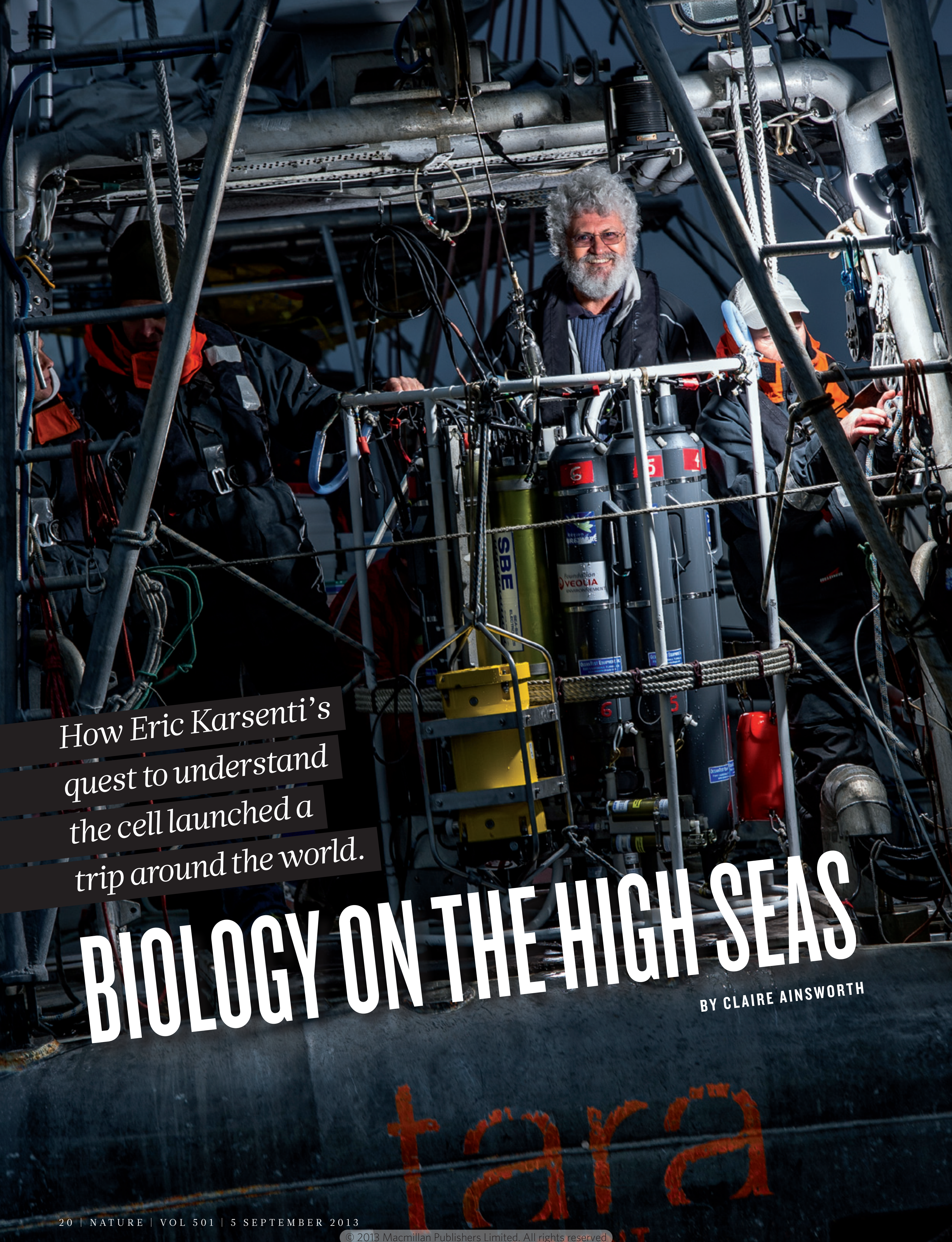

How Eric Karsenti's quest to understand the cell launched a trip around the world.

