’s funding has come from the National Science Foundation, and she has published in journals such as Proceedings of the Royal Society, Environmental Microbiology and Science. Her BS degree is in Biology/ Marine Science from the University of San Diego and her PhD is in Ecology, Evolution and Marine Biology from UC Santa Barbara. Email: sgoffredi@oxy.edu.

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Further reading

Enzymes feel the squeeze: biochemical adaptation to pressure in the deep sea

To the human observer, the deep sea is as extreme an environment as Earth has to offer. Below about 200 metres, there is no light from the surface, the water can be frigid (-2 to 5°C), oxygen and food are scarce, and the pressure is staggering. Of course, to the countless species that inhabit the deep sea, these conditions are not so extreme, and in a statistical sense, they fall fairly close to average, since the deep comprises the planet’s largest habitat by volume. Despite its expanse, we know little about how life persists in an environment so different from our own. Only in the last half-century has technology emerged that allows us to collect and study live deep-sea animals. Diversity, Evolution and EcoPhysiology of Ctenophores (DEEPC, deepc.org, a US NSF-supported research effort) is opening a window on biochemistry in the deep, and specifically on its relationship to high pressure. By determining structural constraints on enzyme function under pressure, we aim to inform models focusing on deep-sea animal colonization, and to find general patterns of protein adaptation with possible applications in protein engineering and biocatalysis.

A short history of pressure physiology

The first investigations on the effects of high pressure on enzymes were undertaken in the early 1940s. Scientists at New York University and Princeton measured the intensity of light emitted by bacterial bioluminescence over a range of hydrostatic pressures. Through a series of experiments, they were able to measure reaction rate changes of the enzyme luciferase and calculated volume changes of the enzyme. Over the following decades, high pressure studies continued on marine bacteria, but most high pressure investigations on the enzymes of animals have been carried out on fishes. The metabolic enzymes of deep-sea fishes generally show smaller effects of high pressure than those of their surface-dwelling relatives. High pressure affects both intrinsic characteristics, such as active site volume and substrate affinities, as well as extrinsic factors, such as the effects of pH and osmolytes. Studies of high pressure effects have only been carried out on the enzymes of a few species of bottom-dwelling invertebrates. By examining a unique group of gelatinous animals called ctenophores, or ‘comb jellies’ (see Box 1), DEEPC aims to understand evolution and diversification in the deep-sea habitat.

Deep questions

The crucial molecular-evolutionary question for the EcoPhysiology branch of DEEPC is How are proteins structurally adapted to high pressure? This leads to a wealth of sub-queries: Is the adaptive evolution mostly parallel or convergent? How many different solutions have evolved in ctenophores to solve the same biophysical problem? Do they vary across protein families or across species? To take a biophysical lens to the initial question, namely, which intrinsic properties of proteins tend to evolve? Because we are biologically focused on ctenophores, we also want to resolve their adaptations to high pressure at an organismal level, requiring us to ask: Which components of ctenophore metabolic pathways are most affected by pressure?

One way to approach the evolutionary questions above is with phylogenetic theory and transcriptomics. To measure convergent evolution and identify metabolic ‘weak links’ heavily affected by pressure, we are using a phylogenetic nonlinear regression analysis, which detects depth-correlated variation in gene sequences and isolates it from the phylogenetic background. Once this analysis is complete, we will be able to score the most commonly substituted amino acids and structural regions proteome-wide. The regressions will also indicate which proteins contain the most depth-correlated substitutions. To answer our questions empirically, we are focusing on metabolic enzymes, such as pyruvate kinase (PK) and malate dehydrogenase (MDH) – components of the vital glycolytic and Krebs pathways. In the cases of PK and MDH, we can make use of prior findings that these enzymes have high-volume transition states and are thus kinetically inhibited by pressure. We also benefit from widely accepted assay chemistry. The latter is important, because precious little is straightforward about studying ctenophore biochemistry under pressure.

Specimens are collected to 20 metres depth by scuba diving, following ‘blue water’ protocols in which the divers swim in open water while tethered indirectly to a small
boat. Collections to 4000 metres are made using remotely operated submersible vehicles (ROVs) belonging to the Monterey Bay Aquarium Research Institute (Figure 1). The specimens are flash-frozen in liquid nitrogen at sea. When samples arrive at the lab, they enter the workflow pictured in Figure 2. This process involves cloning metabolic enzymes from complementary DNA (cDNA), expressing them in fully native form, with no amino acids artificially added to either terminus, and then assaying their activity across a 400-atmosphere pressure range. Subsequently, this analysis is repeated with point-mutated enzymes, to assess the effects of individual amino acids on pressure tolerance. In addition to assaying enzyme activity under substrate saturation, we are also investigating the effect of pressure on the apparent $K_m$ (affinity constant). The cloning and expression steps of our workflow mark our departure from traditional ecophysiology studies, most of which assay tissue homogenates.

**From molecule to ecosystem**

Preliminary results of phylogenetic nonlinear regression have been consistent with a hypothesis from previous work that larger amino acid side chains decrease the overall compressibility of deep-adapted proteins by filling their interior spaces. A typical example is the substitution of

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**Meet the ctenophore**

Ctenophores are a small (~300 species) group of gelatinous marine organisms, which diverged from the rest of known animals near the very beginnings of multicellular life. Their bodies superficially resemble those of well-known jellyfish (cnidarians), but they are evolutionarily far removed. Ctenophores have a body plan fundamentally different from a cnidarian, they are propelled by eight paddle-like rows of fused cilia rather than a pulsing bell (hence the common term ‘comb jelly’), and many use sticky cells on their tentacles to capture prey, in contrast to cnidarian stinging cells.

Ctenophores are uniquely suited to a study of protein adaptation to high pressure because they occupy niches throughout the ocean, from the surface to >7 kilometre depth (where ambient pressure is 700 atmospheres), and from the poles to the equator. Some species have remarkably broad tolerances as well, spanning thousands of metres depth, where others are constrained to the uppermost tens of metres. Phylogenetics suggest that ctenophore lineages experienced several recent and independent range shifts, producing closely related species that live under contrasting physical conditions. These species enable comparative analyses where we can consider pressure and temperature as independent factors affecting protein evolution, while controlling for the background of phylogenetic relatedness.

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**Figure 1:** Ctenophore collection using the remotely operated vehicle (ROV) Doc Ricketts and blue-water diving techniques. Scuba divers can collect between the surface and 20 metres depth, while Doc Ricketts captures specimens and video down to 4000 metres. Ctenophore size is exaggerated in this schematic. Illustration by Kelly Lance, MBARI.
valine for isoleucine in the structure of PK from surface-dwelling ctenophore Beroe forskalii (Figure 3). Initial assays of the same enzyme reflected a decrease in activity when both native-cloned and specimen-derived samples were pressurized to 200 and 400 atmospheres, 2000 and 4000 metres depth, respectively. These trends were consistent with PK pressure studies conducted on deep- and shallow-living fishes.

Through such biochemically focused research questions, we aim to learn about ctenophore ecophysiology at all scales, from individual molecules to the whole organism, and to understand the mechanisms of adaptation to extreme environments.
In the process of investigating pressure physiology in ctenophores, DEEPC will develop some tools of interest to the broader comparative biochemistry community. The first is a cold-shock-induced native protein expression system based on the Escherichia coli cold-shock promoter and a specialized high-specificity variant of the Tobacco Etch Virus (TEV) protease. This plasmid facilitates highly stable protein expression in bacteria or yeast at 15°C, easy purification using a His-tag, and then cleavage of that tag precisely at the protein’s native N-terminus. The second tool is the phylogenetic nonlinear regression-based algorithm mentioned above, packaged as a transcriptome-wide association utility. Any researcher with transcriptomes and quantitative trait data for several related organisms will be able to use this tool to identify amino acid sites associated with the trait, in an analysis controlled for phylogenetic background signal.

Achieving both our biochemical and ecological aims should give insight into the evolutionary past and trajectory of ctenophores, since we will have an idea how much genetic change is needed to enable colonization upward or downward in the water column. More generally, DEEPC will develop some tools of interest to the vast marine ecosystems of which ctenophores are a part. At a molecular level, we want to find out what aspects of protein structure confer pressure tolerance, and how ubiquitous these elements are. We predict that they will be mostly convergent among the ctenophores, and are prepared for a surprise when we ultimately compare them to pressure adaptations in other deep-sea animals. Ctenophores diverged from other animals so long ago, and protein evolution is so path-dependent, that it is possible they evolved largely different means of coping with pressure. On an ecosystem scale, we hope to determine how large a role pressure has in dictating invertebrate species’ ranges in the open ocean, by comparing enzyme functional measurements with our ctenophore sighting records. Some species’ natural depth ranges may come up hard against their physiological pressure limits, while others may be more constrained by different factors such as temperature, predators and prey.

Outside the realm of marine biology, our work has applications in chemical and biological engineering. As the reader likely recalls from introductory organic chemistry, many synthetic reactions, notably organic reductions, are carried out at high pressure and are classically catalysed by precious metals. Biocatalysis by an enzyme, or better yet, biosynthesis by living microbes, is an attractive alternative due to lower reactor cost and greater selectivity, but not all enzymes perform well at the required pressure and temperature. By cataloging evolved solutions to this problem, we can gradually build an enzyme optimization model for the protein engineer’s toolbox.

Jacob Winnikoff is a PhD student in Ecology and Evolutionary Biology at the University of California, Santa Cruz. He has been working on ctenophore physiology and evolution with Steve Haddock at the Monterey Bay Aquarium Research Institute (MBARI) since September 2016. Jacob is interested in a range of marine biochemical subjects, and has previously researched biochemical adaptation to temperature fluctuation in mussels, as well as bioactive secondary metabolites of cyanobacteria. Email: jwinnikoff@ucsc.edu.

Telissa Wilson is currently a master’s student at the Evergreen State College in Olympia, WA. She has been working with Professor Erik Thuesen and has been focused on studies in ctenophore physiology since June 2014. Email: wilitel16@evergreen.edu.

Erik Thuesen is a Member of the Faculty at The Evergreen State College where he teaches Zoology, Marine Biology, Ecophysiology and the science of Symbiosis. He has worked previously at research institutions in Japan, California, Catalonia and Argentina. His investigations have focused on biochemical and physiological adaptations of organisms to life in different marine habitats and the study of marine biodiversity. Email: theuesene@evergreen.edu.

Steven Haddock studies marine diversity, molecular biology and bioluminescence at the Monterey Bay Aquarium Research Institute and UC Santa Cruz. He specializes in fragile gelatinous jellyfish-like creatures that are abundant in the water column of the deep sea and open ocean. In addition to conducting research expeditions around the world, he uses genetic methods to reveal the relationships between organisms and to understand the proteins that they use to make light. He also runs the Bioluminescence Web Page (biolum.eemb.ucsb.edu), the citizen-science project jellywatch.org, and has a textbook for teaching computing to scientists at practicalcomputing.org. Email: haddock@mbari.org.

Further reading

Iron microbe: outfitting organisms for extreme environments

Kelsey K. Sakimoto  
(Harvard University, USA)

As NASA and other space agencies across the world prepare their astronauts to withstand the hazards of space travel and habitation on Mars, tinier adventurers have begun to receive a similar outfitting. For humans to live in extreme environments such as the darkest, coldest, radiation bombarded reaches of space, we must equip useful microorganisms to thrive and survive under similar conditions. This insight has expanded microbial sciences to the materials sciences: blending soft, squishy cells with hard, rocky crystals. And just as billionaire-playboy-philanthropist Tony Stark donned an array of gadgetry to become Iron Man, so too must bacteria and yeast receive the cyborg treatment to augment their functionality for the future of biotechnology.

