

Exercise Improves Strength and Confers Extended Healthspan on Swim-trained *C. elegans*



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Objective

- Device development for direct measurement of *Caenorhabditis elegans* (*C. elegans*) muscular force.
- Establishing swimming as exercise/training protocol for *C. elegans*.
- Extension of force device for study of *C. elegans* lifespan and other physiological parameters.
- Establish *C. elegans* as model organism for studying molecular mechanism of exercise.

Motivation

- Exercise confers powerful health benefits, with anti-cancer, anti-diabetes, anti-sarcopenia, anti-cognitive decline, and possibly pro-immune consequences in humans.
- Molecular/cellular/systems-wide changes by which exercise extends healthspan remain poorly understood



- *C. elegans* has well defined and short life cycle (3 -5 weeks) and are genetically tractable.
- Many basic biological processes in *C. elegans* are also found in humans (~35 - 50% gene homology). [The Future of Aging. New York: Springer, (2010)]
- Remarkable similarity between nematode *C. elegans* muscle cell to that of vertebrate.
- Already an established model organism for aging research.
- Research on exercise/aging may eventually lead to improved healthspan for all humans over a greater time period.

Microfluidic Device

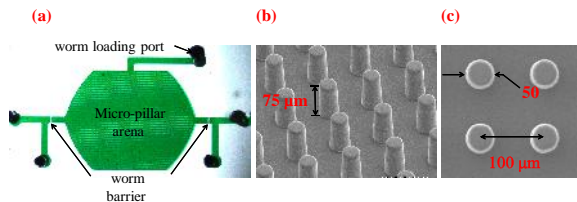


Figure 1: Multifunctional microfluidic device for *C. elegans* muscular force and lifespan measurement. (a) full view of a device filled with green food dye, (b) deformable pillar of height approx. 75 μm arranged in square lattice, and (c) pillar diameter (50 μm) and arrangement (spacing 60 μm).

Method: Force Measurement

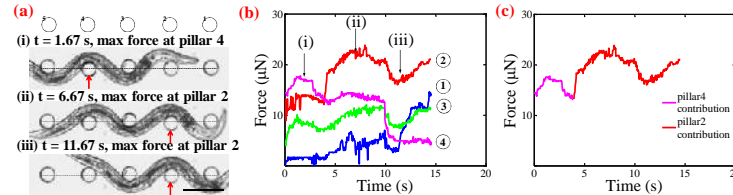


Figure 2: Muscle production in wild-type *C. elegans* (a) Images of the worm interacting with different pillars during a locomotory episode. Scale bar is 100 μm. (b) Force profiles of four pillars the worm is interacting with during the episode. (c) Force signature of a worm constructed by picking up only the maximum force experienced (among all pillars in interaction) at each frame.

Method: Device Characterization

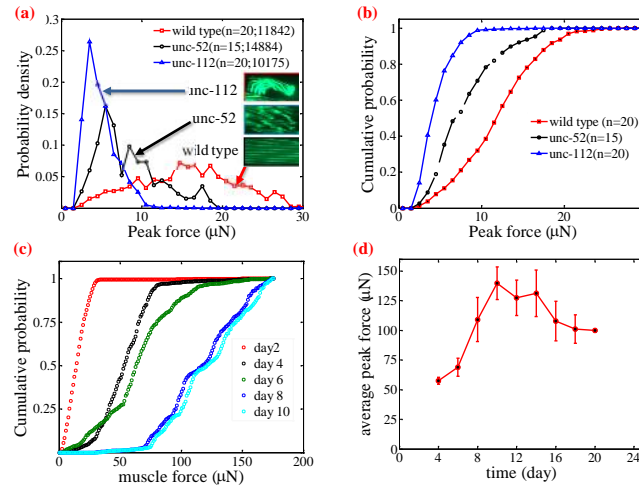
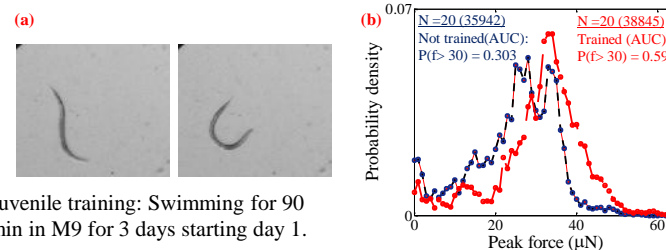


Figure 3: Benchmarking of the device. (a) Comparison of force distribution for the wild-type animals and its muscle mutants *unc-52* & *unc-112*, (b) cumulative probability representation of wild type, *unc-52* & *unc-112* animals, (c) muscular force generation of wild type animal as a function of age, (d) average force production of wild type animal on ageing showing a similar phenomena as human sarcopenia.

Method: Swimming as Training Method



Juvenile training: Swimming for 90 min in M9 for 3 days starting day 1.

Figure 4: Swimming as an exercise protocol for *C. elegans*. (a) two consecutive images shows a trashing instances while swimming, (b) training benefit for juvenile training of *C. elegans*.

Results: Lifespan of Wild type and Age Mutants

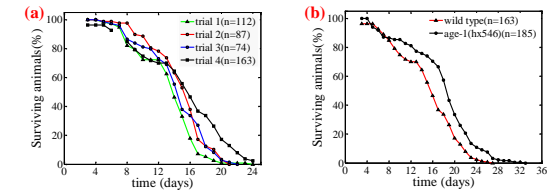


Figure 5: Lifespan study of *C. elegans*. (a) lifespan of wild type animal (Figure shows 4 trial). Wild type animal has a median lifespan of 14.4 days, (b) lifespan of a long lived mutant *age-1(hx546)*. Mutant *age-1* shows a median lifespan of 21 days.

Results: Exercise/Mobility/Healthspan

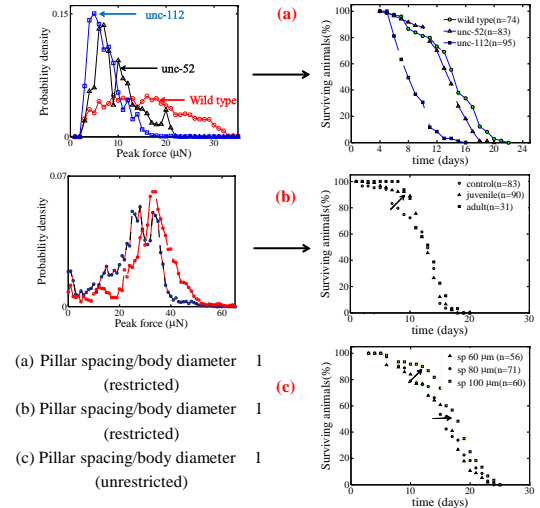


Figure 6: Effect of juvenile training on lifespan. (a) effect of muscle structure and attachment on *C. elegans* lifespan, (b) juvenile exercise shows a better health before median lifespan, (c) increase mobility enhances median lifespan.

Conclusion

- Micro-pillar force sensor measures muscular force directly and reliably.
- Muscular force of *C. elegans* increases with the developmental stages.
- Force device measure lifespan and force simultaneously.
- Swimming provides exercise benefits to *C. elegans*.
- Exercise (Juvenile) enhances median lifespan. It shows swim-train may have greater impact on the animal healthspan.