nagi bioscience

APPLICATION NOTE

Nagi™ B-Age: Biological age measurements for anti-aging interventions.

Pushing the frontiers of healthy aging research.

HIGHLIGHTS

- Measure the Biological Age of the organisms.
- Screen and identify with precision compounds that slow down aging and prolong longevity.
- Mechanisms of action insights: measure the age of different “vital traits”. How are the interventions slowing down the aging process?

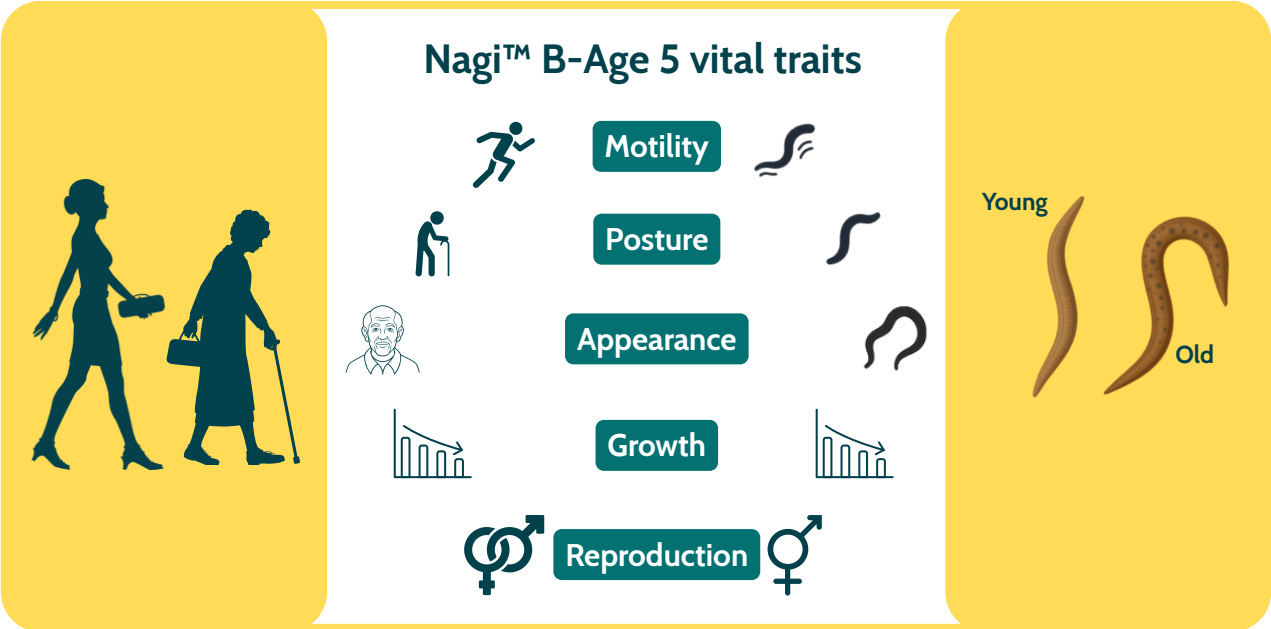
Biological age measurements for anti-aging interventions

As the need for improving **Healthy Aging** emerges as a central biomedical and societal challenge, identifying interventions that counteract age-related decline is essential to extending **healthspan**, the period of life spent in good health. To address this, scientists across industries increasingly rely on **biological age**, a measure of physiological condition that can differ from chronological age. Unlike simply counting years lived, biological age indicates a relatively accelerated or decelerated rate of aging.

Caenorhabditis elegans is an established *in vivo* model for aging research. Its short lifespan, conserved biological pathways, and whole-organism complexity make it ideal for bridging the gap between in vitro systems and ethically constrained vertebrate models. This enables rapid, scalable discovery of interventions that support healthier, longer lives.

Nagi™ B-Age

Nagi™ B-Age is a fully automated, AI-powered assay that measures biological age in *C. elegans* using high-content images acquired through the SydLab™ One platform. This multiparametric approach evaluates over 20 phenotypic biomarkers to assess **five vital traits**. These traits represent how the organism allocates energy across its lifespan. The biological age values are computed for each trait, and then integrated into a single, comprehensive **biological age** for the organism.



