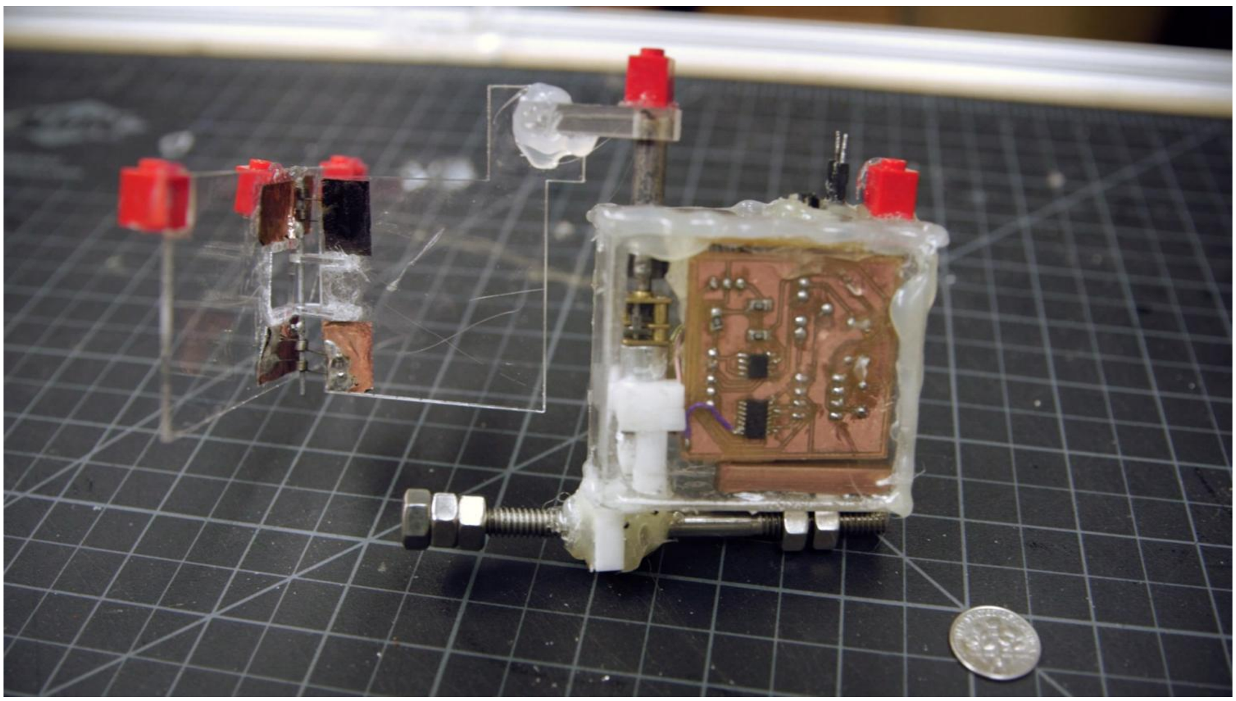
Mystery of tropical human parasite swimming solved

October 31 2016



Researchers in the Prakash Lab created a scaled-up robotic swimmer to learn how the parasite that causes schistosomiasis disease swims. Credit: Kurt Hickman

For several years Manu Prakash, an assistant professor of bioengineering, has gone to field sites to test new, low-cost microscopes as a tool for diagnosing the parasitic disease schistosomiasis. The devices showed promise, but Prakash was perplexed by how often kids treated for the disease were getting re-infected. Prakash quickly turned his attention to preventing infections at the first place.

This new focus led his team to think about a fundamental question in the transmission cycle: How does this parasite actually move in open water to infect a human host? They hope that by understanding the biophysics of how this parasite swims, it might be possible to hinder the movement and thwart infection. The results of this study are published in the Oct. 31 issue of *Nature Physics*.

"We started thinking about the ecological context for the schistosomiasis disease cycle when, out in the field, we were seeing the terrible trauma it inflicts on people," said Prakash, senior author of the study. "It manifests over long periods of time, and if the water body near you is infected, there is a very high likelihood that you will get the disease. So, effectively, you can take drugs that could cure you for some time but you get re-infected again."

