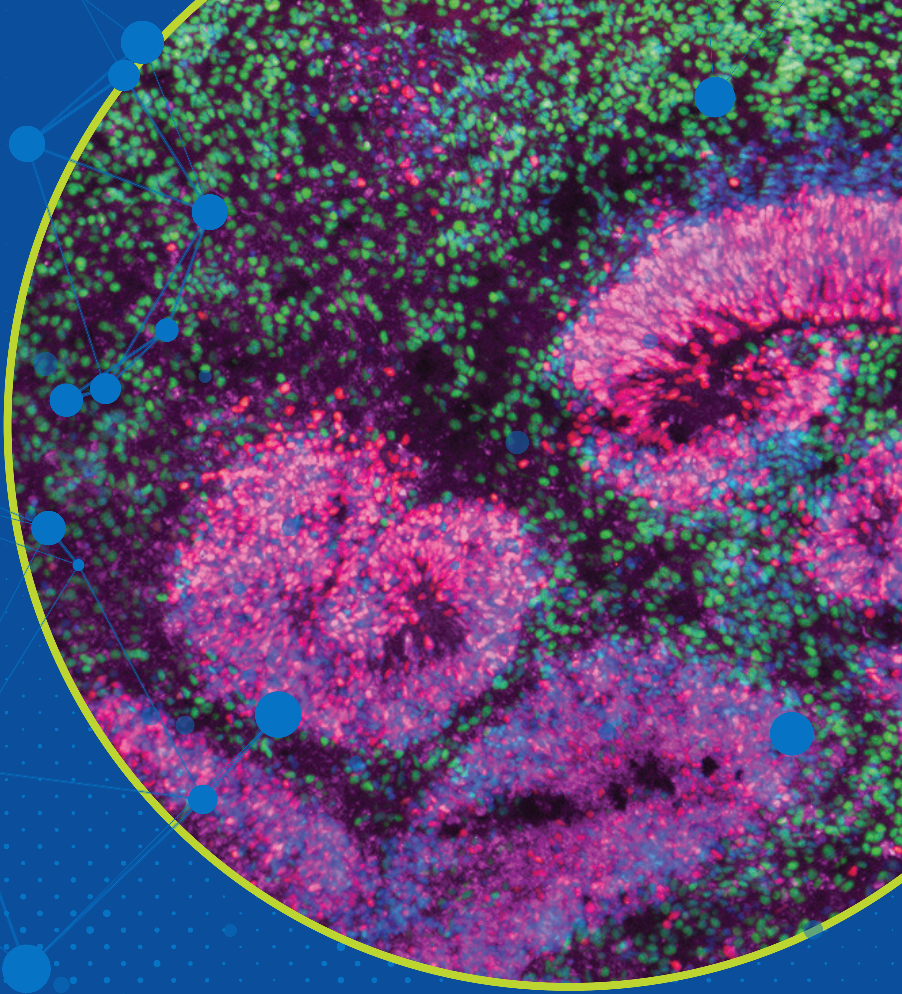

NAMs: Advancing Science and Reducing Animal Use in Laboratories

Animal Welfare Institute

Every year, in laboratories throughout the United States, millions of animals are used for research and testing. Although the shorthand "animal research" or "animal testing" is commonly used to refer to both research and testing, the two are not the same.

- **Research:** This refers to scientific efforts to learn something new or understand something better (such as how the body works, or how a disease progresses).
- **Testing:** This refers to scientific efforts to determine the toxicity and safety of substances—particularly items under development for public use. Among other things, testing is done on consumer products (such as makeup and shampoo), prescription drugs and vaccines, and chemicals that may be dispersed into the environment (such as chemicals from pesticides that could be flushed into waterways).

Of these two, research accounts for the majority of animal use in laboratories.

Many scientists and animal advocacy groups have a shared goal of reducing or eliminating the use of animals in laboratories as nonanimal methods advance. Studies using these nonanimal methods—collectively called "new approach methodologies" (NAMs)—may actually give scientists more insight into human biology than studies using animals.