BIOLOGY ON THE HIGH SEAS

BY CLAIRE AINSWORTH

Eric Karsenti spent a total of three months aboard *Tara* during her 938-day plankton-sampling expedition.

JULIEN GIRARDOT/TARA OCEANS

It is 3 a.m. in mid-December 2010, an hour before dawn, and *Tara* is anchored amid an angry swell near the entrance to the Strait of Magellan. In the lee of Argentina's cliffs, the 36-metre schooner and her crew have sought haven against the impending weather that has earned these latitudes the nickname the Furious Fifties. But as the winds gather to hurricane force, they snap the safety cord that eases tension on the anchor chain. As the crew struggles to replace it, the storm crescendoes, plucking *Tara*'s anchor from the seabed twice before it can be secured again.

Bracing himself inside the aluminium hull is Eric Karsenti. Compact and bright-eyed beneath a bushy mop of white hair, he has the air of a seasoned seafarer. But he is also an accomplished molecular cell biologist who has spent most of his career studying microtubules — rod-like structures that form part of the cell's internal scaffolding. Approaching retirement, he has switched fields, borrowed a famous fashion designer's yacht and launched a 2.5-year expedition around the world to survey ocean ecosystems in unprecedented breadth and detail. Motivated by a love of adventure as much as by science, Karsenti has found his share of both.

"This was really crazy," Karsenti says later, reflecting on the trip from the safety of the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. "I was on the boat for the worst leg of the whole expedition."

The project, called Tara Oceans, set sail from Lorient, France, in September 2009 for a 115,000-kilometre voyage to collect plankton — microscopic marine organisms — at 154 distinct sites around the world. Findings from the expedition are now starting to be published, and the bulk of the data will soon be made publicly available.

Although other surveys, such as the 2004–06 Global Ocean Sampling Expedition, piloted by genomics impresario Craig Venter, have sampled microscopic life in the seas (see *Nature* **446,** 240–241; 2007), the Tara Oceans project is taking a broader approach — to "study it all"[1]. Instead of focusing only on microbes, the scientists collected billions of organisms, from millimetre-scale zooplankton down to viruses 100,000 times smaller.

These marine organisms exert tremendous power over the planet, collectively forming a giant engine that drives the cycling of elements such as carbon, nitrogen and oxygen. Photosynthetic marine microbes produce about as much of the world's oxygen as do land plants. Ocean ecosystems are also hives of evolutionary activity in which countless viruses shuttle genes between organisms.

Understanding how these complex marine ecosystems work requires a holistic approach, says Karsenti. Tara Oceans scientists are identifying the plankton through a range of techniques including genomics, proteomics and automated high-throughput imaging. To link the organisms to their environments, the researchers also measured properties such as the temperature, pH and salinity of the water around each sample, which they plan to cross-reference with the biological data.

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Although the project is limited by its ability to sample areas at only one time, "the data they collect could be used in revolutionary ways", says Jack Gilbert, a microbial ecologist at Argonne National Laboratory in Illinois. By working out how the different plankton species interact with each other and the environment, the Tara Oceans project members hope to understand how ecosystems emerge from the sum of the interactions between their parts. This huge data set, they say, will help researchers to tackle big issues, such as calculating the biodiversity in the oceans, predicting how marine organisms will respond to environmental shifts and, perhaps, gaining insight into how evolution acts on networks of organisms in ecosystems or of molecules in cells[2].

Given his research background, Karsenti would seem an odd fit for this holistic enterprise. For decades, molecular cell biology was a byword for reductionism. But through his work on microtubules, Karsenti, like a growing number of biologists, came to see that reductionism could reveal only half the story, and that cells must be understood in terms of how the interactions between their components form a greater whole.

