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Advancing archaeal research through FAIR resource and data sharing, and inclusive community building

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Over the last two decades archaeal research has expanded into a wide-ranging research field, driven by a fairly small research community. Archaea are now recognized as important players in the One-Health approach and expertise on the biology of archaea has become crucial in the study of a broad range of topics and environments, including the host-associated microbiomes, major nutrient cycles, greenhouse gas metabolism, the cell biology and origin of eukaryotes, adaptation of life to extremes, as well as various biotechnological applications. Here, we summarize existing resources and ongoing efforts in the engaged broader archaeal scientific community to accelerate research and resource sharing guided by FAIR (findable, accessible, interoperable, reusable) data-sharing principles. We highlight ongoing community efforts that: (i) aim to share protocols and best practices for working with archaea (e.g. ARCHAEA.bio), (ii) combine large ‘omics datasets for the dissemination of unified, system-wide results (e.g. Archaeal Proteome Project, KBase) and (iii) provide opportunities for scientists to present their work in a supportive environment and to forge connections and collaborations (e.g. Archaea Power Hour). Together, these resources and projects promise to spur and cross-fertilize research, making archaeal research more accessible to a broader and more diverse audience.

Archaeal research has vastly increased our understanding of life on Earth: from marine nitrogen cycles[1,2] to the origins of Eukaryotes[3], and from extremozymes[4,5] to the first discoveries of CRISPR systems[6], archaea have contributed to numerous scientific breakthroughs, as well as invaluable biotechnological applications. However, despite their environmental, evolutionary, biotechnological, and biomedical importance, Archaea have only been reclassified as an independent domain of life by Carl Woese and George Fox less than five decades ago[7]. Furthermore, they still remain understudied compared to Bacteria and Eukaryotes, resulting in a comparatively small research community.

Historically, archaea were thought to thrive only in extreme environments (e.g., low or high pH, temperature, salinity, water activity, pressure). Although the focus on extremophiles has broadened our view of the limits of life[8,9], putting the spotlight on their versatility of metabolisms and incredible adaptations to these environments[10,11] and even giving rise to biotechnological applications[12], it has also distracted from the ubiquitous distribution of archaea. This delay in realizing the fundamental functions that archaea play in diverse ecosystems was prolonged by difficulties in culturing archaeal species[13]—which unfortunately is still often the case—and detecting them in metagenomic analyses[14–16]. But thanks to the advancements in universal metagenomics techniques in the last decades, the underestimated phylogenetic diversity of archaea and their presence in diverse microbiome, including in plants, animals, and humans, has been revealed[14,17–19]. These connections establish archaea as crucial contributors to a One-Health approach, which reinforces the concept that the health of humans, animals, and plants is interdependent, and reliant on their environment[20]. Archaea form relationships, ranging from symbiosis to dysbiosis, with other microbes in the environment as well as with human, plant, and animal hosts. Therefore, even though intriguingly no archaeal pathogens have been identified so far, archaea can be linked to the well-being of their hosts[21–23]. Furthermore, archaea have a significant impact on biogeochemical cycles and thus affect life on Earth in various ways[24,25]. For example, methanogenic archaea (a specialized group of archaea) are becoming increasingly important in facing climate change dynamics as they are considered the main methane producers on Earth[26–28]. Thus, achieving our global climate sustainability goals necessitates understanding the roles of archaea in diverse ecosystems.

Archaea are now commonly accepted as the root of Eukarya, thanks to the recent discoveries of new species and the ensuing reevaluation of their

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phylogenetic relations (e.g., the presence of eukaryotic signature proteins)[29–32]. However, archaea often have unique metabolism and information processing pathways, requiring the development of novel experimental tools and methods of gene expression, and resulting in shifting paradigms for thinking about Biology. The shortage of established resources, together with unfamiliar or difficult experimental conditions for working with many archaea, has triggered the development of creative and collaborative initiatives to cope with the challenges of working in this research field. Similarly, while other established biological research communities (e.g. yeast, fruit flies, and nematodes[33–37]) have evolved career development pathways and opportunities over time, the archaeal research community has only recently initiated such structures, due to the smaller number of members. This situation provides an opportunity to not only benefit from experiences in other communities, but also to develop innovative and inclusive ways to advance archaeal research.