Natural vs. unnatural photosynthesis

At the frontiers of human exploration – Mars, for example, or more domestic extreme environments like the deep ocean – photons come at a premium, calling for absorbing sunlight at the highest efficiency and converting that energy into biologically useful forms. Yet, some 3.4 billion years ago, evolution made a mistake. The first photosynthetic organisms used complex organic molecules: the predecessors to chlorophylls found in present-day plants, algae and cyanobacteria. While this game-changing foray into photochemistry enabled the transduction of solar energy into biochemical reactions, these same biomolecules handicap natural photosynthesis. Theoretically, natural photosynthesis can only absorb 12% of the sun’s energy. The lovely green colour of plants and algae stems from chlorophyll’s limited absorption of a narrow band of red light and blue light, leaving most green wavelengths (where the sun has maximum emission) futilely reflected back into space (Figure 2). The susceptibility of these organic molecules to photooxidative damage from high-intensity light has also capped the efficiency, forcing ~80% of the photons absorbed on a sunny day (or a photon intensity of 1 sun) to be converted to waste heat. Tallying up these shortcomings has left most plants with a solar-to-biomass efficiency of less than 1%.

For that reason, space exploration relies not upon organic molecular light absorbers like chlorophyll, but inorganic semiconductor solid-state materials. Molecules absorb light at specific wavelengths, represented by peaks in an absorption spectrum, where light between these peaks is not absorbed by the molecule for photochemistry. But semiconductors absorb all light shorter than a specific wavelength (higher in energy), leaving no gaps in an absorption spectrum, meaning more light is absorbed for more photochemistry. This different mechanism of light harvesting caps semiconductor solar-to-electricity efficiency at 32% for a solar panel made out of a single type of semiconductor. Extensive engineering and optimization of semiconducting silicon found in modern solar panels has driven up commercial efficiencies to the range of ~20%. Efficiencies as high as 45% set the record on devices usually reserved for satellites that combine 3 to 4 semiconductors in conjunction to absorb even more light. These impressive numbers lie at the heart of an unnatural form of photosynthesis, so-called ‘artificial photosynthesis’, that employs purely inorganic catalysts and light absorbers. While production of \( \text{H}_2 \) and \( \text{O}_2 \) from water splitting is routine, these abiotic routes have so far struggled with more complex reactions, like \( \text{CO}_2 \) reduction.

Furthermore, high-efficiency semiconductor light harvesters typically incur a high capital cost and extensive infrastructure. Balance of systems costs, which typically include everything beyond the actual photovoltaic module, such as installation, can make up to 70% of the total cost. But anyone who has ever seen a pond covered with a stubborn swath of duckweed knows that biological organisms require very little impetus to start growing rapidly. Thus, one would like to capitalize on the high efficiency of semiconductor light harvesting and combine it with the beautiful (and cheap) self-replication of biology.

Bionic upgrades to photosynthesis

So how do you give cells a bionic upgrade with high-efficiency semiconductor light absorbers? First, researchers have tried to simply introduce inorganic semiconductors to biological systems and see what they do. Leaves of \( \text{Arabidopsis thaliana} \) can take up carbon nanotubes: tiny straws of elemental carbon that absorb light in the infrared range. By travelling along the plant’s native vasculature, carbon nanotubes eventually pass through the cell membrane via local electrical-field-induced deformation of the lipid bilayer: sort of like electroporation combined
with endocytosis. These materials boost the range of plant light absorption and lead to enhanced photosynthesis: photons absorbed by carbon nanotubes can produce electrons that reduce electron acceptors along the electron transport chain linking the oxidative and reductive halves of photosynthesis, thereby increasing the total rate of electron flow.

But could we hijack the powerful capabilities of cells to chart a biosynthetic course to solid-state materials? Diatoms transform silicic acid, Si(OH)₄, trace levels of ‘soluble glass’ found in the oceans, into silicon dioxide, SiO₂. But as an insulator, silica exhibits no photoactivity. By introducing a biocompatible precursor for titanic acid, Ti(OH)₄, growing diatoms produce measureable amounts of TiO₂, a classical semiconductor and photocatalyst capable of splitting water into H₂ and O₂ with the aid of a catalyst. Deconstruction of the original biosilification pathway revealed short peptide sequences that could nucleate the key condensation reaction: Si(OH)₄→SiO₂+2H₂O. A bioinspired version of this peptide, (RKK)₄D₈, in combination with the titanium precursor, encapsulated Chlorella vulgaris in TiO₂, repurposing the biosilification pathway to produce an alternative metal oxide in microorganisms other than diatoms. While these early designs still don’t demonstrate semiconductor-driven photosynthetic capabilities, these biosynthetic routes present intriguing paths to the full library of oxide materials in the routine toolbox of materials scientists and engineers.

**Photosynthesis upgrades to the non-photosynthetic**

The first full-fledged bionic upgrade to light harvesting came to an organism that may have never before seen the light of day. Non-photosynthetic CO₂ fixation, such as the Wood–Ljungdahl pathway found in acetogenic anaerobes,
boasts greater efficiency than the photosynthetic Calvin cycle in terms of ATP requirements, pathway complexity and substrate specificity. For this reason, researchers have photosensitized a non-photosynthetic bacterium, *Moorella thermoacetica*, which fixes CO₂ into acetic acid (Figure 3). Introduction of the normally toxic cadmium cation (Cd²⁺) induces a detoxification pathway in *M. thermoacetica*, whereby a cysteine desulphhydrase liberates sulfide, S²⁻, from cysteine. These two ions precipitate out to form cadmium sulfide, CdS, nanoparticles that decorate the outside of the bacterial cell. When light hits *M. thermoacetica*-CdS hybrids, the CdS absorbs a photon to produce a photoelectron. This reducing photoelectron then hops to a membrane-bound protein, likely a hydrogenase, that produces H₂ and NAD(P)H that enters the Wood–Ljungdahl pathway as normal, though the exact mechanism remains under active investigation. To balance this reaction (every reduction reaction needs a complementary oxidation reaction), a tandem system employs TiO₂ nanoparticles as a photocatalyst for water oxidation to produce O₂. The net effect of this bionic upgrade looks nearly identical to natural photosynthesis (2CO₂+4H₂O→CH₃COOH+O₂), yet functions at ~2% efficiency, compared with less than 1% of typical plants. The bacteria remain viable throughout the whole process, driving a self-repairing, self-replicating feature native to all biology.

The upper limit of this form of bionic upgrade should be much higher, as CdS only absorbs blue photons (500 nm or shorter). But other metal sulfide semiconductors, such as lead sulfide, that absorb significantly more light can boost this efficiency. This methodology links biochemical reactions, like CO₂ reduction, to semiconductor light harvesting and is by no means the only new kid on the block, rubbing elbows with technologies like the ‘bionic leaf’—an electrochemical reactor that cultivates CO₂ and N₂ fixing bacteria, or *in vitro* systems that immobilize enzymes such as hydrogenase and nitrogenase directly on semiconductor surfaces. As this battery of bionic technologies continue to develop, microbes become better equipped to make the most out of the limited sunlight in the deeper reaches of the solar system.

**A spacesuit for bacteria**

While limited light flux on the more distant planets of our solar system poses a challenge to microbe survival, high-intensity light flux of another variety potentially presents a more serious problem. In the absence of an atmosphere and earth’s protective magnetosphere, damaging solar radiation from the UV to the gamma range, along with ionizing radiation in the form of high-energy protons and alpha particles pose a serious threat to living organisms, leading to degenerative DNA damage, and the production of undesirable molecules like reactive oxygen species (ROS), among others. Thus, equipping microorganisms to resist similar threats remains a crucial requirement for bionic upgrades.
Biology itself has in many ways inspired the design of man-made bacterial spacesuits. The hardest microbes intrinsically resist the most damaging effects of radiation. Deinococcus radiodurans exhibits a particularly radiation-resistant proteome that aids in DNA repair following radiation damage (see p37 for an Interview with Professor Michael Daly who works on D. radiodurans). In contrast, Ramazzottius varieornatus, a species of tardigrade, expresses a DNA-associating protein, Dsup, under stress conditions that protects the DNA itself from permanent genomic damage.

A more widespread approach to resisting environmental stresses comes in the form of sporulation. Some bacteria, such as many species of Bacillus, form protective protein or peptidoglycan shells in response to unfavourable conditions of heat, desiccation and other stressors. These protective barriers plunge the cells into a dormant state, allowing them to wait until suitable growth conditions return. This behaviour, however, doesn’t allow the cell to function in adverse conditions, only survive through them.

**Artificial spores – microbial Iron Man suits**

Inspired by bacterial sporulation, man-made cell encapsulation techniques fabricate a biocompatible coating to protect cells against stressful environments, simultaneously allowing them to maintain biological activity in these extremes.

While microbial Iron Man suits made out of passive materials like silica show some protection against ROS, heat and radiation, active materials that catalytically protect their cargo show great performance (Figure 4). Ceria, CeO$_2$, is another crystalline ceramic material widely used in industrial chemical synthesis and technologies like fuel cells. As a catalyst, CeO$_2$ (or more correctly, a mix of Ce$^{4+}$ and Ce$^{3+}$ forms CeO$_{1.85}$) catalyses the detoxifying reduction of ROS ($\text{H}_2\text{O}_2$, $\text{O}_3$–, $\text{OH}$•) to $\text{O}_2$. In addition to reacting with harmful products of ionizing radiation, the nanoparticulate form of ceria used to encapsulate cells demonstrates a light filtering effect, reflecting a portion of harmful UV radiation away from the microbe, yet allowing desirable visible photosynthesis through. Such lanthanide materials (including CeO$_{1.5–2}$ and LnPO$_4$) have protected a range of cells from cyanobacteria and plants to zebrafish embryos.

For as many stressors extreme environments can throw at cells, researchers have developed a laundry list of materials too exhaustive for this article. Exploration of the literature reveals designs that employ metal oxides, polymers, metal-organic-frameworks (MOFs: ionic crystals composed of charged organic ligands linked by cationic metals) and layered composites of all three. Encapsulating microbes in these materials grants protection against desiccation, temperature extremes, osmotic stress, lytic enzymes, and of course, radiation.

**The final (fragile) frontier—protecting environments from microbes**

As much as microbial encapsulation is designed to protect beneficial bugs from their environment, researchers have also concerned themselves with protecting environments from microbes. The history of ecology is nothing if not a cautionary tale against invasive species, and the establishment of NASA’s Office of Planetary Protection testifies to the dangers of introducing foreign organisms to even the most seemingly extreme and inhospitable environments. But a surprising role of microbial encapsulation is the control of cell division. Originally viewed as a flaw, many of the metal oxide shells are too rigid to allow cells to propagate, enabling them to metabolize, but not replicate. This feature now seems crucial in preventing these microbial explorers from infesting other ecologically fragile worlds, but still enabling them to join us on our missions to explore the extreme environments of the universe.

**Further reading**

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Kelsey K. Sakimoto is a Harvard University Center for the Environment Fellow in the Department of Chemistry & Chemical Biology (Harvard University) and Department of Systems Biology (Harvard Medical School). His research pairs microbial synthetic platforms with renewable energy to transform CO$_2$, $\text{H}_2$, water and sunlight into food, fuels, pharmaceuticals and materials. He pioneered the development of the “lyborg bacterium” M. thermoacetica-CdS, and developed the “bionic leaf” platform—a bioelectrochemical device that operates at 10× the efficiency of natural photosynthesis—to produce a microbial biofertilizer from air for use in modern sustainable agriculture. Email: kelsey_sakimoto@fas.harvard.edu.
Pushing the boundaries of life itself

The ability of some organisms to live in extreme environments has always fascinated us. While more complex species such as mammals can live in very cold or hot surroundings, microorganisms definitely take the crown when it comes to being able to survive the most extreme conditions. These extremophiles are very resilient and can survive conditions that would kill other organisms in seconds. Indeed, some researchers believe that life may have begun with such organisms living deep under the ocean on hydrothermal vents. Helen Albert talks to Professor Rania Siam from The American University in Cairo, Egypt, about her research on microbes living near highly salty underwater ‘brine pools’ in the Red Sea. Helen also discusses the remarkable bacterium Deinococcus radiodurans, which is able to withstand high levels of radiation and desiccation, with Professor Michael Daly from the Uniformed Services University in Bethesda in the USA.