Although best known as a lab scientist, Karsenti has been interested in the sea since childhood, when he spent summers on France's Brittany coast. Later, he taught sailing to help fund his education. As his studies progressed, however, he left his fascination with the sea mostly behind. At Paris Diderot University, Karsenti studied the typical range of science disciplines, but he also developed an interest in statistical physics, a sideline that would later change the course of his research. After obtaining a PhD in immunology and cell biology from the Pasteur Institute in Paris in 1979, Karsenti joined the lab of cell biologist Marc Kirschner, then at the University of California, San Francisco, to study the cell cycle and cell division. Karsenti was interested in mitosis — the process of cell division — particularly in the mitotic spindle, an intricate structure that forms during cell division to ensure that new cells inherit only one copy of each chromosome.

Under a microscope, the spindle, formed from microtubules, looks like rigging strung from each end of the cell. Hundreds of proteins collaborate to control this elaborate molecular machine, from the motor proteins that crawl along its filaments to the signalling molecules that synchronize its movements with specific points in the cell-division cycle.

The early 1980s was the heyday of classical molecular cell biology and its reductionist approach, and Karsenti found himself purifying proteins and performing biochemical experiments to identify individual molecules and determine their roles in the cell cycle and mitosis. But it became clear to him that this approach, although extremely valuable, could not fully explain the spindle's complex behaviour. "I started to realize that you cannot understand this by simply identifying molecules: you need to understand how they work together," he says.

In 1985 Karsenti set up his own lab at the EMBL. Returning to his interest in statistical physics, he started collaborating with EMBL biologists Thomas Surrey (now at the London Research Institute) and François Nédélec, as well as Stanislas Leibler, a physicist at the Rockefeller University in New York. They were interested in a phenomenon known as self-organization, and in how it could be applied to biology. Physicists, chemists and mathematicians have long studied self-organization to understand how disordered systems can give rise to ordered, dynamic structures such as ocean currents and gyres. These structures are not organized from the top down, but instead emerge spontaneously from the interactions of individual components. By the 1990s, biophysicists had started to apply these concepts to molecular structures in cells. Karsenti says their work was revelatory. "I suddenly saw how you can with formulas encapsulate the whole biological process," he says.

He also saw links to his own work on the mitotic spindle, which meets three key criteria for a self-organizing system. First, it seems to form a stable structure or pattern, but is actually highly dynamic: its individual tubules are constantly building and demolishing themselves. Second, it requires energy to keep itself going. And third, it involves interactions between fixed, or deterministic, factors — such as the forces exerted by the motor proteins — and random, or stochastic, factors, such as the probability of a motor protein meeting a microtubule. The final product, the spindle, cannot be explained by any simple cause, but instead emerges from this network of interactions.

Karsenti was among a number of researchers who were applying these principles to build computational models of spindle formation. In 2001, he and his colleagues showed how individual interactions between microtubules and motor proteins could result in the emergence of different structures, such as vortices or star-shaped 'asters', at the ends of the spindle[3]. Altering the conditions of these interactions changed the organization: higher concentrations of motor proteins led to more aster formation, for example, whereas slowing down the rate at which the motors move along the microtubules reduced the number of asters.

"I was struck by the similarity to what happens in the formation of fish schools and flocks of birds that can also be modelled using stochastic simulation," says Karsenti. "Yet, both phenomena occur at entirely different scales."

ANCHORS AWEIGH

By 2006, with compulsory retirement looming, Karsenti says, "I had the feeling that I had to do something different." Keen to raise public awareness of biology and evolution, he took some inspiration from Charles Darwin's *The Voyage of the Beagle* (1839). "He really describes in this book how travelling helped him to ask important, fundamental questions about the evolution of Earth and the evolution of life," says Karsenti.

Launching a similar expedition seemed a promising idea — and a timely one, given the impending bicentennial, in 2009, of Darwin's birth (see *Nature*'s Darwin 200 special, www.nature.com/darwin). Karsenti discussed the idea with a friend and colleague of more than 30 years — Christian Sardet, a biologist at France's Oceanological Observatory of Villefranche. They floated a plan to produce a reality-television show centred around such a voyage. When that fell through, Sardet introduced Karsenti to Gaby Gorsky, an oceanographer at the observatory, and the three repaired to a local watering hole, Le Cockpit. "We started to dream," says Gorsky. "If we can get an interesting boat, what kind of project can we push forward?"

