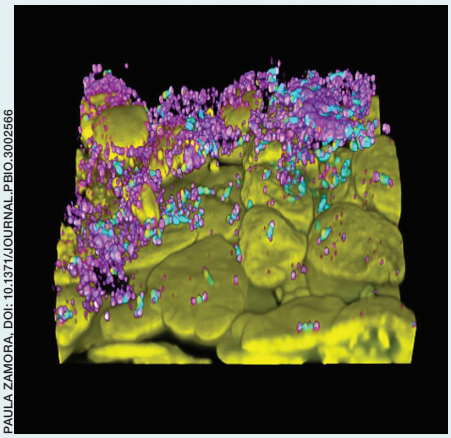
Phage Therapy Leverages our Immune System

With drug-resistant infections alarmingly on the rise but the pace of new antibiotic introductions at a crawl, researchers in the Western world are increasingly turning to phage therapy—an antibacterial approach that some Eastern European countries have relied on for decades. As phages (short for "bacteriophage" viruses) parasitize and kill bacteria, they have so far proven relatively safe and effective, especially in combating multidrug-resistant bacteria. Still, little data exists on how these viruses interact with their human hosts.

Now, a team of researchers at several United States universities, led by Jennifer Bomberger, a professor of microbiology and immunology at Dartmouth University, have completed a study of four phage types and how they interact with human airway epithelial cells in combating the opportunistic pathogen *Pseudomonas aeruginosa*—a bacterium cataloged by the Centers for Disease Control and Prevention as a serious threat to human health. Hospitalized patients, those with compromised immune systems, and people with the genetic disease cystic fibrosis may be particularly vulnerable because some strains of *P. aeruginosa* are resistant to almost all available antibiotics.



PAULA ZAMORA, DOI: 10.1371/JOURNAL.PBIO.3002566

Bacteriophages (purple) attack bacterial biofilms (aqua) on lung cells (yellow).

The experiments showed that human cells detected the phages' presence, precipitating an immune response. Furthermore, the cellular response varied based on specific properties of the phages. For instance, certain phages promoted more of an inflammatory response—a local defense that can aid in bacteria clearance.

"The major takeaway from our study is that phages being used clinically to treat bacterial infections are detected by cells in the respiratory tract and can trigger immune responses," said Bomberger. "We found that the respiratory tract is able to distinguish between different phages, and we think this feature of phage therapy may be considered when selecting a phage for treatment with the potential to choose phages that could have the most therapeutic effect."

Overall, the findings suggest that evaluations of phage therapy moving forward should leverage the human immune system's natural contribution to eradicating pathogenic bacteria.

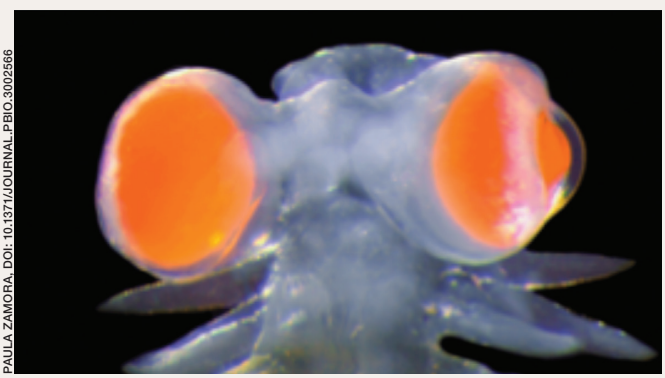
"Currently, the rational design of phage therapy is focused on the selection of phage cocktail formulations that can address the genetic diversity of the targeted bacteria while preventing the emergence of phage resistance," said Paula Zamora, first author of the study and a postdoctoral researcher in Bomberger's lab. "We hope that our findings might add interactions with the human host as one of the factors to be considered." (*PLOS Biology*)

—Adam Hadhazy

Clear Vision in the Dark Sea

Of the thirty-five phyla of animals on Earth, only three are known to have high-resolution eyesight: vertebrates; cephalopods, including squid and octopuses; and arthropods, such as shrimp and spiders.

But some species of deep-water bristle worms or polychaetes (*Vanadis* spp.) possess enormous eyes for their body size—twenty times the size of their heads—that invite questions about the quality of their eyesight. Because they inhabit deep waters, though, these species are difficult to study in significant numbers.



PAULA ZAMORA, DOI: 10.1371/JOURNAL.PBIO.3002566

Keen eyes of a marine bristle worm (Vanadis *sp.*)

A trio of marine biologists overcame this challenge by capturing marine worms in surface waters off the coast of the Italian island Ponza. Though they typically live at about 150 meters or deeper, the worms rise through the waters at night, making them easy to collect by hand using nets or suction.