If you are interested in pursuing a career in science—one that involves, for example, developing lifesaving medicines or testing the safety of products people use daily—but don't want to experiment on animals, NAMs might be part of your path.

NAMs

New approach methodologies—or NAMs—are new techniques that can help scientists learn more about how the body functions and reacts to various conditions (including chemical exposure and disease) without using live animals. You might hear people also refer to NAMs as “replacements,” “alternatives,” or “nonanimal methods” because of their potential to reduce or replace animal experiments. NAMs cannot yet fully replace all experiments on animals, but scientists are working hard to bring new NAMs to the table every day.

Studies that use animals are referred to as *in vivo* (Latin for “in the living”) experiments. In contrast, NAMs, which involve nonanimal technologies, broadly fall into one of three categories: *in chemico*, *in vitro*, *in silico*.

In Chemico (Chemical Analysis)

If you like studying organic chemistry, *in chemico* methods might be your thing! These are relatively simple techniques used to measure the chemical reactivity of something on the molecular level, and they don't require live organisms or even whole cells. For *in chemico* experiments, scientists combine substances they want to test with solutions made up of biological molecules (like peptides, proteins, or DNA) to see what chemical reactions occur. The goal is often to see whether (or under what conditions) certain chemicals may be toxic or cause a reaction, like a rash. Scientists might use *in chemico* techniques, for example, to assess whether medicines, cleaning products, or makeup would cause skin or eye irritation.

IN CHEMICO IN ACTION

In chemico techniques can be used instead of *in vivo* (animal) experiments, sparing animals from painful or uncomfortable experiences in labs. For example, the hemoglobin denaturation (HD) test and the Ocular Irritection test are two *in chemico* alternatives to the ocular Draize rabbit test. The Draize rabbit test was developed in 1944 to test cosmetic and household products for toxicity and their potential to irritate or damage the eye. It involves applying chemicals to the eye of a restrained, awake rabbit, and then measuring the damage to the eye over time, which is often very painful for the rabbits.

Because eye irritation can largely be explained by the denaturation (breakdown) of proteins and plasma membranes in the cells of our eyes (ocular cells), the *in chemico* alternatives combine ocular proteins with solutions of a substance being tested to measure whether the substance causes the proteins to break down. This method can provide crucial information about whether the substance would be harmful to real-life eyes without subjecting live animals to painful procedures.

In Vitro (Experimentation on Cells)

If you are interested in understanding how the body works on a cellular level, or you want to pursue a career developing new drugs or testing product safety, your future might include working with in vitro methods!

In vitro experiments are conducted on cells outside of living organisms. Historically, in vitro studies involved growing a layer of cells on a two-dimensional (2D) plane, such as in a petri dish (the literal translation of in vitro is "in glass"), and then observing them under a microscope to see how they react to various substances. This type of experiment is typically inexpensive and allows for a high degree of control and quick results.

Although 2D cell culture experiments are still useful for answering certain questions, there have been many exciting advancements in other in vitro approaches over the past two or three decades. Scientists can now grow cells in 3D environments that are dynamic and complex, like real organs in a live body. These 3D models—called "microphysiological systems" (MPS)—include "spheroid," "organoid," and "organ-on-a-chip" technologies. MPS are really changing the game for human health research!

Spheroids and Organoids

Spheroids and organoids are microscopic 3D structures made up of multiple cells. Although you may hear these two terms used interchangeably, they do have differences. For one thing, spheroids are less complex than organoids—they are basically clusters of cells that stick to each other.

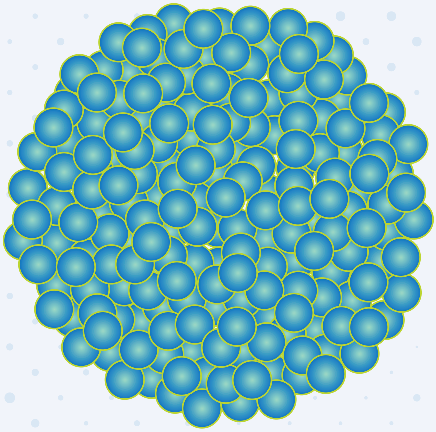

Illustration of a spheroid, a microscopic, 3D cell system.