Both Gorsky and Sardet work on plankton, and the discussions about their research reawakened Karsenti's interest in ocean life. The three decided that it would be fascinating to study planktonic ecosystems as a whole. Other researchers had already begun to apply the principles of cellular systems biology to ecosystems, using total gene sequences, or 'metagenomes', of microbial communities to pick apart all the metabolic processes they are carrying out. Ecosystem modellers were showing how ocean circulation, together with differences in factors such as nutrient content and temperature, cause microbial species to self-organize into defined geographical distributions[4]. Karsenti could see the basic principle of deterministic and stochastic factors working together to create a dynamic system.

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The models were elegant, but they lacked data. Karsenti, Sardet and Gorsky aimed to rectify that deficit — all they needed was to find a boat and money. Through some of Karsenti's old sailing contacts, they found *Tara*.

A schooner is an unlikely candidate for oceanographic research, but *Tara* had a sound science pedigree. She was built in 1989 as a polar-exploration yacht and later owned by Peter Blake, a legendary explorer from New Zealand. After Blake was murdered by pirates in 2001, the schooner was bought and renamed by Etienne Bourgois, a keen yachtsman and the son of the French fashion designer Agnès B. The family established Tara Expéditions, a non-profit organization that uses the vessel to support and promote environmental research. The foundation's outreach work, as well as the boat herself, made *Tara* the perfect choice for a scientific expedition aimed at popularizing biology. And, Karsenti says, "A sailing boat is much more romantic than a motor boat."

Thanks to his connections in the French competitive yachting community, Karsenti was able to arrange a meeting with Bourgois. The pair co-founded the Tara Oceans project and eventually secured financial backing from a range of funders, including the French government and the EMBL. Karsenti now needed to gather his scientific team.

He cast his net wide to secure scientists with the right expertise, including oceanographers, microbial ecologists, taxonomists, cell and systems biologists, bioinformaticians and ecosystem modellers. The project snowballed, eventually including more than 100 researchers, who took turns working aboard *Tara*. Also taking part were non-scientists such as French journalist Vincent Hilaire, who blogged from the ship about the expedition's adventures (see 'Gathering data, logging adventure'). Some 5,000 children also visited *Tara* over the course of the voyage, and the project's outreach continues online with projects such as *The Plankton Chronicles*, a video series about the strange organisms the team found.

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For a slideshow from the Tara Oceans expedition, visit:
go.nature.com/jckavb

STORMY SCIENCE

Doing science aboard *Tara* posed a unique set of challenges. A sailing boat was cheaper and more environmentally friendly than a motor vessel, but dangling delicate measuring equipment hundreds of metres down into the water demanded a stable platform, hard to achieve with a boat of *Tara*'s relatively small size. And because Tara Oceans selected discrete, identifiable water masses as sampling stations, the boat had to get to the right place at the right time and under the right weather conditions. Satellite remote sensing allowed the team to monitor oceanographic features such as currents and gyres in near real-time, and detailed forecasts helped to predict whether the elements were going to cooperate.

They often did not. On the white-knuckle run down the coast of Argentina in December 2010, for example, the researchers wanted to sample from three different water masses. For three weeks they endured a succession of low-pressure systems sweeping through the area. *Tara*'s sturdy design meant they could weather even the storms that nearly robbed them of their anchor, but they had to time their stops carefully. "We tried to reach the sampling station when we knew the wind would go down to 20 knots," says Karsenti. "Then we had 20 hours to do the sampling, then bwough! It started again."