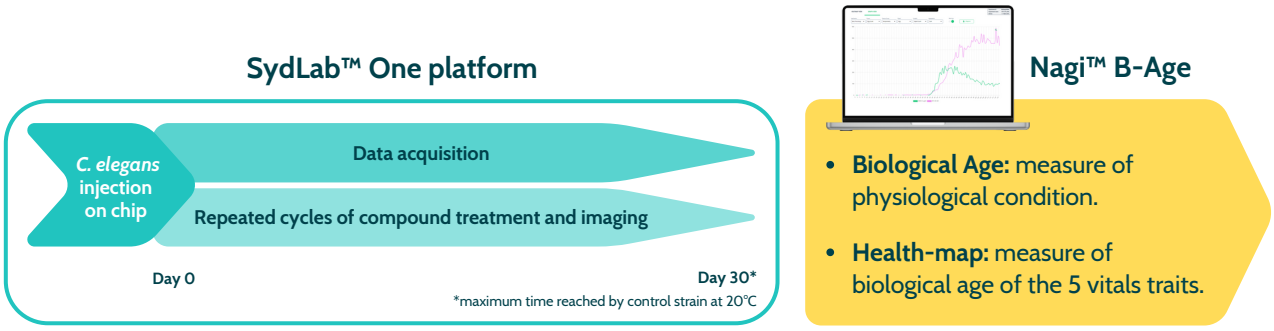
Explore the technology: SydLab™ One Technical Note

Nagi™ B-Age is an ideal solution for screening and evaluating a wide range of interventions, such as supplements, nutrients, microbiotics, and drugs, that aim to slow aging and enhance longevity.

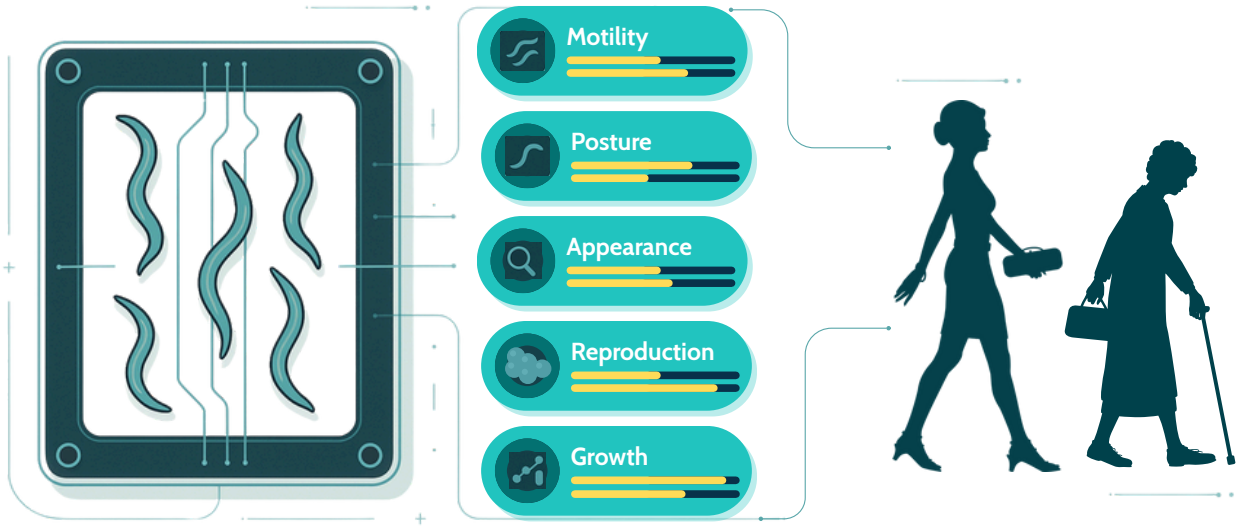
Is the reduction in biological age driven by a global improvement across traits, or by a strong effect on a specific vital function?

Nagi™ B-Age allows you to pinpoint how each intervention influences the biological age of the five vital traits, offering detailed insights into its mechanism of action.

One fully automatic workflow



When combined with the microfluidic precision of SydLab™ One, interventions can be applied through controlled feeding schemes, enabling comprehensive, reproducible testing of all possible longevity effects.



Nagi™ B-Age results

Human populations are heterogeneous, some individuals live significantly longer or shorter than the average. The same variability is observed in *C. elegans*, which naturally forms subpopulations of short-lived and long-lived individuals.

To explore this phenomenon, we used Nagi™ B-Age to track the biological age of wild-type *C. elegans* across their entire lifespan.

