

Pesquisa

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Brazil is expected to revise its industrial policy and R&D incentives in response to the WTO

Two neural pathways control the aggressive behavior of predators

Companies invest in small wasps produced in the lab to combat diseases of the orange groves

Slave women used strategies to purchase their freedom

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Accumulation of DNA lesions, excessive production of free radicals, and a declining ability to replace damaged cells can all lead to the deterioration of organisms



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PHOTO BARANOZDEMIR / GETTY IMAGES

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LETTER FROM THE EDITOR

The science of aging

Alexandra Ozorio de Almeida | EDITOR IN CHIEF

Research on aging is always an interesting read. Most of humankind is trying to some extent to outwit destiny and live longer. To find new ways to delay aging, science must understand the factors at play and how they interrelate. The cover article presents the main lines of investigation on the cellular and molecular mechanisms associated with senescence, highlighting Brazilian contributions. The deterioration of two important mechanisms is central: the cell's capacity to multiply and DNA's capacity to repair itself. Decline of the former complicates the renovation of tissues and organs. Defects in DNA are common, but a reduced capacity to repair them puts many processes at risk. Other processes involve organelles, such as mitochondria; structures, such as telomeres; and factors, such as each individual's genetic profile. In addition to providing definitive answers, state of the art research has revealed the complexity of the problem at hand.

An interesting exercise carried out on behalf of the Science Academy of the State of São Paulo produced a map of the scientific capacity of the 15 administrative regions in the state. São Paulo is the state responsible for roughly 40% of Brazil's scientific output. The output highlights regional specializations, which may help direct private investments and public policies. It also portrays the successes of former public policies targeted at the development of

scientific capacities, some of which are directly or indirectly related to the social and economic challenges faced by the State. Investments by federal and state administrations in the last 20 years have led to the founding of new institutions and the expansion of existing ones. The study also highlights deficiencies: in 3 of the 15 regions, scientific capacity was considered extremely deficient.

*

This current issue of Pesquisa FAPESP international edition also includes an article on Brazil's industrial policy and the ruling by the World Trade Organization (WTO) that considered several of the country's programs to be illegal. Brazil will appeal this ruling. The WTO's conclusion was that an important part of Brazilian industrial policy violated WTO rules through the use of mechanisms such as tax exemptions or suspensions.

*

Another article discusses a study by Elsevier comparing scientific output by women in a range of countries. The data shows a general trend towards gender balance in science over the last 20 years. In Brazil, women account for 49% of the researcher population (2011-2015) – an improvement from 38% female researchers between 1996 and 2000. The articles comprised in this issue are a selection from our monthly editions in Portuguese published between January and April 2017. The four complete editions are available online in English at (<http://bit.ly/Previous>).

COVER



THE MECHANISMS OF AGING

Studies of living cells and organisms identify genetic and molecular phenomena associated with physical and mental decline

Marcos Pivetta and Ricardo Zorzetto | PUBLISHED IN APRIL 2017



Never before have so many people lived so long. Of the babies born today, more than half will reach the age of 65 years, living an average of nearly two decades longer than those born in the middle of the last century.

Increased longevity and reduced fertility are rapidly increasing the age of the global population. In *Developing in an Ageing World*, a United Nations (UN) report published in 2007, projections indicate that by 2050, there will be approximately 2 billion people aged 60 years and older on the planet (22 percent of the total population). In 2005, 670 million people were in that age category, representing 10 percent of the global population.

The global increase in life expectancy can cause problems, including a rapid increase in the size of the elderly population in many countries—including Brazil. In France, it took almost 150 years for the proportion of elderly individuals to increase from 10% to 20% of the overall population. During that time, the country grew richer, and living conditions improved. China, Brazil, and India will show a similar trend within 25 years (see the chart on page 7).

Today, there are 26 million elderly people in Brazil (12.5% of the population). According to projections

by the Brazilian Institute of Geography and Statistics (IBGE), the elderly will represent 29% of the Brazilian population by 2050 (66 million people). “Brazil is aging and will face difficulties as a result,” says Alexandre Kalache, a doctor and epidemiologist from Rio de Janeiro who headed the World Health Organization (WHO) Global Ageing and Health Program for 13 years and now presides over the Brazilian section of the International Longevity Center (ILC), a non-profit organization that investigates population aging and the strategies countries use to adapt to the so-called old-age revolution. “We already have problems with health, employment, education, and sanitation, and very soon, we will also have to deal with a population composed of many elderly people.”

Illnesses associated with aging may become more common. At the same time, more people will remain healthy longer, subsequently changing the work and employment landscape, which will require more flexibility and adaptability from the public, businesses, and the state. “Cities will have to prepare for these new circumstances, creating policies for housing, transportation, social participation, work, and education that consider the elderly,” warns the epidemiologist.

Concurrent with these changes, advances have been made in the field of aging over the last century at an unprecedented rate. A simple keyword search for *ageing* or *aging* on PubMed—one of the largest and most important databases of scientific articles related to health—results in approximately 384,000 papers on the subject from 1925 to 2016 (see the graph on page 9).

In an article titled *The Hallmarks of Aging*, published in the journal *Cell* in 2013, researchers in Spain and France presented a summary of the current knowledge regarding the cellular and molecular mechanisms—the deeper causes—of aging. This report revisits the main points of this topic and presents recent advances, including the contributions of Brazilian researchers.

GENES AND TIME

“Good genetics” is perhaps the biological factor most associated with long life. Experiments involving the manipulation of genes have significantly extended the life span of model organisms, including yeasts, flies, worms, and even mammals. Molecular intervention was successful in *Caenorhabditis elegans*, a 1-millimeter-long roundworm whose genome was sequenced in 1998. The worm, whose normal life span is two to three weeks, was able to live for 145-190 days after its genes were altered. The results of experiments on mice (*Mus musculus*) are more modest but equally positive. Genome alterations have been shown to extend rodents’ life span by a year, from approximately two years to three years.

These results have led some molecular biologists and geneticists to argue that biological aging is a malleable process that can be controlled to some extent. “We can accelerate or slow down aging in animals,” says Portuguese biologist João Pedro Magalhães, head of the Integrative Genomics of Ageing Group at the University of Liverpool in England. “The next step is to repeat this in human beings.” According to Magalhães, studies of model organisms have already identified some 2,000 genes that are capable of regulating aging.

One of the strategies used in the pursuit of a longer and healthier life is to search for cellular and molecular mechanisms associated with good health in those who are extremely old. In 2015, Magalhães coordinated the genome sequencing of the bowhead whale (*Balaena mysticetus*), one of the longest-living mammals in the world. The DNA of this 18-meter-long and 100-ton cetacean from the Arctic could provide clues about how to prevent cancer and survive for as long as two centuries. The paper, published in *Cell Reports*, identifies alterations in a gene linked to thermo-

regulation that may be important to understanding the animal’s low metabolism. A slower metabolism could explain how such a large mammal can live for up to three times as long as humans.

DNA from the longest-living individuals of our own species could also be a source of useful information in the fight against diseases associated with old age and the figurative ticking of our biological clocks. This is the goal of ambitious projects such as the Wellderly study, which was initiated in 2007 by the Scripps Research Institute in California. The project sequenced the complete genomes of 600 healthy elderly people (with no chronic diseases) aged between 80 and 105 years and compared them to those of 1,500 younger adults, with the first significant results being published in 2016.

The most significant difference between the healthy elderly group and the young adult group was that Wellderly participants presented a lower genetic risk of developing cognitive problems. In some healthy elderly people, variants of the *COL25A1* gene were identified that may protect against Alzheimer’s disease. These individuals also had a low propensity for heart problems, although their genetic risk of tumors, type 2 diabetes, and stroke was equal to that of the control group.

“It was surprising to see no difference in genetic risk for the development of cancers,” says Ali Torkamani, director of genome informatics and drug discovery at Scripps. “We also know that there are genetic diseases that influence the speed of aging, usually accelerating it. But overall, aging is a complex process.”

The Human Genome and Stem Cell Research Center at the University of São Paulo (CEGH-CEL-USP) is currently coordinating a Brazilian Wellderly project involving two elderly populations. The first of them includes more than 1,300 São Paulo residents who were over 60 years old when they participated in the epidemiological survey Health, Well-Being, and Aging (SABE), which has been conducted by the USP School of Public Health since 1999. The second population, the 80+ group, includes approximately 130 people in their eighties, all in good health, for DNA analysis.

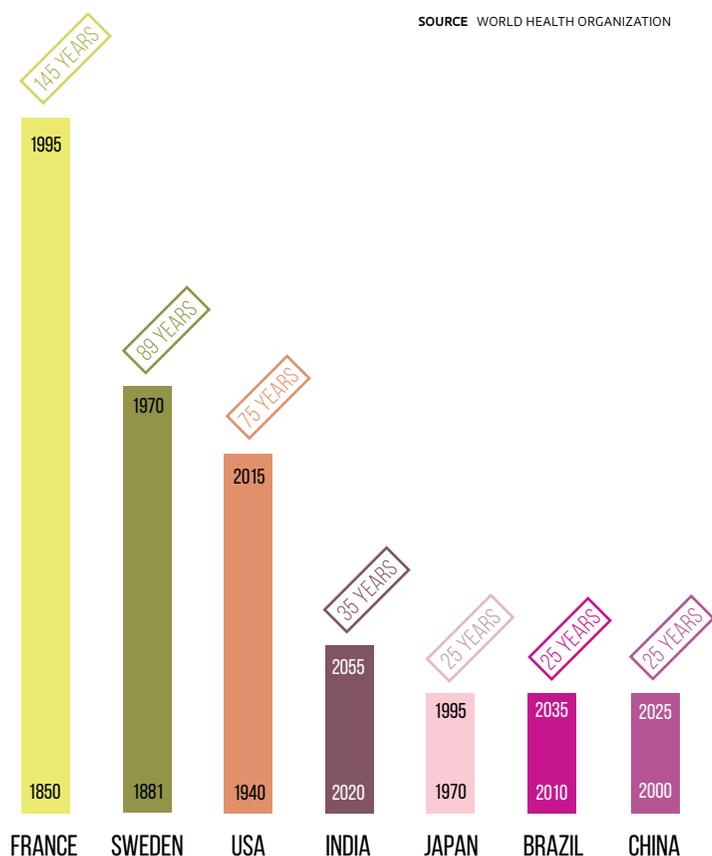
The USP researchers sequenced the exome (the part of the genome that encodes proteins) of the elderly SABE respondents. The first re-

DNA repair failures occur in diseases associated with aging, such as Alzheimer’s disease



RAPIDLY AGING POPULATION

The chart below indicates the time taken for the proportion of elderly individuals to increase from 10% to 20% of the total population



sults from 609 participants were published in the journal *Human Mutation* in March 2017, demonstrating the unique mixture of populations that characterizes Brazil (African, indigenous, and European). The study identified 207,000 genetic variants that had never been described in international biological databases. “This shows the importance of studying our population,” says geneticist Mayana Zatz, co-author of the study and coordinator at CEGH-CEL-USP, one of the Research, Innovation, and Dissemination Centers (CEPID) funded by FAPESP. Each elderly person had an average of 300 genetic alterations, most of which were harmless. Only seven individuals had mutations associated with disease, mostly some form of cancer.

In the coming weeks, geneticist Michel Naslavsky from the USP research center will travel to the United States to begin sequencing the genomes of the 1,300 SABE respondents and the 80+ group subjects. “It will be a long project,”

says Naslavsky, the first author of the article published in *Human Mutation*. The data produced by CEGH-CEL-USP are available on the Online Archive of Brazilian Mutations (ABRAOM).

WAYS TO PROTECT DNA

Most biologists and biochemists today accept the idea that organisms age and die because, over time, their cells lose the ability to perform their functions and die faster than they can be replenished.

Chemical reactions in an organism and environmental phenomena can cause lesions in DNA molecules at any time. Experiments conducted by Swedish biochemist Tomas Lindahl in the 1970s showed that the DNA of a human cell undergoes 10,000 small spontaneous alterations per day, almost once every 10 seconds. In the 3.6 billion years of life on earth, proteins have evolved to help genetic material remain intact, allowing cells to produce perfect copies of themselves and continue to exist.

However, nothing is perfect, and these repair mechanisms can fail. In a study on mice published in the journal *Nature* in 2007, researchers from the United States and the Netherlands proved that stem cells accumulate genetic defects over time and lose their ability to reproduce and maintain tissues unaltered and functioning. Further studies have shown that the same process occurs in human cells, including in syndromes associated with accelerated aging, such as progeria.

At the USP Institute of Biomedical Sciences (ICB-USP), molecular biologist Carlos Menck and his team investigate the causes of genetic alterations that prevent the proper repair of genetic material. For several years now, they have monitored people with the hereditary disease *xeroderma pigmentosum* (see Pesquisa FAPESP, issue No. 199). Sufferers develop skin cancer very easily when exposed to the sun because their cells do not repair the damage caused by ultraviolet radiation. Some may also experience neurological problems and other symptoms similar to those seen in accelerated aging syndromes, which in some cases can lead to death in the first year of life. Faults in these same genes lead to the delayed physical and mental development observed in Cockayne syndrome.

Years ago, Menck began collaborating with a former student, Brazilian biologist Alysso Muotri of the University of California San Diego (UC San Diego), to study phenomena that may affect the neurons of people with Cockayne syndrome. They used chemical compounds to regress skin cells collected from these people to the stem cell stage, from which they can create

other tissues. They then stimulated the cells to transform into neurons and observed that they formed irregular connections with other cells. “The defects observed in the lab-created neurons could at least partially explain the origin of the neurological problems suffered by these individuals,” says Muotri, one of the authors of the article published in the journal *Human Molecular Genetics* in 2016.

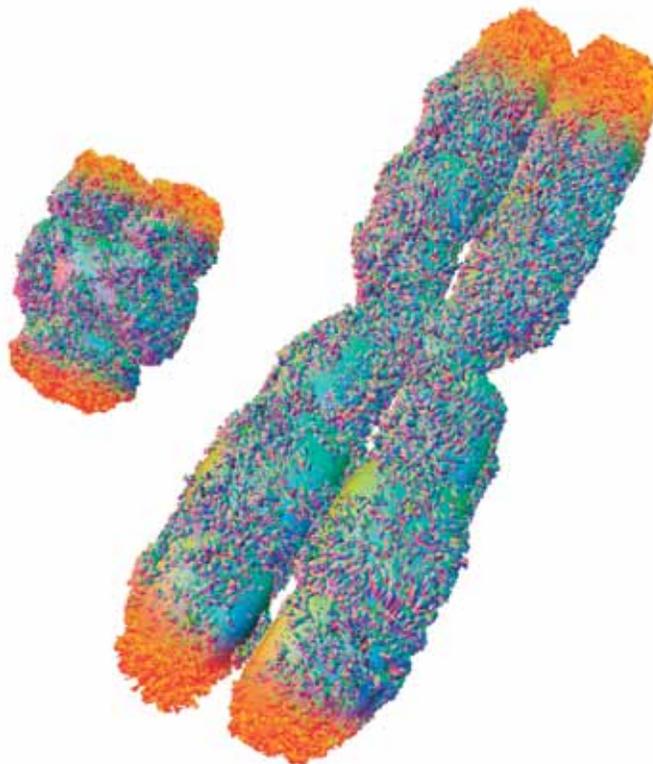
Menck and Muotri also found that these neurons accumulated reactive oxygen species, or free radicals, compounds containing a form of oxygen that easily interacts with and damages DNA and proteins. They suspect that these molecules are produced in defective versions of the mitochondria that are responsible for the production of energy in cells. “We believe that this is the connection to progeria, since high levels of reactive oxygen species have already been linked to aging,” says Muotri. “We are now trying to reverse that process using antioxidant compounds.”

At USP, Menck is working to amplify the damage that reactive oxygen species inflict on the genetic material of people with Cockayne syndrome while trying to determine which parts of the cellular machinery these damages affect. If this strategy is able to replicate the effects of Cockayne syndrome, Menck and Muotri will have a model of accelerated aging that can be used to understand the process of aging in healthy people.

Problems in DNA repair also occur in other diseases associated with aging, such as Alzheimer’s disease, which is more common in people over 80 years old. At the USP campus in Ribeirão Preto, geneticist Elza Sakamoto Hojo and her team have been analyzing the efficiency of DNA repair in people with and without Alzheimer’s disease. They collected blood samples from 13 people aged 65 to 90 years who suffer from the disease (and from 14 people who do not) and subjected cells to high concentrations of reactive oxygen species using hydrogen peroxide, simulating conditions of stress. In an article published in the *International Journal of Molecular Sciences* in 2013, the authors show that the Alzheimer’s cells took three times as long to recover from the free-radical bath as those from the healthy participants.

SHORTENED TELOMERES

During the life of a cell, genetic damage does not occur uniformly throughout the whole DNA molecule; it more commonly affects the two ends, in regions known as telomeres. These segments of genetic material serve to protect the rest of the DNA strand (their role has been compared to the plastic tip on the end of a shoelace). Each time the genetic material



Artistic representation of two chromosomes, the structures that package DNA into cells. The telomeres (in orange) protect the ends of the chromosomes

doubles and the cell divides, the telomeres become shorter by approximately 2%. Only one enzyme, telomerase, is capable of restoring telomere length. In mammals, however, most adult cells do not produce telomerase, which is usually synthesized by stem cells. With a restricted capacity for recovery, telomeres shorten with age. Researchers at Harvard University have shown that telomeres can be artificially lengthened by introducing extra copies of the telomerase gene into cells. But this strategy can be risky, with tumors sometimes becoming malignant after the production of the telomerase enzyme has been reactivated.

In some diseases, telomeres become shortened faster than normal. One example is dyskeratosis congenita, a rare disease characterized by difficulties in producing blood, skin, and lung tissue cells, which can lead to accelerated aging, as seen in progeria. It has been known for some time that the telomeres of dyskeratosis sufferers are shorter than normal. Brazilian biologist Luis Francisco Batista, a former student of Menck and a professor at Washington University in Saint Louis, confirmed the cause: failure in the proper functioning of telomerase.

Using skin cells from people with dyskeratosis, he generated stem cells and found more severe forms of the disease associated to a greater inability to produce active telomerase. Since publishing his results in *Nature* in 2011, Batista has dedicated himself to studying how a lack of telomerase and the shortening of telomeres af-

fect the number of stem cells stored in tissues. “We are trying to uncover the chain of events that follows,” says Batista.

EXHAUSTION WITHOUT REPLACEMENT

In the elderly, there is an accumulation of cells that have reached the end of their life cycle and have lost the ability to copy their own DNA and generate clones of themselves. This symptom of aging has a positive impact: cells that do not multiply can be eliminated by the immune system, preventing the development of tumors.

The problem is that the body’s ability to defend itself against external threats, such as viruses and bacteria, is also diminished, affecting the efficacy of vaccines. “In Japan, which has a large elderly population, they have tested the effects of administering three smaller doses of the influenza vaccine instead of just one,” says biologist Valquiria Bueno, a professor at the School of Medicine of the Federal University of São Paulo (UNIFESP).

Bueno, an expert in immunosenescence, compared the production of defense cells in six men and six women aged 88 to 101 years (participants of the SABE survey) with that of university students under the age of 30 years. The generation of leukocytes (a type of defense cell) in bone marrow was 40% lower in the elderly on average,

which is similar to the findings of international studies. In addition to these findings, which were presented in 2016 in a book titled *The Ageing Immune System and Health*, the blood of these elderly participants was also found to exhibit increased production of another type of cell that can reduce resistance to infections and promote the development of cancer.

There are other more controversial approaches. Recent experiments on animals suggest that replacing old cells with new ones could delay aging or partially reverse deterioration in certain organs. Some of these studies use a controversial technique developed in the mid-nineteenth century called parabiosis, where a young rodent is surgically attached to an old one in order for the latter to receive a transfusion of new blood.

In 2013, a team led by Amy Wagers, a specialist in regenerative medicine at Harvard University, published an article in *Cell* describing how they used parabiosis to identify an increased level of a protein that can combat cardiac dysfunctions linked to old age in old mice that received blood from young mice. Further studies have reported the benefits of this method on brain and muscle tissues.

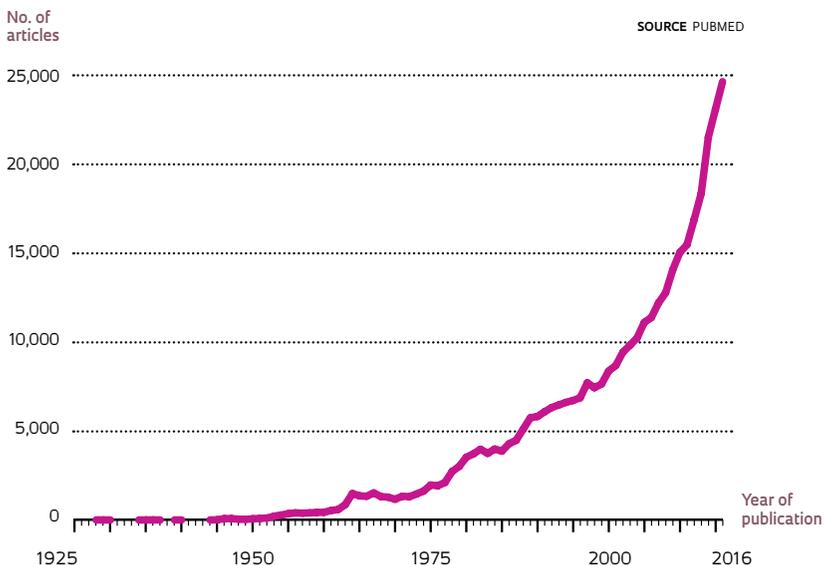
Last November, however, an article published in *Nature Communications* reported that the administration of new blood did not significantly improve biological parameters in old mice and that the health of the young rodents deteriorated as a result of receiving transfusions of old blood. “Our study suggests that new blood alone does not work as a treatment,” said Irina Conboy, a professor at the University of California Berkeley (UC Berkeley) and the lead author of the paper. “It would be more accurate to say that there are inhibitors in the old blood that we need to mitigate in order to reverse aging.”

DAMAGE TO THE ENERGY CENTERS

For many years, mitochondria were regarded as the villains of aging. In 1956, American chemist and physician Denham Harman, at the time a researcher at UC Berkeley, proposed that one cause of the deterioration and death of cells could be the production of free radicals. He suspected that these molecules were able to interact with and damage DNA, proteins, and other cell components. Later experiments supported Harman’s arguments and even led some researchers to recommend avoiding physical exercise, which increases energy consumption and cellular respiration. The opinion today is quite different.

GROWING SCIENTIFIC OUTPUT

The PubMed research database hosts approximately 384,000 studies on aging published from 1925 to 2016



Over the last two decades, experiments have indicated that free radicals play a dual role in cells. At low concentrations, they induce the production of antioxidant compounds, protect cells from aging, and even stimulate cell proliferation. At high levels, however, they cause cell death.