Cramming all the work into the brief weather windows then stowing the samples in *Tara*'s bows as she ploughed to the next station was physically and emotionally demanding. Karsenti — on board for four legs of the voyage, a total of three months — led by example. "He was always ready to do the difficult stuff," says Gorsky. "He was the first to clean the dishes or the toilet — no problem. He was never hiding behind his status as leader."

Back on land, the challenge for researchers has been integrating and interpreting the genomic, imaging and environmental data from the project, and making it accessible to the research community. They analysed 27,882 samples, using DNA and RNA sequencing to estimate the diversity of organisms present and study their gene functions and ecological roles. The researchers are also developing high-throughput imaging systems to scan samples and automatically identify and quantify the species present — a task that

GATHERING DATA, LOGGING ADVENTURE

In addition to scientists and sailors, *Tara*'s passengers included journalists who regularly wrote about their adventures during the 2.5-year expedition.

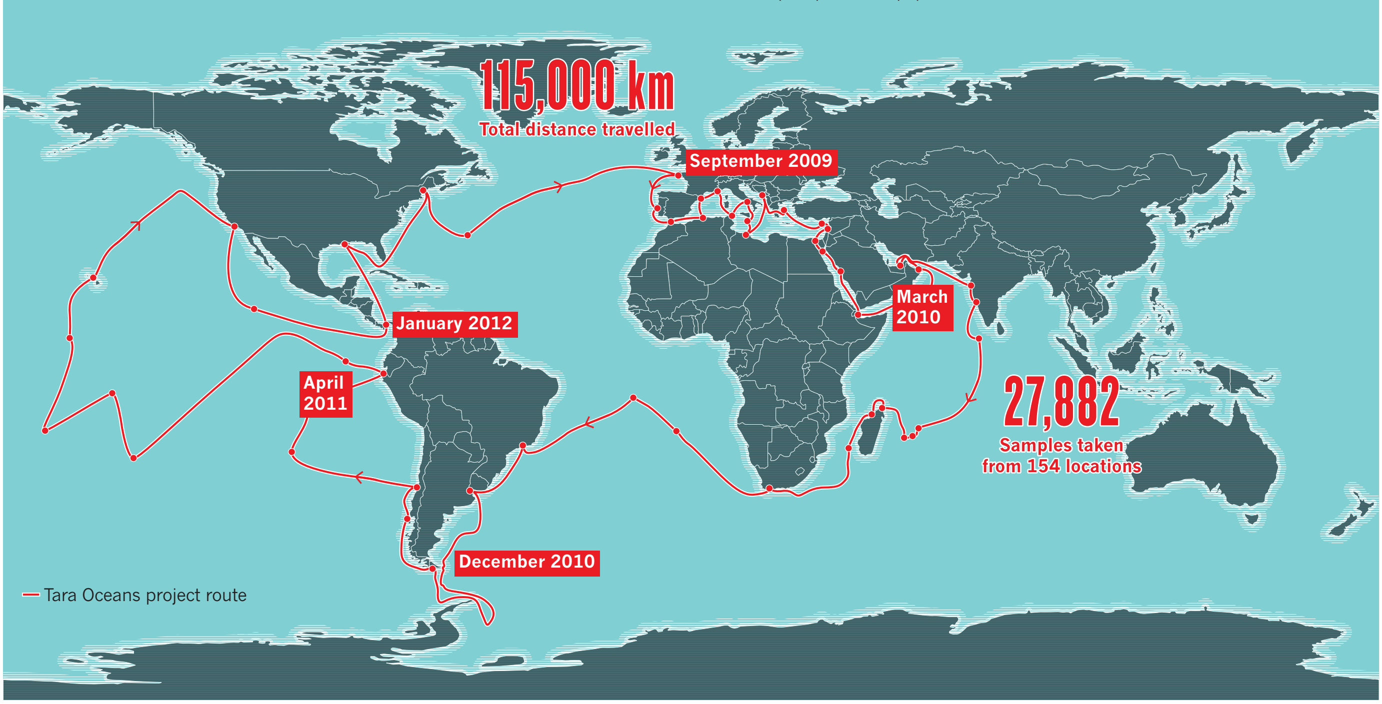
September 2009: *Tara* sets sail from the Brittany coast: *"It is now that the travelling and the scientific work begin."* — Sacha Bollet

