ANA LYONS

Coloured image of the tardigrade *Hypsibius exemplaris* — the organisms are also known as 'water bears'.

TARDIGRADE OBSESSION: MEET THE ANIMAL'S BIGGEST FANS

For water-bear enthusiasts, the creatures are an ideal model organism for systems neuroscience — and it's their legs that are key. **By Benjamin Plackett**

There's no two ways about it: tardigrades are badass.

These eight-legged, microscopic water-dwellers have survived the vacuum of space, extreme dehydration, and temperatures ranging from near absolute zero to above boiling point. In 2021, researchers fired frozen tardigrades from a gun onto a target several metres away, to simulate a meteorite impact, and showed that they lived to tell the tale[1].

Tardigrades are also transparent, skin-shedding and occasionally cannibalistic — traits seemingly at odds with their cuddly appearance and 'water bear' nickname. And they have great PR. They have a dedicated subreddit on which people showcase their tardigrade tattoos and soft toys. There are tardigrade fan clubs and memes, as well as online merchandise. Water bears might not care, but the Internet certainly does. People can't seem to get enough of them.

But for a burgeoning community of researchers getting ready to converge this month on Tsuruoka, Japan, for the 16th International Symposium on Tardigrada, it's all about the legs.

Tardigrades "are one of the smallest animals on Earth that we know of that have limbs," explains Ana Lyons, a neuroscientist at Keio University's Institute for Advanced Biosciences in Tsuruoka City. "At the same time, they also have simple eye spots, a central brain and a peripheral nervous system."

Tardigrades, therefore, exist in a sweet spot: simple enough to study properly and intricate enough for it to be worth doing so. That's one of the reasons that neuroscientists such as Lyons are working to make tardigrades a model organism for studying how neural circuits work — a field of research called systems neuroscience.

Not every organism has what it takes to be 'model', however — there are basic requirements. Ideally, they are easy to maintain and breed in the lab and have a short life cycle. They should also be genetically tractable and, for systems neuroscientists, have well-understood neurocircuitry. It is these latter two issues that scientists need to work on if tardigrades are ever to transition from meme to model organism.

Fortunately, tardigrade enthusiasts are a confident bunch.

"There's work to be done, but I have faith in the tardigrade community," says Jasmine Nirody, an organismal biologist at the University of Chicago in Illinois. "We're determined."

'A little space alien'

Lyons has been into tardigrades since the age of 15. In rural Michigan, where she grew up, there were no advanced science courses available at her school, so she took a course at a specialized 'magnet' school. In search of a topic for a project, she wandered around the local library. An encyclopaedia of North American invertebrates caught her eye.

"It had a black and white [scanning electron microscope] photograph of a heterotardigrade" on the cover, she recalls. "Those are the really cool tardigrades that have all the cilia on their backs and really prominent eye spots and their claws on their legs are very distinct. It just looked like a little space alien to me."

Fascinated, she reached out to the author of the tardigrade chapter and struck up a conversation. That author, Diane Nelson, invited Lyons to visit her laboratory at East Tennessee State University in Johnson City. "I spent my 16th birthday there, learning how to handle and identify tardigrades," Lyons says. They ended up co-authoring a paper when Lyons was an undergraduate at the Massachusetts Institute of Technology (MIT) in Cambridge – although, because there were no tardigrade labs at MIT at the time, she mostly studied fruit flies and yeast.

Lyons returned to water bears during a fellowship year in Germany and continued her work as a graduate student at the University of California, Berkeley. For her postdoc, she joined the lab of neuroscientist Saul Kato. A worm biologist, Kato was looking to branch into a new experimental system when he started his lab at the University of California, San Francisco – he describes tardigrades as "*Caenorhabditis elegans* with feet". They met at a tardigrade conference in 2018, and she joined his lab in 2022.

