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'… all ecosystems have microbes at their most foundational level … Whether one is studying the human gut or frozen lakes in Antarctica, it is all environmental microbiology' – These words encapsulate the message of Roberto Kolters's[1] 'personal interpretation' of the history of microbiology in this volume of the *Annual Review of Microbiology*.

Microbiology came into its own as a unified field, branching out of chemistry, in the second half of the 19th century, some 200 years after microorganisms were first discovered by observation under a microscope. We learnt then that microbes are responsible for various reactions, such as the fermentation of grapes into wine, and are the drivers of major biogeochemical cycles like the sulphur cycle and the nitrogen cycle that sustain life on our planet. We also learnt that some microbes cause disease. With its immediate and obvious impact on human health, this discovery quickly brought a sledgehammer down on unified microbiology, creating a 'schism' (as Kolter calls it) and forming medical microbiology as a specialization within microbiology.

Medical microbiology progressed and occupied a position of great importance and interest in the first half of the 20th century, primarily in the form of antimicrobial discovery and deployment. It was in the second quarter of the 20th century that the second of Kolter's schisms appeared in microbiology. One might consider this as an offshoot of medical microbiology. The discovery of bacteriophages in a clinical context and their study, along with the observation of trait transfer between infectious bacteria variants that eventually led to the identification of DNA as the genetic material. This, over the subsequent decades, would result in the blossoming of molecular microbiology.

The first volume of the *Annual Review of Microbiology* was published in 1947 (ref. 2). By this time, penicillin was well established as a miracle antibiotic and streptomycin, following successful animal testing, was undergoing clinical trials. The golden age of antibiotics had begun. Medical microbiology was exciting. Our understanding of microbial metabolism was expanding. Though the deciphering of the double-helical structure of DNA was a few years into the future, it was already a leading candidate for being the genetic material. The 1947 volume of the *Annual Review of Microbiology* covered quite a bit of ground on the state of our knowledge then. An article on industrial fermentation performed by fungi and bacteria covered the production of economically important molecules such as alcohol, lactic acid and antibiotics. The general bacterial metabolism was represented with an emphasis on nitrogen metabolism. Reflecting the times, medical microbiology took up the lion's share of printed real estate. As expected, the discovery and mechanism of action of antibiotics as well as antimicrobial resistance found a place, as did immunization and the state of knowledge of various microbial pathogens. Though mechanisms of DNA replication and mutation were unknown, work with antibiotics and bacteriophages had established the enormous biochemical plasticity of microorganisms and their ability to adapt to new challenges. This was acknowledged by an article on antigenic variation in bacteria and protozoa, a phenomenon that permits infectious agents to evade the immune system.

Seventy-five years later, we have seen rapid technological developments in molecular and cell biology. In particular, the sequencing of genomes of most microorganisms in pure culture is now routine. We have also been able to sequence genomes of microorganisms, primarily bacteria, living in complex communities directly from the environment without the need to culture them in laboratory media. Such direct environmental sequencing has led to the recent discovery of candidate phyla radiation, which represents ~15% of the total known bacterial diversity, but with only a few culturable representatives[3]. These developments have opened up many new avenues in microbiology, as discussed by Kolter[1] in his article. I will henceforth emphasize my interest in microbiology, which is relevant to the application of molecular approaches to unified microbiology. This is the broad, age-old question of how microorganisms adapt to their environments through genetic evolution and physiological adjustments.

Two articles in this volume highlight the genetic diversity and adaptive capabilities of hitherto underserved types of microorganisms. In the late 1970s, Carl Woese, in a radical departure from the then-common approach of building trees of life using morphological and physiological parameters, had used sequence data of a marker gene to show that the Archaea were a third kingdom of life, distinct from the Bacteria and the Eukarya. As pointed out by Tahon *et al.*[4], human knowledge of Archaea, encompassing only 40-odd years, has recently expanded by leaps and bounds. As one might expect of an ancient kingdom of life that dates back to ~3.5 Bya, the diversity of Archaea is great and covers at least 30 phyla and 20,000 species. These include the so-called Asgard Archaea, first discovered only a few years ago in deep marine sediments. This group of Archaea, all named after Norse Gods, is the closest known relative of eukaryotes, encouraging new research into the evolution of the Eukarya. Though the number of archaeal species mentioned above may pale in comparison to estimates of the number of bacterial species, it is likely that the molecular methods used to discover Archaea are systematically undersampling them.

Fungi are a diverse group of eukaryotic microbes mostly studied as terrestrial or host-associated organisms. Baidouri *et al.*[5] discuss the less-understood category of aquatic and amphibious fungi, most of which are yeasts. Though Bacteria and Archaea are often considered the most dominant denizens of extreme environments, and that may well be the case, yeasts are also known to survive in harsh environments such as hydrothermal vents and polar regions. The authors discuss how aquatic and amphibious fungi face a variety of harsh stresses comparable to classical extremophiles. For example, aquatic yeasts are exposed to high ultraviolet radiation, but adjust by producing melanin. This also increases cell strength, which in turn would enable its producer to withstand high hydrostatic pressures. Amphibious yeasts face high 'differentials of salinity, hydrostatic pressure and temperature' between land and water. How do they adapt? For example, yeasts that enter the ocean must overcome the osmotic shock. However, even terrestrial yeasts, such as those that perform industrial fermentation, can withstand high osmolarity, suggesting pre-adaptation to an amphibious or aquatic lifestyle. Most environmental surveys of microorganisms – called microbiome studies – only emphasize bacterial and archaeal diversity, making Baidouri *et al.*'s call to do more to understand the interactions of fungi with their environment rather urgent.