To fully understand Biology requires studying the molecular, biochemical, genetic, and ecological functions of organisms from across the Tree of Life. Given the unique contributions of archaeal research to our understanding of Biology, coordinated research and education are needed to better predict, understand, and use archaeal biology to address pressing challenges in climate, sustainability, and health. Here we discuss various efforts in building a global archaea community, ranging from providing resources for scientific inquiry to developing an online platform for sharing methods to increase reproducibility across the field, from developing tools for data mining to embracing FAIR (findable, accessible, interoperable, reusable) data sharing principles. Additionally, initiatives aimed at fostering a collaborative community include organizing local and international meetings, online seminars, and discussion forums. All the resources cited in the text, as well as others that may be of interest to the archaeal community, are listed in Supplemental Data 1. We also highlight the remaining hurdles in gaining a fundamental understanding of the archaeal domain, as well as in increasing its visibility globally.

Protocols and methods—learning from each other's mistakes and successes

Although the archaeal research community is expanding quickly, transitioning to this field of research or even starting a new research project focused on a different archaeal species can be challenging, especially if the species falls outside the limited set of well-established archaeal model organisms. Indeed, since many archaeal species studied today are extremophiles, determining ideal culture conditions remains challenging. Undergraduate-level microbiology curricula in many institutions do not introduce students to techniques for growing microbes at extreme pH, temperature, pressure, or strict anaerobicity, and as a consequence, many microbiologists are unfamiliar with and naturally choose to pursue easier-to-cultivate microbes. As a result, while the number of sequenced archaeal species is rapidly increasing, especially through metagenomic analyses, cultivating new species remains a major obstacle, sometimes requiring long-term efforts from multiple research groups such as the recently cultivated members of the Asgard phyla[31,38]. Additionally, equipping a laboratory to accommodate these non-conventional culture conditions can be complex and expensive. So far, only a few archaeal model organisms are well-established[39,40], primarily representatives from the phyla Euryarchaeota and Crenarchaeota that typically grow comparatively fast (doubling time <5 h) and under heterotrophic conditions. While some of them benefit from extensive toolkits on the genetic, molecular, and cell biological level (e.g., *Haloferax volcanii*, *Halobacterium salinarum*, *Sulfolobus acidocaldarius*, *Pyrococcus furiosus*, *Thermococcus kodakarensis*, and several methanogens[40–46]), others still lack the genetic tools and/or established methods necessary for in-depth biological investigations (e.g., *Methanobrevibacter smithii*[47] or Asgardarchaeota[13]).

These challenges in working with archaea necessitate the development of new or adapted media recipes, genetic tools, physiological assays, and specialized equipment. The relatively small size of archaeal research groups means that the burden of protocol development is distributed on a few shoulders. Consequently, synergistic collaborations and effective communication of successful methods are key to advancing the field. Unfortunately, the material and methods sections in journal articles are often insufficient to fully reproduce the described experiments[48–50]. Long chains of references, requiring time-consuming tracing of relevant methods, are paired with a lack of details that can prevent other researchers from understanding and adapting the method. Often, what appears as a minor detail in protocols for the authors is precisely what is missing for their fellow researchers to establish their method in a different lab. In addition, access to publications and their methods sections is often restricted by paywalls, leading to an inequitable distribution of crucial information.

Although direct training with experts in methods or model organisms is often the most efficient way to get started, the global, open dissemination of knowledge, methods, up-to-date protocols, as well as lab-bench tips and tricks would be preferable. For some archaeal phyla, early community efforts resulted in protocol collections like the Halohandbook[51]; in addition, dedicated books with peer-reviewed methods articles have been published[46]. However, while contributions to general protocol-centric journals (e.g., Bio-protocol, STAR protocols) have been made, a central platform collecting protocols for all archaea and distributing them in an open-access format has been missing so far.