With access to considerable numbers of healthy bristle worms of three species—*Torrea candida*, *Vanadis cf. formosa*, and *Naiades cantrainii*—the researchers discovered that they all had eyesight as sharp as some spiders, and sharper than in many other marine worms.

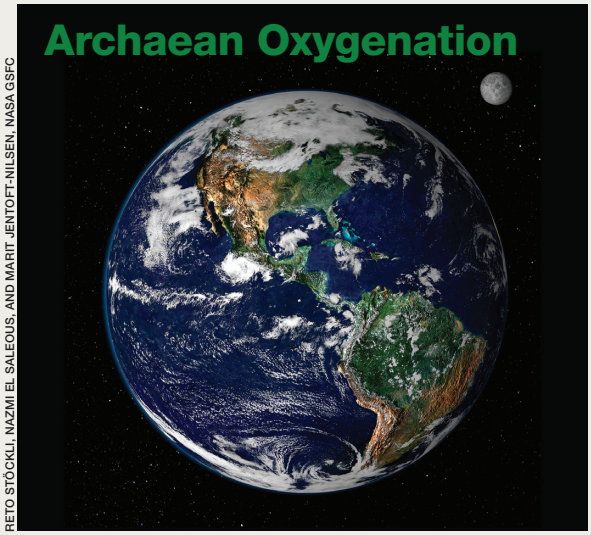
Previous studies had determined that bristle worms had dense photoreceptors especially attuned to green and ultraviolet wavelengths of light. The new findings showed that bristle worms, in addition, have a wide field of vision well-suited for spotting small objects moving in the water column. This may help them hunt for prey, but their eyes—the only solid part of their otherwise translucent bodies—also make them more of a target for bristle worm predators.

The scientists hypothesize that the worms might sense bioluminescence and potentially communicate by using a visual language composed of light—as fireflies do by flashing ultraviolet wavelengths that are invisible to humans.

The evolution of the eyes is a much-debated issue in biology: whether they evolved once or many times. The simple structure but complex functionality of the *Vanadis* eyes, which have developed recently in evolutionary terms, are evidence that eyes have evolved more than once. Bristle worms now rank with vertebrates, arthropods, and cephalopods in having the keenest eyes on the planet.

Further research will help determine how these marine worms use their enormous eyes—and may support improvements in artificial vision as engineers apply principles from the worms' eyes to improve information processing in robots. (*Current Biology*)

—Brittany Steff



RETO STÖCKLI, NAZMI EL SALEOUS, AND MARIT JENTOFT-NILSEN, NASA GSFC

The Earth we know today has an oxygen-rich atmosphere.

An earth science study from the University of Bristol, UK, helps scientists answer a longstanding mystery: how Earth's atmosphere became oxygen-rich during the Archaean eon as the first life emerged. Though geologic records show slow oxygenation throughout Earth's four-and-a-half-billion-year history, the drivers of this process had not yet been discovered.

"Previously, we didn't have a clear idea of why oxygen rose from low concentrations to present-day concentrations, as computer models haven't previously been able to accurately simulate all the possible feedbacks together," said lead author, biogeochemist Lewis Alcott. "This has puzzled scientists for decades and created different theories."

Alcott and colleagues' new model suggests that carbonate buildup in Earth's crust played an essential role in atmospheric oxygenation. Volcanic carbon dioxide entered ocean sediments to form rocks, such as limestone. During tectonic upheavals, as rocks weathered, carbon was released into the air where it could be used by plants in photosynthesis. This movement of carbon would have led to increasing atmospheric oxygenation from the (oxygen) byproduct of photosynthesis.

Availability of other plant-limiting nutrients, such as phosphorus, would also have increased from weathering of volcanic rocks. In their model, the researchers charted carbon, oxygen, and phosphorus changes as a factor of various boundary conditions—planetary temperature, atmospheric carbon dioxide concentration, phosphorus burial records, and carbon isotope ratios. They ran the model 1,000 times with a random distribution of these parameters.