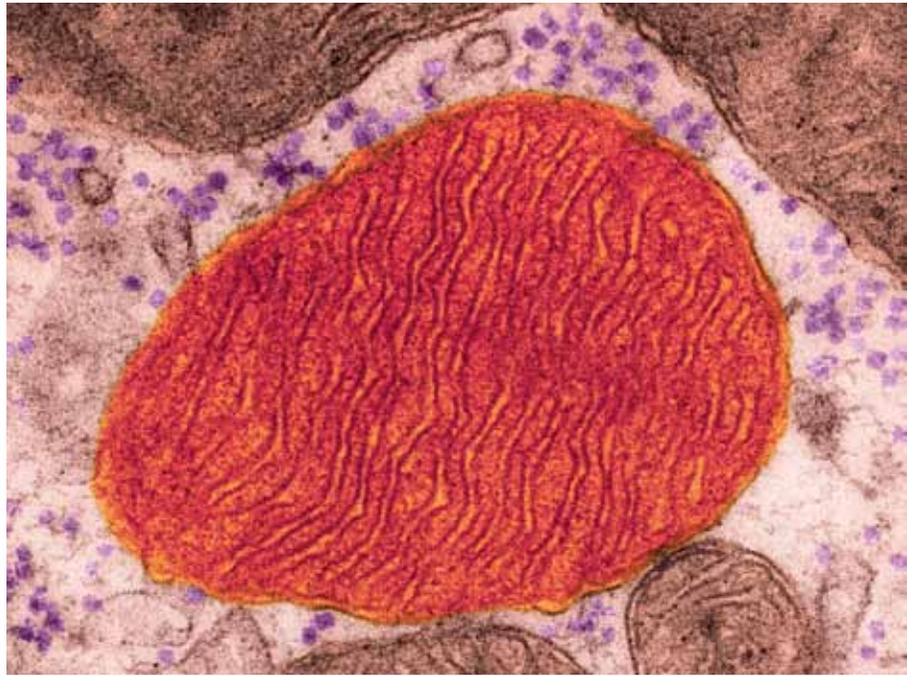
In the late 1970s, during a postdoctoral fellowship at Johns Hopkins University, biochemist and physician Aníbal Vercesi noticed that certain conditions created pores on mitochondria membranes, killing them. Later, after returning to the University of Campinas (UNICAMP) where he is a professor, he found that this effect is due to an increased concentration of free radicals.

In experiments conducted with his team—including biochemists and physicians Roger Castilho and Alicia Kowaltowski, then doctoral students and now professors at UNICAMP and USP, respectively—Vercesi found that inside the mitochondria, the accumulation of calcium stimulates the over-production of free radicals, leading to cellular damage. Proteins, genetic material, and free radicals escape through the pores that open in the membrane of the mitochondria. “We proposed this hypothesis in 2001,” says the biochemist. “Today, it is widely accepted and even used to explain the damage that occurs during heart attacks and strokes, as well as the development of age-related illnesses such as diabetes and Alzheimer’s.”

Biochemist Nadja de Souza Pinto, a former doctoral student of Vercesi’s and now a professor at USP, studies the consequences of excessive free radical production in mitochondrial DNA. While working at the National Institute on Aging in the United States, she studied the brains of people with Alzheimer’s and observed that repair of the DNA lesions caused by free radicals is less efficient in people with more severe symptoms. Back in Brazil, she is working with geriatrician Wilson Jacob Filho and gerontologist José Marcelo Farfel, both from USP, to evaluate DNA repair in the mitochondria of two groups: people with typical Alzheimer’s and asymptomatic carriers who do not develop cognitive problems. In studies on rats, Pinto found that mitochondrial DNA repair increased until midlife and then deteriorated. “We are proposing that the low activity of these repair mechanisms may be a risk factor for Alzheimer’s,” she says.

EAT LESS AND LIVE LONGER

The effect of diet on the life spans of different organisms may be the longest-studied topic related to aging. For nearly a century, we have known that reducing the amount of energy consumed by an animal prolongs its life span. In 1933, American biochemist and gerontologist



Mitochondrion, a cellular organelle that converts nutrients into energy, as observed under a microscope

Clive McCay, a researcher at Cornell University, published a short article in *Science* comparing the longevity of the rats studied by his team in New York with the rats kept in the laboratory of physiologist James Slonaker at Stanford University in California.

McCay’s rodents, fed a more nutritious diet, grew and reached sexual maturity faster, but they only lived half as long as the rats from Slonaker’s laboratory, which gained weight and matured more slowly and lived for an average of 1,200 days. “It is possible that longevity and rapid growth are incompatible and that the best chance for an abnormally long life span belongs to the animal that has grown slowly and attained a late maturity,” argued McCay, hypothesizing that reduced calorie intake would favor longevity to the detriment of reproductive capacity.

For the next 50 years, aging was understood as inevitable and inherent to life. This view began to change in the 1990s with the findings of molecular biologist Cynthia Kenyon. A professor at the University of California San Francisco (UC San Francisco) and vice president of aging research at Calico, a company founded by Google, Kenyon found that alterations in a certain gene doubled the life span of the *C. elegans* roundworm without affecting its fertility.

It was later discovered that this gene encoded a cell-surface protein—a receptor—to which insulin-like peptides are connected. This receptor functions as a nutrient sensor in the extracellular environment. “These advances have sparked a race to study caloric restriction from a molecular perspective,” says biomedical scientist Marcelo Mori from UNICAMP, who investigates life

span-increasing mechanisms that are activated by caloric restriction and physical exercise.

One such mechanism is the production of microRNAs, molecules that modulate the functioning of genes and the production of proteins. In studies on mice during his postdoctoral fellowship at Harvard that continued at UNIFESP and UNICAMP, Mori found that the main source of circulating microRNAs in mammals is adipose tissue (where fat is stored) and that microRNA production decreases with age. In experiments with mice and *C. elegans*, he also found that caloric restriction increases life span by boosting Dicer enzyme activity, which transforms long RNA molecules into microRNAs (see Pesquisa FAPESP, issue No. 212). “Aging decreases the production of the Dicer enzyme and microRNAs and reduces life span, but caloric restriction does the opposite,” says Mori.

At USP, Alicia Kowaltowski and her team are interested in how reduced calorie intake affects the functioning of mitochondria. In an article published this year in the journal *Mechanisms of Ageing and Development*, the researchers noted that in animals fed a restrictive diet, mitochondria are more elongated, less damaged, and replaced more quickly than those in animals fed a normal diet. Previous experiments presented in *Aging Cell* in 2016 indicated that caloric restriction improves the functioning of mitochondria in neurons and increases their resistance to cellular stress, such as increased levels of calcium and free radicals. According to another study by the group, eating less also improves the functioning of insulin-producing cells in the pancreas, protecting the body against diabetes, a disease associated with aging.

Although these findings are encouraging, whether they can be applied to human health remains unknown. “It is difficult to transfer the results of animal models to humans,” says Kowaltowski. In the laboratory, animals are protected, sedentary, and eat at will, which makes them obese compared to those living in the wild. “Even people who live sedentary lives perform physical activity and they do not feed continuously,” says the researcher. “In humans, it is possible that simply maintaining a healthy weight is equivalent to caloric restriction in laboratory animals,” she says.

Marcelo Mori from UNICAMP believes that it is not feasible for most humans to maintain radical caloric restriction throughout their entire lives without damaging their health. He proposes searching for pharmacological or dietary interventions that mimic the effects of caloric restriction in a safe and less demanding way together with regular physical activity, which also

seems to increase average life span and is more easily adopted. “Despite recent advances,” Mori says, “the fact remains that we are still a long way from proposing viable strategies for increasing the longevity of human life.” ■

Projects

1. CEGH-CEL – Human Genome and Stem Cell Research Center (No. 13/08028-1); Grant Mechanism Research, Innovation, and Dissemination Centers (CEPID); **Principal Investigator** Mayana Zatz (USP); **Investment** R\$26,897,714.59.
2. Consequences of lesion repair deficiencies on the genome (No. 14/15982-6); **Grant Mechanism** Thematic Project; **Principal Investigator** Carlos Frederico Martins Menck (USP); **Investment** R\$2,451,302.99.
3. Genomic instability and molecular signaling involving responses to DNA damage and repair (No. 13/09352-7); **Grant Mechanism** Regular Research Grant; **Principal Investigator** Elza Tiemi Sakamoto Hojo (USP-RP); **Investment** R\$624,252.12.
4. Energy metabolism, redox state, and mitochondrial functionality in cell death and in cardiometabolic and neurodegenerative disorders (No. 11/50400-0); **Grant Mechanism** Thematic Project; **Principal Investigator** Aníbal Eugênio Vercesi (UNICAMP); **Investment** R\$3,019,922.94.
5. Dicer, miRNAs and the control of mitochondrial function in the context of aging and caloric restriction (No. 15/01316-7); **Grant Mechanism** Regular Research Grant; **Principal Investigator** Marcelo Alves da Silva Mori (UNICAMP); **Investment** R\$292,429.97.
6. Bioenergetics, ion transport, redox balance, and DNA metabolism in mitochondria (No. 10/51906-1); **Grant Mechanism** Thematic Project; **Principal Investigator** Alicia Juliana Kowaltowski (USP); **Investment** R\$2,210,658.64.
7. Study of cellular responses to mitochondrial DNA damage in the cells of mammals (No. 08/51417-0); **Grant Mechanism** Regular Research Grant; **Principal Investigator** Nadja Cristhina de Souza Pinto (USP); **Investment** R\$292,654.45.
8. Evaluation of myeloid-derived suppressor cells in the elderly: Brazilian and British population (No. 14/50261-8); **Grant Mechanism** Regular Research Grant; University of Birmingham Agreement; **Principal Investigator** Valquiria Bueno (UNIFESP); **Investment** R\$64,197.47.

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Studies of a city in movement

Urbanist who created new disciplines at FAU-USP dedicates herself to studying the São Paulo macrometropolis

Márcio Ferrari | PHOTO Léo Ramos Chaves

PUBLISHED IN APRIL 2017

Regina Meyer enjoyed teaching at the University of São Paulo's School of Architecture and Urbanism (FAU-USP) so much that when faced with the sudden interruption of reaching retirement age in 2011, she decided to "go in denial." "I was in full flight," she says. "I was still researching and trying to create new disciplines." The enthusiasm of her students was contagious, and vice versa. Today, Regina invests her energy in new research projects and in supervising her graduate students.

Born in Guaxupé, Minas Gerais State, she moved to São Paulo in her early years, and the city became the primary focus of study for her entire career. At 22, she married psychoanalyst Luiz Meyer, and together, they moved to France and then Geneva, Switzerland, to study. Facing an impossible labyrinth of a selection process for the architecture college, she decided to try psychology. "I was accepted in 1968. The psychology course at the

AGE 75

EXPERTISE

Planning and urbanism

QUALIFICATIONS

Degree in Architecture and Urbanism from the University of Brasília (1974); Master's from the University of London (1977); PhD from the University of São Paulo (1991)

INSTITUTION

School of Architecture and Urbanism at the University of São Paulo

SCIENTIFIC PUBLICATIONS

53 articles, 22 book chapters, 9 technical papers, 41 graduate students supervised



University of Geneva was internationally renowned thanks to the innovative work of Jean Piaget. But I had to cut my studies short at the end of the second year to return to Brazil.” On arriving in Brasília, where her husband had accepted an invitation to create a new Department of Psychiatry at the School of Medicine of the University of Brasília (UnB), she found that local psychology courses adopted a predominantly behaviorist approach, as opposed to Piaget’s theories. Disappointed, she resumed her long-standing interest in architecture, starting a career that would lead her to urbanism and urban planning.

Regina Meyer, a married mother of two (Diogo, a biologist, and Ana Elisa, who works in publishing), granted this interview in her apartment, which is in a central neighborhood of São Paulo. The building was designed by architect Rino Levi in the 1940s and decorated with tiles by landscape architect and plastics artist Roberto Burle Marx.

Your studies on metropolises, particularly São Paulo, have always been characterized by an intense focus on changes to the practical terrain. What are you currently working on?

I am working with colleagues from FAU-USP, pursuing a project that, in my case, fulfills an endeavor that was started during my PhD days, when I studied the São Paulo of the 1950s, and continued with my observation of the changes taking place in the metropolis in the 1990s. In the early years of the 2010s, our research was advancing towards an enlarged urban scale — that of the macrometropolis; a concept that, although not new, has gained more support in the last few decades because of the enormous territorial expansion of many cities and metropolises. In our case, it is the conjugation of the São Paulo metropolises, which are located in a large territory of 53,000 square kilometers and have a population of 30 million inhabitants across 173 municipalities. This immense set of cities gravitating around a group of metropolises creates an area of almost continuous occupation that radiates from São Paulo on various axes. The study underwent many important developments. At the same time, the São Paulo state government produced an ambitious Macrometropolis Action Plan. There

have not yet been any practical results because plans need time to take root, but formal discussion of this powerful territory — home to 73% of the state’s total population, 83% of its Gross Domestic Product [GDP] and almost 30% of the national GDP — has gained ground, even earning a place in public policy. At the moment, the objective is to write articles that focus on the urban dynamics of this macrometropolitan scale. Raising awareness of this post-metropolitan territorial organization contributes to



Regional hegemony occurs in São Paulo because of many factors, including the organization of capital, the workforce and knowledge

bringing about public policy that takes this scale into account.

Did the functions of each city change with the formation of the macrometropolis?

The formation of the macrometropolis is a historical process. It is an urbanization process that creates distinct urban characteristics during its development. When analyzing urban evolution, as the scale changes, the questions that we need to ask also change. With the São Paulo macrometropolis, recognition of the region’s potential in contemporary terms is very important, and although public policies have always existed, those aimed at strengthening the coordinated functioning of the territory are still new. São Paulo is, and I believe it will continue to be, the nucleus of this macrometropolis because it has the functional characteristics inherent to a powerful center. Just as Paris and London dominate their surrounding areas, regional hegemony is observed in São Paulo because of many factors, such as the organization of capital, to a certain extent the workforce, the research and knowledge based there because of its great universities, the stock exchange, and company headquarters. This does not mean that metropolises the size of Campinas and São José dos Campos, which also host important research centers, will not play important roles in the future. For the time being, São Paulo is where the public and private decision-making institutions are located, even though the workforce and productive innovation are distributed among the other metropolises.

What were the milestones of your career that led you to your current studies?

After my PhD, throughout the 1990s, I wanted to embark on a study of the urban transformations that we were experiencing in São Paulo. To do so, I needed to add other areas of knowledge. With my colleague, Marta Dora Grostein, economist Ciro Biderman, who had recently completed his PhD in urban economics at the Massachusetts Institute of Technology [MIT] and was teaching at the Getulio Vargas Foundation [FGV], and many undergraduate and graduate students, I formed a working group that united FAU-USP and the Brazilian Center for Analysis and Planning

[CEBRAP]. The results of six years of work were published in a book, *São Paulo Metrópole* [São Paulo Metropolis], in 2004 [published by IMESP/EDUSP]. The main objective of the research was to identify and analyze São Paulo from an urban perspective in the 1990s. The data and a large volume of analytical cartography sought to reflect a process of change that had been maturing since the 1970s, which led the metropolis to a stage at which industrial activity began to lose its hegemony. Our central interest was to analyze the urban territory. The research received a decisive boost in the year 2000, when the Center for Metropolitan Studies [CEM] was created as one of the Research, Innovation and Dissemination Centers [CEPID] financed by FAPESP, in conjunction with CEBRAP, the State Data Analysis Foundation [SEADE], TV Cultura and the Social Service of Commerce [SESC; today, the CEM also has offices at USP's School of Philosophy, Languages and Literature, and Human Sciences [FFLCH-USP]]. In 2005, the FAU-USP group separated from CEPID and set up the Metropolis Urbanism Laboratory [LUME]. It was one of the most important initiatives that I participated in at FAU-USP. The creation of LUME paved the way for further research. In the same year, we began a new study that resulted in a second book on the São Paulo metropolis: *A leste do centro: Territórios do urbanismo* [East of the Center: Territories of Urbanism], published by EDUSP and IMESP in 2010.

What was it about?

It was a study focused on urban growth and the transformations of a sector of São Paulo that stretched from the central area to the city periphery. The initial emphasis was on the historical transformation of a region defined as the “vector east of the Center,” covering the traditional industrial neighborhoods, such as Bom Retiro, Brás, Mooca and Pari, as far as the eastern border of the municipality. The research was highly transdisciplinary, including content on the city's historical construction, urban structuring promoted by public transport and an environmental evaluation. We also attempted to define a set of guidelines for urban projects. We introduced a new planning and design tool: the Metro-

politan Interest Zone [ZIM]. We were able to evaluate the impact of the mass transport links between the city center and its more populous periphery, located 30 kilometers away, where the greatest number of housing developments were installed by the government in the 1960s and 1970s. In fact, these developments were constructed with no consideration of the daily commute that residents would ultimately face. The study reinforced the idea that rather than treating cities as “still lifes”, we must work with them as spaces in permanent movement.

How did your activities change after you retired?

Retirement did not signal the end of my academic involvement. I still participate in many activities at the university. I conduct academic research, supervise master's and doctoral students and teach graduate courses, which is a daily commitment. My academic career has been a little *sui generis*. Most professors have taken more diversified career paths. Mine was marked by great didactic activity with new course proposals, working in teams and supervising many graduate theses.

To what do you attribute this singularity?

This choice was not deliberate. In hindsight, and taking a very critical view of the past, I think I enjoyed the academic activities associated with the classroom. Perhaps I could have balanced my activities better and dedicated myself to attending more conferences, for example. I spent considerable time involved with day-to-day university life. I also did not extend my career overseas. The emphasis on getting published in foreign journals came a little late for me. I was recently guest editor for a special São Paulo issue of *Revista de Urbanismo Iberoamericano* [Ibero-American Urbanism Magazine]. It is a very reputable publication that specializes in urbanism and is published simultaneously in Buenos Aires and Barcelona. I have only recently started doing this kind of work.

What kind of disciplines did you create?

I created elective disciplines for contemporary urbanism. Until the 1980s, our courses revolved around modern-

ism. But it became important to teach students the difference between issues of urbanization and those of urbanism. The understanding that urbanization is a process, while urbanism is the effects this process has through the implementation of all kinds of projects, from infrastructure to construction, was introduced at FAU-USP in the 1960s through studies and books by professor Nestor Goulart Reis. It was valuable work that greatly influenced teaching both within the college and outside it. However, despite this methodological collection, some courses still failed to make the distinction, which I considered detrimental. I tried to show, through my courses, that urbanism is inseparable from design and is always propulsive. This was my contribution to the students and young architects who graduated in the 1990s and 2000s.

Why was this emphasis so important to you?

I think it was necessary to be clear about which issues related to urbanism and which related to the urbanization process. In addition, to complicate matters further, there was another issue to be faced in urban planning. At FAU-USP, there is a set of disciplines exclusively concerned with urban planning, taught by some very active and productive professors. However, in terms of approach and production, these subjects differ from those that address urbanism and urbanization. Urban planning promotes a procedural perspective, as is required to implement urban projects. These fields of knowledge, rather than complementary, are totally interdependent. It is interesting to remember that these distinctions were always very clear in courses on the history of urbanism, urban planning and urbanization. The materials that make up these histories are distinct, specific. In addition, in practice, in regard to urban intervention, which is propulsive, it is important to recognize the difficulties that arise from the disconnect between a plan that does not materialize because of the absence of adequate urban projects, and projects and plans that are drawn up without properly considering the urbanization process.

What is the key to solving the city's problems today?

That question is almost unanswerable. Solving the problems of the city and the metropolis is a continuous and complex goal that can only be approached in stages. It is impossible to point to a single, linear path. The word “strategic” has been incorporated into planning vocabulary and gives an idea of the need to constantly review the objectives and above all the tools of action. One possible route to understanding the current dilemmas faced by the city of São Paulo is considering the consequences of its limitless and ungoverned territorial growth, particularly the pattern of outward expansion of its peripheries. One enlightening perspective may come from the evolution, or rather the “devolution,” of its public transport system and this pattern of urban expansion. While working on the themes of the 1950s for my thesis, I realized that in the 1930s, we did not just choose an operational model for the city; we chose a destination. Opting for the construction plan proposed by the mayor at the time, Prestes Maia [1938–1945], we walked inexorably towards a road model. Today, it is clear that one of the city’s greatest problems is the traffic and lack of public transport. Since the arrival of the freeways and with the growing number of motor vehicles, mobility and traffic issues have monopolized urban proposals in São Paulo. The fate of the city was sealed when, in the 1930s, a proposal to build a subway was rejected. Mayor Prestes Maia argued that a subway was the best solution in terms of mass transportation but inadequate as an urban proposal for São Paulo at that time. In his view, it was necessary to first establish a strong and coordinated road system and then to introduce a subway network later. The decision was fatal.

Did the fact that you studied your undergraduate degree in Brasília, a city renowned for its excellent planning, influence your conceptions of urbanism? Brasília at the time was a true laboratory for urban functionalism and architectural modernism. At UnB, there seemed to be no other way of thinking about cities. I studied and lived in Brasília in a very uncritical way. My three-year-old son walked to school alone while I watched him from the window. I boasted about this to mothers I knew in São Paulo who

took their children to school by car. I considered my life on the superblock a wonder. Furthermore, the city was still under construction in the early 1970s, and we all felt similar to “builders” that were a part of the process, despite living under a military dictatorship.

When did you start to see Brasília more critically?

While living there, I got to know many people who worked in Plano Piloto [the administrative region] and lived in the satellite cities (Gama, Taguatinga, Sobradinho). People commuted from a long way away every day and needed to get to the bus station, located in the geometric center of the city. From there, they had to reach their workplaces on the superblocks or in other sectors of Plano Piloto. It became clear to me that there was an unresolved issue. I realized that the plan had not addressed the issue of spatial/urban segregation very well.

And what is your opinion of the Brasília project today?

I think it is a city that was born from a theory, which had already completely defined its adult image during its infancy. In addition, throughout its development, it was not capable of incorporating the transformations it went through, what with being the child of functionalism’s most orthodox theory. There is no denying that Brasília showed its weaknesses quickly; everyday life has made it clear that this is not the best way to design the cities of the future. The closed project, designed based on the conditions of the 1950s, left few openings to incorporate the new. I think it was the intense experience of living in Brasília that led me to urbanism as the subject of my study and work.

How was your vision influenced by the graduate program in London?

I arrived at the Architectural Association School of Architecture [AA] in 1976. The school is at the vanguard of architecture, and I found many texts that were critical of the purposes of orthodox functionalism. I reluctantly realized that I needed to review my preconceptions. What I knew was an urbanism created to solve the problems faced by industrial cities built from scratch, guided by the organization of their functions — living,

working, leisure and movement — all addressed separately. I realized that cities built from scratch no longer represented the challenges of contemporary cities. I did not want to ignore everything I had learned, but I had to bow to the evidence. Almost as a return to that phase of my studies at the beginning of graduate school, I recently wrote an article about the book *Los Angeles: The Architecture of Four Ecologies* by Reyner Banham, published in 1971 but translated into Portuguese just four years ago. In the article, published in the FAU-USP journal *Revista Pós*, I revisit my interests of the 1970s. Banham was a professor at the Bartlett School of Architecture, where I studied during the second stage of my graduate program after leaving the AA. His thinking influenced me considerably at that time.

When you returned to Brazil, were you able to apply what you had learned?

Soon after arriving, I was given the opportunity to lead the city’s Department of Historic Heritage [DPH], associated with the Department of Culture, from 1983 to 1985. I made a great effort to confront the issues and themes related to preservation of the historical heritage specific to São Paulo. After a few months of work, during which time I was involved in the development of the city’s master plan, coordinated by architect and Planning Secretary Jorge Wilhelm, I began to think that the preservation of heritage would be better managed by a planning agency. Secretary of Culture Gianfrancesco Guarnieri was very angry with my position on the matter, and I was dismissed. My participation in the discussions and development of the master plan in the early 1980s sparked an interest in the issues regarding central São Paulo to which I later returned. After leaving the DPH, I took a position at the State Department of Culture, where I managed a project proposed by Secretary Jorge da Cunha Lima called Luz Cultural [“Cultural Light”]. The aim was to create a neighborhood where culture would be the primary focus. It was influenced by projects in Europe that sought to create urban spaces designed for cultural activities which, in turn, would promote urban regeneration processes. In Europe, the migration of large food markets from city centers to

more peripheral areas paved the way for radical redevelopments. Despite the logical intuition of the proposal, I do not think the cultural function would sustain the urban transformations desired for the region.

