

Editorial

A vision on preprints for mitochondrial physiology and bioenergetics

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Abstract A manuscript in preparation for publication on ‘Mitochondrial states and rates’ is the first preprint posted on *MitoFit Preprint Archives* (Gnaiger *et al* 2019). It actually triggered the initiation of a preprint server for mitochondrial physiology and bioenergetics. This editorial presents the story behind starting *MitoFit Preprint Arch*, to develop a vision of science communication beyond traditional journal and preprint publication. This is an open invitation to scientists of mitochondrial physiology and bioenergetics to join the preprint community by submitting manuscripts as preprints. We face the *reproducibility crisis* in the battle to separate doubtful data from relevant information. This is linked to the *inflation crisis* emanating from an exponential increase of scientific articles published per day. Unsustainable exponential growth leads to the *value-impact crisis* in the struggle to forge scientific innovation into knowledge and community benefits.

1. A brief history of preprints

A forerunner of preprint servers was initiated in 1961 at the National Institutes of Health (USA) as 'Information Exchange Groups'. These were shut down in 1967 due to the resistance of publishers rejecting articles that were made available as preprints (Cobb 2017). It took 30 more years to start the modern concept of preprints, when Paul Ginsparg initiated *arXiv* in 1991 for physics, computer science, and mathematics. *arXiv* is maintained and operated by Cornell University (USA). The field 'quantitative biology' was added to *arXiv* in 2003. Ten years later, *bioRxiv* was launched in 2013 by Cold Spring Harbor Laboratory Press in New York as a 'free online archive and distribution service for unpublished preprints in the life sciences', with the intention of complementing *arXiv*. In the same year, *PeerJ Preprints* was launched (Callaway 2013) as the 'pre-print' area of the Open Access journal *PeerJ*, accepting submissions in the same subject areas as *PeerJ* (biological, medical and environmental sciences) and *PeerJ Computer Science*. Similarly, *Preprints* started in 2015 associated with the journals operated by MDPI, based in Basel (Switzerland). Today the majority of scientific subscription journals and Open Access journals accept manuscripts that were previously posted as preprints (www.asapbio.org). A preprint is a 'version of a research paper, typically prior to peer review and publication in a journal' (Tennant *et al* 2019). However, "saying a preprint 'is not published' or 'is not in a journal' merely shifts the ambiguity to the question of what 'published' means or what counts as a 'journal'" (Neylon *et al* 2017; see also Chawla 2017). The days of sending letters and papers as preprints are history. The pre-print may remind us of our environmental responsibility before printing – it is not a 'paper'.

Many discussions on preprints focus on quality standards, peer review *versus* community review (Oakden-Rayne *et al* 2018), and time delays of publication (Vale 2015). An interesting open peer review model is presented by the Open Research publishing platform *F1000Research*: Submitted manuscripts are posted to the journal's website immediately with a DOI and without editorial bias. Subsequently, a transparent peer review is initiated with non-anonymous experts and 'driven by the authors who must suggest the reviewers and who decide when and how to address any criticisms raised by the reviewers'. The reviewer reports, reader comments, and the authors' responses are published, and new versions of the manuscript include explanations of the changes. Completion of the review process entails upgrading of the manuscript as a publication indexed in PubMed and other bibliographic databases. Peer review may be stopped, while the article with a DOI cannot be removed. Then it is equivalent to a preprint, open for submission to another journal for peer review and publication. But what if the original article has been posted as a preprint before submission to *F1000research*?

The increasing impact and popularity of preprints in biology is documented on the basis of 37648 preprints uploaded to *bioRxiv* during its first five years, and >2100 preprints were posted per month by the end of 2018 (Abdill, Blekhman 2019). Preprint statistics are updated in <https://rxivist.org>.

2. A new preprint server for mitochondrial physiology and bioenergetics

Is a new preprint server needed? How can the attempt to offer a new preprint server be justified? These are difficult but decisive questions to be answered when initiating *MitoFit Preprint Archives* for mitochondrial physiology and bioenergetics.

First, launching a preprint server is different from starting a new journal: like all preprint servers, *MitoFit Preprint Arch* does not compete with subscription or Open Access journals, is non-profit, and does not enter the arena of conventional impact metrics. Preprints are not peer-reviewed, but reflect the time-stamped state of the author's work presented to the scientific community. Differences in scientific opinion of authors, referees and editors will not lead to any delay, let alone rejection of a preprint manuscript. 'Journals then may be incentivized to look more toward quality than speed and seek to publish the definitive work that will stand the test of time' (Vale 2015).