More recently, a group of Early Career Researchers, recognizing and experiencing these challenges themselves, started developing an online protocol repository for the archaea community: ARCHAEA.bio, which has received a lot of interest and support from the community. Their mission is to increase knowledge transfer, method clarity, and data reproducibility within the archaeal community. Archaeal researchers are invited to submit protocols including detailed methodology that will be peer-reviewed to be freely and openly available to the entire community, while also being published on the open science platform Zenodo. In this way, protocols will be assigned a Digital Object Identifier (DOI®) that will allow for their citation in material and methods sections of research publications, and the methods will be publicly searchable by keywords and taxa.

Another common obstacle when starting to work with archaea is the limited availability of strains. General culture collections often do not accept archaeal strains due to their specialized culture conditions. Therefore, only a handful of resources distribute a range of existing strains (Supplemental Data 1), including the Japan Collection of Microorganisms, the German Collection of Microorganisms and Cell Cultures (Leibniz Institute DSMZ), and the American Type Culture Collection[52]. However, the deposition of new strains is further limited by many culture collections that only accept axenic samples, while new archaea are often discovered by metagenomics approaches, and many can only be grown in communities or as enrichment cultures. Encouragingly, the Archaea Centre at the University of Regensburg is actively working on creating an archaea-centered strains database, as well as on potential solutions for the isolation and high-throughput distribution of archaeal species. Increasing access to enrichment cultures, isolated strains and generated mutants could also be achieved by the creation of an interactive database of existing strains and corresponding, decentralized research labs from which those strains can be requested. Platforms like ARCHAEA.bio could serve as a hub to generate such databases and connect researchers to these dispersed resources. In addition, ARCHAEA.bio aims to create not only a repository for wet bench protocols but also a collection of data analysis methods, bioinformatics tools, and 'omics databases.

Data sharing—distributing the knowledge, and enabling new analyses

In addition to the availability of strains and methods, data sharing plays a vital role in advancing scientific research and fostering collaborations, especially in a comparatively small research community like the archaeal one. The availability of databases not only accelerates individual research projects but also enables the community to collectively build a comprehensive understanding of archaeal biology. Systems biology and 'omics approaches are rapidly increasing our knowledge about biological processes in archaea while generating large amounts of data that can be difficult to analyze comprehensively, thereby providing striking examples of the usefulness and challenges of data sharing. While "big data" challenges are not unique to the archaea research community, the unique place of archaea in the Tree of Life presents a particular challenge when transferring bioinformatics approaches from far-distant relatives, resulting in lower-confidence functional prediction assignments for archaeal genes and organisms[53,54].

Soon after the first archaeal genomes were sequenced, the Archaeal Genome Browser was developed to provide user-friendly access to gene sequences in their genomic context[55], using sequences deposited to the NCBI GenBank[56]. The Archaeal Genome Browser is not only used to inform common molecular biology experiments but also facilitates the comparison of archaeal genomes, e.g., to analyze sequence conservation and to predict operons as well as non-coding RNAs[57]. Another database that benefited from the increased availability of archaeal genome sequences is the Archaeal Clusters of Orthologous Genes (arCOG) database, which focuses on the functional annotation of proteins in archaea[58]. With limited experimental evidence for protein functions in archaea, public resources like this are invaluable for the interpretation of system-wide analyses.

Combining available datasets to gain further insights into archaeal cell biology is also the aim of the Archaeal Proteome Project (ArcPP), which centers around mass spectrometry-based proteomics[59]. The ArcPP has shown that ʻomics data often contains more information than an initial analysis, trying to answer a specific biological question for which a dataset was generated, revealed. Through unified analyses, the ArcPP gained new information on post-translational modifications, improved proteomic sample preparation, and aided proteogenomic efforts[59–62]. While the ArcPP was initiated solely on data for the model archaeon *Haloferax volcanii*, recent developments extended the database to a variety of archaea.