What changes did you witness at FAU-USP?

Architecture and urbanism were shaken by the impact of the Modern Movement in the 1960s and 1970s, which inevitably affected practice and teaching. There was intense theoretical reform, which should have had a heavy impact on course content, but reviewing our convictions and consequently the teaching methods themselves proved a difficult task. There was a degree of entrenchment against the new theories, particularly those that called aspects of modernism and urban functionalism into question. This opposition to new theories greatly affected urban planning and urbanism. Here is a compelling example: there was an emblematic urban planning agency in London called the Greater London Council [GLC], which coordinated and united all the required information for urban planning and design. It was envied worldwide for its efficiency and forward thinking. The agency was closed in 1983, after Margaret Thatcher was elected prime minister [1979–1990]. The rise of Thatcherism in London's case, and of neoliberalism in general, sent urban planning and urbanism into a rapid retreat. Until the 1980s, the municipal and state planning departments in São Paulo were important agencies. But since the 1990s, they have played a much less decisive role. All this hindered the acceptance of important criticisms that arose at that time.

How did you approach these changes in your teaching?

In 1991, I proposed a new discipline, known as “Intervention in existing cities: the process of urban design.” The objective was to discuss foreign and Brazilian projects with the aim of developing the student's ability to critically analyze contemporary urban projects. We made a great effort to ensure that the exercises developed in class and the course in general encouraged an understanding of the complexity of contemporary cities — existing cities — so that the students



Until the 1980s, the planning departments in São Paulo were important agencies. Since the 1990s, they have played a much less decisive role

could then extract from it the different possibilities of these projects. The determining factors of this complexity should be the starting points of the project. This course was the main reason for my involvement at the undergraduate level.

At the same time, as the planning crisis overseas, Brazil was heading in the opposite direction, with the social functions of housing defined by the 1988 Constitution, the approval of the Cit-

ies Statute (2001), the creation of the Ministry of Cities, the master plans...

This contrary direction actually comes down to important developments in the legal frameworks, some of which are still incomplete and lacking essential elements. The Ministry of Cities itself is not very effective. Despite the dominance of urban areas in Brazil, the ministry does not play a very significant role in how the country thinks about its cities and metropolises. Its only highlight is the introduction of the Minha Casa, Minha Vida program [“My House, My Life”], which has now spent somewhere around R\$300 billion producing housing projects that have all the characteristics of the dismal pattern of peripheral expansion of the 1960s. Planning has taken an almost irrelevant position. Somebody in planning should have checked the cost of building transport links against the value of the land, for example. Many housing projects do not even consider the impact of building a subway line and stations. The contradictions are blatant. The transport network in São Paulo is expanding, and soon the subway will reach areas that are still lacking in basic infrastructure. It is totally disorganized, but we must defend the arrival of mass transport, which is essential to improving the lives of residents.

You have always defended an idea that was once controversial, of increasing the population density in the center of São Paulo.

Defense of the densification was not controversial. There was almost a consensus that the city center was becoming unoccupied. In addition, this is a waste, because there is clearly sufficient infrastructure there to house many more people. There was a time when residents of the city center were moving to the peripheries. I defended the idea, which today is commonplace, that it was necessary to repopulate the center. Population density is a way of taking advantage of the infrastructure already in place. The central region provides the second-largest number of jobs in the city. The sectors of the municipality with the highest traffic today are strictly residential districts of very low population density, such as Morumbi. In contrast, in an area of mixed use, it is possible to get almost anywhere on foot. ■



Industrial policy in check



Fiat Chrysler
factory in Goiana,
Pernambuco State

JUCA VARELLA / FCA / PUBLIC PHOTOS

In response to a ruling by a WTO panel, the Brazilian government considers changes in laws and in the ways in which it encourages R&D

Fabício Marques

PUBLISHED IN JANUARY 2017

The Brazilian government announced that it will appeal to the World Trade Organization (WTO) Dispute Settlement Body to try to reverse the conclusions reached by a panel that found several of Brazil's industrial policy programs to be illegal—they had been formally questioned by Japan and the European Union. The final report of the panel, established in 2014 and composed of three independent arbitrators, was received by the Ministry of Foreign Affairs (MRE) on December 20, 2016 but will probably not be officially released until around February 2017, after fulfillment of a formality: it must first be translated from English into the organization's other two official languages, French and Spanish, and circulated among the 160 WTO members. The document maintains that an important part of Brazilian industrial policy violated WTO rules and denounces the way in which Brazil has encouraged domestic production of automobiles, information technology equipment, and semiconductors—among other items—by granting exemptions or suspensions of tax on end-products that are not extended to imported competitors.

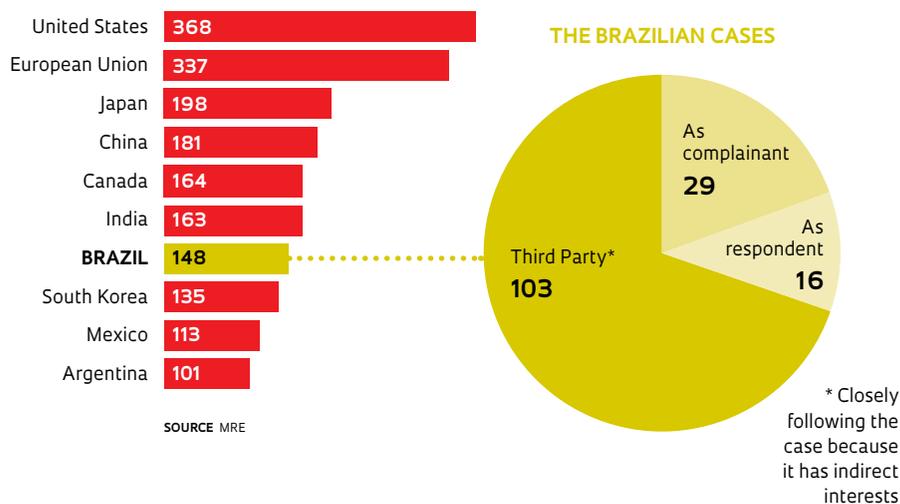
One of the points questioned in the dispute is a violation of the so-called principle of national treatment, understood to mean the granting of incentives to goods and merchandise manufactured in Brazil, in the form of tax exemptions that are denied to similar goods produced in other countries. Another matter involves the requirement that products that benefit from tax reductions contain a certain minimum percentage of Brazilian-made inputs. According to the panel, these problems appear in programs such as Inovar Auto, instituted in 2012 to stimulate the domestic production of automobiles, and the Information Technology Act, which has been in effect for 25 years and grants tax reductions to manufacturers of electronic hardware and components that invest in research and development (R&D).

Also censured in the report is the digital inclusiveness program, which was in effect from 2005 through 2015 and reduced to zero the rates of some mandatory contributions, such as the PIS (Social Integration Program) and Cofins (Social Security Financing Program), whose contributions are normally assessed on sales of computers, tablets, smartphones and other items. Also affected are programs that support technology development in the semiconductor industry (PADIS) and digital TV equipment manufacturing (PATVD), programs that offer tax exemptions in exchange for investment in R&D, and the special regime for the purchase of capital goods for exporters (RECAP), which cuts taxes paid by export industries when they purchase machinery and equipment.

“Brazil had a lot of its industrial policy tools questioned, which is unprecedented,” says economist Sandra Polónia Rios, director of the Center for Integration and Development Studies (CINDES) and a professor at the Pontifical Catholic University of Rio de Janeiro (PUC-Rio). “Initially, the European Union even questioned the existence of the Manaus Free Trade Zone but later abandoned that idea.” From 1995 through 2016, Brazil itself had questioned the policies of WTO member countries on 29 occasions, mostly to challenge barriers to imports of industrial products, and was sued by other countries 16 times. In some cases,

Disputes at the WTO

The 10 members of the organization that have made the most use of the dispute settlement system between 1996 and 2016 – by number of cases



The economic and social balance of the Information Technology Act has been quite positive, says Barbato of ABINEE

Brazil had to modify policies, as in the protest against the Export Financing Program (PROEX) during a late-1990s dispute over the regional aircraft production involving Embraer and Bombardier – a Brazilian and a Canadian manufacturer, respectively. The current litigation of industrial policy is the widest ranging that Brazil has ever faced in the WTO. “This time, several regimes are being questioned, and broader sectors are being affected,” says Ambassador Carlos Marcio Cozendey, undersecretary general for economic and financial affairs at the MRE.

The ruling by the WTO panel caused a commotion in the R&D environment, as companies that had qualified under several of those programs have been investing in innovation in return for tax exemptions. As the panel proceeded with its work, Brazilian diplomats argued that the WTO rules do not prohibit the granting of incentives to local industry or ban encouragement of R&D investments. “These are consistent with WTO rules and objectives to promote development on a sustainable basis, as Brazil sees it,” explains Rubens Barbosa, who was Brazil’s ambassador to Washington from 1999 to 2004 and is an advisor to the

Brazilian Electrical and Electronics Industry Association (ABINEE).

The terms of the appeal that Brazil will file with the WTO will be discussed in the coming weeks by representatives of the Ministry of Science, Technology, Innovation and Communications (MCTIC), the Ministry of Industry, Foreign Trade and Services (MDIC), and the Ministry of Foreign Affairs. It is expected that the 11 judges on the Dispute Settlement Body will rule on the appeal sometime in September 2017. At any rate, the Brazilian government is now preparing to change the disputed programs and negotiate deadlines for implementing those changes. If it does not modify the criticized policies, Brazil will be subject to retaliation by its partners in all areas of world trade. “We are familiar with the case law, and although we believe some measures will be reversed, it is possible that several programs will have to be modified,” says Ambassador Cozendey. Igor Nogueira Calvet, secretary of industrial development and competitiveness at the MDIC, says the new policies must preserve the requirement that favored companies invest in R&D. “We will discuss what the government will be able to offer the companies in order to demand a counterpart in the form of R&D. That is unlikely to take the form of a reduction in the federal value-added tax (IPI), as is now the rule,” he states. “The future will be determined by working closely with the private sector.”

In the case of the Information Technology Act, the government will attempt to preserve its essence by adapting it to WTO requirements. “This legislation was enacted in 1991. It predates the various treaties that form the foundation of the WTO and had never before been questioned,” says Maximiliano Martinhão, secretary of information technology policy at the MCTIC. “The Information Technology Act has become part of Brazil’s tradition and has helped its economic development.” According to the secretary, the law directly created 100,000 jobs, including 15,000 connected with R&D. According to ABINEE data, the amount of revenue lost because of exemptions or reductions in the IPI amounted to R\$25 billion in the years from 2006 to 2014, while taxes collected on the goods that benefited totaled R\$50 billion. Sales by companies of benefited



Ericsson telecommunications equipment facility in São José dos Campos, São Paulo State

products from 2006 to 2014 added up to R\$266 billion, while sums invested in R&D amounted to R\$8.3 billion in that same period. Martinhão believes that it is possible to adapt the legislation while preserving the willingness of companies to invest in R&D. “Europe grants incentives for production within its territory, but they are given to companies, not products. The WTO allows that. One possibility is for us to change the target of the incentive while maintaining the investments in R&D,” he explains.

Another alternative that may be evaluated, says Martinhão, is to accredit foreign companies to receive benefits under the Information Technology Act, requiring them to provide the same R&D counterpart by investing in companies that produce goods in Brazil. The main challenge, he says, is to modify existing programs as quickly as possible. “The worst thing in the world would be to take too long to approve the necessary changes in the law and leave manufacturers in legal limbo,” he notes.

The Information Technology Act grants tax incentives to manufacturers of electronic hardware and components that invest in R&D. The incentive, which is to remain in force until 2029, consists of an 80% reduction in the federal value-

added tax (IPI). Depending on the type of product, R&D investment must be equivalent to 3% or 4% of annual sales of favored goods. Investments can be made within the company itself, at universities, or under contract with third parties—which has led to the establishment in Brazil of a number of private research institutes that conduct custom-ordered studies for other companies (*see Pesquisa FAPESP Issue No. 248*). The law also requires that some of the funds be invested in formal agreements with institutes in the North, Northeastern and Central-West regions of the country. To receive benefits, a company must also adhere to the so-called Basic Production Process (PPB), which determines the amount of domestic content required for each kind of product.

“The Information Technology Act was the result of lengthy debates and legitimate negotiations in the National Congress, where legislators were concerned about maintaining the financial and economic equilibrium of the factories that opted to work under national information technology policy,” says Humberto Barbato, executive president of ABINEE. “The economic and social balance of the Information Technology Act has been quite positive. The scenario designed with the Internet of things will make digital inclusiveness even more present in people’s lives, and the legal framework for information and communications technologies will become more and more essential,” he argues.

The Inovar Auto program was created by a legislative provisional measure in April 2012. It established a regime that grants temporary tax advantages to

automobile assembly plants. The WTO panel rebuke focused principally on the benefits offered in the form of credits against a presumed IPI tax of as much as 30 percentage points per product to companies that satisfy criteria such as the installation of new industrial plants in Brazil or the adoption of new models of production. R&D outlays are among the counterparts required of recipients. According to MDIC data, between 2013 and 2015, approximately R\$15.3 billion was invested in research, development and engineering as a result of the program. Ambassador Rubens Barbosa believes it will be difficult to make modifications to Inovar Auto. “The government will probably have to abolish the program. It was already intended to end in 2017,” he says. Igor Calvet of the MDIC says that a new policy for the automobile industry is beginning to be discussed. “Inovar Auto fulfilled its purpose, which was to attract investment. Several companies established factories in Brazil and set up R&D support structures.”

To economist Sandra Polónia Rios, the outlook for auto assembly plants is the most troublesome of the effects of the WTO ruling. “The automobile industry has enormous idle capacity, which was actually encouraged by Inovar Auto, but there are no prospects of it being absor-

bed within a reasonable time frame,” she says. “This is a very serious problem because Brazil is not in a position to become an auto export platform, and there is little chance of growth in the domestic market.”

According to Rios, the announcement of the Inovar Auto program in 2012 may have been the catalyst that bred displeasure with Brazil in the WTO. “In recent decades, we have established several other industrial policy tools that preserved local content, such as the Free Trade Zone and the Information Technology Act, but they were less aggressive and not challenged,” she says. During the Rousseff administration, however, the use of these tools intensified as part of the 2011 Bigger Brazil Program, to which Inovar Auto was connected. “That made Japan and the European Union uncomfortable,” she suggests.

Representatives of World Trade Organization member countries meet at its Geneva headquarters in 2013

According to Counselor Daniela Benjamin, general coordinator of dispute settlement at the MRE, the concerns in Japan and the European Union about the proliferation of these programs in Brazil influenced their decision to take the issue to the WTO. “At the time, there had been an important discussion in Brazil about extending those regimes to other sectors, such as chemicals, and the complainants were worried that an expansion was going to occur,” said the diplomat at a public hearing held on December 15, 2016 in the federal Chamber of Representatives on the subject of the WTO panel. Soraya Saavedra Rosar, director of the International Negotiating Unit of the National Confederation of Industry (CNI), said at the same hearing that the ruling by the WTO panel creates a new scenario for negotiations about the country’s industrial policy. “Hereafter, when we draft a new law, we will need to more carefully examine the coverage of treaties on international trade that need to be respected,” she said. Redesign of those legal instruments will be a determining factor in shaping the future of the entrepreneurial R&D effort in Brazil, a topic that has gained greater importance since innovation became a key topic in both Brazil’s industrial policy and its science and technology policy. ■



WTO / STUDIO CASAGRANDE



A worrisome calm

The PINTEC survey found stability in the number of Brazilian companies that innovated between 2012 and 2014 and observed increasing difficulties for industry

Fabrício Marques

PUBLISHED IN JANUARY 2017

The 2014 edition of the Survey of Technological Innovation (PINTEC), published on December 9, 2016 by the Brazilian Institute of Geography and Statistics (IBGE), shows that the results of technological innovation efforts by Brazilian companies between 2012 and 2014 remained stable in relation to the preceding three-year period. Of the 132,529 public and private Brazilian companies surveyed in the industrial, selected services and electricity and gas sectors, 36% had introduced or improved products or made innovations in their processes. This percentage, which reflects the so-called overall innovation rate, was slightly higher than the 35.7% recorded in the previous edition of the research study, which evaluated companies during the three-year period of 2009-2011. The latest level remains below the 38.6% obtained in the survey conducted for 2006-2008.

While the innovation rate remained stable, other indicators reveal an increase in the number of obstacles in the path of innovation during the period studied by the survey, especially in the industrial sector, which accounts for 90% of the sample evaluated by the PINTEC. Industries invested 2.12% of their net sales revenue in innovative activities during the period, the lowest level ever recorded in the historical series of the survey. The 2011 rate was 2.37%, and the 2008 rate was 2.54%. These percentages include investment in internal research and development (R&D), acquisition of external know-how, software, machinery and equipment, training, introductions of market innovations, and industrial projects. "Industry was the sector that most strongly reflected the crisis, and the companies' attitude was merely reactive, focusing primarily on innovation in processes rather than products," says economist Alessandro Pinheiro, manager of the PINTEC.

In comparison, selected companies in the services sector increased their investment in innovative activities as a percentage of net sales revenue from 4.96% in 2011 to 7.81% in 2014. However, among electricity and gas companies, although the law requires them to invest in R&D, there was a decline in such in-

vestment, from 1.28% in 2011 to 0.57% in 2014. "Since the historical data series on electricity and gas companies is much shorter than the series for industries, it is best to await upcoming editions of the survey before assessing long-term trends," says David Kupfer, a professor at the Economics Institute of the Federal University of Rio de Janeiro (UFRJ) and coordinator of the university's Industry and Competitiveness Group.

Despite the reduction in investment, the innovation rate in the industrial sector rose from 35.6% in 2011 to 36.4% in 2014. In that universe, 18.2% of firms innovated only in processes, 3.8% innovated only in products, and 14.5% innovated in both products and processes. Some specific areas stood out. Among extractive industries, the percentage of innovative companies rose from 18.9% to 42% between the two surveys. In the case of manufacturing, this percentage increased from 35.9% in 2011 to 36.3% in 2014, but performance varied significantly among subsectors. In the automobile industry, the innovation rate rose from 29.1% in 2011 to 39.1% in 2014, while the chemical industry saw a decline from 59.1% to 49.6%.

"Innovation in Brazil moved sideways during this period," says David Kupfer.

"I was surprised that we did not see a decline. The years from 2012 to 2014 were not years of visible crisis, but respondents were answering the questionnaires in 2015, during a rather pessimistic period, the effect of which is likely to be reflected even more sharply in the next survey." Kupfer observes, however, that some analysts were expecting more robust results. "Brazilian business was coming out of a period of intense mobilization for the sake of innovation. Expenditures on R&D had been rising in several fields," he states.

Economist André Tosi Furtado, a professor in the Department of Science and Technology Policy at the Institute of Geosciences at the University of Campinas (IG-Unicamp), calls attention to the trend in a specific indicator used to measure industry's technological effort: the share of a company's net sales revenue represented by expenditures on internal R&D activities. "An intensification of internal R&D is evidence of the most noble and creative efforts in innovation, but that indicator did not perform well in the industrial sector in 2014. In periods of crisis, companies tend to focus on short-term results and curtail their investments; that seems to have happened with industry, which has been shrinking in terms of Brazilian GDP," he says.



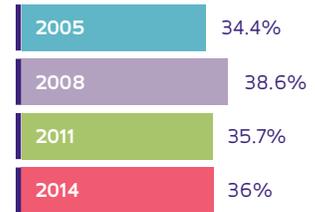
Both in sectors associated with the production of commodities and in those involved in supplying the market, internal R&D investment fell compared with the previous PINTEC, observes Furtado. In manufacturing as a whole, the indicator fell from 0.72% in 2011 to 0.68% in 2014. In some subsectors, the decline was modest. In the case of the automobile industry, despite government stimulus programs, such as Inovar Auto, it fell from 1.28% to 1.1%. In two sectors dominated by large companies that maintain well-structured R&D teams, the figures indicate a more accentuated reduction. In the cleaning products and cosmetics industry, R&D fell from 3.68% in 2011 to 1.1% in 2014, and in the home appliances sector, the drop was from 7% to 1.63%.

“These are not good omens. The retraction occurred in sectors that had been making progress in terms of intensification of R&D, such as pharmaceuticals and others that are vital to the R&D effort in Brazil, such as chemicals and oil,” says Furtado. Despite the bad news, the economist warns that one should not underestimate the ability of Brazilian companies to push back. “This country is still a considerable force in R&D, despite everything people are saying. When we compare ourselves with our neighbors and competitors in Latin America, like Argentina, Chile, or Mexico, we can see that those countries are making much less effort in terms of industrial R&D. I believe our efforts will continue, despite the downturn recorded in the latest PINTEC.”