A Goldilocks-shaped niche

As Lyons and Kato outline in a preprint review posted earlier this year, tardigrades could fill a Goldilocks-shaped niche in the systems-neuroscience space[2]. Mice and fruit flies (*Drosophila*), tardigrade-enthusiasts argue, are too complicated for the field. It's too difficult to isolate and connect behaviours with neural networks in these species. "You have to understand a simple system before you can understand a complex system," says Kato. "We are so far from even having the language or frameworks to truly understand how these large, complex neuro systems work in mice, and arguably it's the same with *Drosophila*."

At the other extreme, nematodes such as the roundworm *C. elegans* are too simple. "You can't get at the question of 'what is the role of the central nervous systems versus the peripheral nervous system when it comes to limb movement' [in worms], because worms don't have limbs," says Lyons.

Tardigrades do; they "have a very trimmed-down neural system but still have a brain and ganglia throughout their bodies and have limbs and can walk", says Lyons. Most organisms that walk need thousands of neurons to do so, she explains, but not water bears. "We don't yet know how many neurons tardigrades have, but they seem to be in the order of 300 to 700," she says.

That simplicity makes it relatively easy – in theory – to tinker with tardigrade neurobiology and observe the consequences. It has also led some researchers to wonder whether tardigrades might be similar to, if not the ancestors of, arthropods: the group that includes insects, spiders and crustaceans. "It is one of the most ancestral states," says Georg Mayer, a zoologist at the University of Kassel in Germany, of tardigrades; studying them "almost enables you to look back in time at a living fossil".

Another string to the bow of tardigrades as a model organism, is their translucency. Pretty much any of their cells can be observed while the animal is alive and in motion. That's especially important when you're trying to study the role of neurons in delivering various behaviours. "You can actually see them," says Lyons. "We're trying to genetically encode florescent reporter proteins so that, in theory, we could see all their neurons."

L: ANA LYONS; R: SAUL KATO

Ana Lyons (left) and Saul Kato think tardigrades could be models for systems neuroscience.

Tardigrades also behave in interesting and unusual ways for such small creatures. "How do they both crawl in a very organized, coordinated fashion, and have their legs move independently and grasp things?" asks Kato. "There seems to be both local control of the limb and top-down control." Kato wants to know more about how the animal's nervous system accomplishes both at the same time.

"There are so many other versions of this type of question in neuroscience and we think this is the perfect animal to study and find out," Kato adds.

And then there's the question of aesthetics – water bears are basically charismatic microfauna. "Tardigrades are definitely cuter than worms," Kato says, "Nobody calls a worm cute." That cuteness, he admits, has probably contributed to the water bears' appeal as a research subject. "They're sort of the darlings of the Internet."

Basic barriers

Given all these potential upsides, why do researchers know more about worms and *Drosophila* than they do about the seemingly ideal tardigrade? Why have water bears been "leap-frogged", as Kato puts it, by people who want to study systems neuroscience?

For one thing, tardigrades were late to the party. Researchers have conventionally gravitated towards either worms or fruit flies, because that's where most of the early grunt work had been done and key genetic tools created. "That's not the case with tardigrades," says Nirody. "We still have to pin down our basic understanding of some of their genetics and neurology."

Researchers aren't even sure which specific type of tardigrade to focus on. There are around 1,300 tardigrade species, and it's not yet clear which would be the most suitable as a model organism. But as a group, they have many traits in common.

For example, says Mayer, tardigrade genomes tend to include lots of duplicated genetic material. "They have multiple copies of some gene families, which is crazy, since they've kept their genome so small," says Mayer. "They have a small generation time and so it's a disadvantage to them to have to duplicate a lot of DNA." Why those duplications exist is a mystery that would be helpful to solve.

Tardigrade researchers are also struggling to genetically manipulate the animals – especially when it comes to inserting genes into their genome, a technique known as knock-in transgenics. At a conference in March on genetic tools for new model organisms, Lyons "was reassured to learn" that tardigrade researchers aren't alone in facing this difficulty. "It's all emerging model organisms, such as cuttlefish," she says. "It seems to be much more straightforward to knock out genes."

