

Frogs: Princely models for science

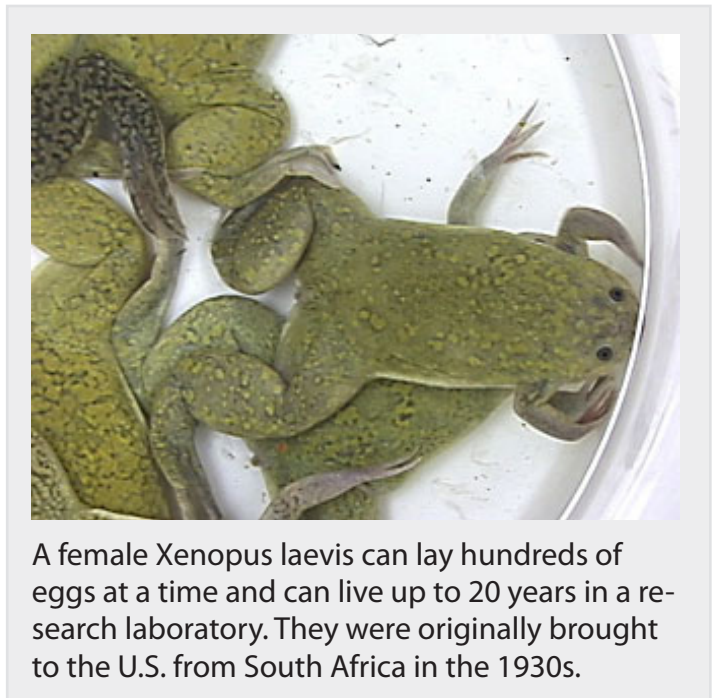
Frogs have no small claim to fame in biology. They've provided us with the first reliable pregnancy tests, donned rubber pants in the name of research, and appeared in many high school biology dissections. Frogs have helped us learn about the connection between nerves and muscles, taught us how to do skin grafts, and have contributed to our understanding of fundamental biological processes such as fertilization, cell division, and development.

What's so special about frogs?

Frogs are ancient creatures, and as such, have many attributes common to all vertebrates. They also possess a host of qualities that make them a princely (or princessly) model for research. The eggs of the female African clawed frog *Xenopus laevis* are quite large, so researchers can not only see them clearly, but can also easily inject substances like drugs or DNA and observe the effects. Embryonic *Xenopus* cells go through divisions very quickly, and they can be stopped at specific points in the division cycle, allowing researchers to extract clusters of cells at the same stage of division. *Xenopus* tadpoles are transparent, so scientists can watch what's happening inside them as they go into metamorphose into adult frogs, which can then live in the lab for up to 20 years. Prolific egg layers, they provide researchers with a continual supply of material.

Fruitful fecundity

The egg-laying talent of the *Xenopus* female was its ticket into the research laboratory—via the family planning clinic. In the 1930s, scientists discovered that a hormone



A female *Xenopus laevis* can lay hundreds of eggs at a time and can live up to 20 years in a research laboratory. They were originally brought to the U.S. from South Africa in the 1930s.

present in the urine of pregnant women could make the female *Xenopus* produce thousands of eggs. *Xenopus* became the basis for a 24-hour pregnancy test, and many hospitals kept populations of them on hand. Now, of course, we can detect pregnancy without amphibians, and researchers use just the pregnancy hormone, rather than urine, to keep frogs producing eggs all year.

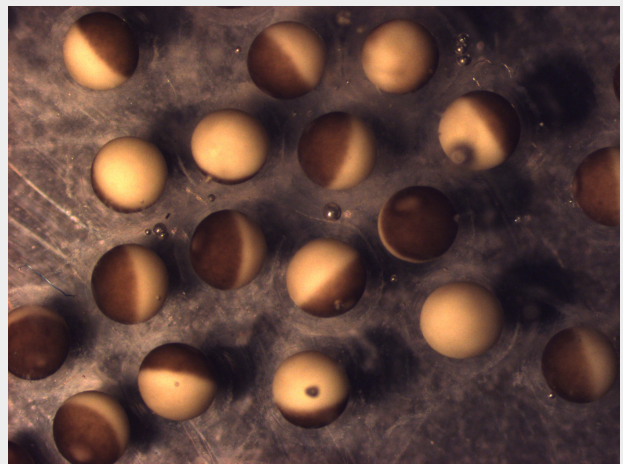
A froggy dance in rubber pants

Long before frog eggs were used to detect pregnancy, they helped scientists discern where new life comes from. Scientists knew centuries ago that sperm existed, but there was considerable debate about its role. In 1777, the Italian scientist Lazzaro Spallanzani (and some fashionably dressed frogs) confirmed that sperm are needed to activate the egg. Spallanzani outfitted male frogs with form-fitting rubber pants, a kind of primitive frog family planning suit. He saw that the pants-wearing frogs didn't produce any tadpoles, but that if he then mixed the pants in with freshly-laid eggs—voilà, offspring.