Professor Rania Siam holds a PhD in microbiology and immunology from McGill University in Montreal, Canada, as well as a medical degree (MBBCh) from Ain Shams University, Faculty of Medicine. She held several post-doctoral positions in the Salk Institute for Biological Studies and The Scripps Research Institute, in La Jolla, California, USA before moving to The American University in Cairo where she is currently Chair of the Department of Biology and a Professor of Microbiology at the School of Science and Engineering. Her research covers medically related aspects of microbiology and molecular biology and, more recently, has shifted towards marine microbiology. Her marine research concerns the microbiology of the Red Sea, specifically of the deep brine pools, and is aimed at understanding the functional and evolutionary basis for life in these extreme environments. Her team has explored the diversity of microbial communities using both cultivation-based and direct metagenomic techniques and has also studied specific enzymes of potential biotechnological interest.

Why is it important for researchers to find out more about extremophiles?

Studying extremophiles and how they live will provide an understanding of the evolution of microbes in these hostile environments. Decoding the genetic makeup of such organisms provides an understanding of the evolution of biological life and peeks into unknown survival strategies. The unique genetic makeup of these organisms allows us to understand how the environment (physical, chemical and geological) skews the genetic content of these prokaryotes. It also can help resolve basic evolutionary questions, on the origin of life. An anaerobic reducing environment and very high levels of volcanic gases characterize submarine hydrothermal vents; these conditions simulate Earth’s early atmosphere. Extremophiles thrive in the submarine hydrothermal vents and studying them would shed light on life Earth’s early atmosphere and how ancient prokaryotes evolved into present-day microbes. We have addressed this in several studies including a study on mobile genetic elements and how they can shape the genetic makeup of extremophiles.

The fact that these organisms are capable of survival under these extreme environments also provides an excellent and natural tool to study different biotechnological processes. These extremophiles, and their genes or proteins, can therefore be appropriately utilized in a broad range of process conditions. For example, we have identified an esterase from the deepest and most secluded Red Sea brine pool, the Atlantis II brine pool, which has unique resistance to heavy metals. Esterases have multiple applications in different industries including the detergent industry.

What is a brine pool and what attracted you to studying the life that lives around them?

Brine pools are topographic depressions filled with geothermal brines. These are extreme environments for life to be found in. Some of the Red Sea brine pools have residual hydrothermal vent activities and therefore this environment simulates the early Earth’s atmosphere. I believe understanding biological life in these pools will provide a better understanding of evolution.

There are 25 brine pools along the central rift of the Red Sea. Each brine pool has different geological and physicochemical characteristics – different temperature, salinity, pH, and heavy metals. For example, the Atlantis II brine pool, one of the deepest and hottest, is characterized by high temperature...
(around 70°C) and salinity, minimal oxygen (anoxic) and a very high concentration of toxic heavy metals and gases. It's interesting to investigate biological life in such a harsh environment.

**How is it possible for living organisms to survive in this high pressure, high salt environment?**

Indeed, how can life exist in such a presumably stressful environment under conditions of high pressure, salt, temperature and toxic heavy metals? We describe these conditions as harsh and extreme. But, these organisms would probably say the opposite, as it is their habitat and they would likely describe their conditions as benign. These organisms have difficulty surviving if they are taken out of their deep, salty, toxic and anoxic environment. This makes it very challenging to culture these microorganisms in the laboratory, since we only have limited understanding of their natural habitat.

The genetic makeup of these organisms allows them to survive in such an environment. For example, halophilic (salt loving) organisms survive in a salty environment by maintaining the physiological osmotic pressure of the cytoplasm. This is achieved by either different cytoplasmic accumulation of osmolytes, or the gathering of molar concentrations of potassium chloride in the cytoplasm. However, this would mean that these intercellular proteins should have the intrinsic capability to maintain activity despite this high salt environment. Several studies have shown that these proteins have halophilic properties (high acidic residues and less hydrophobic residues) that maintain the activity despite the salty surroundings.

Another example is how biological life exists in a toxic heavy metal environment. Mercury is present in very high concentration in one of the Red Sea brine pools – Atlantis II. We’ve researched a Red Sea brine pool mercuric reductase (MerA) that possesses selective amino acid substitutions (increased acidic residues), two short segments near the C-terminal cysteine pair, each containing two basic amino acids and a proline residue. This feature largely contributes to this protein’s ability to survive in a host living in such high mercury levels and also possess halophilic and thermophilic potential.

**In the UK, we are all gripped by the new nature documentary Blue Planet II. How do the brine pools in the Red Sea and the life around them differ from those found elsewhere, such as the ones in the Gulf of Mexico that were recently featured on the programme?**

The physical and geochemical conditions in the deep marine habitats are different. For example, the deepest part of the World’s oceans, the Mariana Trench, is more than 10,000 m deep. The deepest part of the Red Sea is less than 3000 m deep. You can therefore imagine that the hydrostatic pressure imposed on the organisms in the Mariana Trench is much higher than in the Red Sea brine pools.

Brine pools (hyper saline anoxic basins) aren’t unique to the Red Sea. Other well-studied brine pools include Orca Basin in the Gulf of Mexico or Urania Basin in the Mediterranean Sea. The diversity and abundance of microbial communities in each of these deep-sea sites are controlled by the physical and geochemical conditions. The brine pools of the Red Sea can be described as ‘hot brines’ and those of the Mediterranean Sea as ‘cold brines’. Temperature is an important physical factor that can skew biological life. An interest, in my research group, is to understand the thermophilic properties of the enzymes we isolate from the Red Sea brine pools. One of the fascinating characteristics seen in the Red Sea brine pools (in terms of environmental conditions and therefore biological life) is the number and extremity of the environmental conditions. The organisms that live there need to withstand high temperature, salinity,
Interviews

pressure, hydrocarbons and sulphide, in addition to withstanding anoxia, high levels of toxic heavy metals and low levels of light. This we believe is an ‘exceptional combination’ in extreme conditions.

What is metagenomics and how are you using it to study the bacteria you have discovered in the Red Sea?
Metagenomics is a way of understanding the microbial community in an environment by deciphering the genomic content in this environment. Since it is difficult to simulate the natural habitat of such extreme environments (including Red Sea brine Pools), it is difficult to culture the majority of the microbes in these environments. So we utilize a non-culture approach which starts with the collection of water and sediment samples from the different pools, isolate the genomic content and perform shot gun sequencing and 16s rRNA sequencing. The latter is used to look into the prokaryotic community in this environment (bacteria/archea). This would be followed by extensive computational analysis to either describe the community found at individual sites or specifically look for genes or pathways. For example, we made a comparison between the mercury detoxifying enzymes in the different pools (comparative metagenomics). This was, and can be, followed by biochemical analyses, such as mutagenesis and kinetic analysis of the enzymes plus structural studies. This allows us to identify enzymatic features that can contribute to the extremophilic characteristics of the bacteria including the extreme salt tolerance and thermostability.

How can finding out more about these ‘polyextremophiles’ help us to tackle human problems such as antibiotic resistance?
This is in fact one of the issues we investigated in my lab. We looked for antibiotic resistance in the Red Sea brine pools. Identifying antibiotic resistance in such pristine environments will provide a better understanding on the evolution of antibiotic resistance and shed light on antibiotic resistance in extreme environments.

Looking further into the future, we would like to successfully cultivate bacteria from the Red Sea brine pool and get a comprehensive overview of the biochemical pathway of these bacteria. I’d also like to better understand the evolution of the microbes in these pools and to find out what are the important biochemical features that would endorse a single extreme factor (such as thermophilicity, halophilicity and resistance to several toxic metal and gases) and/or ‘pan-extremophilia’. 

On board the research vessel (R/V) AEGAEON of the Hellenic Center for Marine Research during a Red Sea Expedition to the Atlantis II/Discovery Deep brine pools. On the deck in front of the CTD, the water sampling equipment that can also record Conductivity, Temperature and Depth (hence the acronym CTD)
Michael Daly received his undergraduate degree from Queen Mary College, University of London (QMUL), as well as a PhD in genetics. In 1992, following a 3-year postdoc at the National Institutes of Health in Bethesda, Maryland, with Michael Lichten (a yeast geneticist), he started working at the Uniformed Services University (USU), also in Bethesda, where he is currently a professor in the Department of Pathology. He has dedicated the last 25 years to studying the bacterium *Deinococcus radiodurans* – understanding the genetic mechanisms responsible for its resistance to radiation, and then harnessing those mechanisms for practical purposes. These have included a revolutionary method of vaccine production, cleaning up radioactive waste, protecting animals from radiation injury and most recently, gauging radiation resistance in any cell type based on insights gained from studying *D. radiodurans* by electron paramagnetic resonance spectroscopy.

**What attracted you to studying *D. radiodurans* and extreme life?**

That probably goes back to when I was a child and I discovered Sea Monkeys (brine shrimps), which are extremophiles. Later, when I was at QMUL, I studied yeasts, which are remarkably radiation-resistant as well, and this was followed by a postdoc at NIH studying their DNA repair systems. When I moved over to USU, they had these fantastic gamma radiation machines, and *Deinococcus* was there, which set the stage for me, because of all the genetics of DNA repair that I'd done on yeast. We put our research into practice in *Deinococcus* and this gave us the first deep insights into how DNA is repaired in these remarkable bacteria that are not only extremely radiation resistant, but also desiccation and UV resistant.

**How did *D. radiodurans* first get discovered?**

It was discovered back in the 1950s as a contaminant in irradiated meat. Scientists were looking at processes to preserve foodstuffs by cobalt –60 irradiation for the troops in Europe. They found that many of the tins of meat spoiled because they had been contaminated with *D. radiodurans* (originally called *Micrococcus radiodurans*), which survived the radiation sterilization process. Since then, many, many close relatives of *D. radiodurans* have been isolated. You can pretty much find *Deinococcus* species anywhere in the world. They have been found on every continent, often growing in the guts of herbivores, or dried out in desert soils. They require very nutrient rich conditions for survival after drying, so in the gut of an elephant or a cow they have everything that they need to recover. *Deinococci* are then excreted and dry down and sort of turn to dust and get blown into the atmosphere. They then rain down all over the world and because they are so desiccation and radiation-resistant they last for hundreds if not thousands of years and end up as dust everywhere.

**How did they evolve to be radiation resistant?**

In the geologic history of Earth, there have never been such high dose rates of ionising radiation that could explain the evolution of organisms that are as resistant as *D. radiodurans*. It turns out, radiation resistance is a secondary phenotype; it’s a by-product of another phenotype, which is desiccation resistance. Most organisms that are extremely resistant to desiccation are also extremely resistant to radiation. It’s because the mechanisms are closely related in terms of how cells get damaged when things dry as opposed to when exposed to gamma radiation.
Tardigrades and rotifers use the same systems of protection against radiation and desiccation. These protection systems are built on small complexes of manganese with metabolites. These manganese complexes have catalytic activities that very efficiently scavenge and remove free radicals (superoxide) generated from water in cells during gamma-irradiation, desiccation and UV exposure, among other things.

