nature portfolio

Peer Review File

Advancing Archaeal Research through FAIR Resource and Data Sharing, and Inclusive Community Building

Corresponding Author: Dr Stefan Schulze

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
Ithurbide, Buan, and Schulze's piece on community building is remarkable, and it is a constant question I am asked when talking to colleagues from other fields: where should someone go if they want to start working on archaea? Databases are scattered, and protocols must be completed to make them unreproducible. Therefore, there is a growing need to build resources to allow tools and knowledge accessible to scientists and the public.

I have no significant concerns but a couple of suggestions:

1) authors could organize the resources cited in the text as tables. For example, a table for meetings, another for databases etc.

2) It would be nice to add the Bacterial Cell Biology and Development GRC meeting, which comes with the sub-title of “Organization, Dynamics, and Development of Bacterial and Archaeal Cells”

3) It is not essential for the manuscript, but I would love to know more about how other communities (fly, worm, yeast, etc.) successfully develop their community resources. This could be a great addition to the manuscript and allow the archaeal community to learn from others’ pros and cons.

4) The title reads so long and complicated. Archaea is lost in the end. Something like “Cultivating a FAIR Archaea Community: Practices for Inclusive Resources and Data Sharing” would appeal more to the general readership.

Kind regards,
Alex Bisson

Reviewer #2

(Remarks to the Author)
In this manuscript, the authors describe the necessity to increase our knowledge about archaeal biology. They provide insights on how this can be achieved in a community-driven way and discuss the tools and resources that are already available to achieve this goal. The text is an excellent summary for every person interested in working on archaea, to get first ideas about where to start.

To minor points:

Line 91: I’m not sure I would call H. volcanii and S. acidocaldarius rapid growing (especially not in comparison with typical bacterial model systems). This applies to archaeal model systems in P. furiosus and T. kodakarensis, which have a doubling time of 20 minutes. The genetic toolbox of T.kodakarensis (developed by Haryuki Atomi) and quite some methanogens is pretty well developed and should probably be mentioned, too.

Line 94: for the Haloferax volcanii genetic toolbox, a reference by Thorsten Allers should also be provided

Reviewer #3

(Remarks to the Author)
Overall, I think it is a very interesting paper that summarizes the existing resources and ongoing efforts in the engaged broader archaeal scientific community, although most contributions focus on the USA and Europe regions without including other parts of the world in this paper. However, I strongly agree that we should have papers like this one to accelerate archaeal research, as it is a fairly small and young research community compared to others. Nevertheless, I do have some comments on the proposed strategies in this paper.

1. "Platforms like ARCHAEA.bio could serve as a hub to connect researchers to these dispersed resources, or to establish a database of existing strains and corresponding, decentralized labs from which those strains can be requested." I am concerned that the archaeal resources (strains) are very diverse and difficult to centralize, as the culture conditions for different strains vary significantly, making it challenging for platforms like ARCHAEA.bio to undertake this task. I suggest that platforms like ARCHAEA.bio should collect all archaeal strain information, including the lab, culture conditions, and contact details, so that it can assist researchers in easily accessing this information.

2. The virtual Archaea Power Hour (APH) currently only covers the USA and Europe, yet East Asia and other regions should be included, as they also contribute significantly to archaeal research, such as China and Japan.

3. Additionally, I am aware that China and Japan have already established their research societies for archaeal research a few years ago, so it would be beneficial to have some links to these communities for ARCHAEA.bio project team. The chairpersons for the two Archaea Societies are Prof. Meng Li (limeng848@szu.edu.cn) for China, and Yoshizumi Ishino (protein@agr.kyushu-u.ac.jp) for Japan.

Reviewer #4

(Remarks to the Author)
The manuscript is a narrative about the current state of needs of the archaeal research community and the microbiology field in general. It is timely given recent developments in archaeal research including those that relate to expanding the diversity of archaea (e.g., novel methanogen phyla, novel sulfate/sulfite reducers), evolutionary implications (e.g., origin of eukaryotes in ancestors of Asgard, origin of sulfite reduction in Euryarchaea, origin of nitrogen fixation in methanogens), and functioning of ecosystems (archaeal nitrification, anaerobic alkane oxidation). The outline of the resources that are being developed to build capacity and to grow the community (all largely from the ground up) should serve as a wake up call to the broader microbiology community and overall funding environment about the significant advances that are being made in this field and the even more significant advances that could be made for human/ecosystem benefit with even slightly more attention and investment. I offer the following comments to further improve a future version of this paper.