The survey points to a change in the composition of investments in innovation in the industrial sector. There has been an expansion of company purchases of R&D from outside sources, i.e., R&D activities conducted by scientific and technological institutions or other companies. “It seems to be a sign that the so-called ‘open innovation’ is a strategy that companies see as having potential because of the possibility of joining efforts and sharing risks,” concludes Luciana Hashiba, director of the Brazilian Association for Research and Development of Innovative Companies (ANPEI), referring to the process of innovation based on an external network of partners, which may include

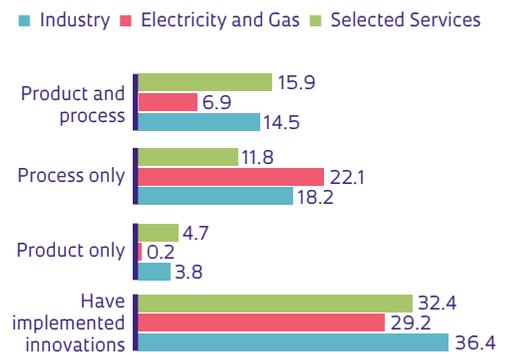
THE INNOVATION RATE HAS STABILIZED

Percentage of companies that innovated in products or processes, according to the last four editions of the PINTEC



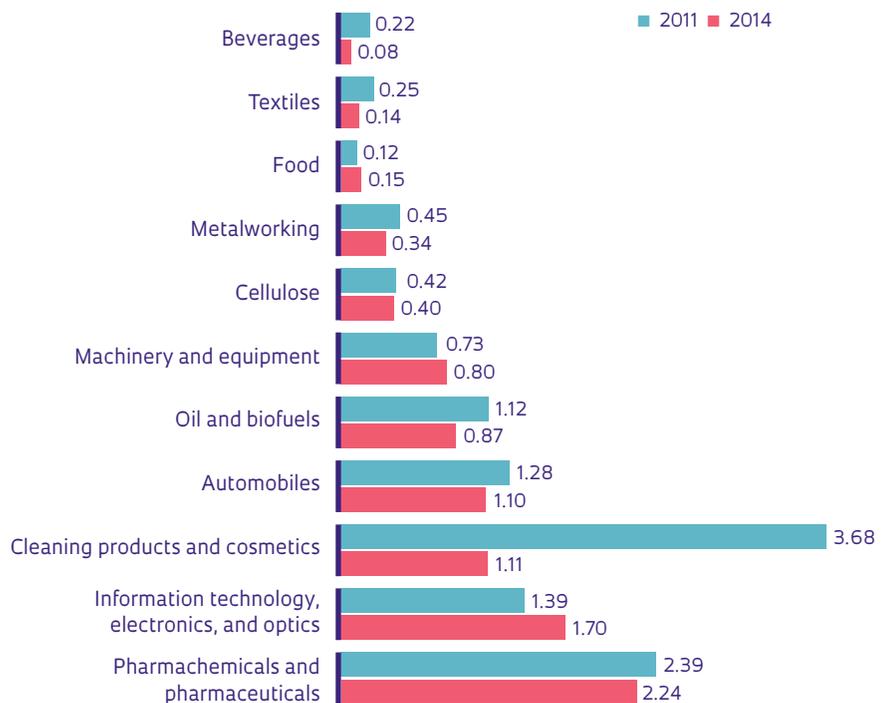
EFFORTS BY COMPANIES, BY TYPE OF INNOVATION

Percentage of total innovating companies that implemented innovations in products and processes, by business sector, according to type of innovation in Brazil, (2012-2014)



INTERNAL R&D ACTIVITIES IN INDUSTRY

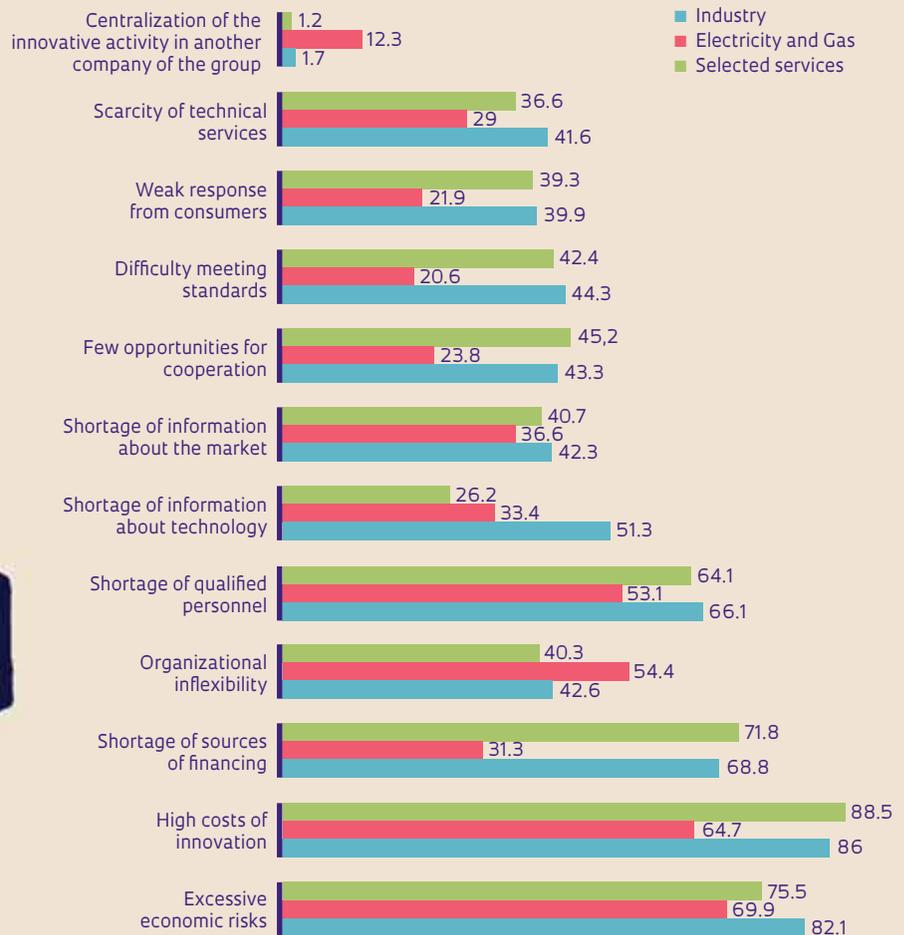
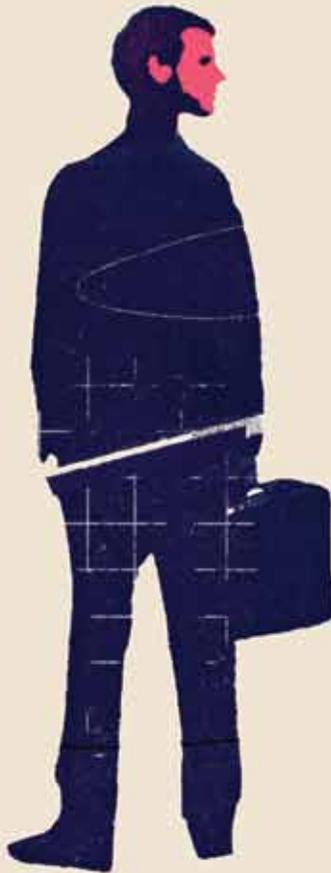
Percentage of net sales revenue invested in internal R&D activities – selected industrial sectors



SOURCES: IBGE, BOARD OF RESEARCH, INDUSTRY COORDINATION, INNOVATION RESEARCH 2014

ROCKY ROAD

Importance attributed to problems encountered by companies that implemented innovations in products or processes, by business sector in Brazil (2012-2014)



universities, nearby partners or partners from other countries, suppliers, and even competitors and customers. “We recently held a workshop at ANPEI and noted that various companies believe it is important to work within a network,” she says.

That trend is more visible in sectors such as cosmetics, where external purchases of R&D rose from 0.07% of net sales revenue in 2011 to 0.51% in 2014. “The search for outside sources is proof of the strategy adopted by companies to survive adverse conditions, but we know that you can’t subcontract all of your R&D. What is acquired elsewhere must be complemented by internal R&D in order for a

company to effectively appropriate it,” Unicamp’s André Furtado emphasizes.

Another important finding was the increase in the proportion of surveyed companies that had benefited from some kind of government incentive to innovate. The rate was 40%, compared with 34.2% in the previous survey. In the industries group, the percentage has been trending upward in the last three surveys, going from 22.8% between 2006 and 2008 to 34.6% between 2009 and 2011, and has now reached 40.4%. “It is reasonable to presume that government support was one of the factors that contributed to stability in the innovation rate,” says Alessandro Pinheiro, of the PINTEC.

The increase in the percentage of companies that declared they had re-

ceived government assistance does not mean, however, that the volume of funds invested has risen. According to a survey by the Federation of Industries of the State of São Paulo (FIESP), investment in R&D by companies that benefited from the so-called “Lei do Bem,” a set of tax incentives for R&D to boost innovation enacted in 2005, amounted to R\$6 billion in 2012, R\$9 billion in 2013, and R\$9.9 billion in 2014, a level lower than that observed in 2008, when it was R\$12.4 billion. “One thing is the percentage of companies that declared they had received support. The amount and form of that aid are something else. For example, the number of companies that used the “Lei do Bem” went up, but direct support via subsidies declined,”

says economist Carlos Américo Pacheco, Chief Executive Officer of the FAPESP Executive Board.

Luciana Hashiba of ANPEI notes that although government assistance programs are becoming more sophisticated, companies still have trouble using those tools. “Access is easier for large companies, and there are also tools for micro-enterprises, but small companies that are transitioning to medium-sized still have problems obtaining support because of the guarantees that are required,” she says, “A culture of innovation is created over the medium and long term. What we need to know is to what extent macroeconomic risk will be reflected in the companies’ predisposition to innovate and whether they will manage to regain their appetite for risk-taking.”

Financing for purchases of machinery and equipment was the main form of government support employed; it was obtained by 29.9% of innovative companies, 4.3% more than in the previous three-year period. Tax incentives for R&D and technological innovation that were available under the “Lei do Bem” were used by 3.5% of innovative companies, compared with 2.7% in the earlier survey. Government purchases of innovative products benefited 2% of the companies that innovated—in the industrial sector, that percentage was 1.4%. This was the first time that the PINTEC assessed the impact of government purchasing programs on Brazilian companies.

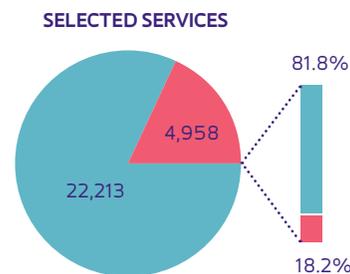
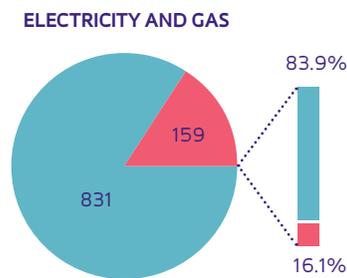
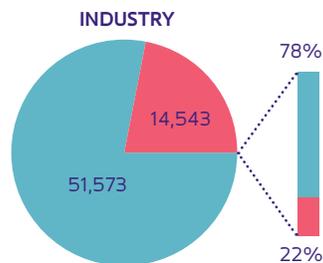
The electricity and gas sector was one of the most affected during the period analyzed by the PINTEC. Innovative companies in that sector represented 44.1% of the total surveyed in 2011 but only 29.2% in 2014. In the services sector, the performance of telecommunications services firms was big news in 2014. R&D investments in telecommunications jumped from just over R\$1.1 billion in 2011 to approximately R\$4.2 billion in 2014. “Investment in telecommunications services peaked in 2014. This was justified by the installation of new technologies and major events like the World Cup,” says Alessandro Pinheiro. “The volume of investments was enormous, and although the services sector in general is given relatively

WOMEN IN R&D

Participation by researchers occupied, exclusively and partially, in R&D activities but not dedicated full-time at companies that implemented innovations (2012-2014)



■ Men ■ Women



little weight in the PINTEC, it can be said that it helped sustain overall performance.” In telecommunications services, expenditures on innovative activities as a percentage of net sales revenue rose from 3.66% in 2011 to 9.99% in 2014. “It is important to note that this growth took place in purchases of external R&D, i.e., these are telecommunications service companies buying research and know-how from other companies, universities, or research institutions,” according to a technical note about PINTEC 2014, published by the Institute for Applied Economic Research (IPEA) and organized by economist Fernanda de Negri and her colleagues.

In 2014, of the total of 94,277 researchers involved in internal R&D activities pursued by innovative companies in Brazil, only 19,660, or 20.8%, were women. This was the first time that the PINTEC included gender in its survey. There are more women working in R&D in industry (22%) than in services (18.2%) or in electric and gas companies (16.1%). Among those involved in R&D activities at companies, 63.4% are researchers, 28% are technical personnel, and 8.6% are assistants. In 2011, there were more researchers (65.3%) and fewer technical staff (26.4%) and assistants (8.4%). Regarding the educational background of people working in R&D, 71.5% had a college education; 61.4% had undergraduate degrees; and 10.2% had advanced degrees. In 2011, 69.2% of all individuals working in R&D had a college education, with 58.5% holding undergraduate degrees and 10.7% advanced degrees. ■



A map of scientific competencies

Study shows where researchers are concentrated and describes the impact of their production in the 15 administrative regions of the state of São Paulo



Fabrcio Marques

PUBLISHED IN MARCH 2017

In February 2017, the Academy of Sciences of the State of São Paulo (ACIESP) introduced a survey regarding the scientific competencies of each of the 15 administrative regions of the state. Titled *Map of Science in São Paulo*, the study assembles a set of indicators from 2002 to 2011 that show everything from the concentration of researchers in each region and their fields of knowledge to the size and impact of their scientific production. Also included are graphs that group the researchers according to the number of articles published in two time periods—over the entire 10 years of the study and between 2009 and 2011. “This is a snapshot of São Paulo science during the first decade of the 21st century. It shows the different kinds of expertise by region in this state that is directly responsible for half of all Brazil’s scientific production,” says Marcos Buckeridge, a professor at the Biosciences Institute of the University of São Paulo (USP) and president of ACIESP. “The idea was to have a data platform that can be con-

sulted by entrepreneurs interested in opening new businesses, for example. There they will find out the location of well-established researchers who could help them deal with their challenges,” says José Eduardo Krieger, dean of research at USP who was president of ACIESP until 2015, when the study was commissioned. The entire map can be seen at bit.ly/MapaCiênciaSP.

Sponsored by Banco Bradesco, the map, as was expected, shows a heavy concentration of researchers along the São Paulo-Campinas axis. However, it also reveals some nuances. The São Paulo Metropolitan Region (SPMR), the site of two USP campuses as well as public universities such as the federal universities of São Paulo (UNIFESP) and the ABC (UFABC) and private institutions such as Mackenzie or the Getúlio Vargas Foundation, has the most scientists in nearly every field of knowledge. However, the lead is more significant in some fields. This is true of Applied Social Sciences, with 59% of the state’s researchers; Health Sciences, with 54.9%;



DENSITY OF RESEARCHERS

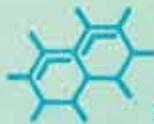
The science occupations of each of the 15 administrative regions of the state of São Paulo, comparing the percentage of the local population with the percentage of researchers in selected fields of knowledge

SOURCE: MAP OF SCIENCE IN SÃO PAULO / ACIESP

São Paulo Paraíba Valley

5.48% of the state's population

HIGHLIGHTS
Engineering, with 15.2% of the state's researchers; and Exact and Earth Sciences, with 10.8%



Presidente Prudente

2.05% of the state's population

HIGHLIGHTS
Human Sciences, with 2.4% of the state's researchers; and Agricultural Sciences, with 2.1%



Piracicaba

3.33% of the state's population

HIGHLIGHT
Agricultural Sciences, with 15.3% of the state's researchers

Araçatuba

1.69% of the state's population

HIGHLIGHTS
Agricultural Sciences, with 3.2% of the state's researchers; and Engineering, with 2.4%

São Paulo Metropolitan Region

51.27% of the state's population

HIGHLIGHTS
Social and Applied Sciences, with 59% of the state's researchers; Health Sciences, with 54.9%; Linguistics, Literature, and Arts, with 54.3%; and Human Sciences, with 51%

Campinas

9.17% of the state's population

HIGHLIGHTS
Agricultural Sciences, with 22% of the state's researchers; Engineering, with 18.5%; Exact and Earth Sciences, with 16.6%; and Linguistics, Literature, and Arts, with 15.1%

Ribeirão Preto

5.76% of the state's population

HIGHLIGHTS
Agricultural Sciences, with 13.6% of the state's researchers; Biological Sciences, with 11.4%; Health Sciences, with 10.5%; and Human Sciences, with 6.3%

São José do Rio Preto

3.8% of the state's population

HIGHLIGHT
Linguistics, Literature, and Arts, with 4.3% of the state's researchers



Assis

1.34% of the state's population

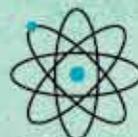
HIGHLIGHT
Linguistics, Literature, and Arts, with 3.3% of the state's researchers



Bauru

3.53% of the state's population

HIGHLIGHTS
Agricultural Sciences, with 11.1% of the state's researchers; Health Sciences, with 6.4%; and Biological Sciences, with 6.3%



Marília

1.1% of the state's population

HIGHLIGHTS
Human Sciences, with 2.7% of the state's researchers; and Applied Social Sciences, with 1.9%



Macrometropolitan region

Region of Jundiaí and Sorocaba

6.4% of the state's population

DIAGNOSIS
Limited density of researchers. Varies from 1.7% of the state's researchers in Exact and Earth Sciences to 2.6% in Human Sciences

Itapetininga

2% of the state's population

DIAGNOSIS
Very low density of researchers. Varies from 0.06% of the state's researchers in Health Sciences to 0.5% in Agricultural Sciences

São Paulo Southern Coastal Region

1.12% of the state's population

DIAGNOSIS
Very low density of researchers. Varies from 0% of the state's researchers in Linguistics, Literature, and Arts, to 0.5% in Agricultural Sciences

Linguistics, Literature, and Arts with 54.3%; and Human Sciences, with 51%. In other fields, leadership occurs but by smaller margins. In Exact and Earth Sciences, 38% of researchers live in the SPMR. The regions of Campinas (16.6%) and Araraquara (15.3%) rank second and third. However, in Engineering, São Paulo is at the top of the list, with 36.8% of all researchers, followed by Campinas (18.5%) and the Paraíba Valley region (15.2%). "The survey shows clearly that, although competencies are concentrated in the SPMR, other parts of the state exhibit specific areas of expertise," says Buckeridge, referring to the Araraquara Metropolitan Region, which boasts USP campuses, the São Paulo State University (UNESP), and the Federal University of

São Carlos (UFSCar) while in the Paraíba Valley an aerospace hub has emerged around São José dos Campos.

There is one field of knowledge in which the São Paulo Metropolitan Region does not contain the largest contingent of science professionals. This area is Agricultural Sciences, in which Campinas appears with 22% of the state's researchers, followed by São Paulo, with 19.3%; Piracicaba, with 15.3%; and Ribeirão Preto, with 13.6%. "What created the equilibrium is the presence in the Campinas region of the Agronomic Institute and the University of Campinas (UNICAMP)," Buckeridge says. "In turn, the significance of Piracicaba relates to the Luiz de Queiroz College of Agriculture, which is part of USP."

Economist Marcelo Pinho, a professor at UFSCar, recommends caution when making comparisons among regions. "The comparability of the data is impaired by the enormous disparity between the dimensions of the mesoregions in both demographic and economic terms," he says. He notes that the SPMR has approximately 20 million residents while the Araraquara region has yet to reach one million. "It would be more prudent to filter that difference by evaluating scientific production per 100,000 residents or by GDP," he says. According to Pinho, the concentration of researchers in greater São Paulo should attract attention only after it exceeds 50%, the figure corresponding to the percentage that the capital city and its vicinity represent in the state population as a whole. "That happens only in Health Sciences and in the group of subject fields associated with Humanities and Social Sciences, including Linguistics, Literature, and Arts."

Having expressed those reservations, Marcelo Pinho says that the data reflect regional concentrations of competencies that were already known. "It is not surprising that the Piracicaba region, which has less than 4% of the state's population accounts for 15% of the researchers in Agricultural Sciences and occupies an even more prominent position, considering researchers that exhibit the highest productivity. Something similar can be said of the Araraquara mesoregion, which includes São Carlos, with regard to Engineering and Exact and Earth Sciences. With approximately 2% of the

A SAMPLE OF THE MAP OF SCIENCE IN SÃO PAULO

Total number of researchers and their scientific production (articles, citations, and citations per article) in the field of Health Sciences, between 2002 and 2011, in the 15 administrative regions



SOURCE: MAP OF SCIENCE IN SÃO PAULO / ACIESP

São Paulo Metropolitan Region

7,708 researchers
65,769 articles
822,764 citations
12.51 citations per article

Campinas

1,398 researchers
10,916 articles
130,672 citations
11.97 citations per article

Macrometropolitan

296 researchers
949 articles
7,052 citations
7.43 citations per article

It takes about 20 years for a scientific competency to become well-established in a region, says UNICAMP's Renato Garcia

state's population, that region is home to 14% and 15% of the researchers in those two fields of knowledge, respectively," he says. According to Pinho, the data confirm the presence of a reasonable degree of spatial distribution of scientific capabilities throughout the state. "This is a positive result of the policies that have been followed for many decades, namely the deconcentration of the locations of universities and research institutions.

To Renato Garcia, a professor at the Economics Institute of UNICAMP, the data from the map suggest that policies

in recent years have encouraged a greater concentration of scientific activities rather than a decentralization. "There has been an expansion of higher education, but most of it occurred near the city of São Paulo," he says, referring to the establishment of the UFABC and installation of UNIFESP campuses in the cities of Santos, Diadema, Guarulhos, São José dos Campos, and Osasco. "In most cases the expansion was not designed to promote regional development," he says. Even in the case of the UFSCar campus installed in Sorocaba in 2011, says Garcia, the local impact will not be felt for some time. "They are hiring researchers who have potential and are already attracting master's candidates, but doctoral students are still opting to attend more well-established centers. It takes about 20 years for a scientific competency to become well-established in a region."

The analysis used as its starting point the figures compiled by the Research Groups Directory (DGP) of the National Council for Scientific and Technological Development (CNPq), which compiles information on Brazilian researchers on its Lattes Platform. When studying the production by São Paulo State researchers on the DGP site, names of other collaborators emerged – expanding the size of the survey universe to 1.2 million résumés. Using information technology tools, the data were checked to prevent double

Ribeirão Preto

1,473 researchers
16,554 articles
183,765 citations
11.10 citations per article

Presidente Prudente

117 researchers
386 articles
2,523 citations
6.54 citations per article

Marília

182 researchers
602 articles
4,891 citations
8.12 citations per article

São José do Rio Preto

322 researchers
1,510 articles
10,615 citations
7.03 citations per article

Piracicaba

462 researchers
5,121 articles
60,704 citations
11.85 citations per article

São Paulo Paraíba Valley

327 researchers
1,809 articles
12,550 citations
6.94 citations per article

Bauru

898 researchers
7,925 articles
76,210 citations
9.62 citations per article

Araraquara

615 researchers
4,858 articles
43,270 citations
8.91 citations per article

Assis

38 researchers
123 articles
1,446 citations
11.76 citations per article

São Paulo Southern Coastal Region

3 researchers
4 articles
50 citations
12.5 citations per article

Itapetininga

8 researchers
30 articles
106 citations
3.53 citations per article

Araçatuba

178 researchers
1,826 articles
11,894 citations
6.51 citations per article

counting and cross-checked against data on citations from Google Scholar. The methodology developed was refined under a project supported by FAPESP as part of its Innovative Research in Small Businesses Program (PIPE) program. “For some years, we had been developing scientific-technological databases and tools for treating and analyzing data, but the PIPE project provided for the improvements and further sophistication of the tools that we used in constructing the Map of Science and in other projects,” says computer engineer Luiz Daniel Lapolla, of Elabora P&D, Computação e Sistemas de Informática.

The survey shows that significant knowledge can be produced even in regions where the concentration of researchers is not particularly notable. The study reports the number of articles produced in each region by field of knowledge, the citations that those papers obtained, and the relationships between articles and citations. Again, taking Agricultural Sciences as an example, we find that the Paraíba Valley produced only 785 articles between 2002 and 2011; however, they were the target of 10,707 citations, resulting in 13.64 citations per article. That ratio is better than the ratio for Campinas (7,684 articles and 67,451 citations) with 8.78 citations per article or for Piracicaba (7,118 articles

with 60,829 citations) with 8.55 citations per article.

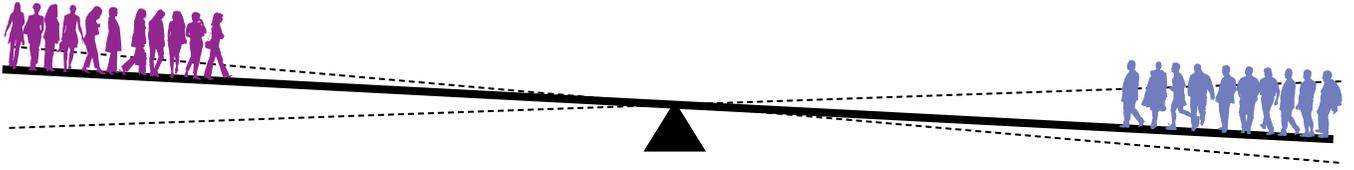
In some regions both the concentrations of researchers and scientific production are low. The extreme cases are São Paulo’s Southern Coastal region, which has 17 municipalities surrounding Itanhaém and Registro, and the contiguous Itapetininga region with 35 municipalities. Both have only a few dozen researchers in each field of knowledge. The gaps in terms of science coincide with areas of low economic activity. The Southern Coastal region includes the Ribeira Valley, one of the poorest areas in the state. Its annual per capita GDP is R\$24,500 according to Brazilian Institute of Geography and Statistics (IBGE) figures for 2013. In Itapetininga, income is even lower at R\$22,600 per inhabitant. In contrast, the per capita GDP in the SPMR is R\$44,400 a year, and in Campinas it is R\$41,600. Marcos Buckeridge compared the data from the Map of Science with the Human Development Index (HDI) for the regions. “There is a correlation with the income indicators from the HDI, but they take off after the number of researchers in a region passes the 2,000 mark,” he says. Buckeridge has observed a relationship, albeit less significant, between scientific performance and indicators of population longevity—but found no correlation with education. “The knowledge

generated by the universities seems to have very little influence on the basic education system.”