Physiological adaptation to changing environments involves sensing and processing a signal and responding to it on time. One such signalling pathway, called quorum sensing (QS), detects molecular markers of cell density. These pathways, best studied in

some model bacteria, trigger various responses, including the formation of biofilms and host colonization processes. Tian *et al.*[6] bring a eukaryote perspective to QS by discussing its mechanisms and roles in fungi. QS in fungi regulates processes like host colonization similar to that in bacteria, in addition to eukaryote-specific functions such as meiosis and apoptosis, but use a different suite of molecular signatures of cell density. This might even allow some fungi to disrupt QS pathways used by certain bacteria, suggesting that QS pathways in fungi might have a role to play in interspecies and interkingdom signalling across microorganisms.

Among the most prominent signalling systems in bacteria is that mediated by the small molecule (p)ppGpp. It is well known that this molecule binds to RNA polymerase, powerfully inhibiting the transcription of various genes, particularly those involved in resource-expending translation. A review by Bange *et al.*[7] explains how the action of (p)ppGpp extends beyond this by binding and directly regulating the activities of a wide range of proteins and even RNA molecules. These proteins are involved in ribosome biogenesis and maturation as well as in the process of translation, among others. The range of dissociation constants for (p)ppGpp binding across its binding partners suggests the prioritization of targets for regulation at different cellular concentrations of the molecule.

Other articles present mechanisms by which various steps in gene expression and activity are regulated. For instance, how is stoichiometric protein synthesis achieved? How are RNases, which can degrade RNA indiscriminately, deployed in a regulated manner? Taken together, this volume of the *Annual Review of Microbiology* does justice to Kolter's unified view of the field by assembling a series of articles representing the state-of-the-art in microbial ecology, molecular evolution and molecular processes of adaptation.

1. Kolter, R., *Annu. Rev. Microbiol.*, 2021, **75**, 1–17.
2. https://www.annualreviews.org/toc/micro/1/1 (accessed on 6 October 2022).
3. Hug, L. A. *et al.*, *Nature Microbiol.*, 2016, **1**, 16048.
4. Tahon, G. *et al.*, *Annu. Rev. Microbiol.*, 2021, **75**, 359–381.
5. Baidouri, F. E. *et al.*, *Annu. Rev. Microbiol.*, 2021, **75**, 337–357.
6. Tian, X. *et al.*, *Annu. Rev. Microbiol.*, 2021, **75**, 449–469.
7. Bange, G. *et al.*, *Annu. Rev. Microbiol.*, 2021, **75**, 383–406.

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In her introductory remarks, Ruth Lehman (one of the editors of this book) brings out the multiple difficulties we faced during the COVID-19 pandemic and how research in life sciences has taken centre stage over the past couple of years. Scientists rose to the occasion, more than did their bit, to understand the various aspects of this disease and helped develop effective vaccines in record time. Most of us, however, suffered in our research output and wet laboratory scientists had to face their problems. For example, I had nightmares about losing my two-decade-old clonal culture of hydra (fortunately, due to the efforts of a dedicated technical officer, it survived). The pandemic also taught us to keep abreast with advances in other areas of human activity, especially science. Normally, primarily due to lack of time, one misses out on reading about interesting works in other areas of research. This is where the *Annual Reviews* series has come to one's rescue. This volume is one such collection of fine articles that I would strongly recommend everyone to peruse. All the articles are certainly not on the same theme, which is understandable because the subjects of cell and developmental biology are vast, but each has something interesting to offer. There are 22 articles which review diverse cellular and developmental phenomena in organisms from bacteria to mammals. These include the role of cytoskeletal components, mechanobiology, cell signalling in animals and plants, regeneration, infection, the spread of viruses, etc.

The first few articles cover the trends in the molecular understanding of structural and functional aspects of cell shape, organelle biogenesis and assembly, phagocytosis and T-cell activation. How a limited number of proteins is responsible for generating the rod shape in bacteria is described from the data obtained from *in vitro* and *in vivo* studies. The current models that attempt to explain the rod-shape formation, maintenance and regulation have been discussed. Microtubules, one of the cytoskeletal components, play multiple roles in all types of cells. Patterning of microtubules inside the cells has been used to describe principles of self-organization in the biological context. Comparing cytoplasmic partitioning in frog eggs before cytokinesis and the longer-lasting syncytia in early *Drosophila* embryos is interesting and illuminating. A detailed description of the self-assembly of the centrosome is the topic of another article. Minute details of the structural organization of the centrosome have been discussed. Up-to-date information on the dynamics of centrosome assembly in cells is reviewed. Changes in the centrosome during development and disease processes have also been discussed. While concentrating on the biochemical events that drive various cellular processes, one often tends to ignore the importance of mechanical sensing in biological processes. This point has been dealt with in an article devoted to activation of T cells, which is important for adaptive immune response. State-of-the-art microscopy and related techniques show how mechanical cues drive T-cell activation through a large number of molecular components. The article on the regulation of phagocytosis makes interesting reading. Phagocytosis is a dynamic process that responds to various cues in an extremely versatile fashion. The combination of a vast array of signals from targets and receptors on phagocytes makes the process dynamic and versatile. Additionally, in the authors' words, 'An exquisite extra layer of complexity is introduced by the coexistence of "eat-me" and "don't-eat-me" signals on targets and of corresponding "eat" or "don't-eat" receptors on the phagocyte surface.'

The work of Lin Margulis on endosymbiosis, which was not well received initially and was apparently rejected by several journals, has changed our understanding of evolution. McCutcheon discusses how intracellular bacterial infections can lead to endosymbiotic relationships. With some interesting examples, he discusses how bacteria escape rejection by the host cell, how their genomes are modified, and finally, though yet to be well understood, how host cells might tolerate these 'permanent guests' that eventually help their hosts in different ways. Understanding how the host tolerates only