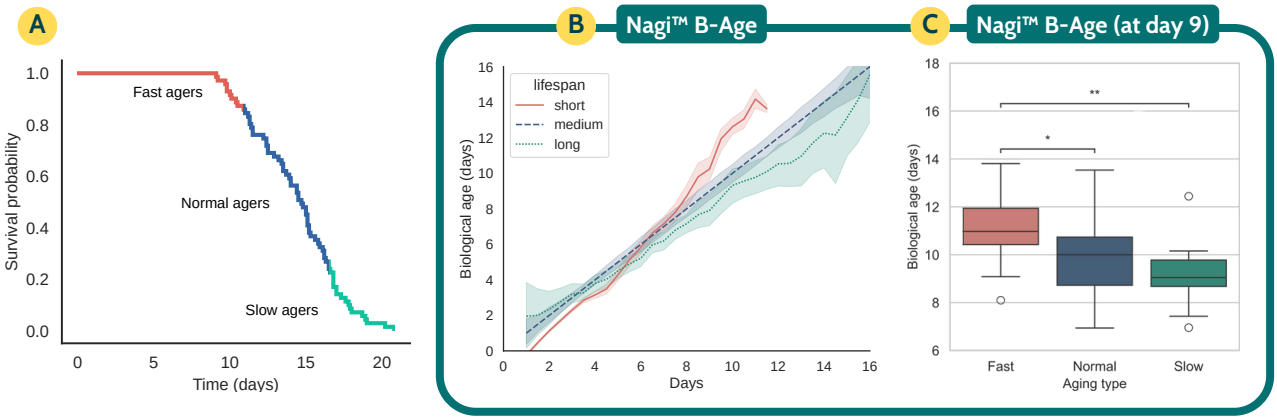


Figure legend: a) Survival curve of wild-type individuals colored according to their aging type (fast, normal, slow). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 16, for the three aging types. **c)** Boxplot of biological age at day 9, statistical significance was assessed with Mann-Whitney U tests.

Remarkably, Nagi™ B-Age was able to detect differences between the three lifespan subpopulations as early as **day 7.5**. Long-lived individuals consistently exhibited a **younger biological age** compared to both their chronological age and the other two subgroups. These results precede what is observed in conventional survival curves, which typically reveal such divergence only at later time points.

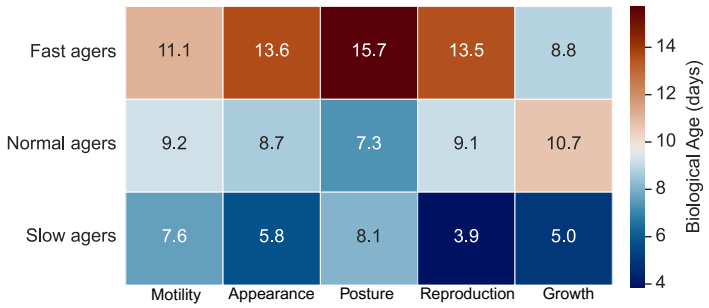


Figure legend: Decomposition of the clock predictions into the vitality traits, the mean of each trait is shown for the three conditions.

By **day 9**, the biological age trajectories of the three groups were distinct. A detailed analysis of the five vital traits revealed that **slow-aging individuals** consistently showed **lower biological age scores** across multiple parameters, highlighting the sensitivity and predictive power of Nagi™ B-Age in identifying aging dynamics early in life.

CASE STUDY 1

Screening anti-aging interventions throughout the life of the organisms

We applied Nagi™ B-Age to screen and evaluate the effects of several known anti-aging interventions in *C. elegans*. This enabled us to monitor the biological age and identify specific longevity improvements across the five vital traits.

Metformin

Metformin, known for its anti-aging activity through enhanced mitochondrial recycling, significantly reduced biological age starting from day 7, with a **clear dose-dependent effect** observed by day 10. Notably, the Motility trait improved substantially (up to 4.4% improvement compared to control), consistent with metformin's role in supporting mitochondrial function and muscle health.