Together, the Archaeal Genome Browser, arCOG, and ArcPP illustrate that the combination of large-scale and system-wide analyses has a greater benefit than the mere sharing of data and knowledge: it can result in new biological insights and the development of hypotheses that, in turn, can be tested experimentally. This efficient use of experimental data is especially important for large ʻomics datasets that are relatively expensive to generate. Notably, the sharing of data is not limited to the mentioned examples for archaea-specific databases. General databases commonly used by archaeal researchers include NCBI's GenBank[56] and Gene Expression Omnibus[63] for genomics data, KEGG[64], ModelSEED[65], and KBase[66] for predicting and modeling metabolism, rrnDB[67], and SILVA[68] for ribosomal RNA sequencing data, and the ProteomeXchange consortium for mass spectrometric data[69]. Importantly, databases like UniProt[70] require community efforts to update entries whenever new information becomes available, to serve as valuable resources with aggregated information that can be used for a variety of tool developments and further analyses. Furthermore, the inclusion of comparative quantitative analyses, and the combination of results from different ʻomics technologies (like the integration of RNA sequencing data in the Archaeal Genome Browser) remain challenging topics for future database developments.

Finally, the sharing of bioinformatic tools and open-source code is crucial not only to reproduce results from published analyses, but also to achieve standardized and unified workflows that allow for comparisons between different datasets. So far, source code is mainly shared through designated platforms like GitHub in the form of isolated repositories. Collections like ARCHAEA.bio (see above) are likely to improve the visibility of these repositories, making it easier to gain an overview of algorithms that are available for specific tasks. Furthermore, platforms like KBase provide access to full workflows integrated into a high-performance computational infrastructure. The reusability of bioinformatic code is also part of increasing efforts to follow FAIR sharing principles, which apply not only to bioinformatic tools but also to the sharing of experimental data. Notably, open-access licenses, the use of unique and permanent identifiers (e.g., DOIs associated with specific datasets or versions of databases), and the sharing of all relevant metadata are increasingly required by journals and funding organizations as well. Having a curated data-sharing platform would not only promote the dissemination of information among existing archaea researchers but would also lower the barrier to entry for new and early career investigators to contribute to the broader archaeal research community by making it easier to identify knowledge gaps, research priorities, and new frontiers.

Community building for collaborations, discussing results, and advancing Early Career Researchers

Sharing and collaborating are at the core of academic research, which involves creating communities that expand beyond geographic borders and scientific backgrounds in order to generate new knowledge. Conferences are still a main avenue for building communities and collaborations, whether they are local or international (Supplemental Data 1). There are two main international conferences focused on archaea that occur alternatingly every other year: the Gordon Research Conference®: Archaea: Ecology, Metabolism and Molecular Biology and the EMBO© workshop Molecular Biology of Archaea. Traditionally, archaea researchers have also been very active in participating in well-established conferences about extremophile microorganisms, such as the International Conference on Halophilic Microorganisms (Halophiles), organized every 3 years and which is currently supported by FEMS, the International Congress on Extremophiles organized by the International Society for Extremophiles every two years and the Thermophiles meeting organized every 2 years Archaea researchers are also well-represented participants of conferences about ecology (ISME Symposia), geochemistry (ISEB, ICGOA) and astrobiology (AbSciCOn) due to the importance of Archaea in these areas.

While archaeal research has long been regarded as a niche within larger microbiology communities and conferences, the ongoing expansion and increased attention of archaeal biology resulted in the inclusion of archaea in new conference titles, such as the Meeting on Regulating with RNA in Bacteria and Archaea, The Bacterial Cell Biology and Development GRC®: Organization, Dynamics, and Development of Bacterial and Archaeal Cells, and the recent EMBO workshop Archaeal and bacterial cell division: beyond the Z-ring. The American Society for Microbiology and other microbiology societies take a different approach, by interspersing archaeal presentations among their general meeting sessions to familiarize a broad swath of microbiology researchers and educators with archaeal microbiology. Further conferences facilitate the transfer of knowledge between the domains of life, including not only bacteria and archaea but also eukaryotes, often through meetings focused on specific research topics such as the Plant and Microbial Cytoskeleton GRC® or Chromosome dynamics GRC®. With the expansion of research topics in archaea beyond extremophiles, the increase in microbiome research, and the revealed evolutionary ties between archaea and eukaryotes, the number of inter-domain conferences is bound to increase in the coming years, helping to build connections between diverse scientific communities.

