Venom With Velocity (p. 4345)

Snakes don't just bite for fun. It's usually a matter of life or death before a snake will bare its fangs. But the obvious drawbacks of working with venomous snakes have meant that no one had directly measured the way they dispense their venom during a strike. However, this did not deter Bruce Young from adapting a technique used for monitoring blood flow to measure how a striking rattlesnake expels its venom.

Rattlesnakes use their fangs for two reasons: hunting and defence. Young wanted to know how the snake ejected venom in both types of strike. Working with Krista Zahn, an undergraduate at Lafayette College, Young operated on four adult diamondback rattlesnakes and implanted a perivascular flow probe around the snake's right venom duct.

Young tested the snakes bite in three ways. First he provoked defensive strikes using mice and rats. Then he induced predatory strikes using mice alone, so that he could directly compare both bite styles on a single quarry. As well as recording the fluid flow in the venom duct, he filmed each strike with a high-speed video camera to catch every detail of the way the snakes wield their fangs at their victims.

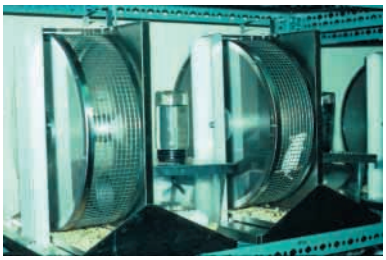
Young accurately recorded three distinct venom flow patterns produced by the snake, and a fourth, where the snake sunk it's fangs into the prey, but failed to release any venom. Although there was plenty of anecdotal human evidence that snakes didn't always inject venom into their prey, it had never been proved before that some snakebites are dry.

He also found that the snake injected ten times the amount of venom during a defensive strike than it does to secure a meal. Young explains that this might not be as cock-eyed as it sounds. The way that snakes digest their food means that it isn't terribly urgent that they successfully capture every potential meal, but an unsuccessful outcome with an attacker would rule them out of the evolutionary race. He thinks that it's simply a better investment for the snake to use a large amount of venom in a defensive strike than one that results in a gastronomic reward.

One constant feature of the flow pattern Young found was that the snakes reversed the venom flow at the beginning and end of each bite. At first, Young thought there was a problem with the data collection, but he says that when he sat and thought about it he probably shouldn't have been surprised. The snake's venom gland and duct are more like a pipette than a syringe, and when you stop applying pressure to a pipette bulb, some of the liquid always sucks back.

Ken Kardong, who has worked with rattlesnakes for more than 30 years, says that the reverse flow found by Young was unexpected, and he agrees that it could be part of a venom mixing mechanism. The snakes have two venom glands along the length of the venom duct. How the secretions from both glands mix had never been clear, but Young's flow reversal could be part of a venom mixing mechanism.

Of course, other species have completely different flow patterns, so Young hopes to repeat the experiments with spitting cobras. The only drawback is that this time he'll have to use his own face to get the right reaction from the snake. Young says that he's tried using mirrors and other targets, but the only sure fire way to get the snakes to spit is if he sits in front and makes direct eye contact. That'll make an interesting Materials and Methods section!



Running Through the Generations (p. 4311)

Anyone who's ever owned pet rodents knows just how much they love running in their wheels. But a team of physiologists in Madison, Wisconsin, have taken this a step further. They wondered how generations of house mice would develop if they were selected for their ability to run long distances. After 23 generations, it seems that the mice have adopted the same approach that the Romans used over 2000 years ago for covering long distances in short times: run fast, but little and often.

Ted Garland Jr began the experiment over 7 years ago, when his team set up a massive selection program to breed mouse super-runners. The experiment was designed so that there were eight separate mouse populations, four that were selected for running, and four control populations. Each population started off with ten families. At six weeks of age, each mouse was given a cage with an exercise wheel. Then they got a week to run whenever the fancy took them, before they ran the keenest-runner-test that decided whether they got to pass their genes on.