A debilitating disease

People become infected with schistosomiasis when the larval form of the parasite leaves the freshwater snail host, swims through the water and penetrates human skin. Once in a person, the larvae develop into adult schistosomes. The female parasites later release eggs, which are either passed out of the body through urine and stool or trapped in bodily tissues, triggering an immune response and large-scale organ damage. When the eggs from urine or stool enter a water body with the freshwater snail hosts, the cycle begins again.

Schistosomiasis infection often produces abdominal pain, diarrhea and blood in the stool or urine. It can also cause learning deficiencies in children and an inability to work in adults that traps families in a poverty cycle. Over the years, adults can develop bladder cancer or severe kidney damage, which reduces their quality of life. In some cases the disease results in death.

The World Health Organization (WHO) estimates that 258 million people required preventive treatment for schistosomiasis in 2014, with an estimated 20,000 deaths. As with many other neglected tropical diseases, schistosomiasis disproportionately impacts people who live in poverty. These people are more likely to be vulnerable to infection because they often have less access to adequate sanitation or to safe water for drinking, chores, recreation, fishing or agriculture. Even after treatment, people are often re-infected through their constant contact with contaminated water.

Where to start

Prakash decided to investigate how schistosomiasis larvae swim to find a human host. This is a valuable question because, in its larval form, the parasite has no feeding mechanism and must find a host within about 12 hours or die. It stands to reason, then, that the larvae likely have some special, extremely efficient swimming skills. It turns out that hunch is correct.

"This was unlike anything I had seen before," said Deepak Krishnamurthy, a PhD student in the Prakash Lab and lead author of the study. "When I looked at this parasite, I was fascinated by the fact that it was swimming in a completely different way as compared to any other microorganism I knew about. The parasite had a mysterious forked tail, something that has never been seen before in any other swimming microorganisms."

The researchers used three different approaches to investigate this odd swimming stroke. They imaged live parasite larvae with high-speed microscopy, they created a mathematical model to understand how the parasite interacted with the surrounding fluid, and finally they translated that model into a scaled-up robotic swimmer as a physical extension to learn more about physical parameters at play.

The T-swimmer

While observing the larvae, the team noticed a few swimming styles that schistosomiasis larvae employ in different situations, and which differ primarily in the position of the forked tail. Of those, one stood out as unique. In this stroke, the larvae stick the tail out perpendicular from the body, like the letter T, prompting the researchers to dub them T-swimmers.

The larvae switch to T-swimming when they are moving against gravity, which they seem to do in order to be near the water's surface, where they are most likely to find a human host. High-speed video of live larvae swimming allowed the researchers to examine in depth how this novel swimming style works.

Members of the Prakash lab in Madagascar studying the larvae that cause schistosomiasis. Credit: Saad Bhamla

"We spent countless hours watching hundreds of these parasites swim - it's like an obsession," said Yorgos Katsikis, a former PhD student in the Prakash Lab and co-author of this study. "Then we developed image-processing algorithms that would process this data automatically without any experimental bias."

These custom algorithms revealed in detail the exact kinematics of how the larvae bend their body and rotate their head, how fast they move and how they accelerate and decelerate and perturb the surrounding fluid.

Creating models

In parallel with direct observations, the researchers developed multiple mathematical and robotic models for how a T-swimmer could swim. The mathematical representations look like three rods, one representing the larvae's forked tail and the other two its bending tail and body. The robots were similarly structured and swam through corn syrup, a 10,000 times more viscous counterpart to the water the larvae infests, to recreate the same physical effects.

With these models, they could make the model larvae do strokes that involved varying combinations of tail stiffness and bending movement. They even raced several robots, each with slight modifications in their tail stiffness.

"In many cases, we try to replicate nature in robots. This was very different," said Krishnamurthy. "On the face of it, it looks like I'm trying to make a robot that swims like a parasite, but the truth is that it was the exact opposite: I was building a robot to actually understand how the biological parasite swims."

What these models and various modifications revealed is the larvae's real swimming stroke was indeed the optimal version.

Prakash and Krishnamurthy have been in Madagascar collecting infected snails and studying the ecology of this parasite in open water in rural villages. They hope their work in and out of the lab will help them understand how these parasites find humans and bring them one step closer to an ecological solution to this widespread disease.

More information: Schistosoma mansoni cercariae swim efficiently by exploiting an elastohydrodynamic coupling, *Nature Physics*, DOI: 10.1038/nphys3924

Provided by Stanford University