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São Paulo supplies more than half of Brazil's sugar cane, which is used to produce ethanol fuel for the car industry.

How science supports São Paulo

Brazil's richest state has a long history of applied research.

BY GUSTAVO FALEIROS

The first cases of what would become Brazil's vicious Zika epidemic were detected in the northeastern states of Maranhão and Sergipe in late 2014. By the end of 2015, the disease had spread across the nation. In October of that year, evidence emerged in the state of Pernambuco that the virus was affecting pregnant women and causing encephalitis (inflammation of the brain) in unborn babies. Public panic unfolded, made worse by a lack of understanding: the virus, first identified in the forests of eastern Africa in the 1940s, was a stranger to South America.

Because of its rich networks of public and private research institutions, São Paulo had a leading role in responding to the epidemic, says Paolo Zanotto, a microbiologist at the University of São Paulo (USP). Previous research carried out in the state, on mosquito-borne viruses such as dengue and chikungunya, helped to make a rapid response possible. Within a year of encephalitis being matched with Zika, discoveries on the behaviour of the virus were published, and funding to enable the development of vaccines, diagnosis kits and mosquito repellents poured into São Paulo laboratories.

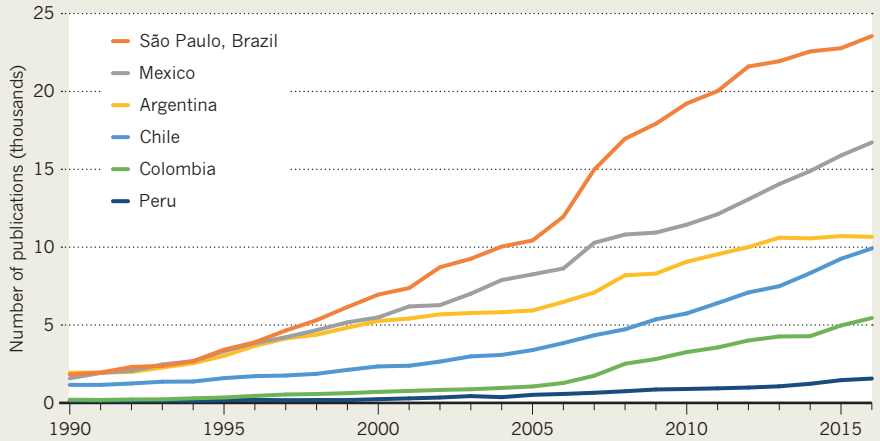
Zanotto led the creation of a network of scientists dedicated to curbing the spread of the virus. Rede Zika (Network Zika), formed in November 2015, aimed to respond to challenges set by the World Health Organization (WHO), which urged member states to find reliable ways of detecting, confirming and managing cases of the disease, and to educate people about the measures they can take to reduce exposure to the virus.

The network brought together several scientists who were involved in virology research in the state, as well as neuroscientists and immunologists. The first samples of Zika arrived at Zanotto's USP lab in January 2016, from Senegal. They were isolated for molecular analysis, and then distributed to other researchers in São Paulo and elsewhere in Brazil. Altogether, Rede Zika had 32 labs working on the project.

In terms of numbers of papers published on the virus, the network has pushed USP ▶

STREETS AHEAD

São Paulo's research output dwarfs that of entire South American nations.



into second place in the worldwide rankings — behind only the Pasteur Institute in Paris, and ahead of the US Centers for Disease Control and Prevention in Atlanta, Georgia.

"By the middle of 2016, the network had already responded to most of the [WHO's] challenges," says Zanotto. Blood tests were implemented, and the scientists developed a retrospective understanding of how the disease had spread across Brazil, which helped them to predict possible future movements. Genetic analysis on children born with encephalitis established the impacts of the virus on brain formation. "With the network, it was much easier to conduct basic and applied research; the quality of the knowledge was diversified," says Zanotto, who adds that, before Rede Zika, most of the country's resources had been dedicated to clinical trials alone.

Research, in some cases, went far beyond the WHO's recommendations. One study, published in April this year, suggested that the Zika virus could be used to combat brain tumours, because it selectively targets cancerous cells (C. Kaid *et al. Cancer Res*. http://doi.org/gdqnv3; 2018).