Encouraging scientific activities in those areas poses a challenge, but in the opinion of José Eduardo Krieger it would not be necessary to establish new universities there. “The resources need to be allocated where scientific competencies already exist. What is essential is to identify local vocations and support them,” he states. Renato Garcia argues that one cannot ignore the effect that the establishment of a university or technology hub has on a city. “A campus can change the face of a municipality. It encourages urbanization and attracts people of a high intellectual level, which generates new demands,” he says. “Even the risk of researchers becoming isolated diminishes because of opportunities to collaborate at a distance using information technology.” Garcia warns that we should not expect the same effect on the transfer of knowledge to companies. “For that to occur, there has to be demand. If there are no companies in the region, demand will not exist.” ■

Project

Elabminer: Order and predictability in web mining workflows. (No. 12/50119-1); **Grant Mechanism** Innovative Research in Small Businesses Program (PIPE); **Principal Investigator** Gabriel Dieterich Cavalcante (Elabora); **Investment** R\$ 78,989.80.



THE SEARCH FOR BALANCE

A report released by Dutch publisher Elsevier on March 8—International Women’s Day—presents an unprecedented statistical comparison of the scientific output of men and women in 27 fields of knowledge. The study analyzed data from 11 countries and the European Union, demonstrating a general trend towards gender balance in science over the last 20 years. Between 1996 and 2000, women accounted for more than 40% of researchers in only one country: Portugal. Between 2001 and 2015, several other countries joined this club, including the United States, the United Kingdom, Australia, Canada, France, Denmark, and Brazil, as well as the European Union.

The full report is available at bit.ly/GeneroCiencia.

The proportion of men versus women was measured by identifying and counting authors published in the journals indexed in Elsevier’s Scopus database, which includes more than 62 million articles published in more than 21,500 scientific publications. Titled “Gender in the Global Research Landscape,” the report highlights Brazil as one of the countries that has made the most progress, according to its indicators. “In Brazil and Portugal, women account for 49% of the researcher population, while in Japan, the proportion of women in science remains much lower,” says microbiologist Holly Falk-Krzesinski, vice-president of academic relations at Elsevier and a member of the project team that pro-

A study comparing scientific output by women in a range of countries highlights Brazil’s improvement

Fabrcio Marques

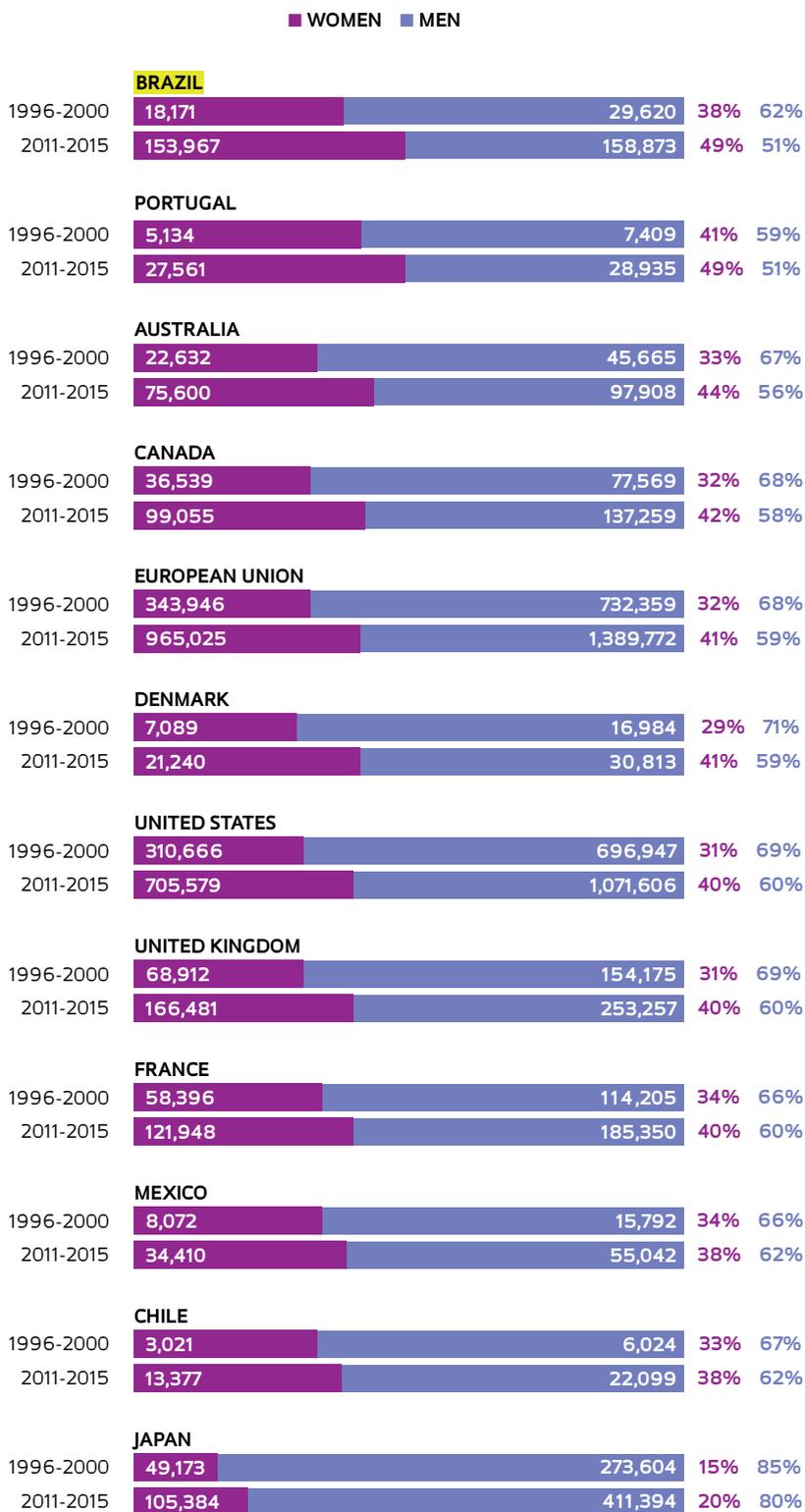
PUBLISHED IN APRIL 2017

duced the report, according to the website Inside Higher Ed. Brazilian authors published between 2001 and 2015 consisted of two nearly equivalent populations: 153,967 women and 158,873 men, accounting for 49% and 51% of the total, respectively. The proportion observed between 1996 and 2000 was 62% men and 38% women, although the indicators for the two periods cannot be directly compared because the number of Brazilian journals in the Scopus database at the end of the last century was much lower than at present.

Brazil also appears to be relatively balanced within a certain indicator subgroup. The presence of female authors in the field of engineering is one example. Of the total Brazilian output in this field between 2011 and 2015, women were the first or corresponding authors of 48% of papers—compared with a rate of 44% in the United Kingdom, 43% in the United States, and 35% in Japan. Another indicator analyzed was the number of female and male inventors, which was 19% women and 81% men in Brazil, less of an imbalance than in most other countries, except for Portugal, where 26% of inventors were women. In Japan, 8% of inventors were women, compared to 14% in the United States 14%—although in absolute terms, these two countries have 60 to 90 times more inventors than Brazil. The number of inventors is based on the number of patent applications registered on the World Intellectual Property Organization (WIPO) database.

MALE AND FEMALE RESEARCHERS

Evolution of the absolute number and percentage of authors of scientific papers in 11 countries and the European Union, distinguished by gender*



* The data refer to researchers who published papers and whose name and gender were declared on the Scopus database or were identified using other software

SOURCES SCOPUS, GENDERIZE, NAMSOR, AND WIKIPEDIA

Biologist and information scientist Jacqueline Leta, a professor at the Federal University of Rio de Janeiro (UFRJ) and an expert on gender issues in science, says that cultural traits and forms of scientific organization in the country may help explain why female researchers in Brazil seem to face fewer obstacles than those in other nations. “Women abroad may be less able to leave household tasks in the hands of others. In other countries, it is more difficult for women to delegate home and family issues,” she says. Certain characteristics of the Brazilian scientific community, whose activity is highly concentrated in public institutions, may also be associated with more stable research careers for both men and women. “Our system is more rigid than other nations, where there is more research activity in industry, links with institutions are often temporary, and researchers have greater mobility between institutions and countries.”

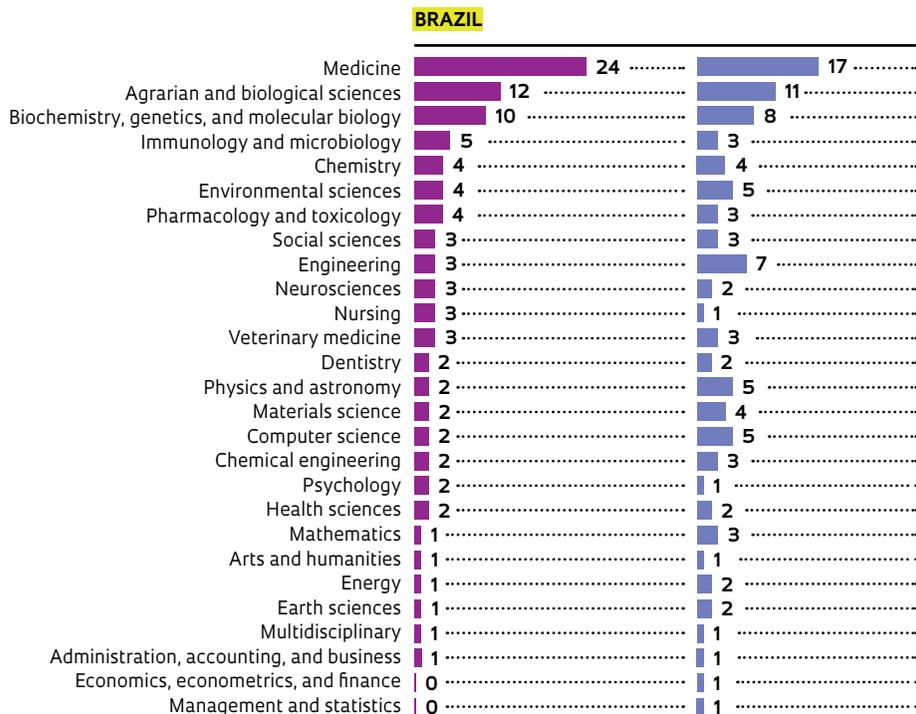
However, this stability does not favor a more egalitarian division in the occupation of university positions, says the researcher. Eight years ago, she conducted a study that analyzed 1,946 professors at UFRJ and concluded that, with the exception of the arts, humanities, and languages, the percentage of women involved in graduate research was always lower than the proportion of women as professors. “UFRJ has never had a female dean. There were two female candidates in the last selection process, both very qualified, but in the end, a man was given the position,” she says.

THE LEAKY PIPELINE

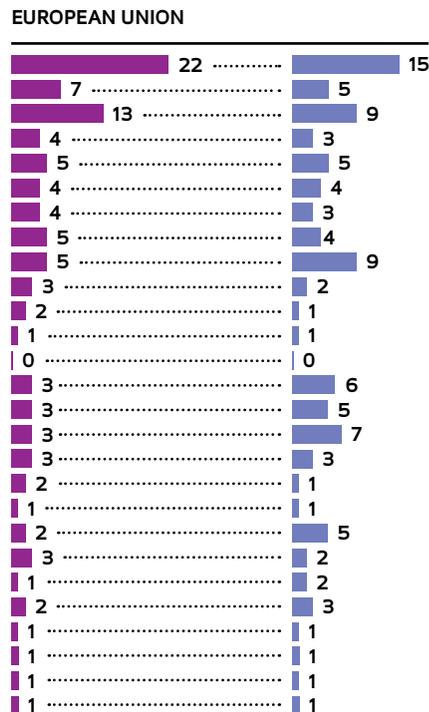
A lack of women in positions of prestige is a problem in many countries. The Elsevier report refers to this phenomenon as a “leaky pipeline,” suggesting that while academics of each gender begin academia together, the proportion of women decreases at each career stage. In an interview published in the report, James Stirling, provost of Imperial College, UK, discusses this problem: women account for 35% of undergraduates in the institution’s science, technology, engineering, and mathematics programs, but only 15% of professors in these fields are female. “Not enough women are coming in to STEM subjects, and when they do come in, they are not reaching the highest ranks in the pro-

ON THE TREE OF KNOWLEDGE

How the authors of scientific articles are divided by gender and field in two regions (in %)



■ WOMEN ■ MEN



SOURCES SCOPUS, GENDERIZE, NANSOR, AND WIKIPEDIA

fession,” he says. As well as participating in a program designed to strengthen the commitment to gender equality in UK research institutes, Imperial College wants to combat the prejudices hindering women in recruitment and career advancement. “It is an unconscious bias, but it can be combated through training programs.” While there is a gender balance among Brazilian authors in general, the situation depends on the discipline under analysis. In a phenomenon common to other countries, women in Brazil account for only 23% of authors in the field of computer science, 24.8% in mathematics, 28.2% in economics, and 33% in physics and astronomy. In other fields, such as nursing (72.9%), immunology and microbiology (58%), neurosciences (55.8%), and medicine (55.4%), they are the majority. The report notes that the percentages of female representation were lower between 1996 and 2000 than between 2011 and 2015. In engineering, the proportion of Brazilian authors was 16% between 1996 and

WOMEN PUBLISH FEWER ARTICLES THAN MEN BUT THERE IS NO EVIDENCE THAT THIS AFFECTS CITATIONS

2000, rising to 29% in the more recent period. “This relatively rapid change over time disputes previous suggestions of ‘sex differences in general intelligence with a male advantage appearing in adolescence’ and suggests instead that the problem is social and cultural in nature,” states the report.

Sociologist Maria Teresa Citeli notes that there are specific explanations for the higher number of females in some fields. “In the past, it was said that the greater participation of women in certain fields, such as developmental biology, was related to female characteristics, such as motherhood. But the fact is that the field of biology was developing at a time when women were entering the labor market. It is easier to enter a nascent field,” says Teresa, who was a researcher in the Department of Science and Technology Policy at the University of Campinas (UNICAMP).

COLLABORATIONS

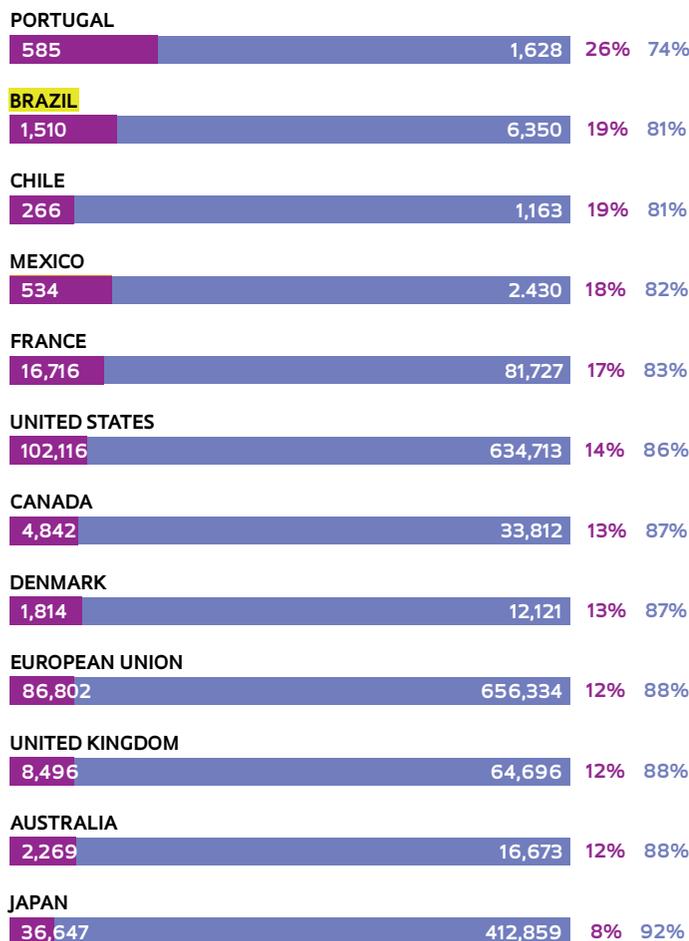
The Elsevier report presents further conclusions on the performance of women in science. It shows that female researchers publish less than men in general, although there is no evidence that this affects citations and downloads of their articles. In Brazil, the mean number of articles published by women between 2011 and 2015 was 1.2, compared

GENDER AND INNOVATION

Absolute number and proportion of inventors by gender between 2011 and 2015

SOURCE WIPO – OCTOBER 2016

■ WOMEN ■ MEN



with 1.5 articles published by men. This score is low compared to other nations: Denmark and Australia averaged 2.2 articles for women and 2.8 for men. The study also indicates that women generally have less professional experience abroad than men and tend to establish fewer scientific collaborations. Finally, female scholarly output has a slightly greater tendency to focus on interdisciplinary fields.

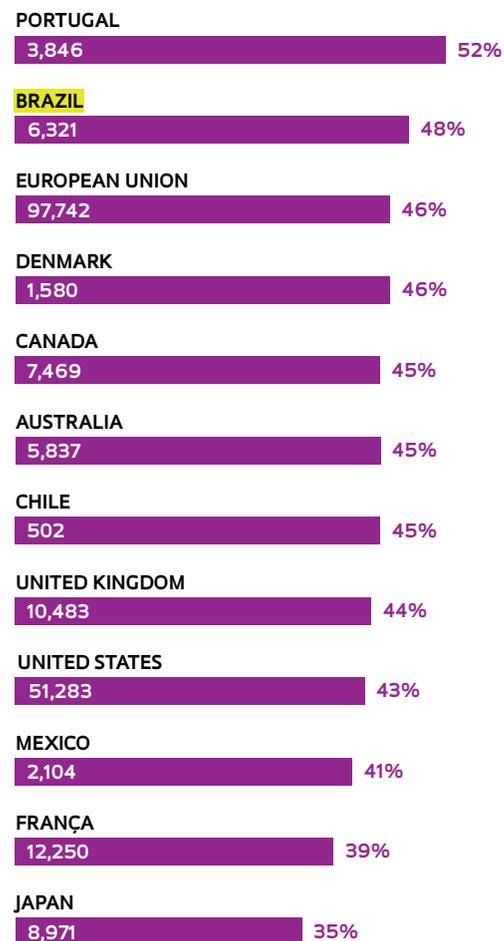
One notable aspect of the survey is its methodology. Although the first name on a scientific paper is usually represented only by an initial, Scopus maintains a record of authors and their full names. However, information about the gender of each researcher is not always

available, so that in such cases, other sources are needed. The study used the Genderize database, which contains thousands of names from 79 countries and the proportions of men and women with each specific name. This was used to calculate the probability that a researcher was female or male, given their name. Not all registered authors were included in the study. A gender was attributed to an author only when the name appeared on Genderize at least five times, and the chance that it was male or female was over 85%. Another data source, called NamSor, uses sociolinguistic data to help identify a name based on the researcher's country—for example, an author named Andrea is

WOMEN IN ENGINEERING

Number and percentage of articles in the field of engineering, where the first author and/or corresponding author are female

SOURCES SCOPUS, GENDERIZE, NAMSOR, AND WIKIPEDIA – FROM 2011 TO 2015



probably a man in Italy but more likely a woman in other countries.

“Most previously published articles used small samples or case studies precisely because of the difficulty obtaining comparable data from several countries, but Elsevier has come up with a way to overcome this barrier,” says Jacqueline Leta. Teresa Citeli believes we need to know more about this methodology before we can properly incorporate it into studies of science and gender. “This is an innovative approach with eloquent and favorable conclusions on the increasing presence of women in science. The result also has political implications, because it could lead to more women starting careers in science.” ■

Weight

across generations

Among rats, the effects of excessive or insufficient feeding can be transmitted to children and grandchildren

Reinaldo José Lopes

PUBLISHED IN FEBRUARY 2017

Experiments conducted on rats by researchers from universities in São Paulo reinforce the idea that being overweight may be a phenomenon that transcends generations. This is not just because children tend to inherit genes that favor calorie accumulation and predispose them to obesity, or because they live in an environment with excessive amounts of food available. Through mechanisms that remain poorly understood, alterations in the female's food supply shortly before or during pregnancy appear to increase the likelihood of producing overweight children and grandchildren.

In a series of experiments, biologist Maria Martha Bernardi and her team at Paulista University (UNIP) fed a high-calorie diet to female rats at the start of their reproductive lives, as well as to rats that were pregnant, to determine what would happen to the first generation of pups and their offspring. The offspring that were born to overfed mothers, as well as those of the subsequent generation, were more likely to become overweight.



The tendency towards excessive weight gain occurred even when the children and grandchildren of these rats were fed only the standard laboratory diet. According to Bernardi, this indicates that the period of fetal development *in utero* is crucial in defining that animal's metabolic regulation as well as the metabolic regulation of at least one subsequent generation.

If these changes only appeared in the first generation, a natural conclusion would be that hormonal alterations resulting from the maternal diet affected the offspring. However, since this effect continues into the second generation, researchers suspect that the propensity to gain weight may be regulated by epigenetic mechanisms—alterations in the way genes are turned on and off—resulting from environmental factors such as diet, and thus transmitted to subsequent generations. Changes to the gene activation profile do not directly alter the DNA sequence, even though they are inherited over generations. Although Bernardi's group has not analyzed the gene activity pattern, data obtained by scientists worldwide indicate that changes to the gene activation profile without alteration of the DNA sequence, may occur in both animals and humans.