Second, *MitoFit Preprint Arch* is not fundamentally different from established preprint servers (Bourne *et al* 2017). The amazing success of *arXiv* can be gauged from its mere size and, importantly, gains from the large number of articles (roughly 757 000 from 1991 to 2012) which helped machine-learning algorithms to detect and analyze patterns of copying published text; thus articles with a high

duplication score are automatically labelled by a plagiarism filter as an alert to readers and authors alike (Citron, Ginsparg 2015). At the start of *MitoFit Preprint Arch*, the very small size sticks out as a specific advantage, when we can expect a gradually growing number of manuscript submissions in the fairly well defined area of mitochondrial physiology and bioenergetics.

(1) In contrast to physics and mathematics, where publication in *arXiv* has become a standard, preprints remain relatively unpopular in biomedical sciences (Chawla 2017; Sarabipour *et al* 2019; but see Learn 2019). Despite the many benefits of preprints for the authors and the scientific community, the perceived “risk of ‘scooping’ is often used to argue against preprints, whereas in reality the opposite is true as a preprint defines precedence and ‘ownership’ of research” (Tennant *et al* 2019). A specific mitochondrial physiology (MiP) preprint server can encourage more authors to engage in preprint publications within the MiP network. According to a search of 7760 preprints, “articles with a preprint received higher Altmetric scores and more citations than articles without a preprint” (Serghiou, Ioannidis 2018).

(2) It is a difficult decision to post a preprint or search for preprints on mitochondrial physiology in big servers such as *bioRxiv* under the categories Biochemistry, Biophysics, Cancer Biology, Cell Biology, Molecular Biology, Neuroscience, or Physiology. The scientific community with well-defined interests in mitochondrial physiology and bioenergetics can find relevant preprints more quickly on *MitoFit Preprint Archives*. Similarly, many successful preprint servers on mathematics were directed to communities of not more than a few hundreds of specialized mathematicians (Jackson 2002). Umbrella servers play the important role of coordinating the information from many smaller servers and centralized archives.

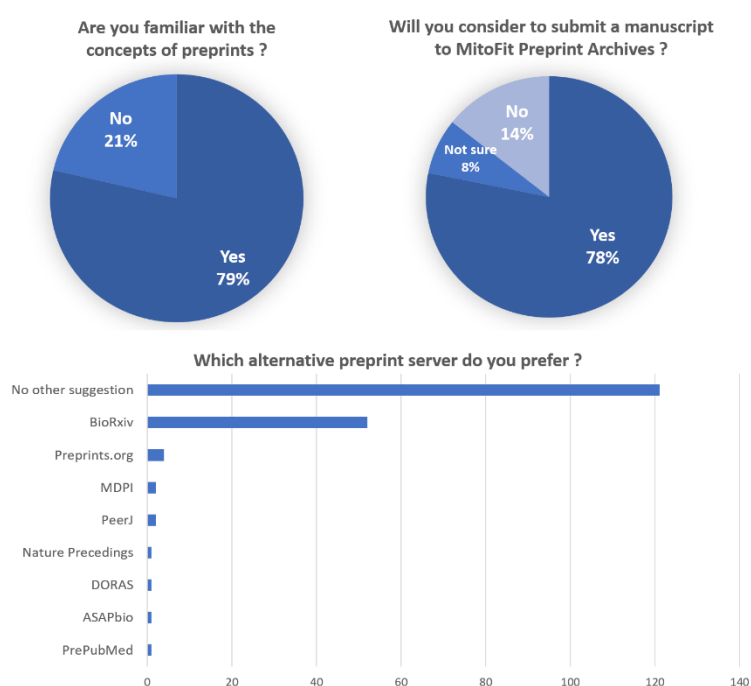
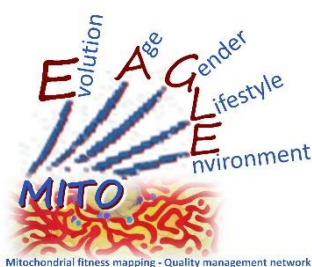


Figure 1. The ‘States and rates questionnaire’: Three questions on preprints were circulated on 2019-02-12 to the 530 coauthors of Version 1 of the preprint [Mitochondrial respiratory states and rates](#). 179 responded by 2019-03-15. 38 coauthors were unfamiliar with the concept of preprints. Among those, 20 responded positively to publish in *MitoFit Preprint Archives*, whereas only 8 were against preprint publication. Note that among ‘alternative preprint servers’ a majority of 67 % (120) selected ‘no other suggestions’, 29 % (52) selected *bioRxiv*, and a few websites were listed which actually do not qualify as preprint servers

(ASAPbio, PrePubMed). Nature Precedings ceased accepting new submissions in 2012. In summary, *MitoFit Preprint Arch* is a positive contribution to make preprints more popular in mitochondrial physiology.