What we have learnt over the last 25 years from Deinococcus is that if you want to survive radiation, the key to survival is that you must protect your proteins! There has been a paradigm shift in the field of radiation biology driven by D. radiodurans. This has moved the focus away from DNA, which is usually what we think about in radiobiology. We now say proteins are the critical targets that must be protected to survive radiation.

What research have you carried out on D. radiodurans?
The big mystery from the very beginning has been why this species is so radiation resistant. Back in the 1990s, we were one of the very first to get a whole genome sequence from D. radiodurans. Since then, of course, there have been thousands of other organisms that have been sequenced, but early on we saw very clearly, and this has been established through many different other analyses since, that a genome sequence cannot predict radiation resistance. That was a big surprise, a shocker on my side. So our emphasis shifted to other things.

In 2004, we published a paper in Science that showed radiation resistance, in bacteria at least, was based on the accumulation of manganese complexes. What was so remarkable about these manganese complexes, once we purified them and reconstituted them in the lab, was that they were immensely radio protective of proteins, but not DNA. Out of that finding came the hypothesis that if you want to survive radiation you must protect your proteins, a model I named ‘Death by Protein Damage.’ In Deinococcus, it’s these manganese complexes that protect the DNA repair and replication proteins that are needed to reassemble broken genomes. In fact, such antioxidant manganese complexes found in all organisms, even human cells, and they have become particularly enriched in cells that are very radiation resistant. Again, this was a surprise because it was antioxidant enzymes that were originally thought to be critical to radiation survival. Not so, it’s the small manganese complexes that give rise to the high levels of radiation resistance that we see across the tree of life.

After we purified the manganese complexes, we discovered a new way of making vaccines in a faster, safer and cheaper way than before. Deinococcus manganese complexes only protect proteins, not DNA. So, imagine you could grow up any pathogen you want. You mix the manganese complexes in with them, stick them into an irradiator and give them a massive dose of ionising radiation (gamma rays). Because the manganese complexes are protecting the protein surfaces of these viruses and bacteria, all their epitopes and all their structures are preserved, but their genomes are destroyed. That is the basis of an ideal vaccine and is one way Deinococcus manganese complexes are being used today. They’ve been used to develop vaccines against the flesh-eating MRSA bacteria, a number of alpha viruses and we are just about to report a new irradiated polio vaccine based on Sabin strains.

These same Deinococcus manganese complexes, when you feed them to mice, confer record-breaking levels of resistance to gamma radiation and can prevent radiation injury. So radioprotection from these manganese complexes can be applied in vitro in the production of vaccines, but also in vivo to protect against radiation.

We’ve also harnessed the manganese complexes from these bacteria for something called bioremediation, specifically cleaning up radioactive waste from the environment.

The Deinococcus Group at USU. Pictured from left to right are: Dr. Rok Tkavc, Dr. Elena K. Gaidamakova, Ms. Polina Klimenkova, Dr. Gözen Ertem, Dr. Michael J. Daly, Ms. Isabel H. Conze, Dr. Vera Y. Matrosova, Dr. Olga Grichenko, and Mr. Robert P. Volpe.
How are you hoping to use this research to protect people and animals from radioactivity?

In our recent mouse study, the manganese complexes were administered before exposure to gamma radiation, and they conferred high levels of resistance afterwards. What we need to do, and what we have good reason to think will happen, is that we will be able to administer the same manganese complexes after irradiation to provide protection that way. Because you never know if you are going to be irradiated, unless of course you are going through radiation therapy and that's a different scenario.

For the past 60 years, there has been very little progress in developing any form of radioprotection for animals or the like. That's because the old paradigm for why radiation is so dangerous was all focused on DNA. Yes, DNA is an important target, but it's not the critical target in irradiated cells. Our work has opened up the door to developing new ways to protect animals from radiation. Perhaps most importantly, \textit{D. radiodurans} has become a 'Rosetta stone' in understanding radiation resistance across the tree of life.

What are you planning to study next?

There is a strong connection between radiation resistance and aging. One of the things we have not yet published, but we have some clear data on, is that there is a strong correlation between the content of manganese complexes in a cell and aging. As cells age, they lose a lot of their antioxidant manganese complexes and then they die. When they are young and healthy, they are absolutely stuffed full of these manganese complexes. So, I am moving directly into the field of aging. We have all sorts of studies lined up looking at the correlation between the manganese complex content in cells and how healthy and how old they are.

**Further reading**

From stars to cells – harnessing the power of the crowd for research

Modern research techniques allow more data to be generated than can be easily analyzed by the scientists who produce it. An original solution to this problem is to recruit volunteers to help with data analysis through online citizen science projects such as the Zooniverse.

The origins of the Zooniverse

It is now over ten years since the first Zooniverse project, Galaxy Zoo, asked for public help with the morphological classification of galaxy images. The unexpected success of this project, which received more than 70,000 classifications per hour for its first few days following launch, led to the application of this approach to other astronomical research projects, including Solar Stormwatch and Moon Zoo, and eventually to the establishment of the Zooniverse platform.

The expansion of online citizen science

Since these early astronomical origins, the Zooniverse has become the world’s largest and most popular online citizen science platform with a community of more than 1.6 million registered volunteers contributing to over 110 research projects across multiple domains. The diverse assortment of projects currently on the Zooniverse platform range from transcribing documents written by Shakespeare’s contemporaries in Shakespeare’s World to aiding the study of climate change in Weather Rescue.

Although broad in research question and goal, these projects share the common principle of taking large data sets and asking volunteers to perform simple data-characterization tasks. Because we can ask more than one volunteer to look at each image, we can attain a level of accuracy greater than that achievable through the efforts of a single ‘expert’. Not only does the application of online citizen science methodology result in large and accurate datasets that would be challenging to produce by other means, the process of having multiple volunteers examining each data point can result in unexpected, serendipitous discoveries; for example, a new class of galaxy was identified by volunteers in Galaxy Zoo, and the first planet in a four-star system was found through the efforts of volunteers contributing to the Planet Hunters project.

Exploring new frontiers

Online citizen science methodology is being adopted by an increasing number of academic communities. One arena that is currently seeing a large amount of growth...
in the number and variety of projects is the biomedical research community. Over the last year, the Zooniverse has launched multiple novel projects in this area, including Etch A Cell and Bash the Bug, with many more projects in the development pipeline.

Although developed by and hosted on the Zooniverse platform, these projects address very different research goals. For example, Etch A Cell, which is a collaboration with the Francis Crick Institute, seeks to improve methods for analysing images produced through electron microscopy. In this project, volunteers are asked to perform the manual segmentation of electron micrographs with a drawing tool, in a task very similar to that which would be performed by the researchers themselves. The data produced by the efforts of volunteers on the Zooniverse platform will be used to advance the automation of image segmentation, which is currently a significant bottle-neck in this area.

Another Zooniverse biomedical research project launched this year is the award-winning Bash the Bug. This project is part of the large-scale international CRYPTIC consortium, which has the goal of improving both the diagnosis and treatment of Tuberculosis (TB). TB is currently responsible for more deaths each year than HIV/AIDS, and like all bacterial disease, Mycobacterium tuberculosis is evolving resistance to the antibiotics used to treat it. The CRYPTIC project seeks to advance understanding of how genetic variance in TB influences susceptibility to treatment with different antibiotics. The knowledge of which genetic mutations confer antibiotic resistance will allow more tailored treatment of patients, through the genetic sequencing of the TB strain they are infected with. Zooniverse volunteers are helping with this effort through classifying which antibiotic dose is effective at killing each strain through examining images from 96-well plates. During the six-months following launch, this project has received nearly half a million classifications.

Engaging communities with your own Zooniverse project

Not only does online citizen science provide a means of collectively accelerating research, it also provides a simple and accessible means for anyone with an internet connection to make a contribution to authentic scientific research. Such increased participation with science can benefit professional and non-professional researchers alike, through enabling research that wouldn't be possible otherwise and providing an opportunity for further education, and encouraging deeper engagement with science.

If you would like to build your own Zooniverse project, please visit the Project Builder interface where it is possible to build a project in minutes. www.zooniverse.org/lab

Further Reading


Dr Helen Spiers is a Postdoctoral Associate in biomedical research and citizen science at the University of Oxford. She is also the Biomedical Research Lead within the international research group responsible for the Zooniverse, the world’s largest and most popular platform for online citizen science. To date, over 110 research projects across multiple academic disciplines have been launched on the Zooniverse, allowing anyone with an internet connection to make an authentic contribution to real research, and for researchers to do studies that would not be possible otherwise. Email: helen.spiers@physics.ox.ac.uk.
The power of online learning

Lorenza Giannella
(Training Manager, Biochemical Society)

We live in an era where technology is embedded in everything we do. We use the Internet and various apps numerous times every day to order our favourite takeaway, keep in touch with friends and book GP appointments. In this digital age, technology is also deeply influencing education and learning, especially in science.

In recent years, many Higher Education (HE) institutions have dramatically expanded their online offering and in line with this have developed web-based learning management systems, such as Blackboard, Canvas or Moodle, on which students can access lecture material, additional reading and exercises, timetables and much more. Lecturers can offer online support and tutorials through webinars, live-web based sessions where students can actively participate, asking questions through chats or talking directly. Distance learning courses are increasing in number, offering the option to fit studies around your life. Virtual laboratories are also becoming increasingly popular, both in science blended learning and online degrees. These fully interactive simulations can be accessed by students to perform experiments and collect and analyze data. Moreover, a few UK Universities have or are building virtual reality (VR) laboratories. VR is used to create a fully-immersive hands-on experience, where students will be able to dissect an animal, fix an engine or walk on Mars. And, although you could spend millions creating a virtual reality laboratory, there are some cheap devices available for as little as £5 that are controllable with apps on a smart phone, making it an approach available to almost everyone. All this may sound impressive, but what’s the actual impact of technology on learning and education, except wearing fancy goggles?

The instant impact of online learning is student engagement. The majority of today’s students carry at least one device, be it a smartphone, a tablet, or a laptop, and a good educator can use this technology as part of the learning experience, instead of waiting for one of these devices to become a distraction. Such technology can allow lecturers to keep engaging students beyond the classroom and extend learning time. VR is an example of how technology can enhance and revolutionize learning: students may be able to visualize and move biomolecules in a fully-immersive setting, providing an experience otherwise impossible. Online learning can also allow students to study independently, which is beneficial for various reasons. By accessing material online, everyone can study at their own pace, for more efficient learning. Students with diverse abilities can use the available technology to improve their educational experience and access opportunities that may have been closed to them in a traditional classroom setting. Independent learning is also strongly linked with the pedagogical concept of student-centred education, which brings the focus from the teacher onto the student, for more personalized learning. Encouraging and assisting students to further explore a topic they’re interested in can deepen their knowledge in a subject and, more importantly, create motivation to study and increase resilience. All students have different strengths and weaknesses and a tailored programme can help them to develop skills that they are lacking or need improvement in. Independent learning can also be easily fitted around a student’s life. Students may need to work or they may have family commitments; online learning can allow them to keep up and not get left behind because of external circumstances.

Despite an undoubtedly positive impact, there are a few important aspects to consider before setting up online learning courses, especially in modules or
degrees that are exclusively taught online. Staff members and students alike need to be trained on how to use the learning management system of choice properly. Millennials aren’t necessarily as digital savvy as people think and an ability to use social media doesn’t help someone to know, for example, how to access the assessment feedback on Blackboard; students need to be taught. Moreover, online learning can be challenging because of social isolation. This can be overcome by creating an online community, where the social presence of both educators and students can become central to the educational experience. This has been shown to positively influence engagement, satisfaction and peer-support. These are just a couple of aspects professionals developing a course need to consider and it is not an exhaustive list. Online learning is a powerful tool, but it can also be complicated to embed in everyday teaching, or use to completely replace traditional education.