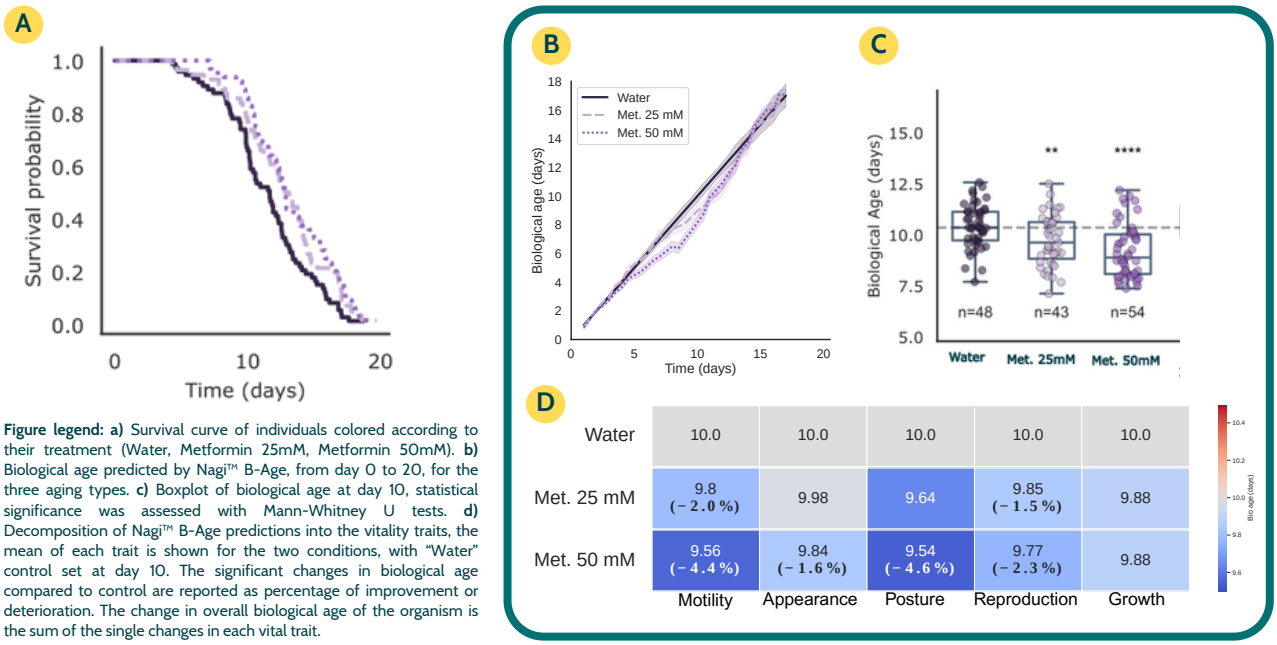


Figure legend: a) Survival curve of individuals colored according to their treatment (Water, Metformin 25mM, Metformin 50mM). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 10, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown for the two conditions, with "Water" control set at day 10. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

CASE STUDY 1

Screening anti-aging interventions throughout the life of the organisms

α-Ketoglutarate

A metabolite involved in protein synthesis and mitochondrial activity, α-Ketoglutarate showed **anti-aging effects only at high concentrations and later in life**. Although overall biological age at **day 10** was not significantly lower compared to controls, trait-specific analysis revealed an overall improvements in all vital traits.

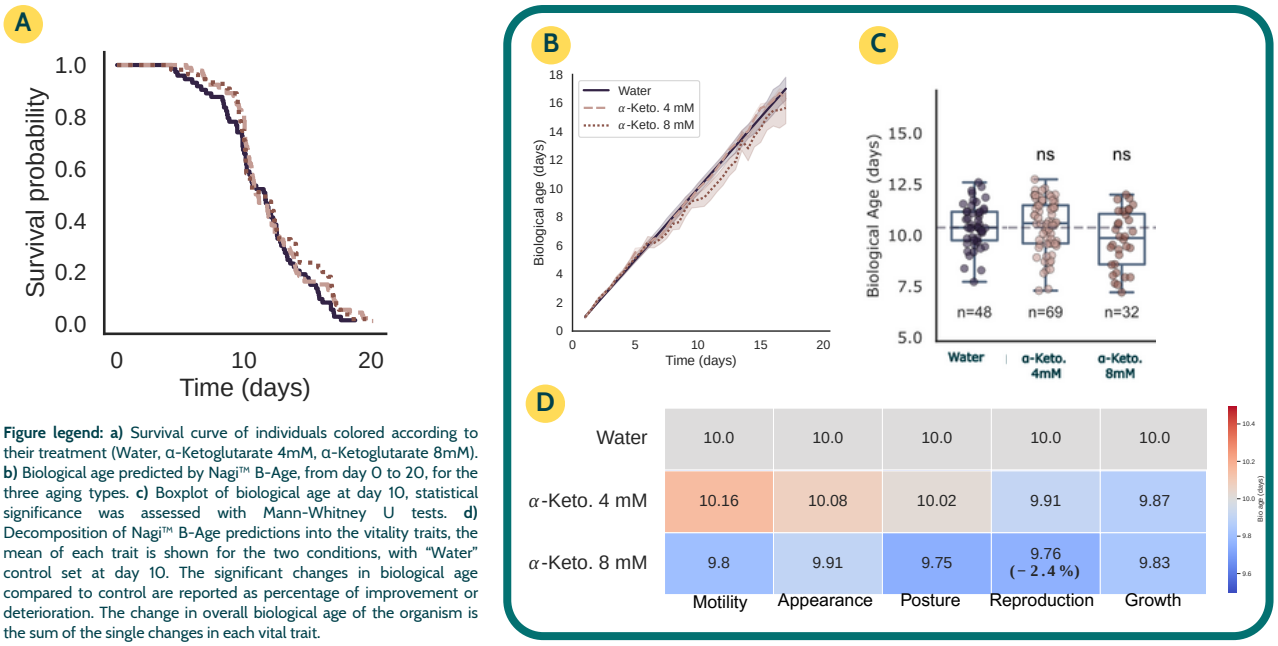


Figure legend: a) Survival curve of individuals colored according to their treatment (Water, α-Ketoglutarate 4mM, α-Ketoglutarate 8mM). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 10, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown for the two conditions, with "Water" control set at day 10. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

Nicotinamide (NAM)

NAM, a precursor of NAD^+ involved in metabolism, DNA repair, and longevity signaling, demonstrated a clear **anti-aging effect at day 10** at its highest concentration, with an overall reduction in biological age. Vital trait analysis showed pronounced **benefits in Reproduction and Posture**, suggesting NAM's broad impact on cellular maintenance.