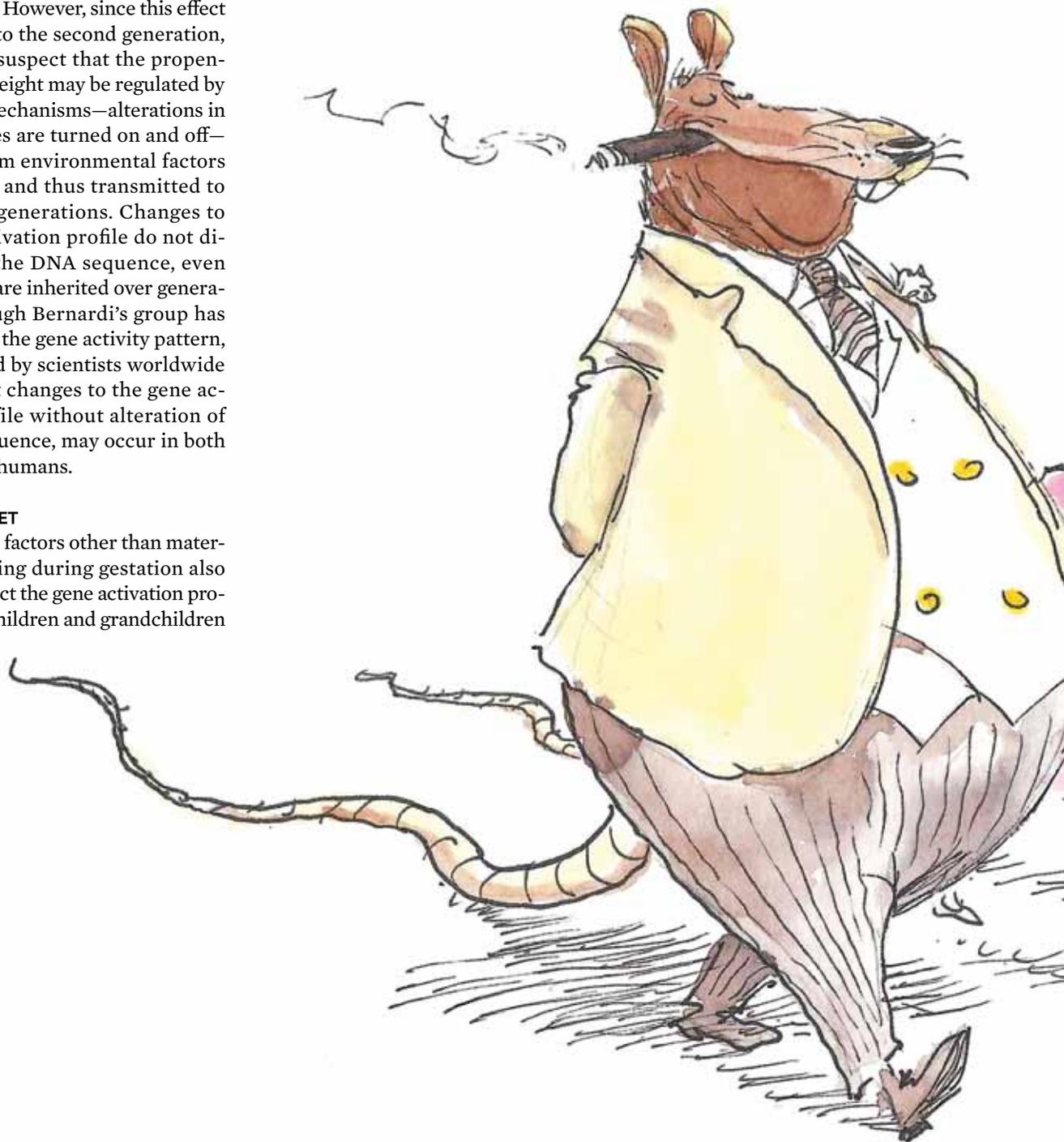
FATTENING DIET

Interestingly, factors other than maternal overfeeding during gestation also appear to affect the gene activation profile, leaving children and grandchildren

Offspring born to overfed mothers were more likely to become overweight

with a tendency to gain weight. In one experiment conducted in partnership with researchers from the University of São Paulo (USP), the Federal University of the ABC (UFABC) and the University of Santo Amaro (UNISA), 12 pregnant female rats received 40% less food than normal, and eight control rats were fed the standard laboratory diet.

The female rats who received the restricted diet during pregnancy gained less than half the weight of the females



who were fed *ad libitum*. Offspring of the feeding-restricted mothers were born smaller and continued to be thinner for some time, even though they received the same amount of food as the offspring fed *ad libitum*. The difference only disappeared when the offspring entered adulthood and the two groups of rodents attained similar weights, although the offspring of the hungry rats had more body fat, particularly visceral fat, which accumulates between organs and is associated with a higher risk of cardiovascular problems.

The most important difference appeared in the second generation. The grandchildren of the feeding-restricted rats were born smaller but then became slightly heavier as adults (from 10% to 15%) than the grandchildren of the rats fed *ad libitum*. These rats had more visceral fat, as well as signs of brain

inflammation. This extra weight gain occurred in the offspring even though their first-generation mothers were fed normally. As per the authors of a May 2016 article published in *Reproduction, Fertility and Development*, it appears as though the food deprivation suffered by the rats in the initial generation led to lasting metabolic reprogramming in their descendants.

Food deprivation in the initial generation led to lasting metabolic reprogramming in their descendants

Regarding this point, the work by the São Paulo team confirms previous studies that found an association between episodes of hunger during pregnancy and the birth of children with a propensity to gain excess weight and the health problems associated with it. Although they did not identify the specific mechanism for this effect, Martha Bernardi and her team suspect that compounds produced by the bodies of the original generation mothers who were deprived of food during pregnancy, activate genes that favor rapid weight gain in the pups. Thus, chemical signals released by the mother act as a warning that food is scarce in the environment and that available food resources must be used efficiently. That signal received by the pups' offspring, could represent the chance to grow and survive in an environment with limited food. "But, it can also lead to obesity, if the food supply returns to normal after they are born," explains Bernardi.

Studies conducted in previous decades described a similar situation among the descendants of women who became pregnant during the so-called *Hongerwinter* (winter of hunger, in Dutch), at the end of World War II, when Nazi armies that were retreating from the Allies cut off a large portion of the food supply to Holland between late 1944 and early 1945. Both the children and grandchildren of *Hongerwinter* survivors had obesity rates and metabolic problems that were higher than those of the general population.



INFLAMMATION IN THE BRAIN

In another study, Bernardi and her colleagues administered hypercaloric feed—a mixture of standard feed plus a liquid supplement rich in different types of fat—to 10 female rats immediately after weaning, while a control group of female rats received normal feed. As expected, the female rats fed the hypercaloric diet as babies were overweight, albeit not obese, upon reaching puberty. Similar effects were observed in their daughters: they were rats that were overweight as adults and suffered metabolic alterations, such as visceral fat accumulation, although they had only been fed a balanced diet for their entire lives. Also published in *Reproduction, Fertility and Development*, this study, as well as others by the group, indicate that being overweight triggered the inflammatory processes that affected the brains of the mothers and their offspring, in a lasting manner.

If it seems strange that excess weight can lead to cerebral inflammation, it must be emphasized that fat cells are more than just calorie deposits. Also known as adipocytes, fat cells produce many substances, including inflammatory molecules, which reach the bloodstream and travel to the hypothalamus, the region of the brain associated with several functions, including hunger control.

Unpublished studies by the UNIP group also indicate that this inflammation affects other areas of the rodent brain. The researchers hypothesize that the inflammatory

Being overweight triggered the inflammatory processes that affected the brains of the mothers and their offspring

process in the brain is related to the re-programming signals transmitted from the mother to her pups, including altered appetite control, which may continue throughout adulthood.

For Alicia Kowaltowski, a researcher at the USP Chemistry Institute who studies the relationship between diet and energy production mechanisms in cells, it is likely that the tendency to become overweight or obese is passed from one generation to the next by means other than inheriting genes that favor weight gain. “The question is to find out which mechanisms are behind these phenomena,” states the researcher.

Among these potential mechanisms, one that has attracted interest is epigenetic transformation. The Greek prefix, *epi*, means superior, and the word epigenetics, coined by English embryolo-



Viewing excess weight from the prism of epigenetics can provide another piece of the puzzle in the global obesity epidemic



gist Conrad Waddington in the 1940s, designates the branch of biology that studies chemical changes caused by the environment that lead to activating or inactivating genes and altering body functions. One common chemical modification that genes undergo is methylation. This occurs when a methyl group, formed by one carbon atom and three hydrogen atoms (CH_3), attaches itself to a section of DNA, preventing it from being read by the cell machinery, resulting in the silencing of that region.

Studies on several species of animals, plants and fungi have shown that methylation profiles can be transmitted from one generation to the next, affecting the characteristics of the offspring.

PATERNAL INFLUENCE

The mother's role in producing overweight offspring seems to be clear. However, what about the father's role? "There is some evidence that there may also be a paternal influence, but this evidence is not as clear," says Martha Bernardi. It would make sense for epigenetic influences to be transmitted paternally, as with other cells in the body, sperm are affected by altered gene activation patterns resulting from environmental influence. If these changes remain after the male cells and the ova come together, the offspring could carry part of its father's epigenetic memory.

A 2015 study conducted by a team led by Romain Barrès from the University of Copenhagen, Denmark, showed that this scenario is plausible by studying the sperm of 16 obese men and the sperm of 10 normal weight men. In the obese volunteers, epigenetic patterns including methylation patterns, particularly those

that are needed to control appetite (and therefore, weight), were concentrated in genes related to nervous system development, which did not occur in the thin volunteers.

Barrès and his colleagues also compared epigenetic markings of sperm from obese men before undergoing bariatric surgery with the markings of sperm from these same participants after the operation. The result: after the surgery, the epigenetic pattern of the cells was similar to that of normal weight men.

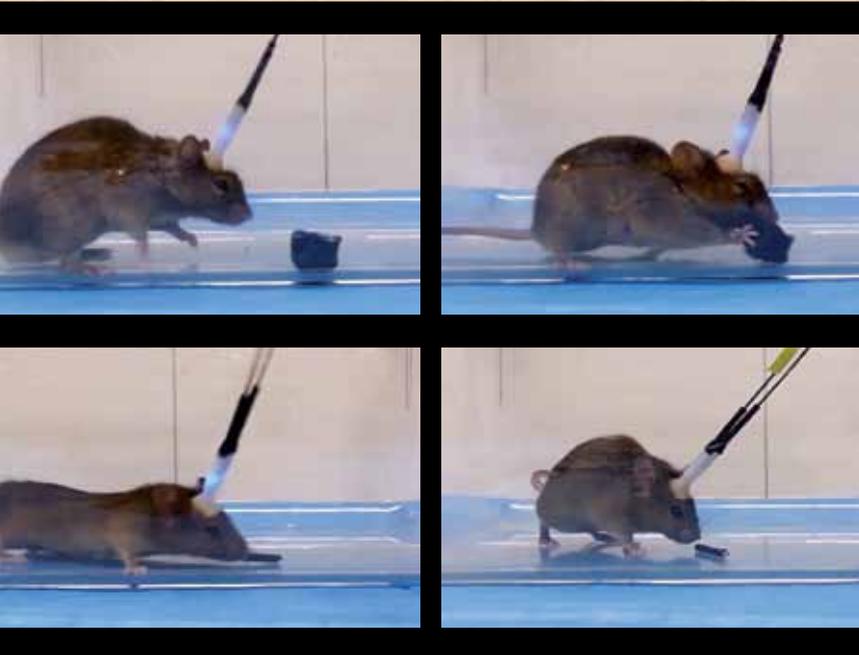
"The most important aspect of these discoveries is that they suggest that these modifications can occur in germinal cells; that is, ova and sperm, and that they can be transmitted to future generations," says physician Licio Augusto Velloso, a professor at the School of Medical Sciences of the University of Campinas (FCM-UNICAMP), who studies the cellular and molecular mechanisms related to the origin of obesity and diabetes. "Epigenetic studies have advanced a great deal in the last decade, and it is hoped that in a not-too-distant future, the mapping of environmental factors and their impact on different aspects of epigenetics will help us to prevent important diseases," affirms Velloso.

Viewing excess weight from the prism of epigenetics can provide another piece of the puzzle in the global obesity epidemic and related metabolic diseases. Historically associated with health and plenty, excess weight has become a significant problem that initially started in rich countries, but today is becoming more common in poorer countries, including Brazil, where almost 60% of the adult population is above the perceived healthy weight, per data from the Brazilian Institute of Geography and Statistics (IBGE). Many developing countries have quickly transitioned from a context in which malnutrition is a serious problem, to another, in which obesity is a great concern. ■

Scientific articles

JOAQUIM, A. O. *et al.* Maternal food restriction in rats of the F0 generation increases retroperitoneal fat, the number and size of adipocytes and induces periventricular astrogliosis in female F1 and male F2 generations. **Reproduction, Fertility and Development**. v. 29, i.7, p. 1340-48. 31 May 2016.

JOAQUIM, A. O. *et al.* Transgenerational effects of a hypercaloric diet. **Reproduction, Fertility and Development**. v. 29, i.2, p. 325-35. 25 Aug. 2015.



Optical fibers transmit laser beams to mice brains. When the light goes on, the mouse is stimulated to hunt. When the light goes off, the behavior stops

NEUROSCIENCE ▲

Hunting circuits

Two neural pathways that originate in the brain's amygdala control the aggressive behavior of predators

Marcos Pivetta

PUBLISHED IN FEBRUARY 2017

A small, almond-shaped brain structure situated in the temporal lobe, the amygdala is commonly described as a group of neurons associated with the processing of emotions, in particular, fear. The classic scenario of a rat paralyzed by terror in the face of imminent attack by its natural predator, the cat, is usually the example chosen to illustrate the result of the activation of this center in the nervous system. However, a study published in the journal *Cell* on January 12, 2017, demonstrates that stimulation of a sub-region of this structure unleashes the cat's predatory behavior rather than the rodent's defensive response. Using a technique called optogenetics, which uses laser to turn specific brain circuits on and off, neuroscientists at Yale University (United States) and the Institute of Biomedical Sciences at the University of São Paulo (ICB-USP) are demonstrating that the amygdala's central nucleus controls the predator's decision to search for prey, capture it and then attack and bite it.

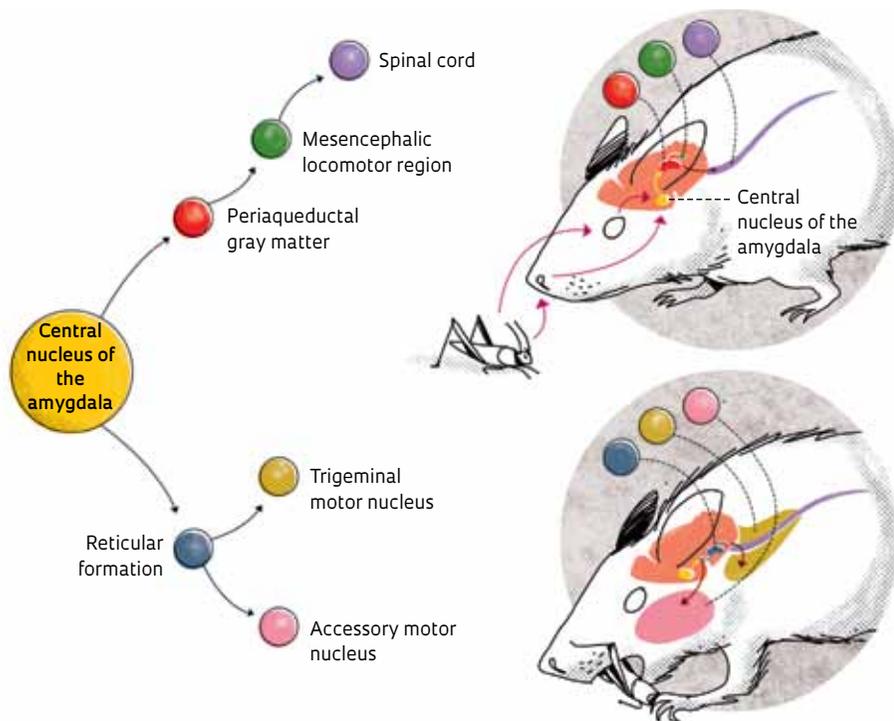
In the study, researchers show that the activation of two independent neural pathways that originate in the amygdala is critical to unleashing the predator's hunt for food (*see box*). When this occurs, rodents chase and then attack almost anything in their path, from actual insects to artificial prey, even bottle caps. "We observed that activating these two groups of neurons is both necessary and sufficient to compel mice to adopt typical hunting behaviors," said Brazilian neuroscientist Ivan de Araújo at Yale University, in whose lab the animal experiments were conducted. Although the neuroscientists do not rule out the possibility that other brain structures may also modulate predatory behaviors, the study's design indicates that stimulating these two circuits is all it takes for the mice to adopt predatory behaviors (*see video at bit.ly/VCircuitoCaca*).

The first pathway stimulated is that related to the pursuit of prey. In nature, this situation occurs when a predator identifies its prey with the help of at least one of the senses (smell, sight or hearing) and begins to move closer to the prey. In experiments with rodents, neuroscientists noted that this behavior is mediated by a projection of neurons present in the amygdala's central nucleus. This circuit relays signals to a structure called the periaqueductal gray matter, which transmits information to the mesencephalic locomotor region. This region then activates the spinal cord, which prompts the animal to mobilize for a hunt.

The second neural circuit controls the very capture and destruction of the prey. This is the moment the hunt is consummated, when the predator attacks the captured prey. The pathway

Stimuli of predatory behavior

Activating two independent neural pathways that originate in a region of the brain known as the amygdala's central nucleus, which is associated with the processing of emotions, prompts rats to pursue, capture and bite prey



PATHWAY OF PURSUIT

Activation of a structure known as the periaqueductal gray matter sends impulses to the mesencephalic locomotor region, which activates the spinal cord. When it sees or smells its prey, the predator initiates a pursuit

PATHWAY OF CAPTURE

Arousal of a diffuse set of neurons, known as the reticular formation, sends electrical impulses to the accessory motor nucleus, which controls the movement of the neck, and to the trigeminal motor nucleus, responsible for opening and closing the jaw. The predator grabs the prey and bites down hard on it

SOURCE IVAN DE ARAÚJO AND NEWTON CANTERAS

that modulates this action also originates in the amygdala's central nucleus, but it takes a different path. The activation of a diffuse set of neurons, known as the reticular formation, carries electronic impulses to the accessory motor nucleus, which controls the movement of the neck, and to the trigeminal motor nucleus, which is responsible for opening and closing the jaw. "When we stimulate only the first pathway and not the second, the rodents pursue their prey, but they don't attack it," explains one of the study's other authors, ICB-USP neuroanatomist Newton Canteras, a specialist in the study of the neural basis of fear and aggression. If, in contrast, the only circuit activated is the second one and not the first, the mice stop what they are doing and simply grab and bite at the air, as if they had an imaginary prey to tear to pieces.

According to the neuroscientists, optogenetics is a technique that can test the functioning of brain circuits in a subtler way than other approaches, such as causing mechanical or chemical lesions in certain areas of the brain to observe their

behavioral or clinical effects. By injecting a virus from a genetically modified population, researchers heighten the sensitivity to light of the neural pathway to be studied. In this way, an optical key that turns the circuit "on" and "off" is created and controlled by the researchers. In the case of the mice in the hunting study, small optical fibers connected to the animals' brains transmit blue laser beams to the amygdala and enable modulation of the two circuits. "In addition to the color, we can control the intensity and frequency of the laser pulse," says morphologist Simone Motta, also a professor at ICB-USP who participated in the study and spent some time at Araújo's lab at Yale learning the technique.

AMYGDALA IN MAMMALS

Work done by Canteras more than 10 years ago inspired the effort to confirm the possible role of circuits tested in the experiment on predatory hunting behaviors. Those studies had already suggested that some neural pathways that originate in the amygdala's central nu-

cleus were more closely associated with predatory stimuli than the expression of fear. Since the amygdala is a structure in the brain that is well preserved in mammals, it may also be involved in regulating hunting behaviors in other vertebrates. The new study brings to the table once again the idea that the amygdala's central nucleus plays an essential role in the organization of responses unleashed by fear. ■

Projects

1. Neuroendocrine and autonomic responses in rats with dorsal premammillary nucleus lesion after social defeat (No. 10/05905-3); **Grant Mechanism** Postdoctoral research fellowship; **Principal Investigator** Newton Canteras (USP); **Grant Recipient** Simone Motta; **Investment** R\$197,050.51 and R\$176,479.88 (Research internship abroad).
2. Role of anterior thalamus and its cortical targets in conditioned defensive behavior to the social defeat context (No. 12/13804-8); **Grant Mechanism** Doctoral research fellowship; **Principal Investigator** Newton Canteras (USP); **Grant Recipient** Miguel José Rangel Junior; **Investment** R\$188,066.58 and R\$96,354.03 (Research internship abroad).

Scientific article

HAN, W. *et al.* Integrated control of predatory hunting by the central nucleus of the amygdala. *Cell*. v.168, 1. 1-2, p.17-9. 12 Jan. 2017.

SHELTER FOR GIANTS

Extinct for 10,000 years, ground sloths and giant armadillos may have built the largest paleoburrows ever discovered on Earth

Igor Zolnerkevic

PUBLISHED IN FEBRUARY 2017

Chamber in Minas Gerais, showing marks resembling scratches on the wall and a hollow that may have served as a resting spot for ground sloths

The Valley of Giants is what paleontologist and oceanographer Francisco Buchmann calls a 250-meter-long stretch of the Esmeril River in rural Rio Pardo de Minas, a municipality of 30,000 in northern Minas Gerais State. There, the steep slopes along the river are covered by tall, dense forest infested with ticks and bees. The vegetation obscures the entrance to six caves of impressive size, which are as long as 40 m and, in most cases, terminate in a spacious chamber 5 to 10 m wide and up to 4 m high. Most strikingly, they may have been dug by large mammals, such as giant armadillos and ground sloths, which lived until approximately 10,000 years ago in what is now Brazil and constituted the class of animals known as South American megafauna.

Buchmann, a professor at São Paulo State University (UNESP) in São Vicente, became aware of these caves in 2012, when geologist Vitor Ferreira, from the mining company Sul Americana de Metais, discovered them by chance while looking for a spot to establish an iron-mining facility in the area. The following

year, Buchmann returned with his team to map the caves and investigate the origin of curious marks etched into the walls.

The tunnels, which feature arched ceilings and walls, as well as grooves in the rocks compatible with scratch marks made by strong claws, led the researchers to conclude that the caves in the Valley of Giants must have been excavated by large animals, such as those belonging to the South American megafauna. In a paper published in the *Revista Brasileira de Paleontologia* in May 2016, the group asserts that these caves did not develop through water erosion or some other geological process. They were likely huge paleoburrows, or chambers dug into the rock by animals, possibly the largest such burrows ever discovered on Earth.

Along with geologist Heinrich Frank of the Federal University of Rio Grande do Sul (UFRGS) and other colleagues, Buchmann has discovered more than 1,500 paleoburrows in southern and southeastern Brazil over the past 15 years. However, they regard the ones in the Valley of Giants as special, along with nine others that were found in three neighboring river valleys within the surrounding eight kilometers. The researchers see these paleoburrows as different because they hold stronger evidence that the animals that excavated them lived in groups: the burrows are close together, and in the innermost chamber of each, there is more than one space that they conjecture served as the animals' resting spot. "A community of ground sloths likely excavated these tunnels," Buchmann hypothesizes. "A family probably lived there."

Ground or land sloths have been extinct for at least 10,000 years and are related to present-day sloths, though they had very different habits. The six species of sloth that exist today spend their lives holding onto tree branches and trunks, where they feed on leaves and fruit. Their arms and feet are not adapted to walking on the ground, which the sloths do rarely and with great difficulty while leaning on their elbows. The nearly 100 species of ground sloths that lived in the Americas between 15 million and 10 thousand years ago used all four feet to walk on the ground and occasionally stood upright,

Land of paleoburrows

Tunnels supposedly excavated by primitive mammals are clustered in southern and southeastern Brazil



SOURCE LOPES, R. P. ET AL. / ICHNOS, 2016.

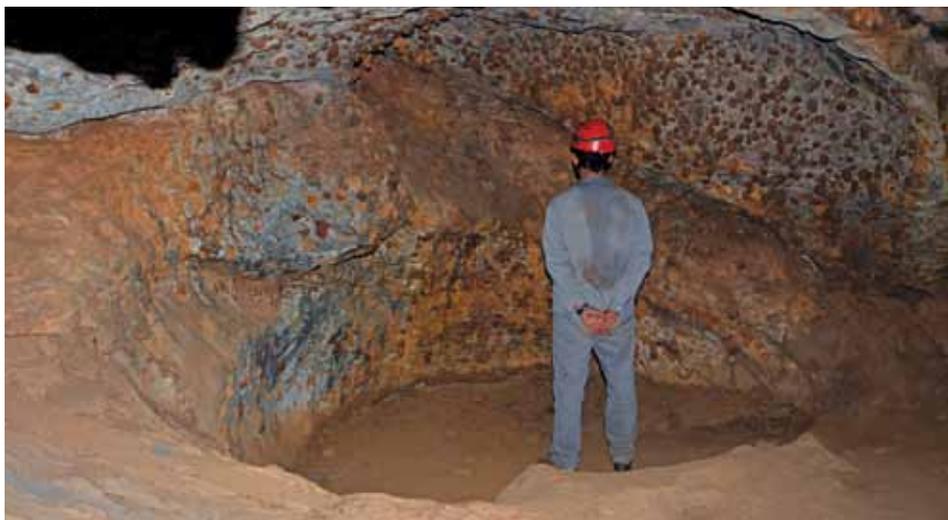
which left their front legs free to grasp fruit or to dig.