Despite this, it is likely that technology will keep playing a central role in education, revolutionizing learning and opening the door to new horizons. FutureLearn is just one example of how online learning is providing access to diverse opportunities. This learning platform, owned by the Open University, is developing a portfolio of postgraduate degrees, professional qualifications and CPD accreditations, in collaboration with leading institutions such as St George’s University of London, the Chartered Management Institute and the British Council. FutureLearn offers a variety of MOOCs (Massive Open Online Courses), and, while completing a MOOC generally doesn’t lead to a qualification, the online platform has announced that users will be able to complete some of its courses to earn academic credits for degrees and MBAs. This is a step forward towards tailored learning and accessibility of Higher Education: in a few years you may be able to access courses from top universities independently of where you are based. And while unfortunately HE does not yet provide open and free degrees, the ‘pay as you go’ approach that many Universities offer for their online programmes, especially at a postgraduate level, may provide more learning opportunities to everyone and hopefully improve social mobility. We just need to wait and see what the digital educational revolution will bring.

Further reading

- FutureLearn, (2017), Press Releases, Available at: https://about.futurelearn.com/press-releases
- Ertmer, P.A., and Ottenbreit-Leftwich, (2013), Removing obstacles to the pedagogical changes required by Jonassen’s vision of authentic technology-enabled learning, Computers & Education, 64, 175-182
- Giannella, L. and Heugh S., (2017), Using a WebLearn course organisation to enhance student engagement, Investigations in University teaching and learning, 11, 100-107
A day in the life of a Further Education teacher

Ursula Lowe is a Further Education (FE) science lecturer at Cambridge Regional College teaching the popular Access to Higher Education courses and day-release BTEC Diplomas. Ursula completed an MSc in Analytical Chemistry at the University of Salford followed by a PGCE in FE at the University of Manchester. Ursula has completed a STEM Insight work placement at the University of Cambridge and won the prestigious ENTHUSE Award for Excellence in STEM teaching (Further Education) in 2016. She enjoys professional development, writes a Wordpress blog STEM527 and tweets @ursula17LO. Lorenza Giannella (Training Manager, Biochemical Society) speaks to her about her work.

How did you get into teaching?

Whilst at University as a post-graduate student, I was asked to be a facilitator in undergraduate practicals and to mark some laboratory reports. The local technical colleges were also looking for suitable people to teach aspects of chemistry and biochemistry. I was recommended by my tutors and was offered some part-time teaching. After university, I studied for a Postgraduate Certificate in Education and then looked for full time lecturing positions in further education.

Can you describe a typical day?

At Cambridge Regional College, the working day is 8.30-17.15. I cycle to work for 8am and check the teaching room is tidy, switch on the computer and prepare the desktop. I print out any materials on coloured handouts for learners with particular needs, set up the room for demos or practical sessions and check my emails for potential student absences. Classes start on the hour and finish so that students can start their next class on time, which often means no break for the lecturer. Lunch is an hour anytime between 11 and 3 depending on the timetable and is often reduced to 25-30 minutes if a student needs to drop in for a one-to-one, or if there are any administrative tasks to carry out. Generally, afternoon classes finish at 16.00 but sessions for part-time students, such as apprentices, can finish much later, so that means my working day is extended too.

What’s the most interesting project you’ve worked on?

My most interesting projects have included my postgraduate work, which involved analysis of pesticide residues using electroanalytical methods, and the Access to Higher Education Science Practical Project. Each year, students pick their own specialism (biology, chemistry or physics) applications, and I support them in carrying out their practical project, building their skills of problem solving, evaluation and analysis. I also learn a lot as I have to research their topics too.

What is your advice for someone who would like to pursue a career in teaching?

Teaching is a vocation. If it’s something you’re interested in, give it a go. In science, most further education lecturers have a degree and a postgraduate or teaching qualification, which can be taken part time whilst on the job. There are

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long hours outside of work and very little thanks sometimes. Like other areas of teaching, Further Education holiday entitlement is usually in peak season and, at 42 days, is less than for teachers in schools. Salaries are typically lower too. However, the curriculum is much broader than in schools (not just GCSEs and A-level), and changes regularly depending on what is best to meet the needs of employers, or what is fashionable.

**What do most people not realize about your job?**
The range of courses and levels that are taught up to level 4/5 HNC/HND and the amount of resources we prepare, since we don't use off the shelf GCSE or A-level material, but more bespoke ones. The timetable changes each year, so a course will run if there are enough students to enrol. If not, you have to find something else to teach, and you do build up experience and confidence to do this.

**What inspires you about teaching?**
I enjoy meeting new people, whether that is students, employers or fellow lecturers and scientists at continuing professional development (CPD) sessions. It's wonderful when you ignite that spark of interest in a learner and see the educational distance travelled. Attending college can also improve their softer skills, such as communication, confidence and team work. I am still waiting to say I have taught a Nobel Prize Winner!

**What's been the greatest challenge in your career so far?**
The STEM Insight work placement I completed at the Department of Biochemistry at Cambridge University during the February 2016 half-term and the accompanying CPD assessments throughout the six months. It's a great way to learn new things, like using social media, network and fresh approaches to learning and resources. It rejuvenates the desire to remain in education, stay student focussed and rise to the challenge of the political and financial constraints placed on FE colleges. In 2017-18, I hope to get to grips with the wonders of Office 365 and undertake further subject specific CPD and continue lifelong learning.

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**Job Profile – Teacher**
A teacher educates pupils in a certain subject, inspiring and supporting them in achieving their full potential. He/she can work in primary, secondary school or in further education colleges, supporting students in acquiring knowledge, develop new skills and prepare them for assessments.

**Responsibilities**
Responsibilities include preparing and delivering lessons, assessing and recording progress, managing students’ behaviour and keeping up to date with the subject area.

**Qualifications**
Minimum standard GCSE qualifications (or equivalent) in English and Maths are essential (grades and qualifications vary depending on country of training). If your undergraduate degree is not a Bachelor of Education (Bed) or a BA or BSc with qualified teacher status/teaching qualification, you will need to complete a Postgraduate Certificate in Education.

Independent schools, free schools and academies may hire teachers without formal teaching qualifications.

**Salary and career development**
Newly qualified teachers start on the main pay range, which rises from £22,467 to £33,160. Teachers may move into year group leadership or management roles, with a subsequent salary increase. Independent schools, free schools and academies set their own salaries.
The Biochemical Society Summer Vacation Studentships offer stipends of £200 per week for 6–8 weeks, and up to £1,600 in total, to support an undergraduate student to carry out a summer lab placement. This scheme not only benefits the student as they get valuable research experience, but the supervisor also gains an extra pair of hands in the lab. Here, a selection of students share their experiences of summer 2017.

**Afra Aabdien supervised by Claire Thornton (King’s College London)**

I thoroughly enjoyed my six-week studentship and learned a multitude of laboratory techniques that have aided me in my experimental design methods, as well as my ability to successfully execute them and make sense of the results which I obtain. My most fond memory was having the opportunity to work with cell cultures and administering peptide drugs to them to test the effect of oxygen glucose deprivation on mitochondrial function. I got the opportunity to visualize treated C17.2 mouse cells on coverslips with confocal microscopy, enabling me to examine how mitochondrial morphology is affected during oxygen glucose deprivation, and whether they have undergone any fission. Two important protein components of mitochondrial fission, Fis1 and Drp1, were fluorescently tagged with secondary antibodies to observe their localisation in the cells.

**Dimitra Papatziamou supervised by Nick Robinson (Lancaster University)**

This internship went above and beyond my expectations; not only has it taught me practical skills and biochemical techniques, but most importantly it cultivated my critical thinking and my confidence as a future researcher. It also helped me reach the decision to pursue a research career in bioscience, as I’ve realised my passion for this field. During this placement I also had the opportunity to engage with other summer interns at Lancaster who also shared the same passion for research and with whom I also attended enjoyable social events. I was also fortunate enough to participate in my first international conference when my supervisor was a guest speaker at the ‘18th Frankfurt Meeting on Genome Function and Gene Regulation in Archaea’. Thanks to an additional travel scholarship from Fylde College, Lancaster University, I was able to attend this exciting meeting where I engaged with both PhD candidates and esteemed professors. This visit enabled me to expand my knowledge of the project beyond the practical work and put my new skills in the context of the latest scientific findings that were presented at the meeting. Overall, this was one of the most rewarding experiences of my life and I’d like to thank my supervisor Dr Nick Robinson for this amazing opportunity. I would recommend it to every student as a highly interactive and essential experience for any aspiring scientist.
Yasmin Rashid supervised by Ewan Main (Queen Mary, University of London)

This placement was an opportunity for me to gain an insight into a real research laboratory, beyond an undergraduate lab. In doing so, I was able to advance the skills that I had already gained from my previous lab experience, along with learning more sophisticated techniques such as large-scale centrifugation, Ni2+ affinity chromatography in protein purification, Size-Exclusion Chromatography and SDS-PAGE, among many others. In particular, I thoroughly enjoyed the process of growing the bacteria and expressing proteins from. Though I was initially unsuccessful in extracting and purifying one of the essential proteins, the translocator protein PopB, I was able to finally do so towards the end of my placement. As such, this was one of the highlights of my entire experience. This studentship was critical in affirming my passion for science and has definitely motivated me to further my studies. Although challenging at times, I found the experience highly rewarding and so would recommend this to any committed individual who has a thirst for knowledge and an avid interest in the research.

Abbie Guild supervised by Laura Spagnolo (University of Glasgow)

My favourite day of the project was in the final week when I was able to look at a protein that I expressed and purified using an electron microscope. My project was looking at Staufen protein which binds to the cytoskeleton through its Tubulin Binding Domain to transport mRNAs around the cell. As part of the experiment I made a complex of Staufen with microtubules to try and produce an image of the complex. Using the electron microscope, I could clearly see protein around the correct size bound to the microtubules which was so exciting. Not only did I get the opportunity to use a biophysical technique that I had learnt about but I was able to use it to look at a protein that I produced which was surreal. As someone who has been interested in science all my life to get the opportunity to use an electron microscope was a dream come true; it was such an exciting and interesting experience!

Joel Reader supervised by Leah Fitzsimmons (University of Birmingham)

Moving from the second to the third year of my genetics degree, I was becoming increasingly aware of the need to decide on what to do next. Thankfully I was able to spend 8 weeks in a research laboratory at the University of Birmingham Institute for Cancer and Genomics. I had previously had the chance to meet my supervisor, Dr Leah Fitzsimmons, and to try out a few relevant practical skills through short visits to the lab in previous years. The financial support from the studentship allowed me to gain a proper insight into academic life. My project aimed to improve our understanding of how the Epstein-Barr virus alters the survival of cancer cells. The range of techniques covered as part of this project was fascinating, especially seeing the ways that they could be combined. Seeing the lives of laboratory staff in person has played an important part in informing my plans after university and has changed them in ways I did not expect. Working on such a project can be challenging, but to any students considering summer studentships, I cannot recommend the experience highly enough.
Before applying for my summer studentship, I was interested in applying for postgraduate research programmes with the overall goal of becoming a research scientist. However, I was really daunted by the prospect of my final year, in particular my lab-based honours project.  
I gained experience in very important biochemistry and molecular biology techniques and had the opportunity to be involved in original research with a supervisor and topic of my choice. I had the added benefit of moving to another university for my studentship, which gave me a feel of a different environment and a chance to meet different lecturers and learn about projects from other PhD students I would not otherwise have known about. I also got to attend university research days which was a great added bonus. Being trained in experimental techniques that I had never done, but had read about in my second year, was very exciting, and getting my first set of results was a great moment! I now have a realistic idea of what being a postgraduate student will be like, and have a good idea of which field of research I would like to go into. For anyone considering applying for Biochemistry/Molecular Biology PhDs or master’s programs in their final year of university, a Biochemical Society summer vacation studentship is ideal.