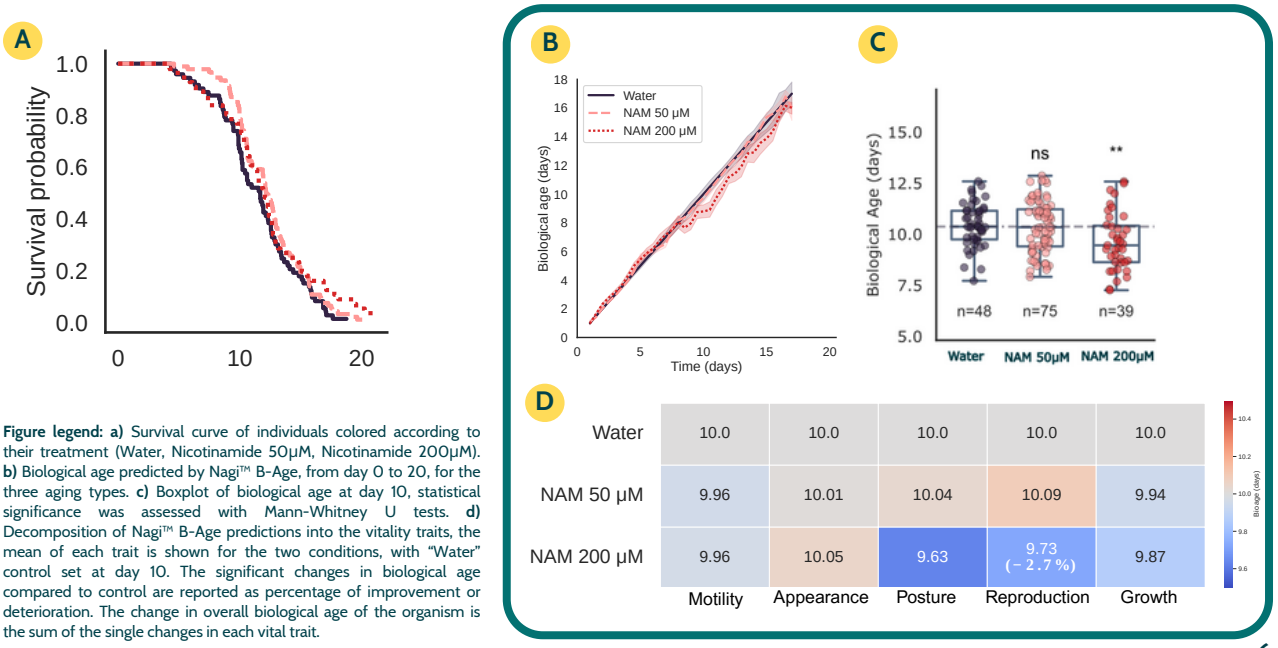


Figure legend: a) Survival curve of individuals colored according to their treatment (Water, Nicotinamide 50µM, Nicotinamide 200µM). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 10, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown for the two conditions, with "Water" control set at day 10. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

CASE STUDY 1

Screening anti-aging interventions throughout the life of the organisms

Doxycycline

Proposed to exert anti-aging effects via activation of protective mitochondrial stress responses, Doxycycline showed a specific impact at high concentrations by **lowering the biological age of the Reproduction trait**, potentially indicating an extended reproductive span.