However, international conferences often put financial strain on resource-limited research groups and tend to disadvantage groups from outside of the US and Europe. Therefore, the virtual Archaea Power Hour (APH) was initiated to develop a community independent of travel to promote best practices in STEM research and education[71]. Based on monthly online seminars and a chat platform, their goal is to foster collaboration, and to provide an equitable forum for discussing science in a decentralized format. The APH was founded by established scientists and is now mainly organized by Early Career Researchers, and encourages participation and presentation from any career level. While it was first established in the Americas, spanning North, Central, South America, and the Caribbean, it has since expanded to Europe and is working on models to facilitate participation from across the globe. The APH is structured as an expandable network that lends easily to launching regional "chapters" to increase speaking and leadership opportunities while maintaining the feel of a small, welcoming community. By using social media platforms and recording presentations for member distribution, community announcements, and research findings are rapidly disseminated worldwide. The APH membership is only limited by an individual researcher's desire to participate and the ability to recruit engaged colleagues to serve on chapter organizing committees.

In addition, archaeal researchers are active in building local communities, often creating dedicated branches out of broader scientific societies

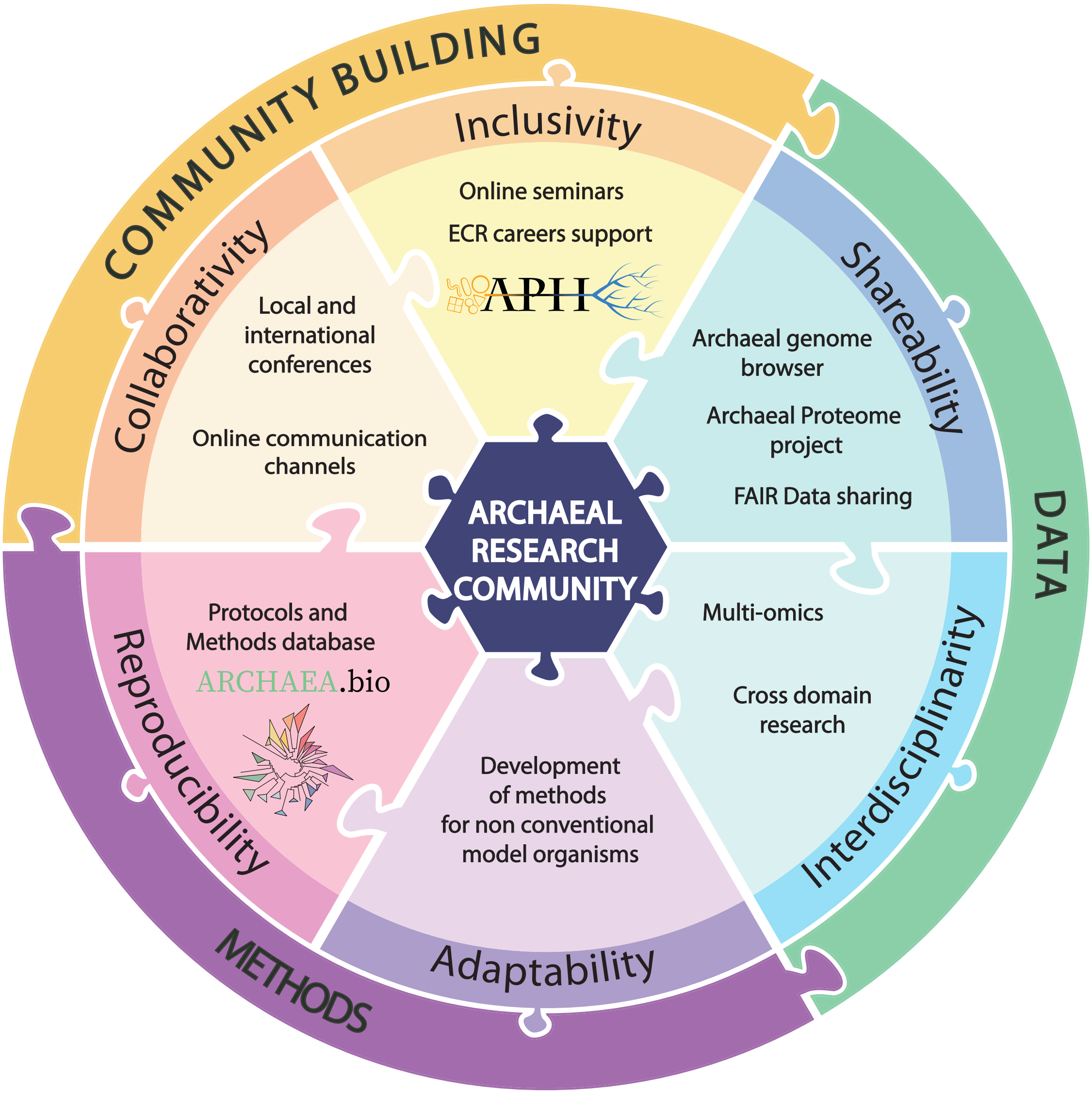

Fig. 1 | The Archaeal Research Community: values and strategies. Archaeal researchers are self-organizing in a dynamic community around three main axes and corresponding values: (i) community building, to foster collaboration and inclusiveness between its members, (ii) data, to ensure its shareability and accessibility and encourage interdisciplinarity, and (iii) methods, to enhance the reproducibility and adaptation of the methods to the archaeal research. Various specific initiatives and general topics are listed as examples of community actions towards these goals. *Usage of ARCHAEA.bio and APH logos were approved by ARCHAEA.bio and the Society for Archaeal Biology and APH and Connor J. Hines, respectively. APH logo attribution is: Connor J. Hines.*