Applications for the 2018 studentships are now open and can be accessed via the Biochemical Society website. The deadline for applications is 23 February 2018.

You can read more examples of student experiences at bit.ly/SVS-2017.
Understanding Animal Research (UAR) is the UK’s only organization devoted solely to helping the public understand why and how animals are used in scientific research and to maintaining a supportive operating environment for such research in this country. Formed in January 2009, following a merger between the Research Defence Society and the Coalition for Medical Progress, UAR has a small staff of around 10 people and a Council of 12 Trustees, chaired by Professor Jeremy Pearson, which oversees our governance. We also have an Expert Network of individuals from across the bioscience sector and related stakeholder organizations that help to inform our work.

UAR is a membership organization and we help our members in several ways. Our policy, education and communications work on behalf of the sector as a whole aims to prevent any reduction in the UK public’s acceptance of the use of animals in research and maintain the favourable operating environment that exists in this country at the moment. Our work on communicating the facts about animal research over the last eight years has helped to reduce the level of illegal animal rights activity in the UK to an almost negligible level, and since the publication of the Concordat on Openness on Animal Research in May 2014 we are now able to have a much more nuanced conversation with the public about the reality of animal research, its benefits and its limitations.

Our Policy team monitors the main UK political parties to ensure that animal research does not become a party political issue. In the run-up to the 2015 General Election we worked with several parties on their early draft manifestos to help them understand the implications of any proposed changes to the existing legislation covering bioscientific research. For the 2017 election, we maintained this effort and ensured that no main party manifesto proposed significant changes to the laws on animal research. We also work closely with the UK Bioscience Sector Coalition, the Home Office and the Office for Life Sciences within BEIS on all relevant policy issues.

Our schools programme has been running for nearly a decade and now organises more than 300 talks in UK secondary schools each year. This equates to around two talks each day of the week in term-time. We train and support researchers and animal techs to go into schools to talk about their work. Our team also gives talks in...
schools and runs workshops and summer schools for larger groups of students, covering the facts on animal research and the ethical dilemmas inherent in this work.

We run two main websites: www.understandinganimalresearch.org.uk and www.animalresearch.info. These provide written information, photographs, videos, infographics, leaflets and fact sheets for the public and for our members to use in their own communications. We also run a small website providing factual reports on instances of animal rights extremism around the world: www.animalrightsextremism.info. Happily, this does not have a great deal of content and does not need to be updated very regularly. Social media takes up a large portion of our communications work: we have accounts on Twitter, Facebook, Instagram, Reddit, LinkedIn and YouTube where we maintain a conversation with the public about why and how animals are used in research in this country.

A major project for us this year has been the development of our www.labanimaltour.org, a 360 degree tour around four UK animal research facilities, supplemented by videos and interviews with researchers and animal care staff.

Support for individual member organizations varies according to each member’s needs, but includes specialist consultancy on planning applications and the building of new biomedical research facilities; round-the-clock media relations support in the case of any claims made by animal rights groups; help with media releases and broadcast interviews and advice on handling Freedom of Information requests. Anybody working within a member organization of UAR can contact us for free help and advice, as can members of Learned Societies, such as the Biochemical Society, that are members of UAR.

We also run a comprehensive programme of training workshops covering various aspects of communicating about animal research. These include formal media training for those who would like to become media spokespeople on this issue; utilizing social media to communicate about research; preparation for debating with those opposed to animal research and preparing to talk to school children about bioscientific research. We offer four free places on these workshops for each of our member organizations each year and are always open to creating bespoke training sessions for our members. Biochemical Society members who would like to take advantage of our training workshops should contact the Society’s Scientific Policy Officer, Emma Sykes (emma.sykes@biochemistry.org).

One of our most important pieces of work over the past few years has been the development and implementation of the Concordat on Openness on Animal Research in the UK, currently signed by 116 organizations. This was prompted by a drop of ten percentage points in public acceptance of medical research using animals, as evidenced by the Ipsos Mori public opinion poll in 2012. It was clear that the sector needed to do something radical in order to rebuild the trust and acceptance that had been lost. The result was that a broad spectrum of organizations including Learned Societies, Universities, medical research charities, Research Councils and commercial organizations have committed to taking practical steps to provide more information and public engagement opportunities. UAR publishes an annual report on progress on implementing the Concordat and we hold an annual awards ceremony to recognise and celebrate the good work that is being done to help the public to access more balanced information on animal research.

More information on the Concordat is available at http://concordatopenness.org.uk.

The year 2014 was a busy one for UAR, in addition to our other work, as we created the European Animal Research Association (EARA), following requests for help from colleagues in Italy, Germany and Belgium. EARA works to set up organizations that help the public to understand animal research in local markets and is also recognised by the European Commission as a pan-European organization representing the bioscience sector.

If you would like further information about Understanding Animal Research and what we do, please do get in touch (wjarrett@uar.org.uk).
Charles McDonald 1953–2017

Charles (Charlie) McDonald obtained his first degree in biochemistry from the University of Stirling, followed by a PhD under the supervision of Jeff Sampson, at the University of Leicester. Here he helped elucidate the role of cAMP phosphodiesterase and its modulation by carbohydrate, during cellular development and aggregation in Dictyostelium discoideum. Charlie emerged from these formative experiences as a gifted experimental biologist. He then moved into the field of steroid control of development, where he obtained a post-doctoral position in the laboratory of Steve Higgins at Leeds, who had followed a similar move from microbial biology to hormonal regulation in mammals, several years earlier. It was the combination of experimental virtuosity, an interest in the application of contemporary molecular biology methodology and the study of complex developmental questions in biology, that made Charlie a welcome addition to the staff in the Department of Biochemistry headed up by Professor Peter Banks, under the MRC’s ‘New Blood’ Lectureship Programme in 1984.

Charlie immediately threw himself into establishing his research group through funding from the MRC, a number of medical charities including Yorkshire Cancer Research and SERC (now BBSRC) funded departmental research studentships. Within five years Charlie had broken the back of a programme to understand the properties of a set of genes encoding proline-rich proteins from the mouse parotid and salivary glands. To give you some idea of the hurdles that Charlie and his group had to overcome: mammalian gene cloning and sequencing was in its infancy in the UK; introns had only been described a few years earlier by Rich Roberts and Phil Sharpe and the mouse parotid is not the easiest tissue from which to extract nucleic acids, let alone proteins. Last, but not least, proline rich proteins are, by their chemical nature, unstructured and have a tendency to aggregate during purification. Charlie's PhD students had to be made of stern stuff!

In fact, amongst his first crop of students were Andy Bannister (now at the Gurdon Institute, Cambridge), Nullin Divecha (University of Southampton) and Stefan Roberts (University of Bristol and Biochemical Society Honorary Meetings Secretary), all of whom have gone onto forge highly successful academic research careers.

Charlie will probably be remembered by most colleagues and students, for his outstanding contribution to undergraduate biochemistry teaching, following the merger of the Departments of Biochemistry, Microbiology and Genetics with the Wolfson Institute of Biotechnology in 1988, under the leadership of Professor Ernie Bailey, to form the current Department of Molecular Biology and Biotechnology. In this ‘second career’, which came after a period of important political service in Sheffield, Charlie re-invigorated Sheffield’s undergraduate laboratory classes (drawing on his wealth of experimental skills) and began to nudge us away from our collective ‘comfort zones’ in our approach to teaching. Charlie was always enthusiastic, rigorous and innovative, and he made an incredibly valuable contribution to both student engagement, course regeneration and ultimately helped MBB to obtain quality recognition and accreditation from the Royal Society of Biology.

Charlie retired from the department on health grounds in 2013 (but only after considerable coercion by his colleagues!), and he continued to fight a brave battle against his illness to the end. We last worked together on a new Molecular Systems and Synthetic Biology course for third year students, which Charlie pioneered and I now enjoy continuing to teach – carefully following his masterplan, of course! Discussing science, education, politics, art, literature and music with Charlie was always a joy if not sometimes a challenge (for me!). Charlie was an avid musicologist and a lover of the ‘great outdoors’, especially the Scottish Highlands, which assumed a greater importance to him towards the end of his life. He is survived by his wife Angela and his three children.

David Hornby
(University of Sheffield, UK)
Upcoming Events

Biochemical Basis of Respiratory Disease
8–10 January 2018, Nottingham, UK

Shaping your career in molecular biosciences: taking a wider view
15 January 2018, London, UK

Industry and Academic Collaboration Award Lecture and networking reception
15 January 2018, London, UK

The Brighton Science Festival, Bright Sparks event
10–11 February 2018, Hove, UK

The motivation to experiment – an art and science exchange, joint with Central Saint Martins
27 February 2018, London, UK

BSGCT Public Engagement Day
15 March 2018, Oxford, UK

The Dynamic Cell III
19–21 March 2018, Manchester, UK

Evolving molecular bioscience education
12–13 April 2018, Chester, UK

New Horizons in ESCRT Biology
17–20 April 2018, London, UK

30th Annual UK RNA Polymerase focused meeting
19–20 April 2018, London, UK

83rd Harden Conference Autophagy - from Molecules to Disease II
3–6 June 2018, Warwick, UK

The Biology and Physics of Bacterial Chromosome Organization 2018
June 2018, Leiden, The Netherlands

Translation UK 2018
5–6 July 2018, Manchester, UK

Small G Proteins in Cellular Signalling and Disease
9–12 July 2018, Cambridge, UK

Meeting Reports

European Drosophila Research Conference 2017

22–25 September 2017, Imperial College London, UK

EDRC 2017 was the largest yet, with 800 delegates from all over the world. The conference opened with four workshops (gut & microbiota, cell competition, immunity and mitochondria), and spectacular opening plenaries. Ruth Lehmann (NYU, USA) presented her lab’s latest work on the diversity of mechanisms through which germ line cells escape somatic differentiation and preserve totipotency and Marc Freeman (Vollum Institute, USA) demonstrated that glial cell function extends far beyond their known role in supporting neuronal homeostasis, to being active participants in neurotransmission.

There were 422 excellent posters. In the student category, Ramya Balaji (Classen lab, Freiburg, Germany) stood out by presenting her work on how the germline influences follicular epithelium cell shape transitions in ovaries. In the postdoc category, John Davis (Tapon lab, Francis Crick Institute, London, UK) won for his poster on mechanical forces in histoblast development.

Fittingly, the sun set on EDRC 2017 with a brilliant plenary on sleep by Amita Sehgal (University of Pennsylvania, USA) who wowed the audience with the delineation of the output circuit that transmits circadian signals from the clock neurons to the fly’s motor centres, as well as the identification of a novel sleep-inducing molecule.

Alex Gould and Nic Tapon
(The Francis Crick Institute)

The 3rd BiKiE symposium

16–17 Sep 2017, UCL Institute of Child Health, London, UK

The 3rd BiKiE symposium aimed to bring together Korean and European scientists working in various fields of Biomedical Sciences, following the recent signing of an International Associate Membership agreement between the Biochemical Society and the Korean Society for Biochemistry and Molecular Biology (KSBMB) to encourage scientific communication and strengthen the global networks between Korea and Europe. Representatives of KSBMB as well as the Korean Academy of Science and Technology (KAST), Korea Institute of Science and Technology (KIST-Europe) and Yonsei University gave short presentations introducing their organisational structures and activities, along with Laura Woodland, Head of Membership Engagement, representing the Biochemical Society.