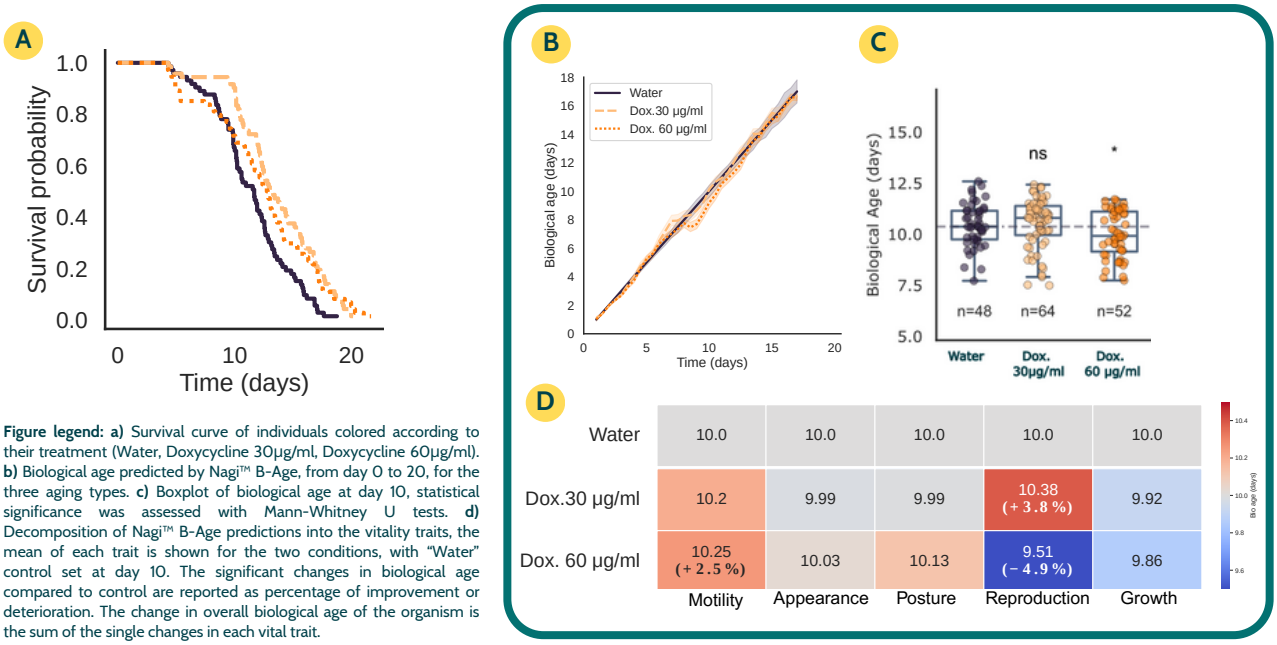


Figure legend: a) Survival curve of individuals colored according to their treatment (Water, Doxycycline 30µg/ml, Doxycycline 60µg/ml). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 10, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown for the two conditions, with "Water" control set at day 10. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

These results highlight the power of Nagi™ B-Age to detect and differentiate the effects of diverse anti-aging compounds at both organism and vital trait-level resolution. By uncovering how each intervention influences specific aspects of biological age, the platform enables precise screening and prioritization of longevity-promoting strategies.

CASE STUDY 2

Screening anti-aging interventions in old organisms

In an aging society, promoting healthy aging is not just beneficial, it's essential. To investigate how anti-aging interventions can influence the biological age late in life, we shifted an old population of *C. elegans* organisms from a normal feeding regime to a regime of caloric restriction. This dietary intervention is well-known for its lifespan-extending effects across species. Switching feeding schemes is done automatically thanks to SydLab™ One's integrated microfluidic technology.

Throughout the experimental duration, we applied Nagi™ B-Age to assess how this late-life intervention impacted the worms' biological age.

