Starving mosquitoes for science

February 22 2024, by Jiayue (Gabriel) Yan

Illinois Natural History Survey medical entomologist Jiayue (Gabriel) Yan peers through a viewing port as he works inside a sealed glove box, using tongs to carefully handle Aedes aegypti mosquitoes. Credit: Fred Zwicky

Researcher Jiayue (Gabriel) Yan is part of the Medical Entomology Program at the University of Illinois at Urbana-Champaign. His recent study appears in *Communications Biology*. In this article, he describes his

work.

Working with mosquitoes and live dengue virus

On a scorching summer day, I'm at work in the heart of the arthropod containment laboratory of the Medical Entomology Program. I place my hands in the rubber gloves that reach into a sealed workspace called the glove box, swiftly maneuvering to grab fully engorged mosquitoes. These insects have just fed on a blood meal infected with live dengue virus. They are now resting calmly on a chilled Petri dish, thanks to the low temperatures provided by the ice below.

Although my hands and arms are protected, I'm on high alert. This is the notorious yellow fever mosquito, Aedes aegypti, a potential carrier of dangerous vector-borne pathogens such as dengue and the Zika virus.

Like other mosquitoes, Ae. aegypti undergoes distinct stages during metamorphosis. In its aquatic larval phase, it eats microorganisms and organic debris. As an adult, it depends on plant sugars and vertebrate blood. Changes in its food quality or availability can induce nutritional stress, potentially affecting its ability to transmit pathogens.

A blood-fed Ae. aegypti mosquito, also known as the yellow fever mosquito. Credit: Fred Zwicky

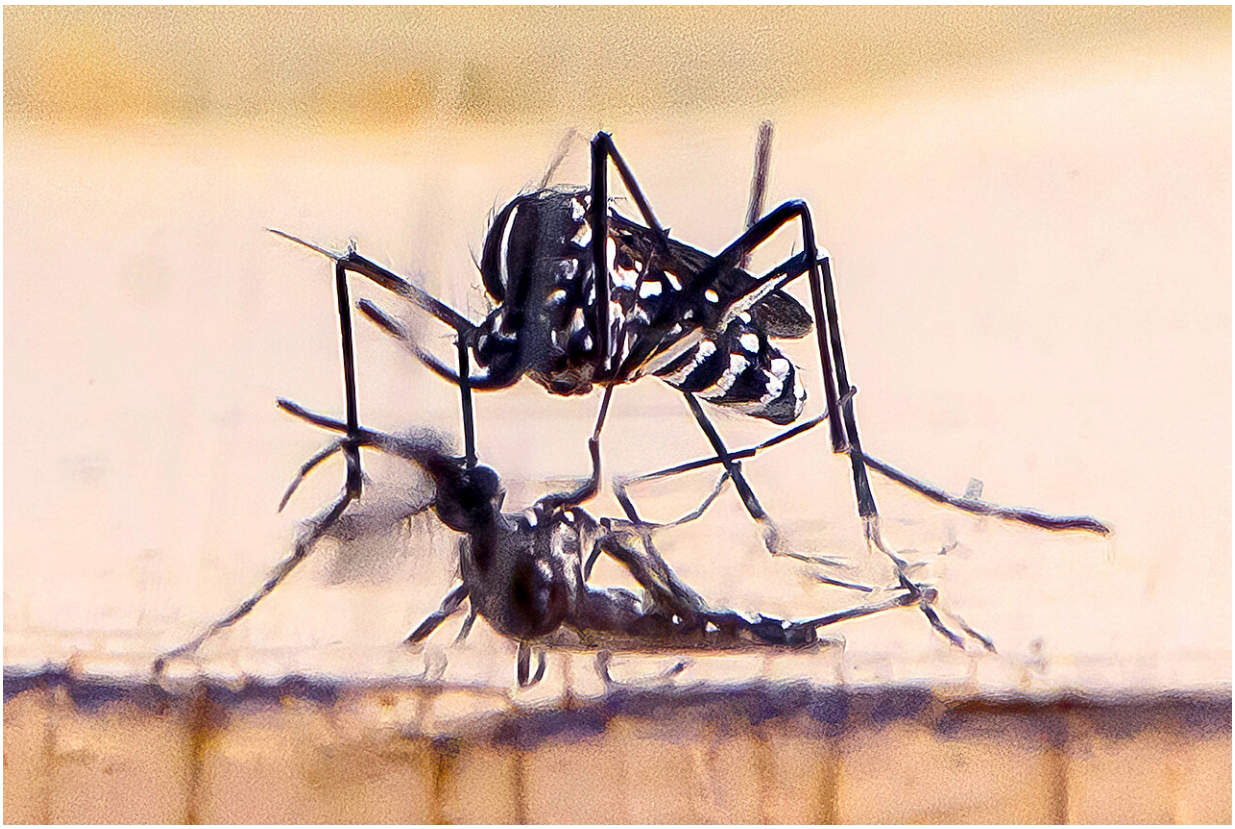
The abdomen of adult Ae. aegypti mosquitoes swell as they extract a blood meal through a membrane-covered feeding device. Their weight can quadruple from the feast. Credit: Fred Zwicky

For me, this is a high-stakes field of research. I am determined to unravel the mysteries surrounding how diet affects these mosquitoes. Previous studies have produced conflicting findings. I want to know how nutritional stress—during both larval and adult stages—influences the mosquitoes' susceptibility to dengue infection.