(3) Many readers are experts in the field, can become voluntary members of the ‘International editorial board’ or simply join as active commentators, and thus help as team players to improve, increasing reproducibility and traceability. Readers and editors may provide critical and constructive suggestions after a preprint version has been posted, in the spirit of open communication in contrast to anonymous peer review. “Most retractions in biomedical journals have been prompted by post-publication review, where the readership of a journal has detected serious flaws in the published research. .. Manuscripts that make bold claims are more likely to be discussed and shared, and are

therefore likely to be more thoroughly reviewed at the preprint stage” (Oakden-Rayner *et al* 2018). By mutual agreement between authors, editors and contributing readers, relevant sections of editorial correspondence may be published as a supplement added to follow-up preprint versions, or as a joint commentary with an independent DOI.



Our analysis of the ‘States and rates questionnaire’ (Fig. 1) provides visible support for launching a preprint server for mitochondrial physiology. *MitoFit Preprint Archives* is as such a product of the COST Action CA15203 MitoEAGLE (www.mitoeagle.org), unequivocally supported by the Management Committee in an eVote. *MitoFit Preprint Arch* is expected to grow with and beyond the MitoEAGLE consortium under the umbrella of the international Mitochondrial Physiology Society (www.mitophysiology.org).

3. Bioblast, MitoPedia, and Gentle Science



The website Bioblast (www.bioblast.at) was brought to life in 2010 by Oroboros Instruments as a glossary and index for high-resolution respirometry. Bioblast was presented at the Mitochondrial Physiology Conference 2010 (Renner-Sattler, Gnaiger 2010), including the ‘MitoPedia’ as a Wiki, driven by scientists with an Open Access concept. Without being familiar with the concept of preprints, we considered the section on ‘Publications’ to provide “a portal for sharing, disseminating and commenting relevant literature in mitochondrial physiology, with context–related ‘filters’ for references. Bioblast allows the evolution of a scientific publication – providing space for open discussions and extensions of an otherwise static *paper*”.



MitoPedia (www.bioblast.at/index.php/MitoPedia) is an ongoing effort to establish a high-resolution terminology, as a dynamic tool for summarizing definitions of terms, symbols and abbreviations. Catalytically working as an *Information synthase* (the logo is derived from the painting ‘ATP synthase congregation’ by Odra Noel), MitoPedia supports the decentralized evolution of a glossary of scientific terms, for developing a consistent nomenclature in the growing field of mitochondrial physiology (Gnaiger *et al* 2019).



The MitoPedia section on Preprints (MitoPedia: Preprints) was added in conjunction with the launch of *MitoFit Preprint Archives*, emphasizing the spirit of Gentle Science (www.bioblast.at/index.php/Gentle_Science). We suggest to connect and collaborate with preprint ambassadors (see ASAPbiol). The Bioblast Wiki provides a platform for Gentle Science in the spirit of Scientific Social Responsibility, and *MitoFit Preprint Archives* constitutes a timely fit in this context.

4. The inflation crisis of scientific publications

Science is progressively turning into an industry with unchecked floods of publications in the business channels of scientific journals. A recent whirl of commercial Open Access journals driven by predatory publishers, and the non-profit wave of accelerated preprint publication leads to further swelling of the stream. Many labs celebrate a new team publication with a toast. The number of scientific publications posted per day is growing faster than the motivation to throw another party and overrides the capacity to turn scientific innovation into knowledge. Publications as a currency of scientific output are subject to an increasing inflation rate, just as economic inflation is driven by excessive money supply. More *papers* add to the inflation crisis. Scientific papers are a currency, in contrast to scientific output in terms of goods and services provided by research. Reproducible results, reliable databases, relevant information, meaningful knowledge obtained by putting information into

context lead to scientific output, such as a test for early Alzheimer diagnosis and a therapeutic formula for treatment of dement patients, or novel strategies for effective preservation of environmental resources.