Despite the name giant sloths, these animals varied considerably in size. The largest ones belonged to the family Megatheriidae, which could reach six meters tall when standing upright. Studies of fossilized bones suggest, however, that the articulation of their arms did not enable the megatherids to dig easily, despite their enormous curved claws. This fact and a comparison with the marks found in the paleoburrows in Minas Gerais led Buchmann's team to suspect that these caves were sculpted into the rocks by species of the family Mylodontidae, which grew as tall as two meters.

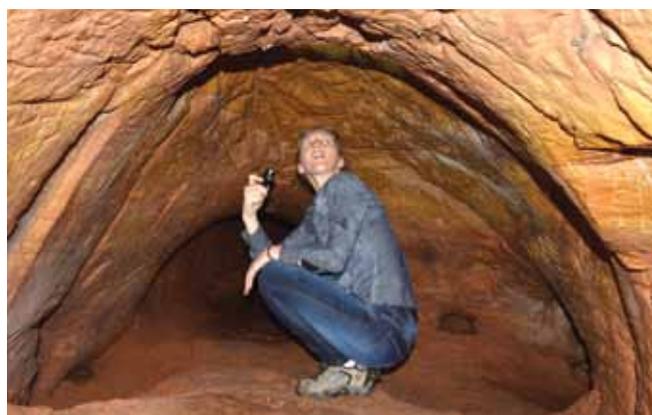
UNESP and UFRGS paleontologists interpreted the hundreds of grooves etched into the walls of the paleoburrows as marks left by the animals' claws as they opened the tunnels. At present, these marks are the principal indicators of the identity of the excavators, given that no primitive sloth fossils have ever been found in the paleoburrows of Brazil.

Buchmann compared silicone molds of these marks against specimens of fossilized feet from ground sloths found in Minas Gerais, which are all preserved at the Museum of Natural Sciences at the Pontifical Catholic University (PUC) in Belo Horizonte. The marks on the walls of the paleoburrows compared more favorably with the claws of mylodontids of the genus *Valgipes* than with the claws of other potential excavators, such as the extinct giant armadillos of the genus *Pampatherium*, which inhabited what today are the Pampas of Argentina and southern and southeastern Brazil during the same period.

The researchers noted another feature common to the 15 paleoburrows



Geologist Vitor Sandin observes a hollow in a paleoburrow in the Valley of Giants (above) in Minas Gerais, and geologist Milene Fornari inspects a paleoburrow in Doutor Pedrinho, Santa Catarina (right)



in northern Minas Gerais. In the last chamber, next to the claw marks, there were always one to three hollows in the wall very close to the ground, each one measuring 1 to 3 meters wide (see the photo on page 46). "The surface of the hollows is smooth and appears to be very polished," notes Buchmann. He believes that these surfaces were beds, the mylodontids' favorite resting spots.

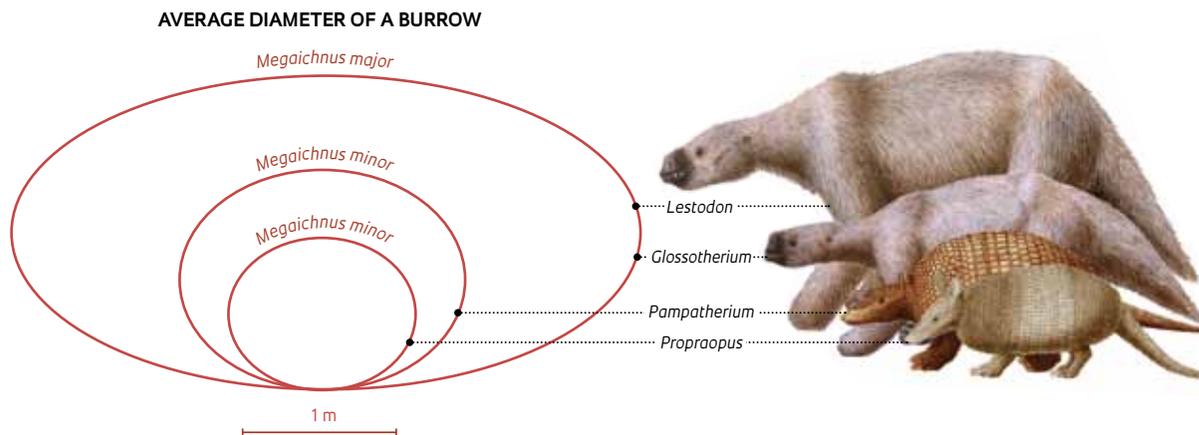
Paleontologists have already raised the possibility that at least some spe-

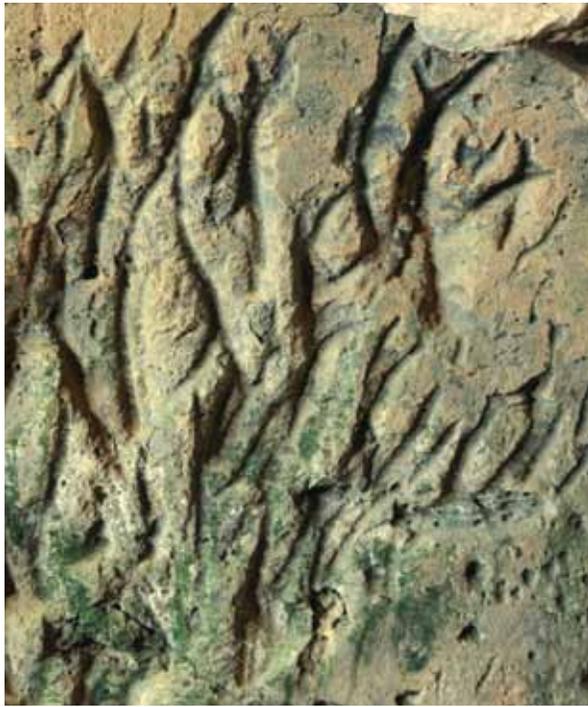
cies of ground sloths may have lived in groups. Buchmann favors this hypothesis to explain how sloths were able to open such large tunnels in the Valley of Giants. "When I think about the volume of sediment excavated, I can't imagine how a single individual could have done this," he says. "I think it's most likely that there was a colony of animals living and digging together."

"These discoveries represent a milestone," says Cástor Cartelle, a paleon-

Sizes of burrows and their possible excavators

Ground sloths of the genera *Lestodon* and *Glossotherium*, which likely had the ability to open the largest burrows (*Megaichnus major*), while armadillos of the genera *Pampatherium* and *Propraopus* created the smaller ones (*M. minor*)





Fossilized claw of a giant sloth of the genus *Valgipes*, which is compatible with marks (left) made on the walls of paleoburrows in Minas



they are not as large. The tunnels attributed to excavation by giant armadillos or ground sloths are ichnofossils of the genus *Megaichnus*.

This new genus has been divided into two species. The largest and widest paleoburrows, attributed to sloths, belong to the species *Megaichnus major* (see illustration on the facing page). Most of these have been found in southern Brazil and a few others in the states of Minas Gerais and São Paulo. In 2015, one was discovered in Acre State and another in Rondônia State. The latter, found on the outskirts of the city of Porto Velho, is the most recent and extensive of the paleoburrows, measuring 600 m long.

The narrower and more abundant paleoburrows were given the classification *Megaichnus minor*. Most of these are filled with sediments brought in by flooding. The few open tunnels stretch for more than 30 m and may bifurcate and form galleries. On their walls, researchers have identified marks from claws, fur and carapace plates from giant armadillos of the genera *Pampatherium* and *Propropus*.

Buchmann heads the Palaeoburrows Project carried out by researchers from six Brazilian institutions, who have identified thousands of such tunnels over the past 10 years. The group is working to identify and map the paleoburrows and to publish what is known about them in southern Brazil, where many were known to the local populace but have been mistaken for caves or attributed to excavations performed by indigenous peoples. ■

Scientific articles

LOPES, R. P. *et al.* *Megaichnus* igen. nov.: Giant paleoburrows attributed to extinct Cenozoic mammals from South America. *Ichnos*. v. 24, i.2, p. 133-45. 15 Sep. 2016.
BUCHMANN, F. S. *et al.* Evidência de vida gregária em paleotocas atribuídas a Mylodontidae (preguiças-gigantes). *Revista Brasileira de Paleontologia*. v. 19, i.2, p. 259-70. May-Aug. 2016.

tologist specializing in prehistoric mammals and curator of the museum at PUC-Minas. “The work of Buchmann’s team has yielded numerous interesting pieces of evidence that the animals occupied these burrows for at least some time and left marks on the walls there.”

Cartelle is not convinced, however, that the burrows were occupied by sloths. He says that there is considerable variation in the size and shape of sloth claws, even among individuals of the same species, and he questions the identification of the marks. “Why would a sloth dig a burrow?” he asks. “A burrow this size would not provide protection against a predator such as saber-toothed tigers.” In his opinion, the most likely explanation is that the burrows were made by giant armadillos, such as *Pampatherium*.

Buchmann suspects that the burrows were probably not excavated for safety reasons because sloths had few predators. He and his colleagues think that the most likely hypothesis is that the sloths were excavating in search of shelter from the climate, which, at that time, was colder and dryer. Ground sloth anatomy suggests that, similar to present-day sloths, they had difficulty maintaining their body temperature.

Cartelle raises other possibilities to explain the size of the burrows and the signs of occupation by several animals. There may have been large fissures in

the rocks of these mountains, in which case, the animals merely completed the openings rather than carrying out the full excavation. Another possibility is that one animal occupied the burrow, left its marks, and some time later, another member of the species did the same.

“I agree that occupation at different times by animals of similar size is a more plausible explanation for the existence of more than one resting place in these burrows,” says Renato Lopes, a paleontologist at the Federal University of Pampa (UNIPAMPA) in Rio Grande do Sul State, who has performed collaborative work with Buchmann and Frank. “We know of no xenarthrans [an order of mammals that includes armadillos and sloths] that form familial groups beyond mother and offspring.”

SIZES S AND L

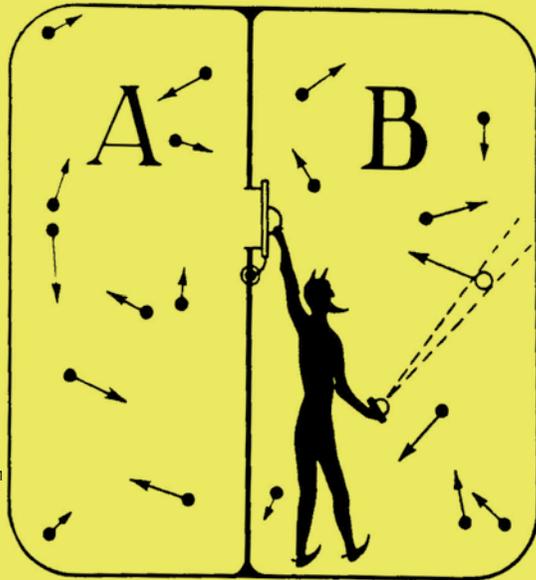
The Brazilian paleoburrows are considered to be the world’s largest ichnofossils—marks made by animals that are preserved in rock, such as footprints and burrows. Similar to living species and fossils, ichnofossils are classified into genus and species. Lopes, Buchmann, Frank and Felipe Caron, from UNIPAMPA, published the first official designation of paleoburrows found in Brazil, Uruguay, Paraguay and Argentina in the journal *Ichnos* in September 2016. There are paleoburrows in other regions, but

Quantum trickster

A Brazilian group controlled the heat generated by atomic nuclei

Igor Zolnerkevic

PUBLISHED IN JANUARY 2017



A 1975 paper by Russian mathematician Alexander Lerner includes a depiction of Maxwell's demon inside a container of gas molecules to be selected

The random generation of heat in the microscopic world is one of the main obstacles to advances in nanotechnology. As nanodevices become smaller and more complex, with parts the size of molecules or even atoms, there is a greater chance that they will generate dangerous quantum fluctuations while operating. These fluctuations are abrupt, unpredictable energy variations that are governed by the probabilistic laws of quantum mechanics and can damage nanomechanisms. A group of Brazilian physicists led by Roberto Serra, a professor at the Federal University of the ABC (UFABC), presented a technique that is able to attenuate the production of these heat fluctuations at the subatomic level in early December 2016 in *Physical Review Letters*.

The microscopic fluctuations in energy and heat affect nanomachines in a way similar to how uncontrolled overheating can damage a conventional macroscopic motor such as a car engine. During the Industrial Revolution in the nineteenth century, one of the motivations behind the development of classical thermodynamics—the area of physics that establishes how energy in the form of heat is converted into mechanical energy and vice-versa—was to understand the operation of pressure valves and refrigerators, devices that made the operation of steam and internal combustion engines safer and more

efficient. Anticipating advances in nanotechnology, Serra and his colleagues are part of a community of physicists who have been developing a more general and detailed theory of thermodynamics, called non-equilibrium quantum thermodynamics, that can ensure the efficient operation of molecular- and atomic-scale devices in which quantum effects occur.

To develop a new control technique, Serra and his colleagues were inspired by “Maxwell’s demon,” a fantastic being invented by Scottish physicist and mathematician James Clerk Maxwell (1831-1879). Maxwell was one of the first to understand that the temperature of a given volume of gas depends on the average speed at which the molecules in it move. The faster the molecules, the hotter the gas. In an 1867 letter to his colleague Peter Tait, Maxwell posited a microscopic, intelligent being that is able to measure and record velocities of all gas molecules. In this mental experiment, the being controlled a valve that separated two identical containers, both containing a gas at the same temperature. Opening and closing the valve quickly, the creature separated the molecules of gas, leaving the slower-than-average ones—which were thus colder—in one container and allowing the faster ones into the other container.

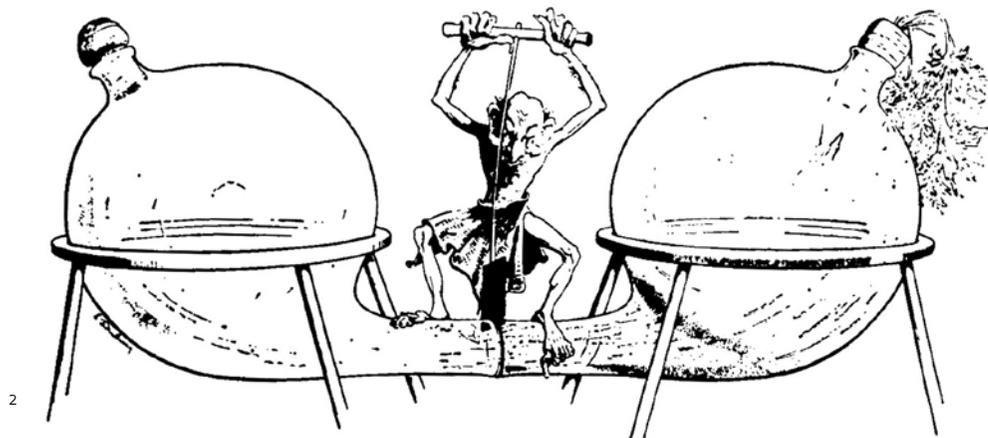
THERMODYNAMIC SIN

In a *Nature* article in 1874, Irish physicist William Thomson, who is better known as Lord Kelvin, called the intelligent being a demon, to emphasize that the creature, by heating gas in one container while cooling gas in the other, committed the sin of violating the second law of thermodynamics.

This law states that an isolated body, or a set of isolated bodies, has a property called entropy, which always tends to increase over time. For a set of particles, entropy corresponds to the possible number of arrangements of all of them in a given situation.

When ordering gas molecules according to their speed, the demon supposedly reduces the number of possible arrangements of the system, which reduces its

In an article published in 1955 in the *American Journal of Physics*, the imaginary figure controls the flow of gas molecules from outside the containers



entropy. After Thomson's article, physicists still wondered: is the demon a mere fantasy, or does the mental experiment indicate a failure to understand the laws of thermodynamics?

More than a century later, in 1982, American physicist Charles Bennett, then a researcher at IBM, realized that to work effectively, Maxwell's demon would need to record information on the speed of gas molecules on a physical substrate, such as the memory bits of a computer. However, writing and erasing data in memory cannot be done without generating heat, which was something discovered years earlier by Rolf Landauer, another IBM researcher. Furthermore, heat generation always increases entropy.

When assessing the increase and decrease of heat in both stages of this process, one notes that the second law of thermodynamics is never violated: the demon can reduce entropy inside gas containers by selecting molecules, but the heat generated to record the speeds of the molecules in memory increases entropy outside the containers much more. The calculations show that Maxwell's supernatural creature obeys all physics laws and that its function can be performed, in practice, by an automatic mechanism, controlled by computer memory.

Experiment with a chloroform molecule and electromagnetic pulses reproduced the mental experiment proposed in the 19th century

Since then, researchers have created increasingly smaller mechanisms in the laboratory, similar to that imagined by Maxwell. The current project being carried out by Serra and his colleagues is the first to design a completely quantum Maxwell's demon. In a laboratory at the Brazilian Center for Physics Research (CBPF) in Rio de Janeiro, the

researchers shot a pulse of electromagnetic waves at a solution of chloroform molecules—each one consisting of a carbon atom, a hydrogen atom, and three chlorine atoms (CHCl_3). The pulse was adjusted to cause quantum fluctuations in the energy of the nuclei of carbon atoms of the molecules. At the same time, physicists shot additional electromagnetic waves at the molecules with the goal of adjusting the interaction between the carbon and hydrogen nuclei of each molecule.

The researchers managed to use the hydrogen nucleus as a Maxwell's demon, storing information about the state of the carbon nucleus. Depending on the energy level of the carbon nucleus, the hydrogen nucleus activated and restricted the energy fluctuations of its neighbor. The actions of hydrogen nuclei caused the energy fluctuations of the carbon nuclei to occur in a way that produced the least possible entropy. "We designed this process based on a mathematical equation that we derived, relating information, entropy and energy," says Serra. "The equation is quite general and can be applied to any quantum system, such as electrons and photons, not just to atomic nuclei."

"It is an exciting study," comments Vlatko Vedral, a physicist at Oxford University, England, who participated in an experiment carried out in 2016, in which laser beams were used to produce Maxwell's demon. "They tested a formula that describes the production of entropy in quantum systems under generic conditions. It is still unclear why the entropy of the Universe must always increase, and this approach could help explain the origins of the second law of thermodynamics." ■

Project

National Institute of Quantum Information Science and Technology (No. 08/57856-6); Grant Mechanism Thematic Project; Principal Investigator Amir Caldeira (UNICAMP); Investment R\$1,977,654.30.

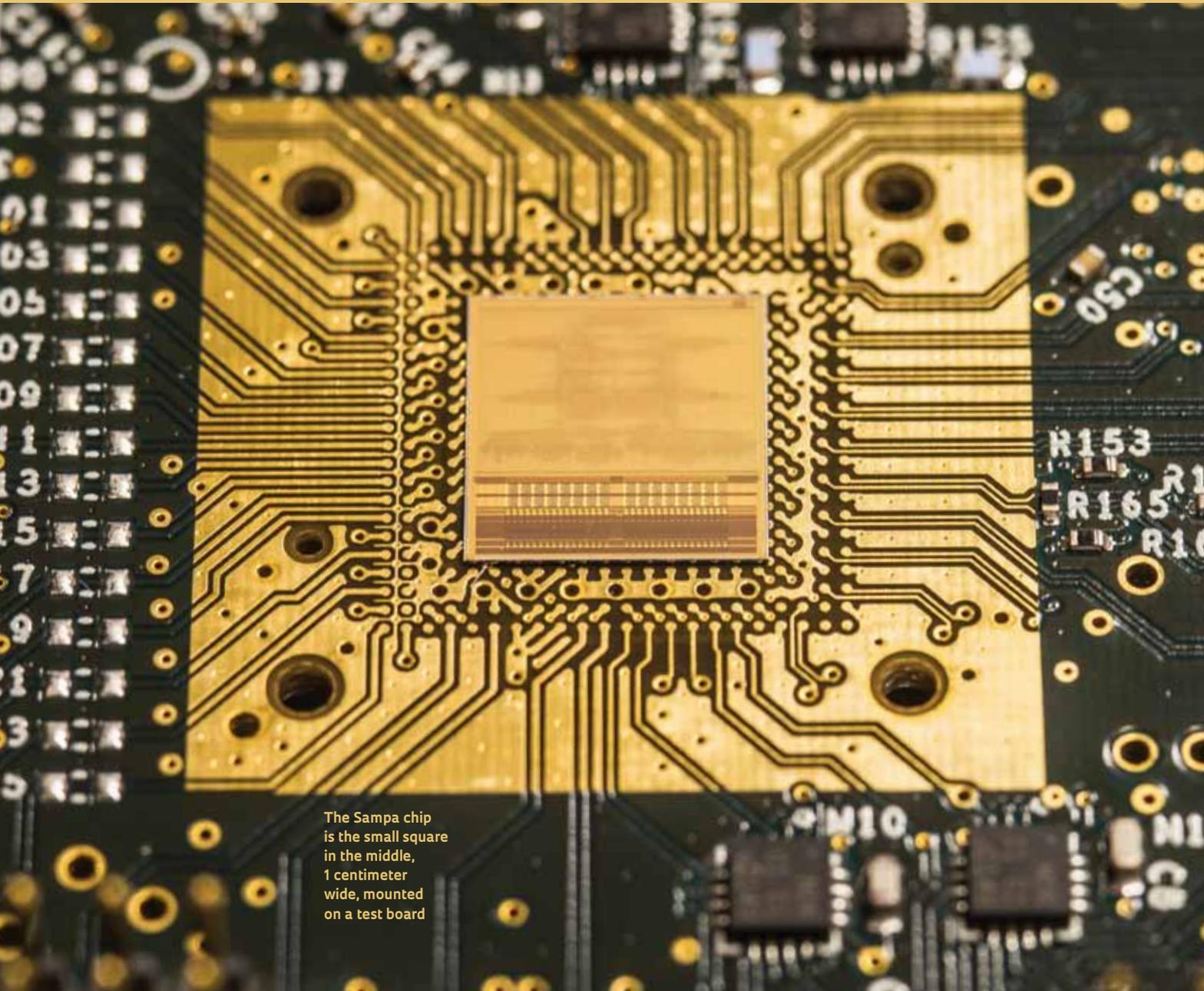
Scientific article

CAMATI, P. A. *et al.* Experimental rectification of entropy production by Maxwell's demon in a quantum system. *Physical Review Letters*. v. 117, 240502. 5 Dec. 2016.