General comments:

The paper would go a lot further by providing specific examples of research outputs from Archaea that have changed our understanding of microbiology. E.g., Brock/Zinder discovering thermoacidophilic Sulfolobus, Stetter/Huber/Takai and their many discoveries involving hyperthermophilic archaea, Delong and the marine nitrogen cycle, Orphan/Delong and ANME, Doudna/Banfield and CRISPR loci, Thauer/Kaster and electron bifurcation in methanogens, among many others. Biotechnological revolutions could also be better highlighted such as Metallosphaera and mineral leaching, Pyrococcus and polymerases, or application of alkaliphilic archaeal enzymes in the paper industry. Various works by Fournier, Martin, Boyd, on archaea as the progenitors of the first cells could also be highlight. In this way, the average reader can develop a better appreciation for the paradigm-challenging revolutions that derive from the archaeal field and thus be more capable of seeing how additional support could further this field and lead to even more revolutionary ways of thinking about archaea in natural and engineered ecosystems.

I wonder if a figure to illustrate biogeochemical cycles (C or N cycle) could be useful. Highlight what they looked like before marine ANME or AOA were discovered (flux or just cycle wise) and what these cycles are now known to comprise? I believe Thauer 2008 Review highlighted some of the CH4 flux numbers that one could use. There may be more refined numbers now for this and marine N cycle now that one could use.

Some of the overarching themes conveyed in the manuscript could be made for any field (e.g., Lines 97-108; lines 230-231). It is suggested to use more specific examples to differentiate this field from others so that you can validate the case.

Specific Comments

Line 17 and again in line 62: “young” lacks context here. Arguably, some of the most successful researchers are old, yet I don’t think that is what the authors are going for here.

Line 20: Remove “the” from host-associated microbiomes. More importantly, however, g, archaea are not major players in host associated microbiomes, correct? Even in humans <30% of people are colonized by archaea. Perhaps give examples to make this more accurate (e.g., ruminants).

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Line 38: Again, I don't think that many view archaea as major contributors to health. Provide an example or two to make this more clear and accurate as to where this is definitely true.

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Line 299: Ken Timmis is driving the International Microbiology Literacy Initiative (https://imili.org/) to develop curricula and activities to promote microbiology literacy globally, starting at a young age. One could envisage contributions from this group to better highlight archaea and thereby push the authors agenda earlier from a grass roots level.

Version 1:

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Overall，I think authors have well addressed my concerns and provided a good response. I have no more comments. Well done and hope you have more contributions on the archaeal community.

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It is quite remarkable that the authors were so dismissive of many of the suggestions made, in particular the suggestion to improve the perception of archaea as contributors to Earth systems that are of societal consequence. Again, the idea is to motivate people to consider studying Archaea (difficult imagining someone joining the archaeal research community or caring about resources available to it if they are not compelled to join the community).

Regardless of the above, I can support publication.

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

Ithurbide, Buan, and Schulze's piece on community building is remarkable, and it is a constant question I am asked when talking to colleagues from other fields: where should someone go if they want to start working on archaea? Databases are scattered, and protocols must be completed to make them unreproducible. Therefore, there is a growing need to build resources to allow tools and knowledge accessible to scientists and the public.

I have no significant concerns but a couple of suggestions:

1) authors could organize the resources cited in the text as tables. For example, a table for meetings, another for databases etc.

The authors agree that a table summarizing all the resources/initiatives and materials mentioned in the text would be of great benefit for our readers. A corresponding table has been added as Supplemental Data 1 in this new version.

2) It would be nice to add the Bacterial Cell Biology and Development GRC meeting, which comes with the sub-title of “Organization, Dynamics, and Development of Bacterial and Archaeal Cells”

Thank you for this additional conference; it has been added in the text (Line 247) and in the new table.

3) It is not essential for the manuscript, but I would love to know more about how other communities (fly, worm, yeast, etc.) successfully develop their community resources. This could be a great addition to the manuscript and allow the archaeal community to learn from others’ pros and cons.