(Supplemental Data 1). For example, The Thematic Group Archaea (Groupe Thematique Archees) is a dedicated section of the French Society for Biochemistry and Molecular Biology (SFBBM). This group organizes monthly online seminars for early career researchers (ECRs) to present their work and an annual retreat for connecting French archaeal researchers. In the UK, the Archaea Group is part of the Genetics Society and is organizing the Annual UK Workshop on Archaea. In Germany, The Archaea specialist group is part of the Association for General and Applied Microbiology (VAAM). In China, the Archaea Professional Committee, a subcommittee of the Chinese Society for Microbiology, is locally promoting archaeal research and is aiming to organize international conferences together with archaeal researchers from Japan and South Korea. Furthermore, internal communities also have arisen based on events with specific research topics, such as the Frankfurt Meeting on Genome Function and Gene Regulation in Archaea, the International Workshop on Geo-Omics of Archaea, or organizing a centralized mailing list to share knowledge on haloarchaea.

Recently, the ARCHAEA.bio project team founded the first independent archaea society: The Society for Archaeal Biology. Its primary mission is to support the development of the ARCHAEA.bio platform, which initially will focus on the sharing of protocols, but in the future aims to provide a global resource not only for archaeal researchers but also for educating the general public about archaea, their biology and their importance on our planet.

Future perspectives and challenges

As we discussed above, the archaeal community has a compelling incentive to develop a collaborative and inclusive research environment based on three main areas: Community building, Data accessibility, Methods development, and reproducibility (Fig. 1), with a wealth of early career and established researchers motivated in pursuing these efforts.

These promising initiatives are likely to solidify and expand the archaeal research community and its global impact. Indeed, similar successful initiatives have arisen in other fields of biology, with examples of yeast, fruit fly, nematode and bacterial research communities that have developed online tools and databases to share data, methods, and more, such as yeastgenome.org[72], flybase.org[35], WormBook[36] or SubtiWiki[73], respectively. Recently, efforts within the *Acinetobacter baumannii* research field also led to the establishment of a database[74] that combines genotypic and phenotypic data, as well as a resource hub website[75]. These examples show not only a strong desire of researchers to connect, collaborate, develop tools, and share data within their disciplines but also the need for community building and database solutions that are specific to the respective research field. Efforts within the archaeal research community are thus likely to further accelerate our understanding of archaeal biology and its potential applications.