The scientific sessions represented the diverse areas of active research and recognised the excellent scientific achievements from Korean scientists. The oral presentations, on the themes of proteomics, genomics, molecular structures, biomaterials and cellular functions, along with poster presentations and small group meetings chaired by senior scientists stimulated much interest and provided many opportunities for engagement and networking. Fifty participants, comprised of Korean scientists currently based in Europe (including academics, PhD students and pharma industry employees) and eminent scientists from top Korean research institutes and universities, enjoyed the event organized by BiKiE, the European branch of KSBMB. The event has provided a strong base of collaborative relationships between the two Societies in the run up to the IUBMB Congress to be held in Seoul, Korea in June 2018.

Soo Hyun Kim
(St. George’s, University of London)
to know one another.

for the delegates and speakers to interact, discuss their work and to get

programme was the discussion sessions which provided opportunities

getting delegates comfortable with new and established technologies

'Advances in platelet signalling' session.

us to invite international research leaders to share their expertise in an

research. The generous support from the Biochemical Society enabled

attendees. Delegates were joined by 29 experts from research laboratories

The European Platelet Summer School meeting attracted over 90

Two new initiatives were introduced into this year's Summer School

programme: the inclusion of a statistics and data analysis talk and

associated practical session; and an informal question and answer careers

session where three invited speakers shared their experience with the

audience on developing a career both within and beyond research.

Overall the meeting was a huge success. The organising committee of 2017

would like to thank the Biochemical Society for their financial

support which contributed to the success of this unique independent

meeting in the field of platelet research.

Jon Gibbins, Alice Pollitt, Chris Jones, Craig Hughes and Sakthi
Vaiyapuri (University of Reading)

Ambassadors are a key group of members that help us to raise awareness of the Biochemical Society, promote its activities, recruit new members and act as the Society's point of contact at their institution. If you would like to get involved as an Ambassador, please contact: membership@biochemistry.org.

Alex Conner is a Senior Lecturer of Medical Sciences at the University of Birmingham. Alex teaches "the easy bits of the medicine course before we need clinicians" and has a research group studying the structure and function of large membrane proteins in health and disease. He is especially interested in human aquaporins and the exploitation of their structure and function for treating brain oedema. Alex increasingly works in science communication facilitating discussions, talking about science to people without a traditional science background and showing off on stage. Alex is a Senior Fellow of the Higher Education Academy and a Fellow of the Royal Society of Biology. He is validated by external titles apparently!

What motivated you to become a scientist?

My main motivation to become "a scientist" was that getting a proper job was hard and I wanted people to call me Dr Conner. My motivation now is that I really love working with and teaching exceptional people. Partly so I can ride the coat-tails of scientists much cleverer than I am.

What inspires you about molecular bioscience?

Figuring out how very small changes to individual proteins can not only explain fundamental physiological processes but also provide a platform for future therapies. Our aquaporin research has directly persuaded a neurosurgeon to start a human clinical trial application. That is both unexpected and very cool. I'm also consistently inspired by the realization that the more I combine research with communication, the more involved I get in public engagement and the better I become at research. Being forced to simplify my explanations led to an ABSOLUTE requirement for clarity of thought.

What are you reading at the moment?

The Long War by Stephen Baxter. I am intrigued by the concept that we are

a single point of energy in a natural hologram and that multiple universes

might exist; this book plays with that a little bit.

What's on your lab bench or desk right now?

A cup of coffee. A big list of admin tasks I don't want to do. A free textbook fantastically called 'The Top 100 drugs' that isn't as fun as it sounds and an augmented reality headset so I can try and teach from inside a beating heart. Normal desk really.

What's been the greatest challenge in your career so far?

The acceptance that I am not as good at science as I am at explaining science to interested people. This meant dealing with the hurt pride that I am less likely to get the plaudits (and promotions) that come with major research grants and Nature papers. However, a preference for science communication and teaching means I am genuinely looking forward to going to work every day. That makes life a lot of fun.

What is your advice for someone who would like to pursue a career in molecular bioscience?

Definitely, unequivocally and without hesitation, make sure you are choosing the thing that you think is a hobby. If you would do it anyway, the success will follow. Ask yourself which bits of the field of molecular bioscience you are thinking about when you should be doing something else and go out and get experience or a PhD or a Fellowship in exactly that area. For me, this is about how aquaporins move around the astrocytes and why. I also think about explaining this to people who aren't qualified scientists. So that is what I do.

What do you do in your spare time?

I do public engagement. Stand-up comedy in science (Bright Club), explaining science on stage (Famelab) and facilitating events and training sessions. I also play Xbox with my sons and try and teach my one-year old how to walk. She's terrible at it. Especially in wellies.

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Royal Society of Biology News

Making the most of new opportunities

The close of the year is inevitably a time for reflection – to consider what we have been doing enabled and supported by the Biochemical Society in the final quarter of 2017, before turning to what we hope to achieve in 2018 and beyond.

In October, we ran our sixth annual Biology Week, by many measures the most successful to date, and we thank our Member Organisations including the Biochemical Society for helping us reach out and bring this annual celebration of the biosciences to even more people than ever before.

Over 100 events took place across more than 50 locations globally, engaging with thousands of people worldwide, with more than 600 bioscientists also joining in on Twitter for our first ever #iamabiologist social media campaign.

Two of our events were in collaboration with the Biochemical Society, including our annual debate hosted by the Royal Institution (Ri), and our Policy Lates discussion evening on mental health and wellbeing.

The debate, Genome editing: where do we draw the line? took an expert look at the rapidly expanding field of genome editing, which brings technical challenges and options, and raises fundamental questions of ethics and values.

The Ri was packed to the rafters with an audience ranging from school children to professors who came to listen to bioethics experts and genetic researchers discuss the facts and opinions surrounding this hot topic.

A vibrant discussion followed the panel discussion, organized in collaboration with the Biochemical Society, British Ecological Society and Physiological Society, on the biological research underpinning our understanding of mental health and mental health policy. It was again encouraging to see such a diverse cross section of people speak openly and progressively about mental health research and policy challenges for the future.

Recently we’ve also responded to a number of consultations, including most recently the life sciences Industrial Strategy enquiry, the Migration Advisory Committee call for evidence on EEA-workers, and the call for evidence by Defra on digital sequence information and the Nagoya Protocol.

We are working to ensure our members’ voices are heard and that decisions made at a Government level are in the best interest of the biosciences community, especially as Brexit discussions continue. The RSB is feeding into the High Level Stakeholder Group on EU Exit, Universities, Research and Innovation, co-chaired by Jo Johnson, MP, Minister of State for Universities & Science, from BEIS and Robin Walker from the Department for Exiting the European Union. Movement of people, skills and regulation have of course featured prominently.

In September, we hosted a discussion workshop on Open Access for learned society publishers across all specialisms. There are over 600 learned societies in the UK, and just under half of these publish academic journals and conference proceedings, including the Biochemical Society.

The health of our specialist research communities is tightly bound to their publishing activity and surpluses and understanding the current business threats and opportunities is key.

We launched our HE Bioscience Technician of the Year Award for the very first time this year, in collaboration with University Bioscience Managers Association. We want to showcase the essential work technicians do in labs and universities across the UK, and the award is a new and visible step in our efforts to do this.

RSB Director Rachel Lambert-Forsyth has also joined the Department for Education’s Healthcare Science Technical Level panel to advise on the content of their new education programmes. Through this panel, we hope that we will be able to help shape the new programmes that will deliver a thorough and robust training programme for the next generation of technicians.

As we move into the New Year, we will also be moving into the final year of our three–year strategy, and of course will be thinking how to progress beyond 2018 with a refreshed strategy.

We look forward to developing further in partnership with the Biochemical Society and our other member organizations and hope the members of the Biochemical Society will continue to be closely involved in our progress.

Mark Downs
CSci FRSB
(Chief Executive, Royal Society of Biology)
The Biochemical Society has been an important part of my scientific life. I suspect like many of you reading this, my first foray into the 'grown-up' world of science as a graduate student was at a Society-organized event. In my case, this was the 30th Harden conference held in 1988. In the intervening almost 30 years (a number that only slightly terrifies me), I have been fortunate enough to hold a number of positions within the Society. This started with me taking on the role of the General Editor of The Biochemist, and continues today in my role as the Chair of the Portland Press Board.

Whilst I have no doubt that everyone reading this will have heard of The Biochemist (it is, after all, the magazine you are holding or the web-page you are visiting) I am far less certain that many of you will really know what Portland Press is, and how its relationship with the Society works. In brief, Portland Press is the wholly-owned publishing subsidiary of the Society. It is a for-profit publisher gifting all profits from its publishing activities back to the Biochemical Society. This enables the Society to carry out its charitable works in support of the biochemical community and molecular biosciences more generally. Portland Press is in business for scientific benefit, providing sustainable support for the advancement of science. Working together and towards the same objectives, the Biochemical Society and Portland Press support innovation and the advancement of science through the circulation of knowledge and the sharing of scientific research across the community for the benefit of both scientists and science.

Currently, Portland Press publishes a stable of seven journals representing a mixture of titles that publish either predominately primary research (e.g., the Biochemical Journal and Clinical Science) or predominately review articles (e.g., Emerging Topics in Life Sciences), using a mix of subscription and open-access models. Portland Press is also the publisher for The Biochemist. It is, perhaps, easy to fall into the trap of thinking of Portland Press as a UK-centric publishing company. Nothing could be further from the truth. At the present time, 92% of authors submitting articles to our journal portfolio and 85% of our institutional subscribers are based outside of the UK.

The Portland Press Board, of which I have been Chair since 2013, is composed of a mixture of Executive Directors (publishing professionals from within the Biochemical Society) and Non-Executive Directors (who have a raft of experience in academia and/or scholarly publishing) to help guide and direct the activities of the organization. The purpose of the Board is to manage, monitor and direct strategic investments and overall direction of the Society’s commercial publishing activities. In recent years, the Board has overseen significant changes: Portland Press has ceased a number of loss-making activities, and has upgraded and modernized almost every aspect of the publishing work that we do. As a consequence, Portland Press is now a lean and focused organisation that is, I believe, exceptionally good at what it does.

But how can a small organization like Portland Press compete against the behemoths of commercial academic publishers? There are undoubtedly economies of scale for publishers who control hundreds, or even thousands, of titles. But we believe we can better serve the molecular bioscience community because we are part of that community. We care about the community and want to ensure that our journals publish work that is of the highest possible quality and do so in a way that supports our science. Being a Society-owned publisher also has the advantage that we can be extremely nimble and agile. Change has become something of a constant in the publishing world for as long as I have been involved in it. Rather than having to turn the metaphorical oil tanker around, Portland Press is able to respond quickly to, and often be extremely proactive towards, changes in the publishing landscape. In a world of fast-moving researcher needs, growing librarian expectations and varying research-funder policies across nations, Portland Press will continue to craft relevant workflows, improve researcher experiences, and, by building on its ethos of collaboration and inclusivity, set high standards in scholarly publishing. For example, the Board has recently been considering how to respond to potential introduction of new scholarly communications licenses and how this might influence our current business model.