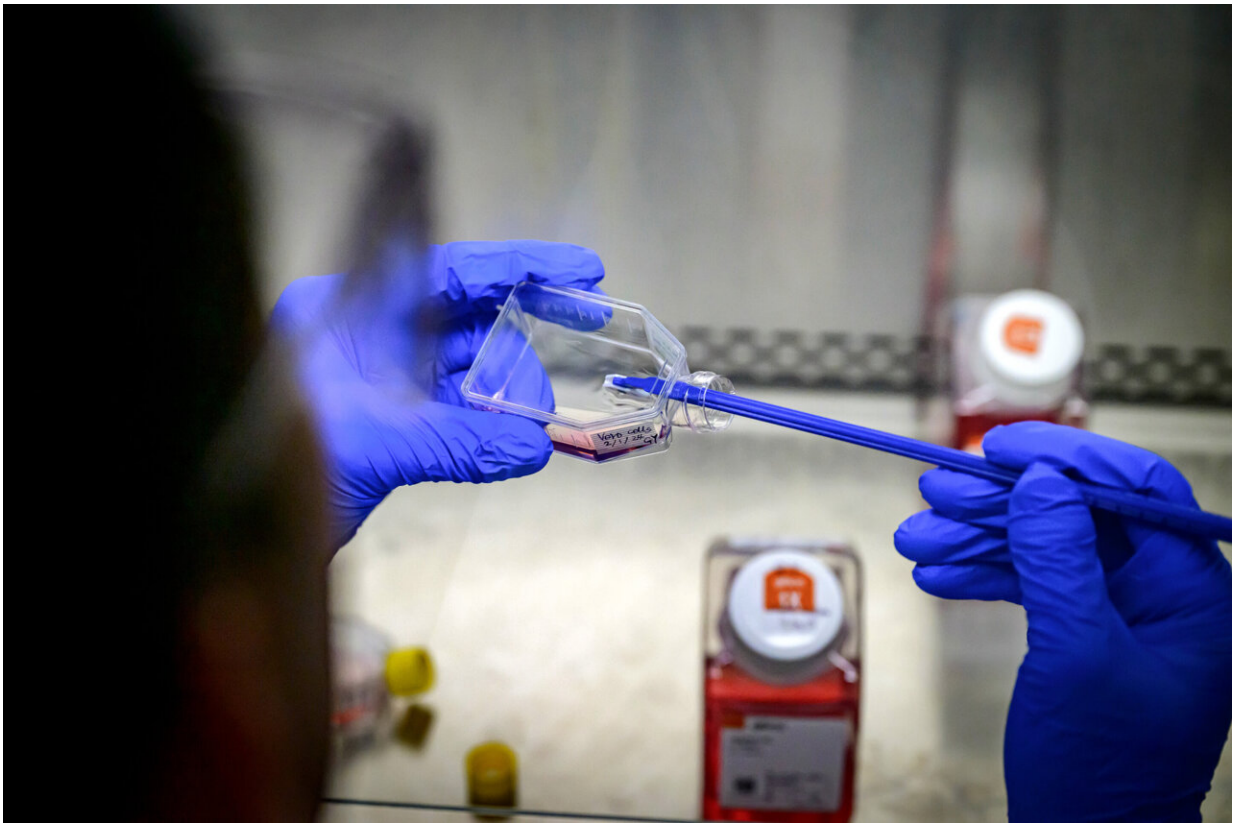
To tackle this problem, I must handle an army of more than 10,000 larvae and 4,000 adult female mosquitoes. Each mosquito is randomly assigned to one of four nutritional treatment groups. Half of the larvae get a full meal while the others get only half as much. For the adult

mosquitoes, half get a 10% sucrose solution and the others get a 1% sucrose solution.

The smaller portions or concentrations of food in their diet serve as proxies for nutritional stress experienced at each life stage. Each of the four groups also must be provided with blood meals—half containing dengue virus and half without. Those not infected with dengue will be used as a control so that I can measure any differences between the groups.