The authors agree that it would be ideal to access this knowledge and to learn from each other's fields/community development. Assessing the advances and drawbacks in other communities has the potential to fast forward the community development of emerging fields of research like ours. However, a comprehensive review of this information is beyond the scope of our manuscript. Nevertheless, we included a short statement in the introduction (lines 72-77), as well as a short paragraph in the Future perspectives (lines

307-318) with a few references to other well-established communities, which may spark efforts to assemble the corresponding knowledge into a separate manuscript.

4) The title reads so long and complicated. Archaea is lost in the end. Something like “Cultivating a FAIR Archaea Community: Practices for Inclusive Resources and Data Sharing” would appeal more to the general readership.

We have modified our title, which now reads: “Advancing Archaeal Research through FAIR Resource and Data Sharing, and Inclusive Community Building” (line 1).

regards,
Alex Bisson

Reviewer #2 (Remarks to the Author):

In this manuscript, the authors describe the necessity to increase our knowledge about archaeal biology. They provide insights on how this can be achieved in a community-driven way and discuss the tools and resources that are already available to achieve this goal. The text is an excellent summary for every person interested in working on archaea, to get first ideas about where to start.

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Thank you for pointing this out; we have modified the rapid growth statement and included additional model systems (lines 107-114).

Line 94: for the Haloferax volcanii genetic toolbox, a reference by Thorsten Allers should also be provided

We agree and have added additional references (line 112).

Reviewer #3 (Remarks to the Author):

Overall, I think it is a very interesting paper that summarizes the existing resources and ongoing efforts in the engaged broader archaeal scientific community, although most contributions focus on the USA and Europe regions without including other parts of the world in this paper. However, I strongly agree that we should have papers like this one to accelerate archaeal research, as it is a fairly small and young research community compared to others. Nevertheless, I do have some comments on the proposed strategies in this paper.

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We realized that this section was confusing for the reader. Indeed, as mentioned, the envisioned role for Archaea.bio is not to physically collect/store strains but to create an interactive resource that could help researchers to find information and contacts to access these strains more easily. This paragraph has been rewritten accordingly, see lines 158-161.

2. The virtual Archaea Power Hour (APH) currently only covers the USA and Europe, yet East Asia and other regions should be included, as they also contribute significantly to archaeal research, such as China and Japan.

Addressed by adding the following text (lines 269-275): “The APH is structured as an expandable network which 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.”

3. Additionally, I am aware that China and Japan have already established their research societies for archaeal research a few years ago, so it would be beneficial to have some links to these communities for ARCHAEA.bio project team. The chairpersons for the two Archaea Societies are Prof. Meng Li (limeng848@szu.edu.cn) for China, and Yoshizumi Ishino (protein@agr.kyushu-u.ac.jp) for Japan.

Thank you for the information that we have missed previously. It is indeed important for us to highlight the initiatives of all the communities worldwide. Unfortunately, online information about these societies is very limited or inaccessible. Therefore, we have reached out to Prof. Meng Li and Prof. Yoshizumi Ishino to learn more about these societies and any other related initiatives in their local communities. Based on their responses, we have included additional information in the text (lines 283-286) and in the new Supplemental Data 1 table.

Reviewer #4 (Remarks to the Author):

The manuscript is a narrative about the current state of needs of the archaeal research community and the microbiology field in general. It is timely given recent developments in archaeal research including those that relate to expanding the diversity of archaea (e.g., novel methanogen phyla, novel sulfate/sulfite reducers), evolutionary implications (e.g., origin of eukaryotes in ancestors of Asgard, origin of sulfite reduction in Euryarchaea, origin of nitrogen fixation in methanogens), and functioning of ecosystems (archaeal nitrification, anaerobic alkane oxidation). The outline of the resources that are being developed to build capacity and to grow the community (all largely from the ground up) should serve as a wake up call to the broader microbiology community and overall funding environment about the significant advances that are being made in this field and the even more significant advances that could be made for human/ecosystem benefit with even slightly more attention and investment. I offer the following comments to further improve a future version of this paper.

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highlighted such as Metallosphaera and mineral leaching, Pyrococcus and polymerases, or application of alkaliphilic archaeal enzymes in the paper industry. Various works by Fournier, Martin, Boyd, on archaea as the progenitors of the first cells could also be highlight. In this way, the average reader can develop a better appreciation for the paradigm-challenging revolutions that derive from the archaeal field and thus be more capable of seeing how additional support could further this field and lead to even more revolutionary ways of thinking about archaea in natural and engineered ecosystems.