4.1. Distinguishing scientific goods and services from inflation of the publication currency

A scientist lists her publication record to obtain an academic degree and position or to support a grant application. Publications in research may be compared to a bank account in the world of investors. Evaluation of a currency depends on how much money can buy. Of course, the Syrian pound (SYP) is not rated equal to the British pound (GBP); a paper in a local journal is not rated equal to a publication in a globally distributed international journal. But does this justify any arguments on superiorities of British (or European) over Syrian culture (Harari 2018)? Academic productivity is measured by widely applied publication metrics, such as the journal-impact factor or h-index (Carpenter *et al* 2014). The focus on publication currencies, however, detracts from the question of value: How powerful is the currency for transactions into goods? Irreproducible results published in traditional journals or preprints have a negative impact on the scientific community, and on society—if any. Is the number of patents a better metric for innovation (Silver 2012) compared to publications? What is the *value-impact* on society of a high *journal-impact* publication, versus the value of a preprint that may be influential irrespective of conventional publication metrics? Good measures of scientific impact on society may not yet be available. A value-impact factor is difficult to define. Many young researchers feel to be trapped in a *value-impact crisis*. But this should not detract us from searching for intelligent solutions, their optimization and implementation. Both, traditional journal publications and preprints contribute towards progress in improving the scientific goods and services, even at an increased inflation rate and decline of the currency value of each unit of scientific publication. However, preprints are free of charge, whereas “US academic libraries paid \$1.7 billion for serial subscriptions in 2008 alone. Library budgets, in contrast, are flat and not able to keep pace with serial price inflation” (Klein *et al* 2018).

4.2. Worthless but useful – like nails

PubMed lists 8, 13, 26, and 46 publications per day in 1988, 1998, 2008, and 2018, when searching for ‘mitochondr*’. At a publication charge of € 1 100 per article, scientists (*i.e.*, their sponsors) would have expended € 50 000 every day in 2018 for ‘selling’ their output to journals, and the actual figure can easily be doubled (Van Noorden 2013). How many of those heavily priced papers did I miss without being aware of their possible relevance for my research or the manuscript currently in preparation for submission? Is another *paper* added to the masses still considered as a potential building block of human culture? Reviews have been a help in science and teaching. But a review published today will be outdated tomorrow. So what’s the point of reading or even citing it?

We need intelligent tools that help to bring validated data into focus (Maciocci *et al* 2019). This requires software-supported screening for results that (1) have been reproduced by different research groups; (2) are backed up with a rigorous quality management, such as pre-publication of time stamped protocols, access to raw data of the complete data set, including calibration procedures and data analysis algorithms; (3) are published explicitly by including ‘negative’ results, which can be compared with corresponding ‘positive’ findings. Similarly, intelligent tools should become available which put a red flag to publications with conclusions drawn on false statistics. Based upon such and other quality control measures, software detecting plagiarism may be developed further by machine learning into powerful tools for improved filtering of specific research topics, generating databases and context of segmented publications. This will not make the scientist redundant, but re-searchers will have the task to validate such databases as indispensable tools for the advancement of science. A corresponding output metric will be the measurement of the impact of a publication on a database, the value-impact of a database on the knowledge system, and the cultural and socio-economic impact. The publication currency may lose the power to buy the opinion of granting agencies or to serve as an index of scientific prestige. A paper will be traded: many papers are needed to buy a valuable tool or

gadget. Even if the individual paper is of little value, many papers together are essential for the whole thing.

An industrially produced nail is not worthwhile picking from the street. In context, all publications are potential nails, which need an architect's plan, quality control for being straight, having the right length, and being made of the proper material. Together with the nails a hammer is needed to build a meaningful structure. Many more nails are needed of sufficient quality and properly inserted to build a structure and hold it together.



5. A mission for mitochondrial physiology

5.1. Quality control

Acceleration of publication presents a recognized advantage of preprints (Vale 2015). This does, however, not resolve the *inflation crisis* nor the *reproducibility crisis* (Ioannidis *et al* 2014; Baker 2016) of scientific publication. Beyond acceleration, quality control (QC) is required, which is critically important and expensive. How can preprints provide QC for free?

Hindle and Sadari (2017) propose an attractive model of journal clubs focusing on preprints (www.prereview.org). These are analyzed in detail and discussed in the format of a review, which is communicated with the authors of the original preprint. As a result, a preprint commentary may be published, complete with an independent DOI and thus searchable and citable. This is particularly attractive for early-career researchers, who not only gain experience in the peer review arena, but can list the published reviews in their CV. Similar models of publishing helpful comments on preprint websites or as independent commentaries make the QC contributions as visible as achieved in an Open Review system (Sarabipour *et al* 2019).