However, archaeal research still suffers from limited funding and awareness, making it challenging to recruit, retain, and promote people among the ranks. Contrary to the current trend of decreasing allocations to fundamental research, increased funding would be needed, for example, to explore cultivation methods, develop genetic tools and other techniques, as well as for large-scale microbiome studies. These research topics can lead to original scientific discoveries, as well as biotechnological and biomedical applications. Despite numerous examples of archaeal research leading to paradigm shifts in knowledge and new technologies, including the first glimpse of the ribosome[76], the discovery of life-saving drugs[77,78], and ability to generate clean-burning energy[79], to name a few, funding agencies are often reluctant to support these topics, in part due to poor representation of archaeal researchers in these agencies, and correspondingly little awareness of the widespread impacts of archaeal research on society. However, we cannot understand Biology as a whole or implement successful bio-based technologies without considering the critical archaeal components of every biological system. This chicken-and-egg problem should be tackled on multiple fronts. Although science dissemination and outreach are important aspects of a researcher's job, it is often overlooked in annual workplace evaluations or tracked as a productivity metric. Promoting outreach and education in the archaeal research field, in particular, would be critical to gain much-deserved public and academic visibility.

While archaea are gaining visibility in the academic and scientific field, these organisms remain mostly unknown to broad communities. Even at universities with Microbiology programs, it is fairly rare that students are exposed to in-depth material dedicated to archaea unless archaeal researchers are teaching in these programs themselves. Instead, archaea are often just a side-note compared to bacteria, and updated information about archaea (e.g., their ubiquity rather than limitation to extreme environments or their evolutionary relationship to eukaryotes) is seldom conveyed. These educational gaps are probably a direct reflection of the still relatively small size of the archaeal research community and teaching force, as well as the lack of dedicated teaching materials about archaea, which would allow educators to create course contents more easily, and improve the learning experience for students. A few books about archaea exist but even fewer are written to target a general or young audience[80–83].

With the Internet emerging as a major resource for learning and education, books may also no longer be best suited as modern teaching materials. However, only a few educational videos, podcasts, or blog posts about archaea are available online (see Supplemental Data 1), and Wikipedia entries are not as developed and up-to-date as other topics. Online learning is further increasing, especially since the COVID pandemic, and may represent a promising avenue to educate a broad audience about archaea. A subgroup of the APH is producing a podcast about this domain of life, "The ArchaeaCast," to showcase the fascinating world of these microorganisms in an accessible manner, and the Society for Archaeal Biology is aiming to encourage science communication articles for the general public. In addition, several examples of teaching experiments focusing on archaea exist, with the idea to provide hands-on experience for high school and undergraduate students to integrate into existing biology curricula[84–87]. Further protocols for educational experiments will be collected by the ARCHAEA.bio project and could be integrated into existing educational and outreach programs such as the International Microbiology Literacy Initiative[88]. With these joint efforts from the community, we can hope for increased awareness and education about archaea in the future, both for students and the general public.

In the meantime, archaeal researchers must use any available resources to efficiently demonstrate the significant impact that funding in this area can have. Collaborative, interdisciplinary research, FAIR sharing of protocols, strains, and data, as well as international networks to support Early Career Researchers and minoritized scientists, are essential to building a strong foundation for archaea research and innovation now and into the future.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

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Author contributions

S.I. and S.S. wrote the first draft of the manuscript, and N.R.B. contributed to significant changes. S.I. created the figure and supplemental data table and modified them in discussion with S.S. All authors read, commented on, and edited the manuscript, resulting in the final version.

Competing interests

The authors declare the following competing interests: S.I. and S.S. declare no competing interests. N.R.B. has disclosed a significant financial interest in RollingCircle Biotech, LLC and Molecular Trait Evolution, Inc.

Additional information

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