We have highlighted several additional groundbreaking findings in the introduction to emphasize the importance of archaeal research (lines 37-49). We also want to note that this manuscript is not meant as a review of archaeal research findings, but is focused on community efforts amongst archaeal researchers. Based on this limited scope, not all suggestions of the reviewer were included, even though we agree that they represent invaluable contributions to the field.

I wonder if a figure to illustrate biogeochemical cycles (C or N cycle) could be useful. Highlight what they looked like before marine ANME or AOA were discovered (flux or just cycle wise) and what these cycles are now known to comprise? I believe Thauer 2008 Review highlighted some of the CH4 flux numbers that one could use. There may be more refined numbers now for this and marine N cycle now that one could use.

We appreciate the thoughtful suggestion to include a figure of biogeochemical cycles. However, we think that a review of specific archaeal research topics is beyond the scope of this perspectives article. We mention nutrient cycles and methanogenesis a couple of times in the introduction, along with other current topics to provide an overview of the importance of archaeal research (lines 37-49).

Some of the overarching themes conveyed in the manuscript could be made for any field (e.g., Lines 97-108; lines 230-231). It is suggested to use more specific examples to differentiate this field from others so that you can validate the case.

We agree that some of the overarching themes apply to other fields as well. However, we are not aiming to focus exclusively on themes that are unique to archaea, and instead aim to highlight some potential solutions (to both general and more specific challenges) and efforts that are specific to the archaeal research community. We would also like to point out that in many instances we intentionally use more general statements to introduce a topic (e.g. on the theme of international conferences) before narrowing the view to archaea. Where applicable, we have also expanded our explanations on archaea-specific challenges (e.g. for culture collections). In addition, we added a paragraph on community efforts in a few other, well-established research communities as suggested by reviewer 1.

Specific Comments

Line 17 and again in line 62: “young” lacks context here. Arguably, some of the most successful researchers are old, yet I don’t think that is what the authors are going for here.

Thank you for raising this point. We have rephrased the sections to avoid the misconception that we were focusing on chronologically young researchers rather than the relative development of the research field as a whole.

Line 43 now reads: “Furthermore, they still remain understudied compared to Bacteria and Eukaryotes, resulting in a comparatively small research community. “ and Line 72 now reads: “Similarly, while other established biological research communities (e.g. yeast, fruit flies, and nematodes30–34) have developed career development pathways and opportunities over time, due to the smaller number of members, the archaeal research lacks many of these structures, providing an opportunity to not only benefit from experiences in other communities, but also to develop innovative and inclusive ways to advance archaeal research.”

Line 20: Remove “the” from host-associated microbiomes. More importantly, however, g, archaea are not major players in host associated microbiomes, correct? Even in humans <30% of people are colonized by archaea. Perhaps give examples to make this more accurate (e.g., ruminants).

Although not numerically dominant, research shows all humans have archaea in their microbiomes. Early 16S amplicon sequencing failed to amplify archaeal DNA, which led to the misconception that archaea were absent. Please see https://journals.asm.org/doi/full/10.1128/mbio.00824-17, https://academic.oup.com/femsre/article/39/5/631/530150, and https://www.sciencedirect.com/science/article/pii/S2452231716300148 for recent reviews on this topic.

Line 35: While I don’t think the authors were trying to make a taxonomic argument here, it would nevertheless be cleaner to replace “class” with “domain”

The word “class” has been removed as part of the restructuring of the Introduction.

Line 37: change “is” to “are”

Thank you for pointing out this typo. The change has been made as suggested.

Line 38: Again, I don’t think that many view archaea as major contributors to health. Provide an example or two to make this more clear and accurate as to where this is definitely true.

Thank you for raising this question. As the research advances, investigators are finding a stronger link between archaea and human health. Although no archaeal examples of frank pathogens have been identified, archaea are increasingly associated with microbial dysbioses and show complex relationships with host symbionts and pathogens. Please see https://www.sciencedirect.com/science/article/pii/S2452231716300148 and https://pmc.ncbi.nlm.nih.gov/articles/PMC11286065/ as examples of recent reviews of the link between archaea and human health. We have included an additional sentence in the Introduction to clarify this point (line 57), reading: "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 wellbeing of their hosts."