A 2024 paper from a Japanese group showed limited success with one approach[3] that used the editing tool CRISPR to insert genetic material into a tardigrade genome. But not at scale. Researchers need to be able to routinely knock-in hundreds of base pairs, and that isn't yet possible.

"We don't yet know the best way to do knock-in for tardigrades," Lyons concludes. "Is it CRISPR? Transposons? Viruses? Or something else? Do we target tardigrades when they're early-stage embryos? Or do we try to get in through the ovaries of the mother tardigrade?"

Once scientists answer those questions, they'll need to work out how to do it without popping the egg or killing the embryo. "That took a long time to figure out in *Drosophila*, for example, but once we realized you slightly dehydrate the embryos and then replace the liquid, boom. That was it. So, there are lots of little things like that which we need to know," says Kato.

One not-so-little unknown for systems neuroscientists is basic neuroanatomy. Tardigrade enthusiasts don't know how many cells the typical organism has, let alone how many neurons. Nor do they know what types of neuron the animals have, nor what they do.

Lyons is applying a battery of fluorescence-microscopy techniques to find out. "I'm finding all kinds of weird and cool cell morphologies," she says, "and some of the suspected neurons look very different from what we see in worms or fruit flies. To be sure they're all neurons, we really need to confirm the presence of synapses using electron microscopy."

The other key difficulty that tardigrade proponents face is that they are, for the moment, using experimental tools that weren't designed with the tardigrade in mind. Those techniques will probably need tweaking to be optimally functional for tardigrades, given the creature's unique biology, says Kato.

"There's going to be a lot of trial and error and we're likely to encounter new biology, new phenomena that are present in this animal, that aren't obviously present in other animals. Those are the 'unknown unknowns'," says Kato.

In a strange way, that's a nice problem to have. "Either we get this done in a reasonable amount of time and then we have this wonderful new model organism, or we're going to learn new things," says Kato. "There's a hypothesis, for example, that tardigrades have better defences [than other organisms] to protect their DNA from damage, and if we find that out, that's going to be amazing. There could be all kinds of applications in medicine for a protective DNA mechanism."

By meticulously investigating and describing every neuron and gene in tardigrades, Lyons hopes to help build a "neural atlas". That would give researchers who are interested in systems neuroscience a reliable map from which to work. But it's not a one-woman job. "It really needs to be a synthesis of experimental biologists who want to do the grunt work of genome engineering – which I'm happily trying to contribute towards – and neuroscientists who are skilled in neuroanatomy and people who know about different types of microscopies," she says. "It's going to be a community effort."

"There's work to be done, but I have faith in the tardigrade community."

And 'community' is exactly what the organizers of the conference in Japan hope to foster: a community spirit in which fellow tardigrade enthusiasts can teach each other what they've learnt, exchanging findings and tips on techniques – and establish collaborations.

Sae Tanaka, a molecular biologist at Keio University who works with Lyons, is one of the conference organizers and will be presenting her progress with TardiVec, an *in vivo* expression system that she and her colleagues have developed for imaging protein dynamics in live animals[4].

"We can now investigate molecular changes occurring directly within tardigrade cells," says Tanaka, who will be hosting a tutorial session on the method at the conference. TardiVec, she says, could accelerate the work of other tardigrade researchers, and she hopes to use the conference to encourage them to use it.

A noble pursuit

With so much basic work that needs to be done before tardigrades can achieve their full potential as model organisms, you'd be forgiven for thinking that few people would respond to Lyons' clarion call to work on a neural atlas.

But, as Kato says, scientific jewels are likely to be uncovered along the way, and scientists who help with the neuron atlas will have opportunities to publish their work. You don't have to talk to a tardigrade researcher for long before you realize that there is a genuine community of scientists emerging around this common goal.