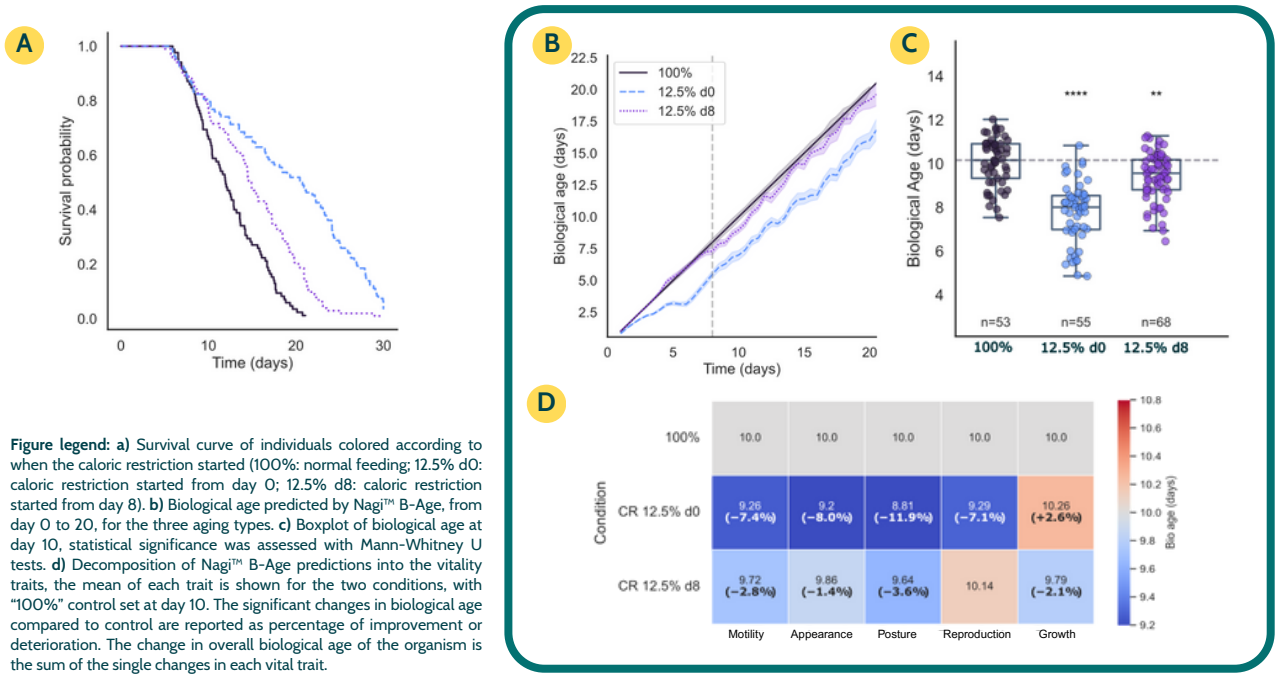


Figure legend: a) Survival curve of individuals colored according to when the caloric restriction started (100%: normal feeding; 12.5% d0: caloric restriction started from day 0; 12.5% d8: caloric restriction started from day 8). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 10, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown for the two conditions, with "100%" control set at day 10. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

The results showed that caloric restriction significantly slowed the aging process, as evidenced by a lower biological age in treated worms compared to age-matched controls maintained on a normal diet. **The vital trait-specific analysis provided further insight:** Reproduction showed no improvement, as expected, since the animals were already past their reproductive phase. In contrast, all other vital traits evaluated were significantly improved, revealing those traits to be implicated in the mechanism of action by which caloric restriction exerts its beneficial effects, even when applied late in life.

These findings demonstrate that Nagi's Aging Clock can sensitively detect the impact of anti-aging interventions even in late life stages. It enables precise, trait-level insights into how longevity-promoting strategies modulate biological age beyond reproductive capacity.

CASE STUDY 3

Measuring accelerated aging in a Progeria model

To further validate the sensitivity of Nagi™ B-Age, we tested its ability to detect accelerated aging in a genetic model of premature aging. We used *C. elegans daf-18* mutants, which lack the ortholog of the human PTEN gene, and is emerging a model for progeria and age-related disorders.

These mutants exhibit a significantly shortened lifespan and show early signs of physiological decline, making them a relevant model for accelerated aging. We conducted longitudinal imaging of *daf-18*, short living mutants and measured their biological age over time using Nagi™ B-Age.