However, the goal of this manuscript was not meant to make the case for archaea and health and we feel it would be distracting for the reader to expand further on this topic at this point in the manuscript. Instead, we will focus the text on community-building activities to promote archaea research overall.

Line 43: While ubiquitous, I think most researchers still believe Archaea inhabit niches that impose chronic energy stress on cells (e.g., Valentine 2007). This is true for extremophilic methanogens and nitrifiers due to energy limitation, etc. even though they are typically not viewed as inhabiting extreme environments. In other words, Archaea have either created or adapted to inhabit environments where Bacteria have vacated or been unable to successfully compete in.

Please see our response to your question below. Due to technical limitations, earlier research has led to entrenched misconceptions about archaeal biology, which is why we urgently advocate for building and growing the archaeal biology research community.

Line 45: I am unaware that it has ever been difficult to detect archaea in metagenomic datasets?

Thank you for your question. Early metagenomics relied on amplicon sequencing, which relied on "universal" primer sets that do not amplify archaea. Over time, 16S primer sets have been expanded to better identify archaeal taxa, and researchers are increasingly using primer-independent methods, resulting in a rapid expansion of archaeal sequences in genome databases. Please see https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0043093 and other manuscripts describing these issues. However, even with new sequencing methods, bioinformatic tools and pipelines that are based on early biased datasets propagate error in mischaracterizing archaea and archaeal genes in metagenome datasets.

Line 86: I don't see the logical connection between being extremophilic and being difficult to cultivate. One could argue that some of the best studied environments (e.g., hot springs) are extreme b/c of their simplified diversity that enables cultivars to be more readily obtained (e.g., Sulfolobus).

Thank you for raising this issue. In our personal experience when speaking with other microbiologists, many have not had the opportunity to learn how to cultivate extremophiles, and/or found growing extremophiles to be too challenging to pursue as a research topic. Difficulty isolating or growing extremophiles is often cited as a barrier to entry to the field. We have added the following text to better explain why growth under extremophilic conditions can add to the challenge of cultivating extremophiles (lines 99-102): "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 and naturally choose to pursue easier-to-cultivate microbes"

Lines 211-215: Thermophiles conferences has a good showing of archaeal researchers. Oftentimes archaeal researchers are featured at the ISME conference and ISSM conferences.

Thank you for providing additional suggestions as conferences of interest to the archaeal community. We have included them in the text (lines 236-243) and in the new Supplemental Data 1.

"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 organised 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."

Line 271: A great place to highlight some of the societal benefits of archaeal research are.

Thank you for this good suggestion! We have added the following text to highlight certain key impacts of archaea research (lines 319ff): "Despite numerous examples of archaeal research leading to paradigm shifts in knowledge and new technologies, including the first

glimpse of the ribosome73, the discovery of life-saving drugs74,75, and ability to generate clean-burning energy76, to name a few, funding agencies are often reluctant to support these topics …”

Line 299: Ken Timmis is driving the International Microbiology Literacy Initiative (https://imili.org/) to develop curricula and activities to promote microbiology literacy globally, starting at a young age. One could envisage contributions from this group to better highlight archaea and thereby push the authors agenda earlier from a grass roots level.

Thank you for sharing this information. We now included this initiative in line 355.

Reviewer #3:
Remarks to the Author:
Overall, I think authors have well addressed my concerns and provided a good response. I have no more comments. Well done and hope you have more contributions on the archaeal community.

Thank you for the supportive feedback.

Reviewer #4:
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It is quite remarkable that the authors were so dismissive of many of the suggestions made, in particular the suggestion to improve the perception of archaea as contributors to Earth systems that are of societal consequence. Again, the idea is to motivate people to consider studying Archaea (difficult imagining someone joining the archaeal research community or caring about resources available to it if they are not compelled to join the community).

Regardless of the above, I can support publication.

It was not our intention to be dismissive of the reviewers comments. We appreciate the thoughtful suggestions and have tried to incorporate them to the best of our abilities in the previous revision. However, we are limited in the scope of this manuscript. Nevertheless, we have included an additional sentence to highlight archaeal contributions to Earth systems (line 58-59) in the introduction, as well as additional references on methanogenesis (line 62).