A pair of Ae. aegypti mosquitoes mate inside a plexiglass enclosure at the Medical Entomology Laboratory. The eggs will be used in future research. Credit: Fred Zwicky



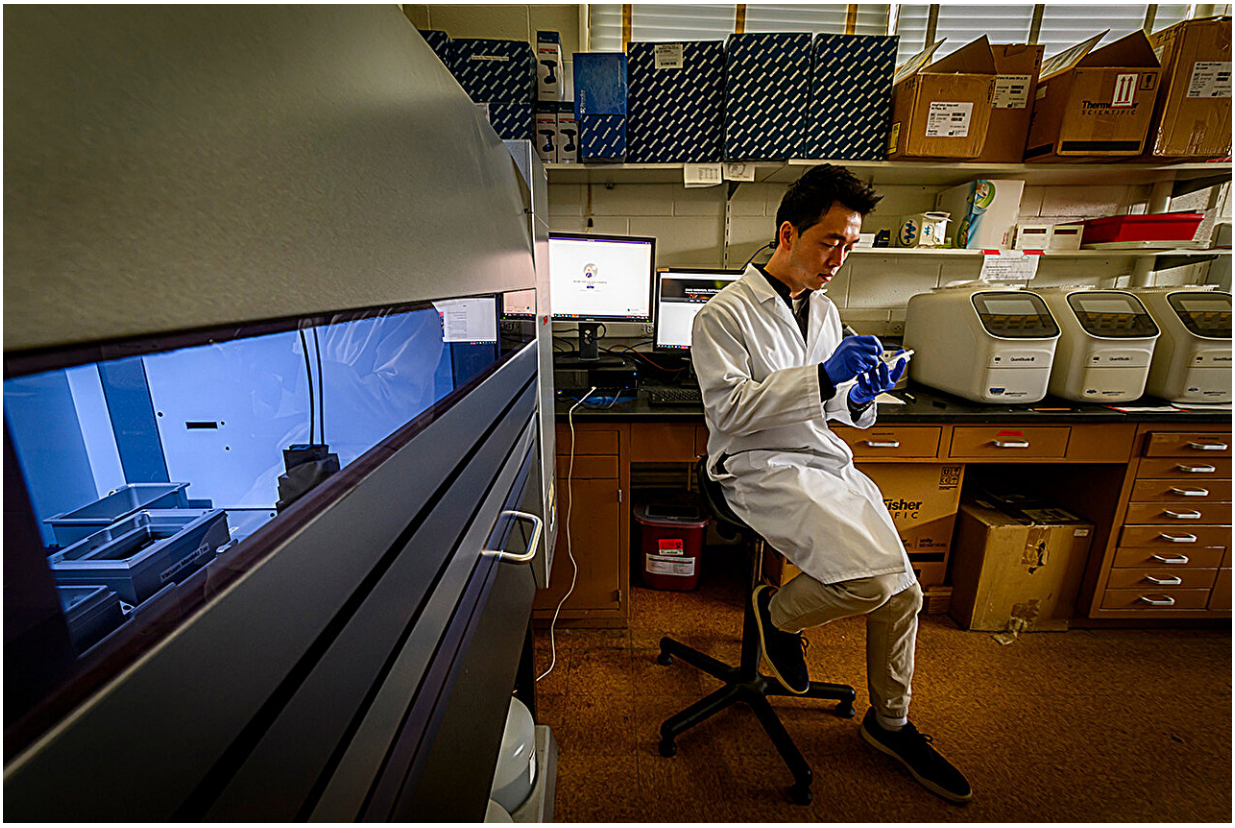
Yan works with live dengue virus to prepare a blood meal for the mosquitoes. Credit: Fred Zwicky

I aim to have at least 100 fully engorged mosquitoes in each of the eight treatment groups. I pick out 800 of the blood-fed females by hand, carefully transferring each into a specific cup in the sealed box. When mosquitoes feed on blood, their weight can double, triple or quadruple. Handling each one with fine-tipped forceps requires extra caution due to their increased fragility in this blood-fed state.

My mission extends beyond the initial feeding. I must meticulously inspect each cup twice daily. If a mosquito has died, I delicately transfer it to the -80 °C freezer for future molecular testing. I also count the eggs

laid to measure their fecundity. Mosquitoes typically live a month or two in the wild, but in the lab some last for more than three months, demanding additional time and attention.

All this hard work is paying off. My colleagues and I have found that the mosquitoes that undergo both larval and adult nutritional stress produce fewer eggs and are less fertile. Under the strain of nutritional stress alone, adult mosquitoes have shorter lifespans.



Yan labels a PCR plate before conducting dengue virus detection using a PCR machine. Credit: Fred Zwicky

Yan extracts mosquito pupae from larva-rearing trays. Credit: Fred Zwicky

]When we look at what's going on at the molecular level, we see that a poor diet in both the larval and adult stages triggers a downregulation of mosquito immune genes and antimicrobial peptides. These components serve as mosquito defenses against pathogens. Adult nutritional stress becomes a chink in the mosquito's armor, heightening its susceptibility to dengue infection.

Understanding the intricate dance between what mosquitoes consume and their disease-spreading potential is important to human health. We now know that a mosquito weakened by a poor diet is a more effective transmitter of diseases like dengue. Our new understanding could help us

find new ways to manage mosquito populations and curb disease transmission.

More information: Jiayue Yan et al, Nutritional stress compromises mosquito fitness and antiviral immunity, while enhancing dengue virus infection susceptibility, *Communications Biology* (2023). DOI: 10.1038/s42003-023-05516-4

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