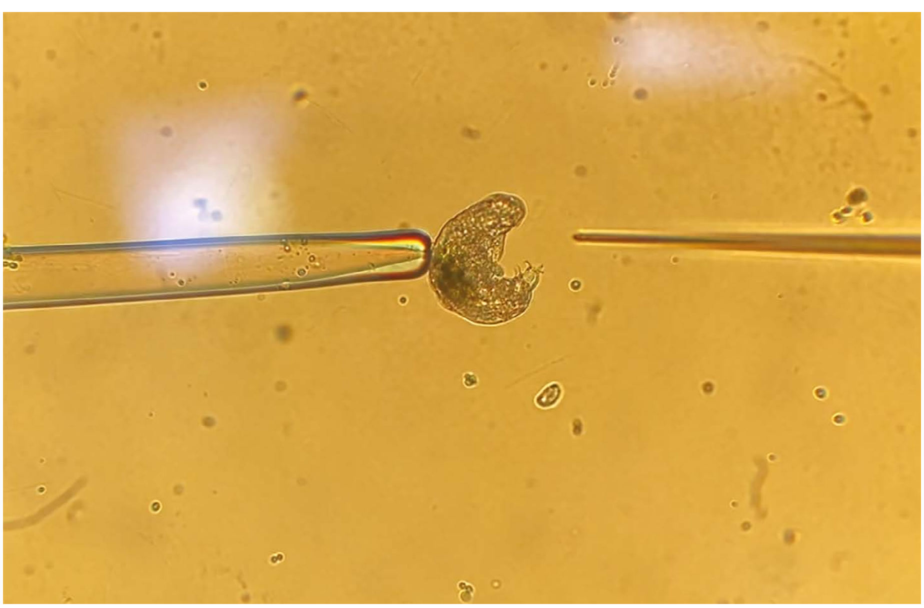
And, says Nirody, tardigrade researchers are a friendly bunch. "In mature fields, where a lot of work has already been done, people can feel as though they're competing with each other for discoveries," says Nirody. "With tardigrades, that's just not the case" – people are working towards a common goal, and are "cooperative and kind," she adds. "It also helps that we come from different fields, each bringing our own expertise and tools with us."

That's certainly the spirit that the organizers of the upcoming symposium are hoping to foster. Lyons hopes to learn from the mistakes that others have made in trying to address the unique challenges of water-bear biology. She's also looking forward to helping them learn from her work. "It's a friendly community and we're really looking forward to it," she says.

Kato, who is heading to Japan for the conference, hopes to meet a breadth of researchers from different fields this year. At his first tardigrade conference, in 2018, he says, he was surprised that there were so few molecular biologists and neurologists in attendance. "It was mainly people debating over the taxonomy of tardigrades and where they fit in the evolutionary tree," he recalls. Since then, the tardigrade community has been going like "gangbusters", he says. As many as 120 people could attend the conference this year, Lyons adds.

That growth in the community, which Kato says has brought different expertise into the fold, makes him optimistic that tardigrades could become a genuine model organism soon. "Years, not decades," he predicts.

Benjamin Plackett is a science journalist in London.



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A tardigrade is injected with genome-engineering cargo using a micropipette.

1. Traspas, A. & Burchell, M. J. *Astrobiology* **21**, 845–852 (2021).
2. Lyons, A. M. & Kato, S. Preprint at arXiv https://doi.org/10.48550/arXiv.2501.06606 (2025).
3. Kondo, K., Tanaka, A. & Kunieda, T. *PLoS Genet.* **20**, e1011298 (2024).
4. Tanaka, S., Aoki, K. & Arakawa, K. *Proc. Natl Acad. Sci. USA* **120**, e2216739120 (2023).

Correction

This feature mistakenly described Ana Lyons as being based in Tokyo and over-estimated the number of attendees expected at the 2025 tardigrade conference.

Corrected 25 June 2025