At *MitoFit Preprint Archives* we are open to experimentation with various models of QC, which will finally result in higher quality publications and improved reproducibility of published results. QC and reproducibility rely on methodological detail made specifically available in conjunction with published data. Reporting the rationale of failed experiments can be more helpful for the full understanding of an approach than merely presenting the final polished results. While traditional journals today offer the option to provide details on methods and experimental protocols as a supplement, this important information can and should be integrated into the main body of a preprint.

QC must be applied to all levels, including the pillars of trust by the scientific community in the governance and sustainability of a shared infrastructure (Bilder *et al* 2015) that will maintain *MitoFit Preprint Archives* alive: the insurance is based on an international scientific community (Mitochondrial Physiology Society) and financial support.

5.2. Scope, formats and manuscript types

Today scientists can decide to submit manuscripts exclusively to journals which accept the concept of preprints. *MitoFit Preprint Archives* accepts submissions on a non-commercial basis, independent of the use of any products related to commercial interests of scientific organizations and companies including Oroboros Instruments. The areas covered in *MitoFit Preprint Archives* include mitochondrial physiology, bioenergetics and ergodynamics. We recommend other preprint servers for manuscripts which do not belong to areas covered by *MitoFit Preprint Arch*. The formats are manuscripts in English. We plan to accommodate several manuscript types:

(1) Experimental: (a) Original research articles, including 'negative' results (irrespective of supporting a working hypothesis); (b) Methods sections with application examples (prior to full

manuscript submission); (c) Confirmative or contradictory results related to previous publications (reproducibility)

(2) Theoretical: (a) Theoretical work with novel concepts; (b) Focal reviews with meta-analyses; (c) Commentaries

(3) Perspectives: (a) Editorials; (b) Educational perspectives, including concerns about minority groups, scientific corporate responsibility, resources and environment

(4) For specific scientific events: (a) Extended abstracts; (b) Slides of oral presentations; (c) Posters.

References to methods papers should inform about original publications. It is inappropriate to refer in the methods section to a previous paper, where reference is made to another paper, which finally may not even describe the relevant methodological details.

6. Conclusions

We are looking forward to preprint submissions and feedback. We cordially invite mitochondrial and bioenergetics scientists to join the MitoFit editorial team. All scientists of mitochondrial physiology and bioenergetics are encouraged to join the preprint community. With joint forces it will be possible to find solutions to the reproducibility crisis of scientific reports, the inflation crisis of scientific publication, and the value-impact crisis faced by the individual researcher.

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Competing financial interests

EG is founder and CEO of Oroboros Instruments, Innsbruck, Austria. *MitoFit Preprint Archives* is operated by the team of Oroboros Instruments. Guidance by the expanding Member and Scientific Advisory Boards adds to our mission of handling submissions on a non-commercial basis, independent of the use of any products related to commercial interests of scientific organizations and companies including Oroboros Instruments.

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8. Weblinks

1. **ASAPbio**: Accelerating Science and Publication in biology - <http://www.mitofit.org/index.php/ASAPbio>
2. **Bioblast**: the *mt-information synthase*, from Richard Altmann's Bioblasts to mitochondrial physiology - <http://www.bioblast.at/index.php/Bioblast>About>
3. **F1000Research**: an Open Research publishing platform for life scientists - <http://www.mitofit.org/index.php/F1000Research>
4. **Gentle Science** - http://www.bioblast.at/index.php/Gentle_Science
5. **Mitochondrial Physiology Society** - <http://www.mitophysiology.org>
6. **MitoFit Preprint Archives**: the Open Access preprint server for mitochondrial physiology and bioenergetics - http://www.mitofit.org/index.php/MitoFit_Preprint_Archives
7. **MitoPedia**: high-resolution terminology - matching measurements at high-resolution - <http://www.bioblast.at/index.php/MitoPedia>
8. **MitoPedia: Preprints** - <http://www.mitofit.org/index.php/MitoPedia:Preprints>
9. **MitoEAGLE** COST Action CA15203: Evolution-Age-Gender-Lifestyle-Environment: mitochondrial fitness mapping - <http://www.mitoeagle.org>
10. **PREREVIEW**: start and run a preprint journal club - <http://www.mitofit.org/index.php/PREREVIEW>
11. **Rxivist**: trending open science - <https://rxivist.org>