Each family sent its best male and female runner to found the next generation. Of course, they weren't always the best runners in the whole population, in fact 'some were real duffers' says Girard, but it was important to make sure that close relatives never mated.

After the mice had been selected for ten generations, they were tested to see whether their performance had changed. The mice from these selected populations easily out-strode their unselected rivals.

After a total of 23 generations had passed through the banks of running wheels, Girard and Matt McAleer watched over 1000 hours of mouse running footage. They chose each mouse's top performance for detailed analysis of their running behaviour. Girard says, 'we all had the impression that the mice were running more intermittently'. In the final analysis Girard found that the experiment hadn't produced a super breed of muscle bound mice that ran fast for extended periods; the mice had found another way round the problem. They were running at top speed in frequent short bursts.

Girard thinks that the mice probably evolved a new running behaviour because they may have maximised their physiological response at an earlier stage of selection. The only way they could continue to improve, once they'd optimised their speed, was to combine their improved physiology with a new style of behaviour.

She says 'I think normal mice could do it too, but these mice want to run more'. Justin Rhodes believes that this is because the mice process dopamine differently, which increases their motivation to get their jogger's high. This is similar to the neurological bases of Attention Deficit Hyperactivity Disorder (ADHD) in children. Having started off asking a physiological question, Garland's team discovered that neuropsychology is a big part of the answer. Understanding the neurological behaviour of these marathon-mice could eventually produce improved therapies to relieve the disturbing symptoms of ADHD.

The Fats of Life (p. 4271)

Cell membranes can be made up of incredibly complex mixtures of lipid molecules. Some animal cell membranes have over 100 different types of phospholipid molecules, distinguished from each other by differences in their head groups and hydrophobic fatty acid chains. But the phospholipid bilayers that make up a membrane are

only half of the story; the remaining fraction is made up of cholesterols and proteins, such as transporter proteins. How the lipid environment affects the protein's function wasn't clear until Tony Hulbert and his colleagues in Wollongong, Australia, found that the physical properties of the lipid mixture have the biggest effect on membrane protein activity.

Years ago, Hulbert's colleague, Paul Else, wondered how swapping the membrane protein hugging lipids might affect the protein's function. He hit on the sodium/potassium ATPase pump as an ideal test case. Else knew that the membrane's lipids differed between toads and rats, so he tested how well a rat ATPase functioned in a toad membrane. Amazingly, the rat protein changed, so it behaved more like the toad protein.

Was the different chemical composition of the two membranes modulating the protein in some way, or were the physical characteristics of the membrane regulating the pump's activity? Until now, most lipid physical characterisation had been carried out on homogenous samples, and certainly nothing as complex as a brain cell membrane, so Ben Wu stepped back into the undergraduate lab, where he used a Langmuir Trough to measure the mechanical properties of complex membranes from rat and toad tissues.

Brain and kidney membranes are packed with sodium/potassium ATPases, so Wu began preparing both membranes from rats and toads. He tested the ATPase activity from all four sources and then began to characterize the membrane's chemico-physico properties after he'd extracted the protein component.

To Hulbert's surprise, the types of unsaturated lipids varied enormously between the four sources, but there was no single type of lipid that could fully explain the differences in enzyme activity. However Wu's biophysical data proved to be more promising. In membranes where the lipid molecules packed together tightly, ATP turnover by the ATPase was slower than the rate measured for ATPases from looser membranes.

Recent evidence has begun to emerge that cell membrane composition could be playing a crucial role in a variety of serious medical conditions, such as schizophrenia and insulin resistant diabetes. People who have a diet rich in oily fish tend to suffer less from depression, and this seems to be correlated with a high proportion of Omega-3 fatty acid chains in the fish's membrane lipids. Hulbert believes that it is likely that the physical properties of the fatty acid chains might directly influence the function of key target molecules in these diseases. He says 'it appears that the physics of lipids has an important effect on membrane protein activity'.