A HISTORY OF SCIENCE SUPPORT

São Paulo has a strong tradition of applied science and, according to the *Times Higher Education* ranking, it hosts the two best universities in Latin America: USP and the University of Campinas (UNICAMP). The state, which is located in southeast Brazil, is also home to 34 technological institutes, which specialize in specific research and development (R&D) activities. One of them, the Agronomic Institute of Campinas (IAC), was founded 131 years ago and is one of the oldest research institutes in the country.

The state has 45 million inhabitants and is the richest and most industrialized in the country, generating 32% of Brazil's gross domestic product (GDP). It is also responsible for 52% of the scientific papers published in the country, and alone outperforms all South American nations other than Brazil itself, in terms of research output (see 'Streets ahead'). São Paulo city, the state's capital, is the largest metropolis in South America.

In 2016, Brazil spent 79.2 billion reais (then about US$20 billion) on R&D. In 2017, São Paulo state alone spent 25.8 billion reais on R&D, more than half of which came directly from the private sector. According to official indicators, more scientists work in the state's private laboratories than in its universities.

SWEET SUCCESS

This strength in science has helped São Paulo throughout its history. The IAC's role in improving sugar-cane yields, for example, has been vital to the state's growth. Although agriculture represents only 1.59% of the state's total GDP, São Paulo supplies more than half of Brazil's sugar cane.

In 1933, the IAC started a programme to boost yields from 50 to 80 tonnes per hectare, by selectively breeding sugar-cane species. These new varieties were also more resistant to drier climates and better adapted to poor soils. Marcos Landell, who directs the IAC's sugar-cane programme, says that the modern-day institute is now working to increase productivity to up to 100 tonnes per hectare for all producers, something that the leading mills in São Paulo are already managing.

ONE STUDY SUGGESTED THAT THE ZIKA VIRUS COULD BE USED TO COMBAT BRAIN TUMOURS.

The technology underpinning this growth comes not from genetics, but from engineering. As a grass species, sugar cane is planted directly into soil, and the growth of its bulbs is uncontrollable and unpredictable. But by growing stalks in greenhouses before planting them, farmers can monitor and control the crop's development more effectively.

"This allows a better deployment of [harvesting] machines. Before, nobody knew exactly how many canes would grow from one seedling. Now we are talking about precision agriculture," says Landell.

The IAC's effort has contributed to a revival of Brazil's sugar-cane ethanol industry over the past 20 years. Vehicles powered by ethanol, a fuel alcohol produced by the fermentation of sugar-cane juice and molasses, were developed in the 1970s to curb Brazil's dependency on oil, but the sector collapsed in the 1990s as global oil prices dropped and sugar prices rose.

Technology implemented by car manufacturers at the turn of the century, however, enables vehicles to run with any mixture of petrol and ethanol. These 'flex-fuel' vehicles helped to revive the sugar-cane sector. Brazil is now the largest producer of sugar cane in the world, and the second-largest ethanol producer, behind only the United States.

BRAZILIAN BIODIVERSITY

Lúcia Lohmann, an evolutionary biologist at USP's Institute of Biology, has, over the past six years, led an interdisciplinary research group investigating the connections between geology and species evolution in the Amazon. Lohmann has received funding from Biota, a programme launched in 1999 and supported by the São Paulo Research Foundation (FAPESP).

Biota's purpose was to investigate Brazil's vast biodiversity, and it has had a lasting effect on policymaking and education nationwide. The first ten-year phase focused on São Paulo state alone, and the data collected during the investigation were used to produce government guidelines for conserving the state's biodiversity.

The programme's second phase will end in 2020. Its specific remit is to ensure that the project reaches beyond academia, says Carlos Joly, a biologist at UNICAMP and one of Biota's coordinators. The programme has already produced educational materials, including school books for children and teenagers, and videos about the natural landscapes of Brazil and its ecosystem. Environmental policy is a hot topic in Brazil at the moment (see 'Tropical Trump').

The second phase also has a larger remit geographically: university researchers funded by Biota–FAPESP are investigating biodiversity across the whole country. Special attention has been paid to the Amazon rainforest, which stretches 6.5 million square kilometres over Brazil and the rest of South America.