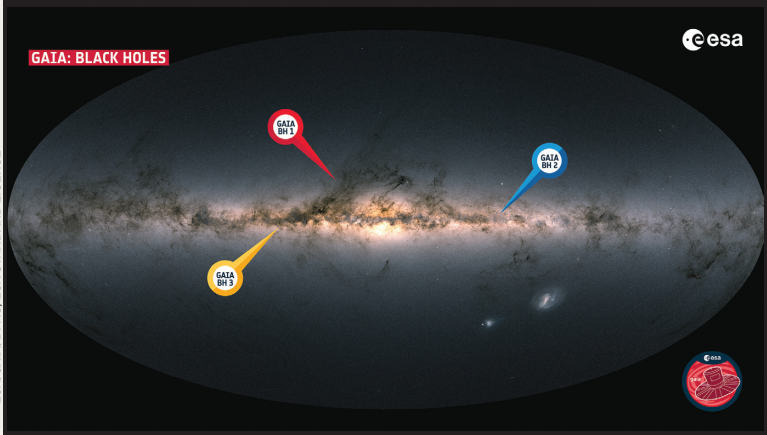
When they ran the model without factoring in any carbonate buildup in Earth's crust, there was a clear mismatch between the model and atmospheric data. For example, while there is other strong evidence for less than one part per million of oxygen in the Archean atmosphere, their models offered no low-oxygen scenarios.

However, when taking into account crustal carbonate buildup, the model yielded results that agreed well with atmospheric records. In this study, the modeled Archean oxygenation event was much more aligned with atmospheric data than in previous studies.

"This breakthrough is important and exciting because it may help us understand how planets, other than Earth, have the potential to support intelligent, oxygen-breathing life," said Alcott. The results suggest that atmospheric oxygenation is possible but is likely limited to older planets and/or planets with rapid crustal turnover that have built up stores of crustal carbon.

(*Nature Geoscience*) —*Majlis Walker*

A Heavyweight Black Hole In the Milky Way



ESA/GAIA/DPAC, ESA STANDARD LICENSE

Map of black holes found in the Milky Way by Gaia, including the heaviest, BH3

A large international team of astronomers, using *Gaia*—a satellite that measures the motions of stars with unprecedented precision—has discovered a record-breaking "stellar-origin" black hole with a mass thirty-three times that of the Sun. Stellar-origin black holes form when stars much more massive than the Sun exhaust their nuclear fuel and collapse under their own weight, becoming so dense that gravity does not even permit light to escape. Although so-called "supermassive" black holes, millions to billions of times the mass of the Sun, are formed by collisions between black holes at the centers of galaxies, the most massive individual stellar-origin black hole found in the Milky Way, until this recent discovery, is only about twenty times the mass of our Sun.

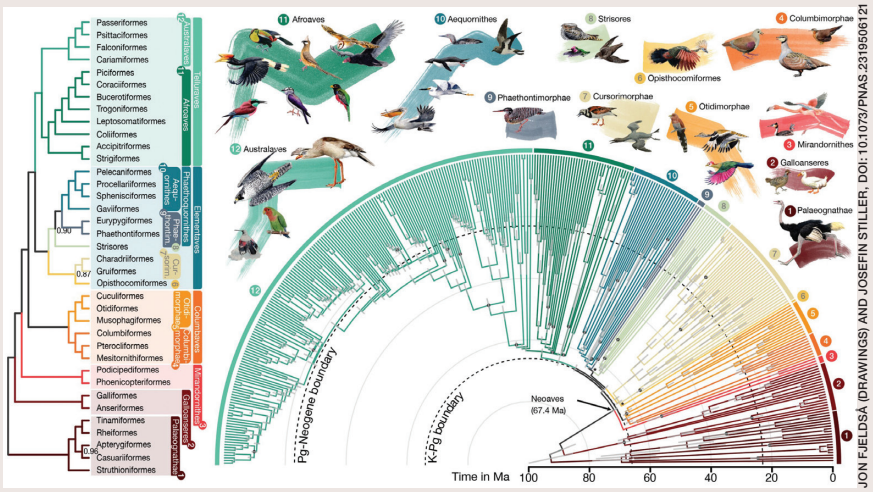
Isolated black holes emit no light and are therefore undetectable, but a black hole in a system with two adjacent stars makes its presence known by its affect on its companion star. If the black hole is very close to its companion, gas from the star can be pulled into the black hole, producing energetic X-rays and light that signal its presence. But if the black hole is further away, such that no gas is exchanged or radiation produced, the black hole can still be detected by the wobble it induces in the motion of the companion as the two orbit around their common center of mass.

The *Gaia* team, taking advantage of the exquisite positional sensitivity of their satellite, searched for such "dormant" black holes, finding one they designated *Gaia* BH3, whose companion appeared to be orbiting around an unseen object that was far too massive and faint to be anything but a black hole. At 1,500 light years from Earth, BH3 is well within our own galaxy, making it an easy target for further observations that can help in the understanding of how stellar-origin black holes are produced, whether there are limits to their size, and how the composition of their companion stars influences their formation.