March 2010: The crew locates a massive plankton bloom in the Gulf of Oman. *"Tara found herself transformed into a proper beehive, what with everyone lending a hand and busying around enthusiastically."* — Jérôme Bastion

December 2010: *Tara* hunkers down near Argentina. *"The gusts of wind were so strong that we could hardly stand up. Around the boat, the water was fuming."* — Vincent Hilaire

April 2011: The crew reaches its 100th sampling station, 2,200 kilometres off the coast of Ecuador. *"The endurance of the teams and the upkeep of the equipment have proven to be the key to the success of the Tara Oceans expedition."* — Anna Deniaud

January 2012: *Tara* scientists take samples from both ends of the Panama Canal to compare the biodiversity of the oceans it connects. *"The new team will continue the work of their predecessors, smoothly performing their first sampling station."* — Yann Chavance



SOURCE: TARA EXPÉDITIONS

would take an eternity to do by hand.

Preliminary data are rolling in, and the numbers presented by Karsenti at the 8th Annual Genomics of Energy and Environment meeting in Walnut Creek, California, this March, are impressive. Genome data suggest that the oceans hold hundreds of thousands or even a million different kinds of eukaryotes, nearly all of which are not yet known to science. The researchers are now using single-cell sequencing to study these organisms in more detail. There is also an abundance of diverse viruses, including a number of giant viruses — enigmatic viruses that are larger than many bacterial cells. One litre of water from the ocean's upper, sunlit reaches contains about 45 million of them.

SEA OF POSSIBILITY

Beyond the big numbers, the team is working to deduce potential ecological relationships. Seeing which organisms occur alongside others in samples, for example, can suggest possible interactions. Hiroyuki Ogata, a Tara Project collaborator and microbiologist at the Mediterranean Institute of Microbiology in Marseille, France, and his team dug through Tara Oceans data and found that a family of giant viruses called Megaviridae occurred alongside filamentous organisms known as oomycetes[5]. Evidence of gene transfer between the two organisms gives the first hints, say the researchers, that oomycetes might be hosts for giant viruses. Karsenti says that such discoveries show how Tara Oceans data could help to unpick the parasitic and symbiotic relationships that have shaped evolution in the ocean.

Tara Oceans is now taking part in an arctic sampling mission, and scientists around the world will be able to access data from its first global circuit later this year, when the raw sequences, together with the environmental measurements, will be released in an open-access database hosted by the EMBL European Bioinformatics Institute in Hinxton, UK.

Researchers will then be able to compare the Tara Oceans data with results from other large marine surveys, such as Venter's Global Ocean Sampling Expedition and Spain's 2010–11 Malaspina project, which focused on samples from deep marine ecosystems. They can also compare the data with the plethora of smaller, more local marine-ecological studies that sample the same area over time so that scientists can see how the ecosystems change. Gilbert says that it is crucial that the data from Tara Oceans be viewed in the context of other longitudinal studies, because the static view from a single voyage is limited. "This has always been the criticism of these kinds of biogeographic surveys," he says.

Robert Friedman, chief operating officer at the J. Craig Venter Institute in San Diego, California, agrees: "For us to truly understand the oceans, one was not sufficient; two is probably not sufficient. We're going to need many more."

Karsenti hopes other researchers will take up that challenge and that some of them will, as he did, step outside their comfort zones to do so. Today's cell and developmental biologists, he suggests, should look beyond their yeasts, fruitflies and mice, and observe the extraordinary creatures inhabiting the seas. Perhaps future cell biologists will look first to the oceans, inspired by the tale of a sailor who peered into the heart of a single cell and caught a glimpse of the world. ■

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