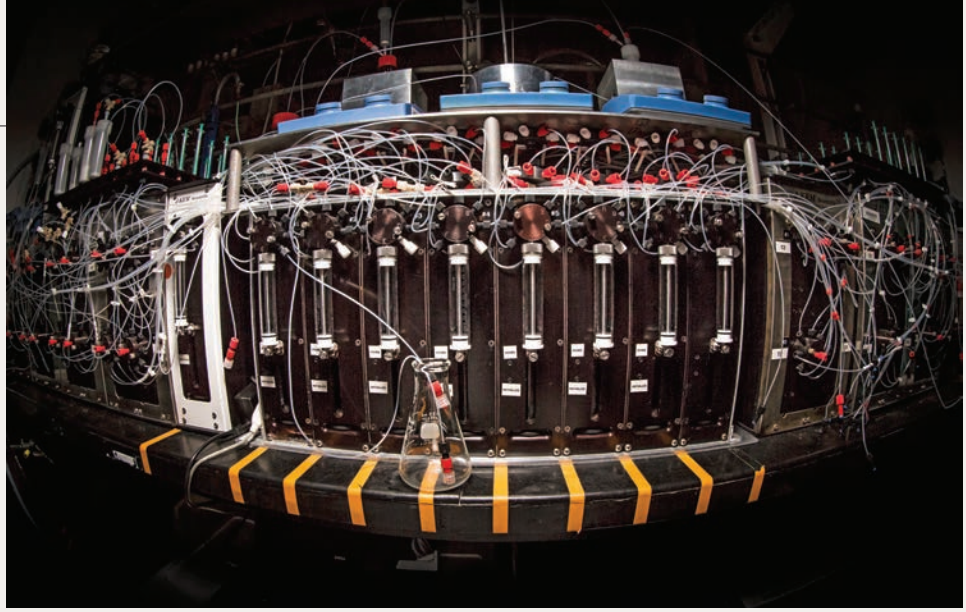


Taking cues from nature, this molecule-making machine couples chemical building blocks to create small molecules.

Made-to-order Molecules

A new invention acts as a molecular 3-D printer.

WHEN CHEMIST FRIEDRICH WÖHLER accidently made synthetic urea about 200 years ago, he stumbled upon a feat that has occupied scientists ever since: the synthesis of small molecules.

Today, we use small molecules everywhere. You can find them in most medicines, foods, scientific research – even coffee sweeteners and light bulbs. Yet when it comes to the vast possibilities arising from small molecule production, we've barely scratched the surface.

"The bottleneck is synthesis," says Martin Burke, an HHMI early career scientist at the University of Illinois at Urbana-Champaign. To date, making small molecules has required a customized approach achievable only by highly trained specialists.

But now, Burke and his team have developed an invention that extends that ability from a select few to anyone with a computer. "We've created a machine that can do on-demand small molecule synthesis – kind of like a 3-D printer for small molecules."

Burke says the machine, described in *Science* on March 13, 2015, was inspired by living organisms. "Nature makes most small molecule natural products through very simple building-block chemistry. ... So in a sense, nature is already telling us the answer."

The machine takes basic chemical modules and stitches them together to create small molecules. When mixed and matched in different combinations, these building blocks can generate a plethora of new small molecules – made automatically and using relatively little effort.

"History speaks strongly to the major impact that can be achieved when you take a powerful technology like molecule making and put it into the hands of everyone," says Burke, whose long-term vision is to have a website where anyone in the world – a chemist, biologist, engineer, or high school student – can order small molecules to be made and shipped directly to themselves. For now, the machine is already enabling a new biotech company to enhance its drug development efforts; it has the broader potential to expand possibilities in many fields of scientific research. *– Anzar Abbas*

in a virtual reality arena to observe the insect's neurons as it walks. The study, published May 14, 2015, in *Nature*, focused on a part of the fly brain called the ellipsoid body, a donut-shaped structure suspected to be involved in directional movement.

The researchers saw a strong relationship between the fly's orientation relative to its visual surroundings and the neurons activated in the ellipsoid body. When the fly changed direction, even in total darkness, neuronal activity shifted from one part of the ellipsoid body to another, much like the needle of a compass.

"We think we have a window into the fly's internal model of its world," says Vivek, who believes ellipsoid body neurons may share characteristics with human head direction cells. "We're starting to see increasing evidence that the fly may have a lot to tell us about how our own brains work, even when it comes to more complex aspects of cognition."

RARE MUTATION MAKES FLU FATAL

While catching the flu might be an inconsequential annoyance for many of us, the flu virus can prove life threatening in some people. Research led by HHMI Investigator Jean-Laurent Casanova at Rockefeller University tackled the question of why some patients respond differently to the virus than others.

The study, published April 24, 2015, in *Science*, describes a two-year-old girl who had been treated for a severe case of the flu at the Necker Hospital for Sick Children in France. The researchers sequenced her exome to hunt down the reason for her immune system's weakened response to the virus.

What they found was a rare mutation in her *IRF7* gene, known to be responsible for the production of antiviral molecules called interferons. Without the functional protein, a patient would have an inadequate response to the flu virus.

"Now we have proof that life-threatening flu, an infectious disease, can also be a genetic disease," says Casanova, whose past work has identified other mutations that make patients more vulnerable to a variety of infectious diseases.

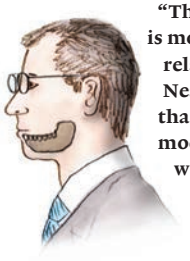
Understanding *IRF7*'s role in fighting the flu virus may allow doctors to consider other treatment options, such as administering interferons, when faced with severe unexplained flu.

JAWBONE REVEALS NEANDERTHAL ORIGINS

Scientists have successfully retrieved and examined DNA from a 40,000-year-old bone.

And not just any old bone. This human jawbone, found in 2002 in a Romanian cave called Peștera cu Oase, dates back to a critical period of Europe's history when modern humans were replacing Neanderthals. Scientists have always wondered how this transition happened. Now, the bone's DNA indicates that it belonged to a modern human whose recent ancestors included Neanderthals.

On average, humans today living outside Sub-Saharan Africa owe about 2 percent of their genes to Neanderthal ancestors. The study, published August 13, 2015, in *Nature*, shows that 6 to 9 percent of the Oase bone's DNA came from Neanderthals.



"The sample is more closely related to Neanderthals than any other modern human we've ever looked at before," says David

Photo: L. Brian Stauffer, Illustration: Leif Parsons