EPHYRA PUBLISHING
Journal: **Systems Aging**
https://doi.org/10.63751/15ic

An inaugural editorial for Systems Aging

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Abstract

With this very first Editorial, we would like to introduce a new actor in the field of aging research and communication. This new actor is Systems Aging, an open access peer-reviewed journal dedicated to advancing aging research through the use of computational and systems biology. It is published by Ephyra Publishing, a small new publisher intending to spread knowledge and attract interest to aging research, targeting both scholarly and general audiences. We hereafter describe the scientific scope of Systems Aging, its target authors and readers, as well as its editorial processes. We sincerely believe that the scope and values of Systems Aging, grounded in goal-oriented pluridisciplinarity, reproducibility and epistemology, will lay the foundations for sharing both exciting and rigorous research.

Fundamental and applied research in aging biology has already started to reveal many of its distinctive hallmarks and important pathways, demonstrating that biological aging can be measured, predicted, and altered by molecular and environmental factors. Nevertheless, the multifaceted nature of aging remains hard to grasp, as crucial mechanistic knowledge is still lacking and overarching causal paradigms are still to be proposed (Gladyshev et al., 2024; Gems and de Magalhães, 2021; Cohen et al., 2020). In particular, aging involves numerous interconnected molecules, pathways and emerging phenotypes: the interactions, feedback loops, and regulatory relationships linking them in a dynamic manner are still far from being elucidated.

Computational and systems approaches are promising avenues to address this complexity (Cohen et al., 2022). A systems view of aging conceptually integrates many dependent molecular, physiological or epidemiological observations into abstract mathematical representations, better suited to work with interconnected phenomena. This not only requires appropriate models, but also appropriate algorithms to computationally estimate the parameters of such models from the data before any biological hypotheses can be tested. A plethora of promising methods have already been proposed by computational biologists, bioinformaticians and biostatisticians over the years in the context of systems biology: even more need to be used, developed and tailored for the specific needs of aging biology. Although several journals are already publishing systems-oriented interdisciplinary studies at the interface of biology, mathematics and computer science, there is no journal entirely dedicated to them in the field of longevity research. This is one of the gaps Systems Aging is going to fill. Its is intended for authors from very different backgrounds, like for instance biologists who would have applied existing methods and analysis pipelines to understand large, -omics datasets about aging, but also bioinformaticians and mathematicians having developed novel algorithms to investigate longevity. Needless to say that Systems Aging is also a perfect fit for any interdisciplinary researcher in between.

The originality of Systems Aging does not only reside in its scope, but also in its editorial choices. While computational and systems biology are full of potential, they are not sufficient to robustly advance our knowledge of longevity and age-related diseases. In fact, increased volumes of data and computational pipelines bring their own methodological challenges, a few of them exemplified in the following lines. Computational approaches often have many hyper-parameters to tune, with few guidance available to do so properly. Mathematical models and algorithms often embed strong assumptions about the data that should be clearly identified and verified. Large multi-factorial datasets offer more opportunities for data snooping and p-hacking. Machine learning

Received: 02 May 2025
Published: 02 May 2025

models still suffer from limited explainability, especially in high dimensional settings and in presence of correlated variables. Finally, reproducibility issues are not restricted to experimental biology, as the outputs of analysis pipelines can also be unstable and vulnerable to noise.

Computational systems biology is therefore nothing without a sound epistemology, i.e. the study of knowledge, and how to acquire it. This is, undoubtedly, at the core of the scientific method. The goal of Systems Aging is to ground aging research in a rigorous epistemic framework, and thus fuel the production of trustworthy findings. This will be embodied in several features of our editorial process.

- We will welcome **replication studies and incremental results** in a dedicated category, too often rejected elsewhere because of their lack of trendiness and novelty. We would like Systems Aging to become a platform for these consolidating findings, that are crucial to strengthen existing knowledge, increase reproducibility and the efficiency of aging research in the long run.
- A study reporting **negative results** will not be penalized in our editorial decisions as long as the method is sound. Turning unknowns into negative results is still deeply needed to advance reasoning and the creation of new research hypotheses.
- The presence of an **epistemic box** where researchers will clearly state their working hypothesis, what is expected under this hypothesis, what observations would falsify it, how they tested it. These considerations are at the heart of any research endeavour, and great pedagogic additions to academic papers, however they are too often implicit or sometimes flawed in existing literature.
- After the double blind peer-review phase is complete, Systems Aging will **make the peer-review exchange transparent**. By publishing it alongside accepted articles and encouraging reviewers to sign their comments, we hope the foster honest, enriching and cordial scientific dialogue.

We sincerely believe that the scope and editorial values of Systems Aging will lay the foundations for publishing both exciting and rigorous research. Our hope is that researchers will join our efforts and soon contribute to this new resource.

Received: 02 May 2025
Published: 02 May 2025

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Received: 02 May 2025
Published: 02 May 2025