While it's easy to make light of the image of frogs in togs, the importance of Spallanzani's experiment shouldn't be underestimated. He put to rest the notion that new life could arise from either the egg or the sperm alone. He didn't know, however, what the contribution of the sperm actually was. That discovery would have to wait until researchers saw fertilization, the fusing of the sperm and egg nuclei, in sea urchin eggs.

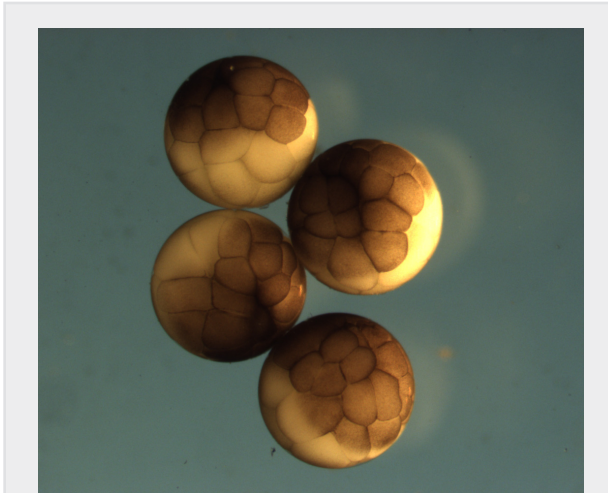
Size matters

Today, *Xenopus* eggs are still used for research, in part because they're big enough to be manipulated easily. Their size—about 1 millimeter, huge compared to most other animals (human eggs are about 1/10 as large)—makes it relatively easy for scientists to inject genes or chemicals. The egg then becomes a kind of factory, pumping out thousands of copies of the protein that that gene codes for. In many cases, the protein will



These frog eggs have just been fertilized. The dark portion will become the back of the frog, the lighter part will become the front. These eggs are very large compared with those of many other animals, making it easy to study fertilization and development.

function normally even though it's being made and is functioning in a frog egg rather than a human cell. This kind of protein-manufacturing capability allows researchers to quickly test the effectiveness of a wide variety of drugs, and researchers have used this technique to assess effects on a diverse array of proteins, from those involved in brain function to ones that regulate the growth of tumors.

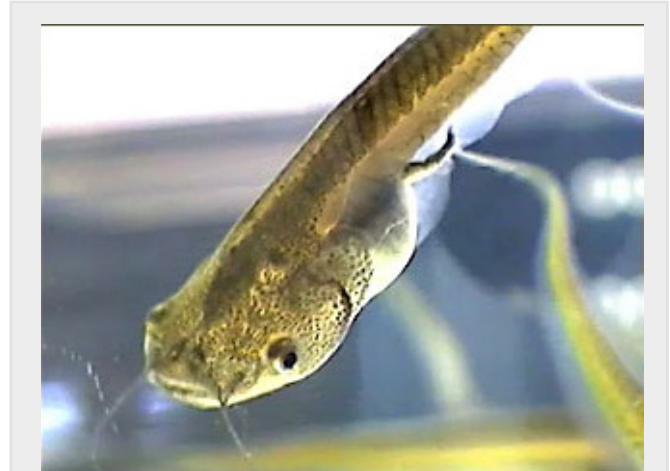


As this early embryo develops, the dividing cells begin to assume some order.

A pondful of uses

The frog's contribution to science goes beyond its egg. Scientists watch developing *Xenopus* embryos to learn how tissues differentiate, and study metamorphosing tadpoles to gain insight into how organs are formed. Both of these paths may lead to a better understanding of how to create medical applications for human organ or tissue generation. Researchers also use developing frog embryos to understand the mechanisms underlying vertebrate body plans; they use tadpoles to look at formation of the nervous system; and the list goes on.

Despite all its contributions to basic research, *Xenopus laevis* isn't the best model for studying genetics, because of its unique chromosome arrangement: Each cell has four copies of each chromosome rather than the single pair common for humans and other animals (This four-copy arrangement is called *tetraploidy*, a geneticist's nightmare!). However, the single-paired genome of a close frog relative, *Xenopus tropicalis* is currently being sequenced. It has many of the same advantages of its claw-footed cousin, but will be an easier model for genetic research. So *Xenopus* will continue to contribute to our knowledge for years to come.



The process of metamorphosis, in which tadpoles transform into adult frogs, is one of the most fascinating feats in the biological world. In this picture, notice the tiny legs that are forming. These legs are among the first signs of transformation to the adult form.

Vive les grenouilles! Long live the frog!