According to a FAPESP report published last year, Biota has supported 299 research projects and trained 288 PhD students in the past 18 years (A. R. S. Garraffoni *et al. Brazilian*

'TROPICAL TRUMP'

Brazil's new leader and science in São Paulo

On 1 January 2019, Jair Bolsonaro will succeed Michel Temer as the president of Brazil. The country's newly elected leader has a mixed record on science and conservation.

"It's a major, major disaster for Brazil, not a temporary blip," Paulo Artaxo, an atmospheric physicist at the University of São Paulo, told *Nature* after the presidential election last month.

Although the right-wing politician and former military captain's election campaign suggested that he would initiate a series of austerity measures — including axeing half of the country's 28 ministries — he seems to have softened on science and technology in the election's aftermath.

Marcos Pontes, Brazil's first (and so far only) astronaut, will lead the ministry of science and technology, and Bolsonaro has promised to increase its budget from 8.5 billion reais to 10 billion reais. If confirmed, the amount would take the ministry's budget to a level similar to that of other prioritized federal sectors in Brazil, such as public security.

Some of Bolsonaro's allies have indicated that his government will push for major changes in the educational system, which will affect universities. The new president himself has suggested that Brazil should invest more money in remote learning, and less in recruiting school teachers and faculty members for public institutions.

One area of concern among scientists is the administration's environmental policy. Bolsonaro, who was once caught fishing in an environmentally protected area, has not been supportive of measures to mitigate Brazil's greenhouse-gas emissions. The country is currently the world's sixth-heaviest polluter.

While campaigning, Bolsonaro threatened that, if elected, he would pull Brazil out of the Paris Climate Agreement — a stance that, along with his fiery rhetoric, earned him the moniker 'Tropical Trump'. Days before the election, however, he said he intended to keep Brazil in the agreement. G.F.

Biodiversity Research: A Promising Future; 2017). During that time, it has produced and stored information on approximately 25,000 species, discovered more than 3,000 new species and published 2,200 articles in scientific journals.

Joly thinks the next phase of the programme must involve private-sector partnerships, especially when it comes to agricultural production. He acknowledges that encouraging businesses to invest more in applied sciences is a challenge, but he thinks the sector can be convinced that conserving and restoring natural landscapes should be a priority. He cites the example of maintaining local bee populations: "Without the pollinator, we wouldn't have crops such as coffee and orange that are so important to the state."

FINDING FUNDING

FAPESP has played a crucial part in funding both Rede Zika and Biota. Created in 1962, the institution has been a driving force for science and innovation in São Paulo. By law, 1% of the state's revenue must be invested in R&D. (In 2017, the total tax income in the state was 205 billion reais.)

Although this commitment is standard throughout Brazil, most states often fail to guarantee the whole percentage to their foundations. FAPESP, the largest of these foundations, is the only one always to have received its tax revenue on time.

FAPESP operates a programme of incentives for small enterprises, known as PIPE. This has been running for 20 years with the goal of transferring knowledge generated at universities to local companies. If a company lands PIPE funding, it must work in partnership with a public university. If the collaboration yields a product, the company shares the intellectual property with FAPESP. The foundation's scientific director, Carlos Henrique de Brito Cruz, says that for each real of public money invested through the PIPE programme, another 11 reais are invested by the private sector.

One of PIPE's projects, led by Danielle Leal de Oliveira, a virologist at USP, is in partnership with a company called Inovatech. The aim is to produce a test kit that can identify whether someone has been infected with the Zika virus. Existing methods cannot distinguish between Zika and other viruses transmitted by insects and ticks, such as dengue and yellow fever.

Leal de Oliveira had not previously worked with the private sector, and she says that the experience has been "challenging", but that the partnership needed to happen. "It is a union of aims: the company wants profit, and we want to promote the public good at the university," she says. "If the new kit manages to hit public hospitals and be made part of prenatal exams, hundreds of women can enjoy the special moment of their pregnancy."

Coordinating 32 laboratories during the Zika crisis "did not coming from nothing", says de Brito Cruz. "If seeds hadn't been planted before, it would have taken at least ten years to create an effective network." ■

Gustavo Faleiros *is a journalist in São Paulo and the editor of InfoAmazonia.org.*