Finally, I would like to encourage you to publish, and continue to publish, your academic work in our journals. Doing so will not only bring you the exposure that your science deserves and needs, but will also support the outstanding work that the Biochemical Society undertakes.
Covers that never happened

Freddie Theodoulou
(Science Editor)

One of the changes I instigated in my eight years as Science Editor of *The Biochemist* was to invite design staff to the magazine’s Editorial Advisory Panel meetings so that we could consider the visual angle for each issue (and also so that I could interfere incessantly with the cover designs). Sometimes thinking up novel cover concepts was tough, especially when the default option is to use a chemical structure but more often than not, dreaming up effective ideas for each issue proved an amusing exercise. Rather like practical jokes, sometimes the fun is in having the idea and it’s usually better not to go ahead with the execution. But just for your amusement, I recount the stories behind some of the covers. Here are four cover concepts that it’s probably just as well never appeared in their original incarnation and one that should have been slightly different.

**Science Fact/Science Fiction (December 2012)**

We usually try to have a bit more fun with the Christmas issue, aiming for a playful concept but still delivering some serious science writing. This remains my favourite issue not only because then Executive Editor Mark Burgess secured a super feature article from Anne Simon, science advisor for *The X Files*, but also because of the cover. I was very keen on having a pastiche of a 1950’s horror movie poster with a stereotypical mad scientist, a monster and a screaming woman. Initially we toyed with the idea of Mark and I dressing up as the characters and even got as far as taking a few photographs but quickly realised that we would need costumes, make-up and professional lighting to get an acceptable result. I was uncharacteristically quite camera-shy but Mark rose to the challenge beautifully! In the end, graphic designer Rowena Weedon spent several days masterfully combining and manipulating images to produce the retro-looking final version.

**Metals (October 2012)**

This was a tricky topic for good images and the email conversation about the Metals issue went something like this:

MB: Any ideas for the cover?
FT: How about someone sprayed with metallic paint à la Shirley Eaton in Goldfinger? Not me, obviously.
MB: I’ve just spilled coffee on my keyboard.

Thankfully for all concerned, the end result was somewhat more conservative, though still visually arresting, I think.

**The Seven Deadly Sins (December 2013)**

Another Christmas issue, for which an Adam and Eve-themed cover was my top pick. We toyed with several possible versions but this was another occasion when it was suggested that Mark and I could don lab coats and pose as the eponymous couple. Naturally a combination of reticence and laziness meant that we had to think on our feet for a new idea as the press deadline loomed. I
I dearly wanted to feature the BBC’s Clangers in lab coats. However, a colleague subsequently pointed out that the cover should ideally have featured a digital human and not an animal silhouette. Not only would this have avoided the controversy over featuring an animal image but it would also have more accurately represented the concept of animal replacement. However, a colleague who worked on that issue, came up with this great image of DNA being intercepted by radar dishes which I felt expressed the topic beautifully.

Replacement in Research (June 2014)

This was a genuinely tough call: the sensitive nature of the topic dictated that we had to be very careful. We wanted something to symbolise the three Rs (Reduce, refine, replace), whilst acknowledging the importance of animal research. Early cover concepts featuring Petri dishes looked a little sterile and failed to convey the notion of animal replacement (at this stage we had also decided not to use the word ‘animal’ in the title). It met with quite a lot of opposition, but I felt that this cover with a digital rat and some stylised tissue culture cells neatly embodied the concept of animal replacement. However, a colleague subsequently pointed out that the cover should ideally have featured a digital human and not an animal silhouette. Not only would this have avoided the controversy over featuring an animal image but it would also have more accurately represented the ultimate goal in replacing experimental animals.

Astrobiology (December 2014)

I dearly wanted to feature the BBC’s Clangers in lab coats on this cover (which I recall was the then Honorary Meetings Secretary, Sheila Graham’s idea), but this was vetoed due to copyright issues and the fact that our international and younger readers might not pick up on the reference. In the end, Tony Crowley, the designer who worked on that issue, came up with this great image of DNA being intercepted by radar dishes which I felt expressed the topic beautifully.
Delusions of Gender’ and ‘Testosterone Rex’ by Cordelia Fine

Creating a level playing field for women to have successful careers in research is something many in the scientific community are actively working towards, as those of us on Athena Swan committees will attest to. But we might also admit that it seems very hard to make real change, because while new policies in flexible working and shared parental leave make a huge difference, a major unsung barrier is the entrenched notion that women are primarily carers while men are competitively goal-orientated and career driven. And we cannot claim that this notion is just ingrained in our senior faculty colleagues; it is embedded in all of us, because from the day we are born boys and girls are treated differently; by the age of three we are conscious of which toys are for boys or girls, and by the time we are seven years old our gender views have become entrenched.

Many would argue that gender differences are real, and scientific bases for (apparently) male and female traits have been widely reported. What Cordelia Fine does in her 2010 book Delusions of Gender is to lay bare how gendered our society is, and how this is perpetuated as we raise our children. She then looks beyond the headlines which claim scientific proof validates sex differences, to examine the underlying data critically and thoroughly. In study after study, Fine finds that data are only weakly supportive of conclusions, or that there are inherent flaws in the studies, or that tenuous claims are amplified in discussion. She also highlights the multitude of published studies which fail to find any biological basis underlying apparent male and female traits. In Fine’s recent book, Testosterone Rex, she goes on to address the popular consensus that ‘boys will be boys’, that testosterone is the driving hormone behind male dominance, competitiveness and aggression. With the same rigour, and drawing on countless studies in humans and many other species, Fine convincingly deflates this argument from multiple angles.

And if you think this all sounds like a heavy read, you’re wrong. Fine writes in a witty, personal and engaging manner, and the result is two books I found hard to put down. Indeed, Testosterone Rex won the 2017 Royal Society Insight Investment Science Book Prize. In my view this is thoroughly deserved, and these books have had a greater impact on me than anything else I’ve read in a long time. So if gender differences are a social construction and we can accept that there’s no biological basis for women to be carers and men to be competitive, then we really can break down barriers. Read these books, and tell your friends and colleagues to do the same. If we can raise the next generation, male and female, with these notions embedded then maybe we truly can create a level playing field for women in the workplace of their choice, scientific and beyond.

Emily Flashman (University of Oxford, UK)

Science in the Soul By Richard Dawkins

In this anthology of collected writings: essays, letters, lectures and speeches, Richard Dawkins brings an eclectic mix of science-orientated subjects to the lay reader. Although the author’s introduction was written last year, many of the pieces date from much earlier, with added notes to update them, where necessary, for today’s reader. The forty-one pieces which Dawkins has selected reflect his enormous enthusiasm for all aspects of scientific thought, and his desire to explain it to the rest of modern society.

The essays, articles, letters and lectures were produced and delivered over a period of 30 years, and span a substantial part of Richard Dawkins’ professional career.

The book is divided into eight sections, the titles of which generally relate to the essays within, sometimes somewhat peripherally. Dawkins is an internationally famous science educator, whose views, always didactic, often controversial, excite and inflame readers in almost equal measure. Some of the content of this volume is predictable: the author is a committed Darwinian and describes himself as a passionate rationalist; articles on theology and religion appear, as expected. For the reader with a science background, his demolition of the arguments of creationists in their attempt to limit the scope of science teaching in schools in the state of Alabama in the US is a masterpiece of deductive reasoning. In other essays he demonstrates his unerring skill as a science communicator in his discussion of the value and values of science, in the pursuit of truth and the importance of evidence.

For regular readers of Dawkins’ previous works on many aspects of popular science, who have sometimes struggled with his dense prose and opinionated arguments, this book is a revelation. As many of the articles are short, and the subject matter so varied, it is a delight to dip into Science in the Soul for a period of most satisfying entertainment, or education in an area that is unfamiliar. I have no hesitation in recommending this book most highly. My only warning is that anyone buying it as a present for someone else might be reluctant to pass it on.

John Albert (University of Cambridge Institute of Continuing Education, UK)
**Junk DNA: A Journey Through the Dark Matter of the Genome**
*By Nessa Carey*

Since the first sequencing of the human genome in 2003, we have been left with the puzzling question of why we differ so much from other organisms when our genes are so like theirs. In her second book, Nessa Carey has now chosen to tackle this subject, and describes in detail how so-called ‘junk’ DNA serves multiple purposes, including regulation of the genome and cell cycle.

This is a wide-ranging topic, which has the potential to quickly become unwieldy, but Carey navigates it with aplomb, resulting in a book that is both accessible and enjoyable. Acknowledging from the outset that ‘junk’ is a controversial term, with multiple connotations, Carey is careful to give a clear definition of what it means within the context of this book. The reader is then taken by the hand, and easily guided through this complex topic, making it accessible to the general audience. The conversational tone of much of the text is engaging, and means that the book never becomes dry. Through numerous case studies, including Friedrich’s ataxia and Fragile X syndrome, Carey introduces the concept that organisms drastically differ from each other because of ‘junk’ DNA, and that these non-coding regions are vital for the regulation of much of the genome.

Carey has geared *Junk DNA* to both the general audience and those with a more in-depth knowledge of the field. The result is a well-paced, well explained, and thoroughly absorbing book.

**Matthew Sinton** (University of Edinburgh, UK)

**People in white coats**
*By Benoît Leblanc*
(http://peopleinwhitecoats.blogspot.co.uk)

Aimed at graduate students in the field of green chemistry, the book seeks to generate interest in areas that students might not be familiar with. In this it attempts a difficult balancing act between giving broad overviews of topics and more in-depth, focused research. Experts will find many of the review-style chapters lacking in technical detail, whereas the more focussed research can make for difficult reading for non-specialists. Together these give good insights into both current research areas, and how such research is carried out.

On the whole, this volume is well-targeted at graduate students. Specialists will be familiar with many of the theme. However, the level of technical detail will be overly complex for general audiences. By covering such a range of research, graduate readers, or those with a background in chemistry, will be able to find interesting and generally well-written topics, accompanied by clear figures that help explain often complex ideas.

**John Steele** (John Innes Centre, UK)

**Green Catalysts for Energy Transformation and Emission Control**
*By Ruey-An Doong*

Human activities have profound effects on the environment, from the release of greenhouse gases during energy generation, to the release of pollutants as industrial by-products. This volume presents some key works from an ACS symposium addressing the use of green chemistry to limit or remediate such pollutants. The authors seek to cover a range of topics: detection of environmental pollutants, greener energy generation by reducing greenhouse gas emissions or catalysing hydrogen production, photocatalytic degradation of organic contaminants using various metal oxides, and several chapters covering the formation, characterisation, and improvement of transmission metals for photocatalytic reactions.

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**John Steele** (John Innes Centre, UK)
Crossword Competition

Win

This month’s crossword prize is a soft toy Waterbear (Hypsibius dujardini) from Giant Microbes.

Simply email the missing word, made up from letters in the highlighted boxes to biochemist@biochemistry.org, by Friday 5 January 2018. Please include the words ‘December crossword competition’ in the email subject line.

Congratulations to October’s winner:

Tomas Voisin from Imperial College London

The missing word from last issue’s competition was METHYLATION.

Tomas received a copy of ‘A Crack in Creation: The New Power to Control Evolution’ by Jennifer Doudna and Samuel Sternberg and ‘The Epigenetics Revolution: How Modern Biology is Rewriting our Understanding of Genetics, Disease and Inheritance’ by Nessa Carey.

Terms and conditions: only one entry per person, entrant must be a current Biochemical Society member; closing date Friday 5 January, 2018. The winner will be drawn independently at random from the correct entries received. The winner will receive a soft toy Waterbear (Hypsibius Dujardin) from Giant Microbes. No cash alternative available. No employee, agent, affiliate, officer or director of Portland Press Limited or the Biochemical Society is eligible to enter. The winner will be notified by email within 7 days of the draw. The name of the winner will be announced in the next issue of The Biochemist. The promoter accepts no responsibility for lost or delayed entries. Promoter: Biochemical Society, Charles Darwin House, 12 Roger Street, London WC1N 2JU; do not send entries to this address.
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19:00–20:00 Drinks reception

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