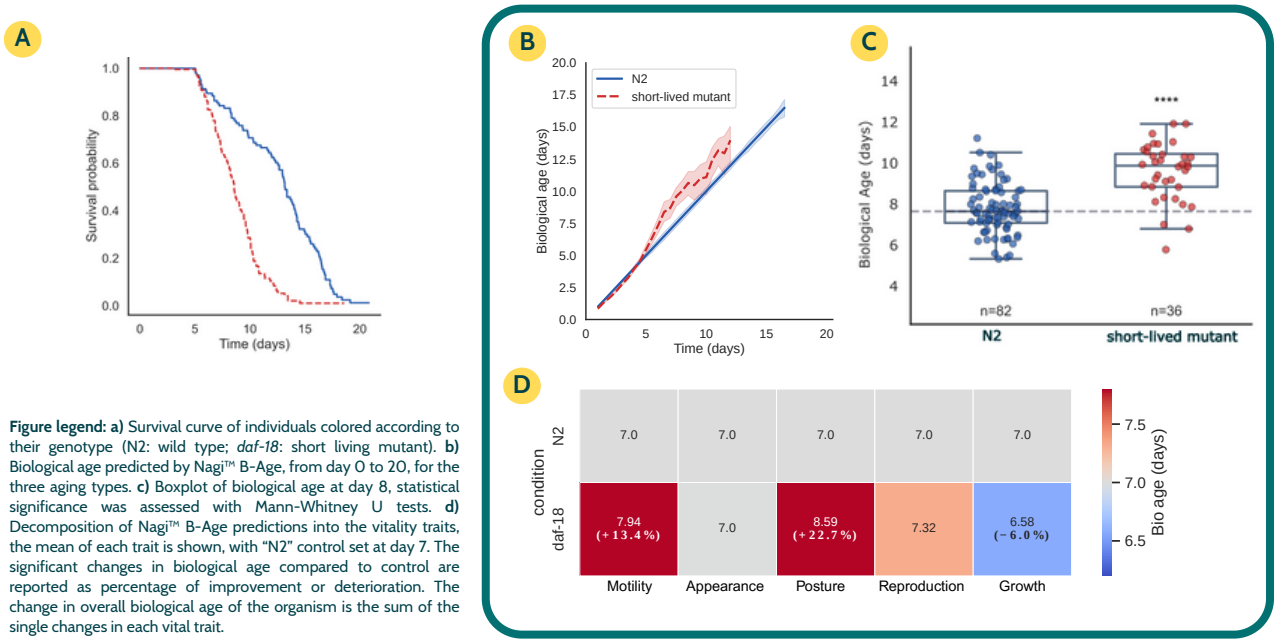


Figure legend: a) Survival curve of individuals colored according to their genotype (N2: wild type; *daf-18*: short living mutant). **b)** Biological age predicted by Nagi™ B-Age, from day 0 to 20, for the three aging types. **c)** Boxplot of biological age at day 8, statistical significance was assessed with Mann-Whitney U tests. **d)** Decomposition of Nagi™ B-Age predictions into the vitality traits, the mean of each trait is shown, with "N2" control set at day 7. The significant changes in biological age compared to control are reported as percentage of improvement or deterioration. The change in overall biological age of the organism is the sum of the single changes in each vital trait.

The results revealed that *daf-18* mutants consistently exhibited a higher biological age than age-matched wild-type controls, confirming their prematurely aged phenotype. Importantly, this difference was already detectable at early time points, demonstrating the power of Nagi™ B-Age to capture early-onset aging phenotypes.

The analysis of the 5 vital traits provided mechanistic insights: Motility and Posture dynamics were strongly impaired, reflecting systemic functional decline.

Altogether, these findings demonstrate that Nagi™ B-Age is not only effective in evaluating anti-aging interventions but also robust in identifying accelerated aging phenotypes, providing a powerful tool for both therapeutic discovery and disease modeling.

Comparison of Nagi's Aging Clock with the gold standard molecular clock

Several types of aging clocks have been developed for humans, each based on distinct biological markers. An approach is using the transcriptomic clock, which estimates biological age based on age-associated shifts in gene expression (mRNA levels) across tissues.

A transcriptomic clock has also been developed for *C. elegans*, providing a molecular benchmark for aging studies in this model organism. We used this established method to evaluate the performance of Nagi™ B-Age by comparing biological age measurements across wild-type, short-lived mutants, and long-lived mutants.

The results revealed a strong correlation between the biological age scores provided by Nagi™ B-Age and those obtained from the transcriptomic clock across all three groups. This alignment with an independent, gold-standard molecular method demonstrates the validity and reliability of Nagi™ B-Age in accurately capturing biological age in *C. elegans*.

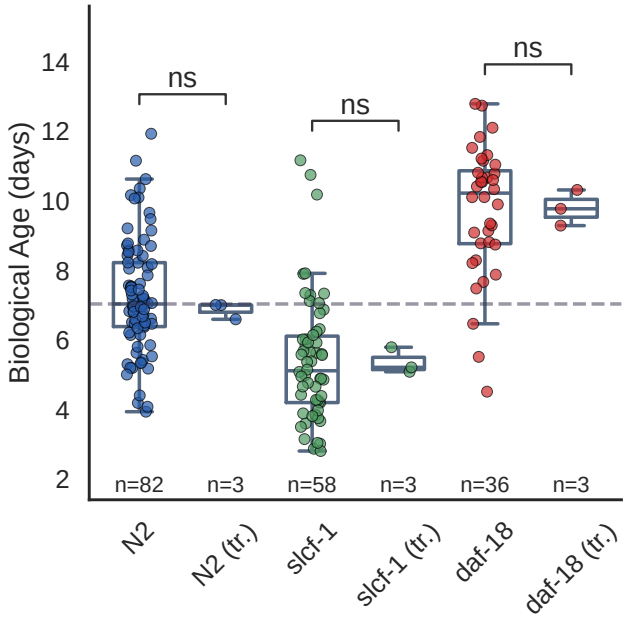


Figure legend: Boxplots of biological age assessed using Nagi™ B-Age and transcriptomic age (tr.) assessed using the BiT Age clock at day 8. Statistical significance was assessed with Mann-Whitney U tests.

Nagi™ B-Age offers a powerful and scalable solution for measuring **biological age** in *C. elegans*, providing a high-resolution, phenotypic readout that captures the complexity of aging beyond what chronological time alone can reveal. By quantifying the biological age of five vital traits, it enables a detailed understanding of how different interventions impact the aging process at a functional level.

Whether assessing combinations of known longevity compounds or exploring novel molecules, testing interventions late in life, or modeling accelerated aging, Nagi™ B-Age provides a unique platform to **screen, compare, and prioritize anti-aging interventions** with unprecedented precision and speed. Its full automation and *in vivo* relevance, provides an essential set of results for advancing the discovery of interventions that promote healthy aging and longer life.

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APPLICATION NOTE

Explore our technologies and research solutions

Discover the capabilities of SydLab™ One with the Discovery Pack experience

Let's connect

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