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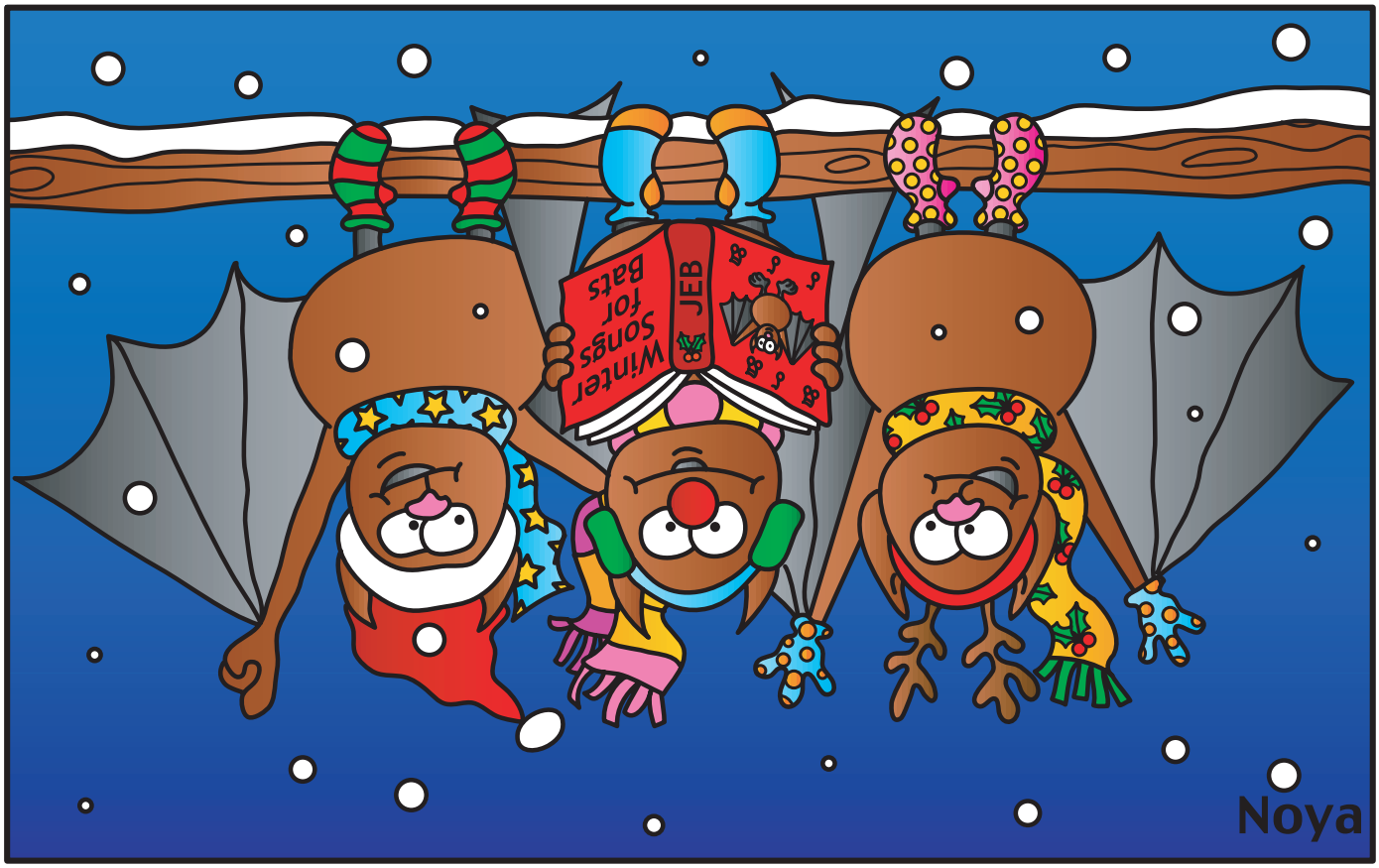
The Journal of Experimental Biology 204, i-ii (2001)



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