SPHEROIDS IN ACTION

Scientists use tumor spheroids (clusters of tumor cells) to better understand the microenvironment of tumors and gauge the potential effectiveness of medical treatments on tumors.

Organoids, on the other hand, are miniature 3D versions of organs or tissues that are grown from stem cells. Since organoids closely mimic the structure and function of organs and tissues in the body, they are used to help scientists learn more about the “parent” organ that the organoid represents.

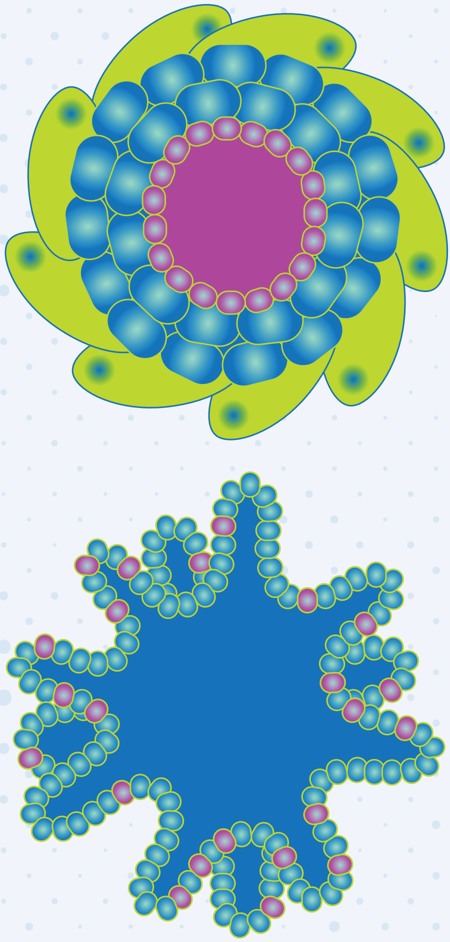

Illustration of a cardiac (top) and intestinal (bottom) organoid.
Organoids are miniature, 3D versions of the larger organs.

GET TECHNICAL: STEM CELLS

Stem cells can follow their own genetic instructions to divide, differentiate, and organize themselves into all the myriad organs and tissues in the body. They can also be used to grow organoids in the lab. (Conversely, the cells in spheroids cannot self-assemble or regenerate.)

Organs-on-a-chip

Organs-on-a-chips—or "organ chips"—are the most complex *in vitro* technology. They are small devices made of clear plastic (normally the size of a USB flash drive) that contain tiny hollow channels lined with living human cells. They are designed to create a dynamic environment in which blood, oxygen, and lymphatic fluids can flow and different types of cells can interact. This allows them to simulate bodily processes and mimic how organs work in real life. For example, the lung-on-a-chip mimics a working human lung, with lung cells in contact with capillary blood vessel cells and simulated breathing.