Pasquale Panuzzo of CNRS' Observatoire de Paris, the lead author on the BH3 paper, remarked on the broad implications of the finding by his team: "It's a real unicorn. . . the kind of discovery you make once in your research life."

(*Astronomy and Astrophysics*) —*Laurence A. Marschall*

New Bird Family Tree



JON FJELDSÅ (DRAWINGS) AND JOSEFIN STILLER, DOI: 10.1073/PNAS.2319506121

Updated bird family tree based on tens of thousands of genes

While the end-Cretaceous mass extinction 66 million years ago wiped out many family lineages, others, such as birds, rapidly diversified. Fully parsing the evolutionary history of the bird family tree has long been a goal for evolutionary biologists, but relationships have remained hazy across major lineages, with debates over the most accurate sampling methodology. With technological advances in genomic research, however, evolutionary histories have quickly become more accurate and complete.

An international team of scientists, led by Siavash Mirarab at the University of California San Diego (UCSD), has reconstructed the evolutionary history of 363 bird species, representing 92 percent of taxonomic bird families. To create this new bird family tree, the researchers used the *Expanse* supercomputer at UCSD to analyze over 60,000 genomic regions from a wide variety of bird species. The team combined genome sequencing strategies to create the most accurate evolutionary lineage, using both a breadth of species and a depth of many genes per species, when available.

The results shed light on how bird evolutionary history was altered by the mass extinction event, demonstrating rapid increases in effective population size, substitution rates, and relative brain size in the aftermath. The researchers concluded that, with the loss of many predators and competitors in the mass extinction, bird capacity for flight likely allowed them to quickly exploit many new habitats and diversify.

Mirarab and colleagues found that sequencing many genes per bird species had a greater effect on the overall family tree, but that sequencing many species was vital to accurately parse the branching of families. The researchers also recognized that complex biological processes, such as hybridization, continue to make the analysis of evolutionary relationships in certain families quite difficult.

The paper was published concurrently with a companion piece in *Nature* focusing on a single family lineage, exploiting the researchers' innovative techniques to reassess the evolutionary relationship between doves and flamingos. Both papers are part of the international Bird 10,000 Genomes (B10K) Project, which plans to generate representative genome sequences from all living bird species. "Our goal is to reconstruct the entire evolutionary history of all birds," said Mirarab. (*Proceedings of the National Academy of Sciences*)

—Liam Engel

Certified Large Mammal Protection

More than a quarter of the world's tropical forests are used for commercial logging, which can have a negative impact on ecosystems. Several forest certification organizations, such as the Forest Stewardship Council (FSC), are expected to promote forest management practices that protect biodiversity. Assessing the effectiveness of these programs, however, has been a challenge because of limited sample sizes in previous studies, among other factors.

To provide a more substantial database, a group of researchers, led by Joeri Zwerts, a biologist at Utrecht University, the Netherlands, conducted a four-year study of logged tropical forests in Africa. They found that FSC-certified forests had a higher relative abundance of large mammals than comparable non-certified forests.

To measure mammal abundance, the team placed 474 camera traps in fourteen logging concession areas in Gabon and the Republic of Congo. Each FSC-certified forest was paired with a similar non-certified forest as a control. Over the four years, the researchers collected more than 1.2 million photos, which were fed into a software program that used machine learning to identify African wildlife.

JOERI ZWERTS, DOI: 10.1038/S41586-024-07257-8

*Camera trap image of African forest elephants (*Loxodonta cyclotis*)*

While previous studies had focused on mammal diversity, or number of species, this study examined mammal abundance—the number of individuals—estimated by encounter rate. Fifty-five mammal species were identified.

Large mammals, such as gorillas and buffalo, were 2.7 times more likely to show up in the FSC-certified forests. Primates overall were 1.8 more common in certified forests. And African forest elephants (*Loxodonta cyclotis*), which are listed as Critically Endangered by the IUCN Red List, were observed 2.5 times more often in certified forests. Smaller animals, such as rodents, were encountered at the same rate within each pair of forests.

Large mammals play a role in many ecological processes of a forest, such as seed dispersal, nutrient cycling, understory growth, and prey population size fluctuations. But logging creates roads through the forest that allow easier access for hunting, putting pressure on these large mammal populations.

"This, in turn, has a profound impact on the ecosystem," said Zwerts. Sustainable hunting practices, such as those required by FSC certification, will be key for sustaining these ecologically important species in tropical forests around the globe. (*Nature*)

—Kati Moore