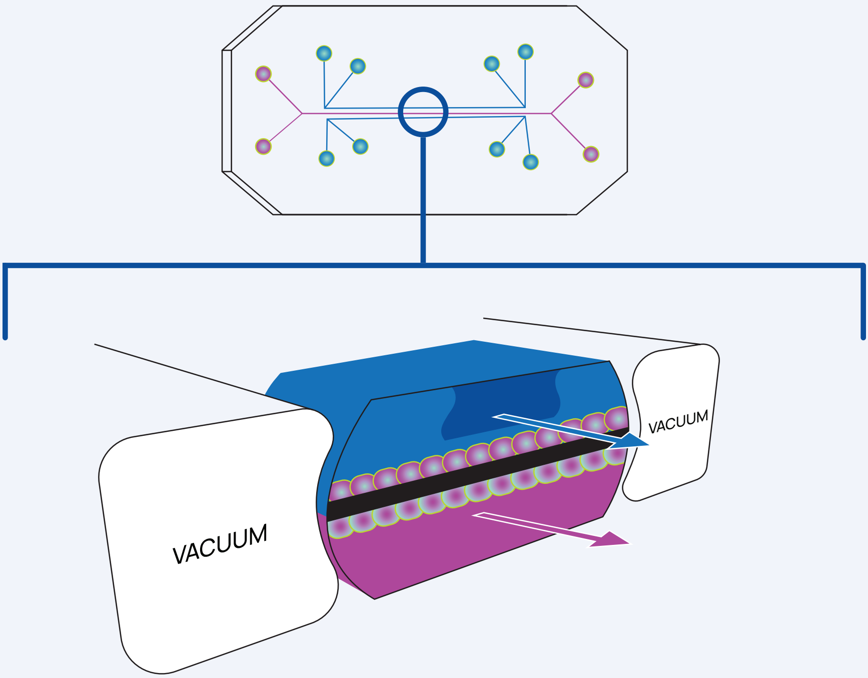

Illustration of a lung-on-a-chip. Air flows above and blood flows below the membrane lined with human lung and capillary cells. Oxygen, white blood cells, and other molecules can move between lung and capillary cells. Application of cyclic suction in the vacuum-side channels mimics breathing.

ORGAN CHIPS IN ACTION

Organ chips can be used in many ways, like investigating a medication's effectiveness or toxicity, the way a disease functions, or even the impact of space travel on organs and tissues. They have also been used to gain insights that aid wild animal conservation efforts. Virtually any organ can be mimicked using organ chips. Personalized organ chips can also be created using an individual's own cells, and multiple organ chips can be linked to form multiorgan interactive systems. One day, researchers may even be able to create an entire "body-on-a-chip"!

In Silico (Computational Modeling)

If computers, math, and AI are your jam, you might like *in silico* NAMs! *In silico* refers to experiments performed by a computer via techniques such as mathematical modeling and simulation, machine learning, and artificial intelligence (AI). Using data from previous *in vivo*, *in vitro*, or *in chemico* experiments, scientists can create digital versions of human organs or body systems that can predict how diseases would progress and how drugs would interact with those body systems. AI and machine learning are extremely useful for combing through large datasets or scientific literature, because these technologies can scan, extract, and clean data much more quickly, efficiently, and accurately than a human scientist ever could. Computer technologies are also able to simulate and test thousands of potential drug options or disease progression iterations in a matter of moments, saving scientists from having to do trial-and-error testing on animals to see what works and what doesn't.

Where Do NAMs Currently Stand Within Science?

Animals are used for various scientific purposes, including research and testing. The rate of NAMs development and adoption for each purpose varies, and at this stage, we appear to be much closer to replacing the use of animals in safety and toxicity testing than in more exploratory research contexts. Specifically, safety testing of cosmetics, personal care, and household products will likely be the first to fully transition away from using animals. This is partly because of consumer demand for "cruelty-free" products (products that have not been tested on animals). Dozens of nations, as well as multiple US states, have banned animal-tested cosmetic products, and this has forced the industry to accelerate its development and adoption of alternative testing practices. Next up, in all likelihood: Scientists will be able to scale up the use of NAMs to test the safety of drugs, vaccines, and other medicines, as well as chemicals such as those found in pesticides or certain plastics that may disperse into the environment. Farther out on the horizon, scientists hope to develop NAMs sophisticated enough to answer more complex scientific questions—the kind often asked in discovery research settings.

With excitement around NAMs growing, it's a great time for young scientists to get involved—the future of science awaits!

Looking for more resources?

awionline.org/content/nam-resources-students

ILLUSTRATIONS
Irene Armas, modified by Molly Benson

PHOTOS
page 1: Jose Soto, Bhaduri Lab; page 3: Gorodenkoff;
page 10: Rawpixel.com; page 12: Vasiliy Koval

Animal Welfare Institute

900 Pennsylvania Avenue SE
Washington, DC 20003

awionline.org