Chip for particle collisions

Brazilian researchers develop and test a device to be installed in the Large Hadron Collider at CERN

PUBLISHED IN MARCH 2017

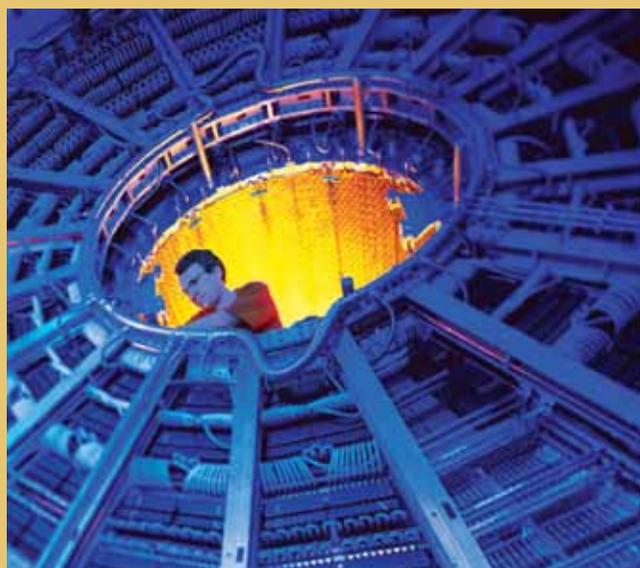


The Sampa chip is the small square in the middle, 1 centimeter wide, mounted on a test board

A small chip measuring less than 1 centimeter square will be one of Brazil's contributions to the detection of elementary particles in the Large Hadron Collider (LHC), located on the border between France and Switzerland and run by the European Organization for Nuclear Research, known as CERN. Called Sampa, the device is being developed by researchers at the University of São Paulo (USP), the University of Campinas (UNICAMP) and the Technological Institute of Aeronautics (ITA). The project started in 2013 and today has completed the second prototype, which is undergoing tests at laboratories in Brazil, Norway, Sweden, France, Russia and the United States. It is estimated that it will begin to be used in 2020.

Sampa will be installed in one of the four LHC particle detectors, called ALICE (short for A Large Ion Collider Experiment), on which 1,800 researchers from 174 institutions and 42 countries—including Brazil—work. “The objective is to reproduce—in the LHC—the plasma of quarks and gluons that would have existed for only a few microseconds after the Big Bang, which was the great explosion believed to have given rise to the Universe,” explains physicist Marcelo Gameiro Munhoz of the USP Physics Institute.

Quarks and gluons no longer exist separately in nature. They are enclosed within hadrons, particles of greater mass that can be categorized into baryons and mesons, such as protons, neutrons and pi mesons. “When you try to separate them, there are no free quarks. But, when colliding very high-energy lead nuclei, the quarks and gluons form a plasma, a sort of particle soup that flows like a liquid,” explains Munhoz. The main purpose of the ALICE experiment is to study this plasma. The Time Projection Chamber (TPC) is one of the devices used in it. Munhoz explains that the TPC is shaped like a barrel, 5 meters (m) in length and 5 m in diameter, full of gas, traversed longitudinally by a channel made of beryllium, with almost no air inside. “Beams of lead ions pass through this channel, at a speed just below the speed of light, in opposite directions, and collide,” says Munhoz. “The collision generates large numbers of various types of particles.”



ALICE experiment chamber, at CERN, where Sampa will replace two other chips, one analog and the other digital

When passing through the gas, the particles generated in the collision tear off electrons that then flow to the ends of the TPC, where two types of chips are installed. An analog chip receives and amplifies the charge and generates an electric pulse that is sent to a digital chip. Transformed into bits (digital signals), these pulses are stored for further analysis by researchers. With these data, they can determine which particles were generated in the collision in addition to verifying if the plasma of quarks and gluons was formed. “Sampa will replace these two chips, doing the work of both,” explains Wilhelmus Adrianus Maria van Noije, from the Integrated Systems Laboratory (LSI) of the USP Polytechnic School (Poli), coordinator of the chip development project.

The need to develop Sampa arose in 2012, with CERN's decision to update the LHC to increase the rate of collisions by a factor of 10 beginning in 2020. One of the current limitations is that today's chips cannot process such a high rate of collisions. According to Van Noije, Sampa will solve this problem. “It will have 32 channels to read the data, twice that of the devices used today,” he says. Munhoz says that when the LHC upgrade program was being developed, discussions began about which groups involved in ALICE could contribute to the modernization effort. “They were lengthy discussions to identify what needed to be built and the knowledge and experience of each group,” says Munhoz, who already knew of Poli's Integrated Systems Laboratory.

“After the presentation and the first internal discussions in Brazil, we invited some European researchers from ALICE to visit us and meet the LSI group. They came and agreed to allocate the responsibility for creating the device to the Brazilian groups.” Sampa's design was developed by Brazilian researchers, and the physical production of the two prototypes was conducted by the Taiwan Semiconductor Manufacturing Company (TSMC). “Unfortunately, there is no company in Brazil capable of manufacturing an integrated circuit like Sampa,” explains Munhoz. The Taiwanese company will produce 80,000 Sampas and deliver them to the LHC by 2020. ALICE needs 50,000, but 30% of the total could be damaged during the assembly stage of the printed circuit boards. “Our part was to carry out the intellectual work of designing the chip, its components, and the circuits, satisfying CERN's specifications,” says Munhoz. ■

Projects

1. Development of scientific instrumentation for the ALICE experiment at the LHC-CERN (No. 14/12664-3); **Grant Mechanism** Regular Research Grant (Special Projects); **Principal Investigator** Wilhelmus van Noije (USP); **Investment** R\$5,531,559.62.
2. Design of a signal acquisition and digital processing ASIC for time projection chamber of ALICE experiment (No. 13/06885-4); **Grant Mechanism** Regular Research Grant; **Principal Investigator** Wilhelmus van Noije (USP); **Investment** R\$1,218,001.52.
3. High-energy nuclear physics at RHIC and LHC (No. 12/04583-8); **Grant Mechanism** Thematic Project; **Principal Investigator** Marcelo Gameiro Munhoz (USP); **Investment** R\$4,277,589.35.

Hard and lifeless

Even though they resemble Earth, the crusts of some rocky exoplanets may be too rigid to be habitable

Igor Zolnerkevic

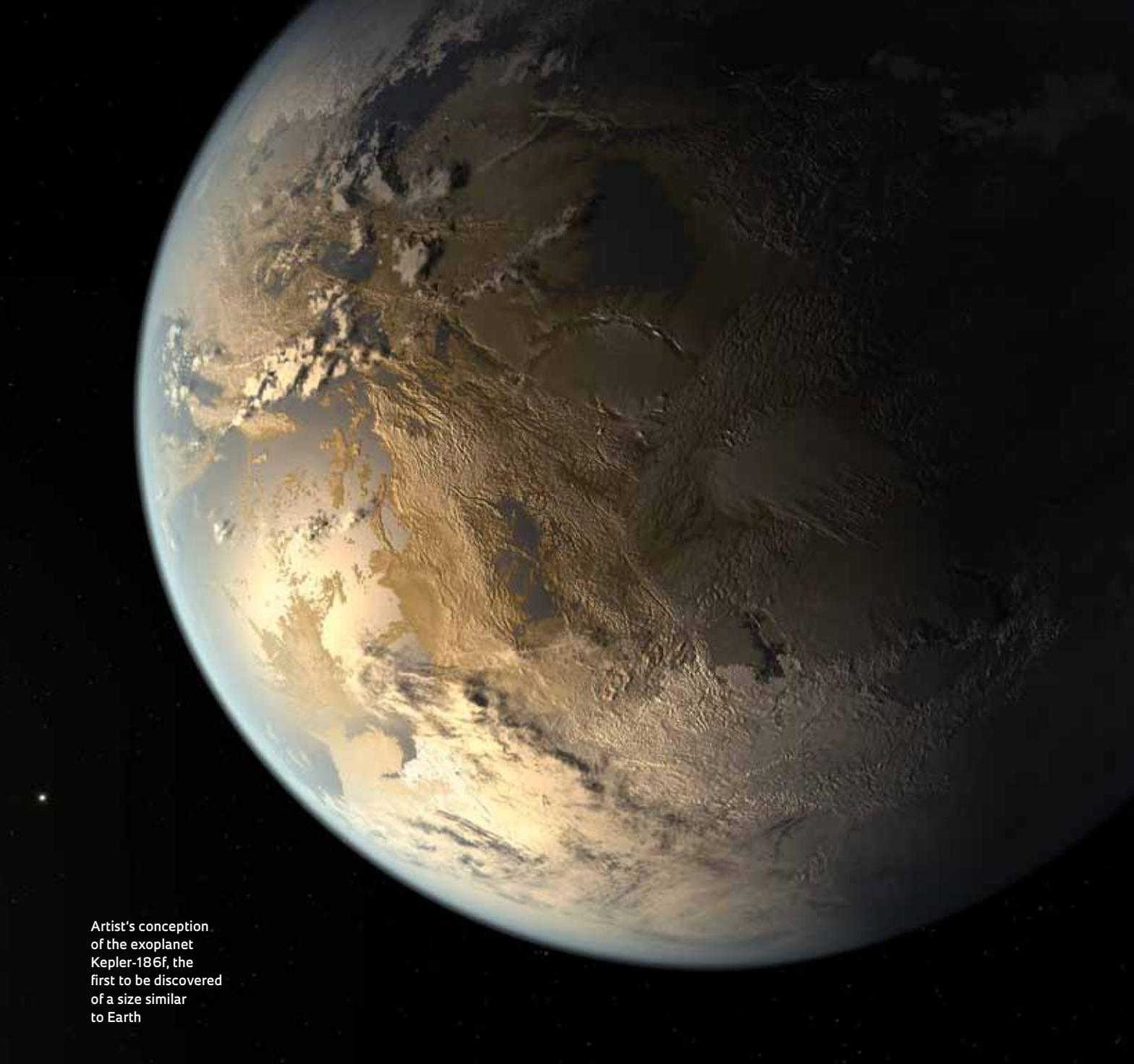
PUBLISHED IN APRIL 2017

The illustration on these pages shows how one artist imagined the exoplanet Kepler-186f in April 2014. At that time, astronomers confirmed that the mass and size of this planet 500 light years from the solar system was similar to that of Earth. Observations made by the Kepler space telescope also suggested that the distance between this planet and its star, the red dwarf Kepler-186, would allow liquid water to exist. For this reason, researchers announced that Kepler-186f

was the first rocky exoplanet discovered in the habitable zone of its star. Inspired by this discovery, the artwork shows the surface on Kepler-186f resembling that of Earth, with continents and oceans, creating a landscape conducive to the development of life forms similar to those of our planet.

However, new observations of its star suggest that the surface of Kepler-186f may be very different to and much less favorable for the existence of life, at least, to life as we know it. Working with an

international team of researchers, the astronomer Kátia Cunha from the National Observatory in Rio de Janeiro and her doctoral student Diogo Souto conducted the first detailed analysis of the chemical composition of the star Kepler-186. Their study was published in February of this year in the *Astrophysical Journal* and presents the chemical analysis of another red dwarf, Kepler-138, which is orbited by the smallest rocky exoplanet discovered so far, with a body the size of Mars. This was the first time that astron-



Artist's conception of the exoplanet Kepler-186f, the first to be discovered of a size similar to Earth

omers were able to measure the chemical abundances of red dwarf stars with accuracies resembling those possible when observing stars similar to the Sun.

The analysis of the light emitted by a star, which is known as the star's spectrum, provides a general understanding of the abundances of the chemical elements that comprise it. However, Souto explains that the temperatures in the atmospheres of red dwarf stars are low enough to allow the formation of water, titanium oxide and vanadium oxide mol-

ecules. When these stars are observed in the visible light range, titanium oxide masks the presence of several chemical elements. Even so, Souto showed that, by using infrared, it is possible to identify and measure the abundances of 13 chemical elements in red dwarf stars.

Souto and Cunha used data obtained from APOGEE, a high-precision spectrograph installed on a telescope in New Mexico, to estimate the concentrations of different chemical elements in the two stars and concluded that Kepler-186f

contains more silicon than the Sun. This excess silicon would cause the planets around the red dwarf to be made of rocks so hard that they would prevent the formation of tectonic plates in their crusts.

Without tectonic plates, there would be no processes to recycle gases, liquids and rocks, which, on Earth, over billions of years, have determined the chemical compositions of the atmosphere, the continents and the oceans. Without oceans or continents constantly altered by the movement of tectonic plates,

Kepler-186f would have a relatively unchanging and possibly desert surface.

The other red dwarf, Kepler-138, showed silicon levels similar to those of the Sun, so its small rocky exoplanet would have a composition that could favor the formation of tectonic plates. Even so, it is too close to the star to have liquid water on its surface.

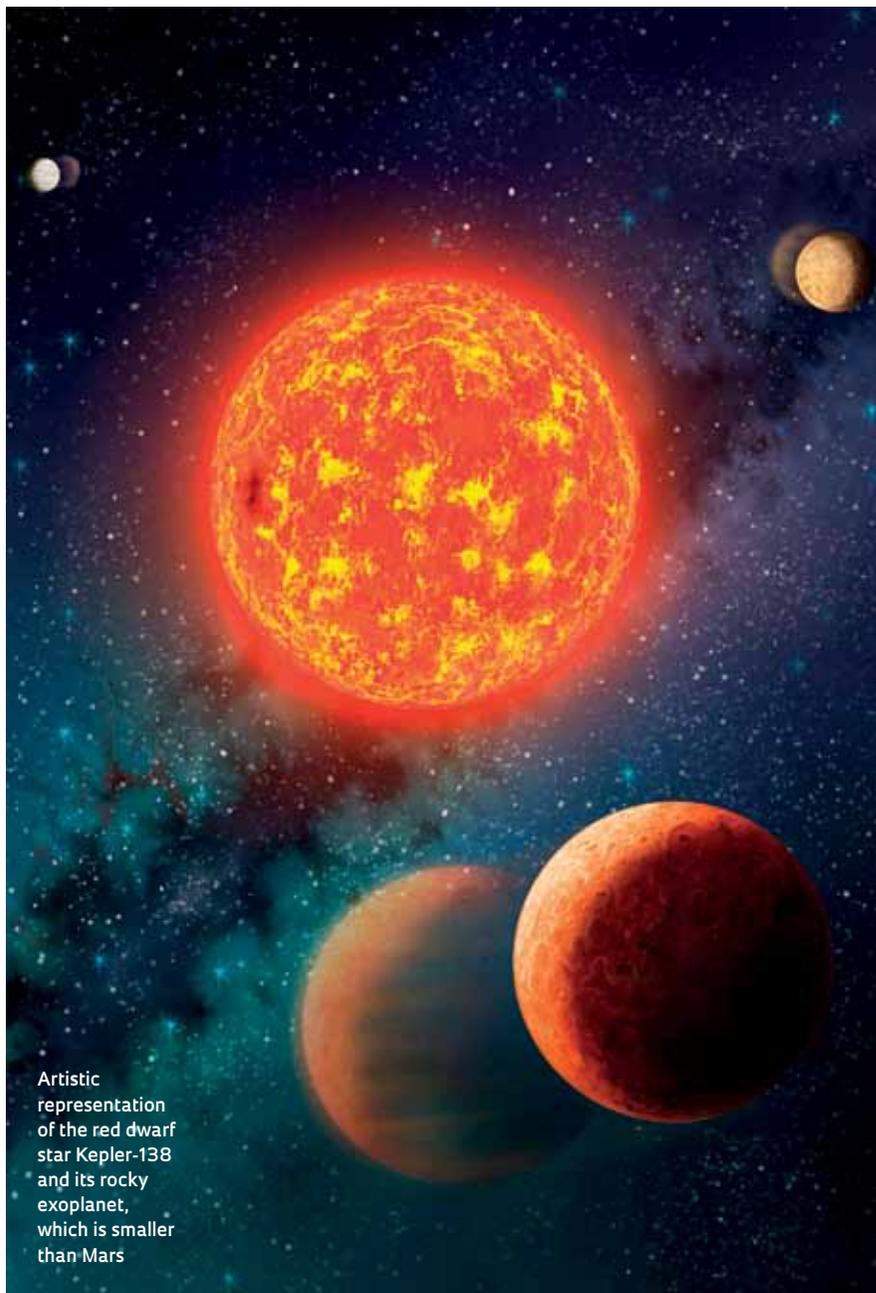
“Studies like this are of great importance for the astronomy of exoplanets,” says Souto. “A future NASA mission, TESS, will look especially at low-mass stars, which are the most abundant in the galaxy, and allow detailed study of their chemical composition, which is important for understanding the properties of their exoplanets.”

IRON, OXYGEN, AND OCEANS

The conclusions made by Souto, Cunha and their collaborators about the surface of Kepler-186f result from the application of a mathematical model developed in 2016 by the American geophysicists Cayman Unterborn of Arizona State University and Wendy Panero of Ohio State University. The model uses astronomical observations of the chemical composition of a star to estimate the mineral compositions of rocky planets formed around it. “The composition of the star serves as a reference for the possible compositions of its planets,” says Unterborn.

Unterborn and Panero based their model on what astronomers and geophysicists know about the composition of the Sun and the formation of the solar system. The planets formed from a disk of gases and dust made of the same primordial material that produced the Sun. A series of collisions that occurred over hundreds of millions of years between the materials in this disk caused the specks of dust to stick together, forming increasingly larger bodies until they formed the rocky planets. It is this process of planetary formation that the American geophysicists’ model simulates in a simplified manner to calculate the mineral compositions of exoplanets from the chemical makeups of their stars.

One of the model’s main conclusions is that the abundance of the element oxygen in this protoplanetary disk can restrict the sizes of the cores of these planets. A rocky planet like Earth has an iron core, which is surrounded by a



Artistic representation of the red dwarf star Kepler-138 and its rocky exoplanet, which is smaller than Mars

If part of the crust is denser than the material in the mantle, the planet can develop a dynamic of tectonic plates

thick mantle; this, in turn, is covered by a thin crust that forms the planet’s surface. “In the mantle, oxygen reacts with the iron and creates oxides that are too light to sink to the center of the planet,” explains Unterborn. “Instead, these oxides remain in the mantle and affect the compositions of minerals.” The quantity of oxygen also controls the presence of water in the mantle and the chance that the planet will have oceans.

While the core is made almost entirely of iron, the mantle and the crust are composed of minerals containing a variety of elements but are mostly silicon. “In estimating the chemical composi-

tion of the silicon-rich portion of the planet outside the core, we can model the process that heats up the rocks in the mantle and forms the crust,” adds Unterborn. “If part of the crust is composed of a material that is denser than the mantle beneath it, the planet can develop a dynamic of tectonic plates.”

To test this model against astronomical observations, Unterborn and Panero have been working since the middle of last year with Johanna Teske of the Carnegie Institute and other astronomers using the APOGEE spectrograph mounted on the Sloan Foundation telescope at the Apache Point Observatory in New Mexico. APOGEE has already analyzed the spectral lines in the infrared frequency range of approximately 200,000 stars in the Milky Way. The main objective is to use the chemical compositions of these stars to understand the history of the galaxy’s formation (see *Pesquisa FAPESP*, issue No. 232).

Some of the stars APOGEE has observed were also the target of the Kepler space telescope, which was designed to look for signs of exoplanets in variations of the brightnesses of their stars, and are now being investigated by Teske and her colleagues. They are applying Unterborn and Panero’s model to deduce the properties of the rocky exoplanets identified by the Kepler telescope around these stars.

SILICON AND THE CONTINENTS

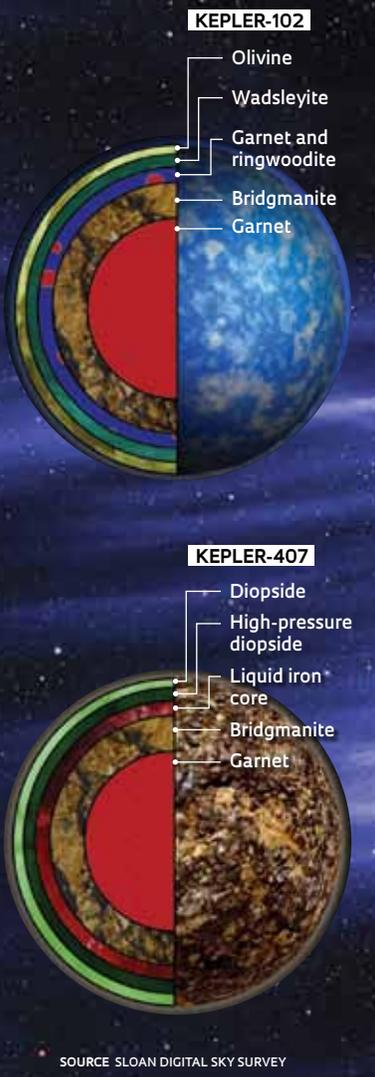
At the meeting of the American Astronomical Society held in Texas in January of this year, the team presented the first results of its assessment of the chemical compositions of planets orbiting two stars similar to our Sun, which is a yellow dwarf. The researchers used the differences between the chemical compositions of Kepler-102 and Kepler-407 to demonstrate how the abundance of silicon in a star is a strong indicator of the most common minerals found in its orbiting rocky planets.

In the case of Kepler-102, which has a silicon concentration similar to that of the Sun, the researchers predict that its rocky exoplanets have mantles and crusts which are rich in olivines, a group of minerals which are also abundant in the Earth’s crust and mantle. Meanwhile, Kepler-407 has silicon concentrations far exceeding those of our Sun;

The chemistry of the planets

The concentration of the element silicon changes the stiffness of the crust

The images below show the possible mineral compositions of the planets formed around the stars Kepler-102 and Kepler-407. The silicon concentration of Kepler-102 is similar to that of the sun but that of Kepler-407 is higher. Kepler-102’s planets are rich in olivine and could have plate tectonics like those of Earth; Kepler’s-407’s planets have more garnets and diopsides and probably have a rigid crust



its planet Kepler-407b has dimensions similar to Earth and is expected to have a crust rich in diopside and a mantle with an abundance of garnets, minerals that are tougher and denser than olivines, which are the most abundant on Earth. This combination, according to Unterborn, would prevent the formation of tectonic plates.

Because of these denser minerals, Kepler-407b may have a greater mass than Earth, although its radius would be similar. Future observations of the planet made with a new generation of more powerful telescopes could confirm or disprove this prediction. “For now, the uncertainties in the measurements are still significant,” says Unterborn.

As the work by Souto, Cunha, and their colleagues has shown, the model by Unterborn and Panero can also be used to estimate the compositions of exoplanets orbiting other types of stars, not just yellow dwarfs like the Sun. Most important of all are the red dwarfs, which represent 70% of the stars in the Milky Way; yellow dwarfs make up 7% to 8% of the stars in the galaxy. Because they are small, less than half the size of our Sun, red dwarfs facilitate the detection of exoplanets passing in front of them. Since these stars are smaller, when their planets cross in front of the stars, the planets cause greater and more easily detectable reductions in the light that arrives at Earth.

This year, astronomers working with the NASA Spitzer and Hubble space telescopes and the TRAPPIST terrestrial telescope at the European Southern Observatory found a record seven planets around a red dwarf, Trappist-1. These planets have similar sizes and masses as Earth, and three are in the star’s habitable zone. “Trappist-1 is in the southern hemisphere, and we will only be able to observe it when APOGEE-2 is installed in the Las Campanas Observatory in Chile,” says Souto. “We put in a request to observe it before November and hope to have some results about its chemical composition by the end of the year.” ■

Scientific article

SOUTO, D. *et al.* Chemical abundances of M-dwarfs from the Apogee survey. I. The exoplanet hosting stars Kepler-138 and Kepler-186. *The Astrophysical Journal*, v. 835, i. 2, 31 Jan. 2017.

Alternative uses for a plant fiber

Brazilian companies are investing in nanocellulose, a promising material for reinforcing plastic and cement, and the production of prostheses and sensors

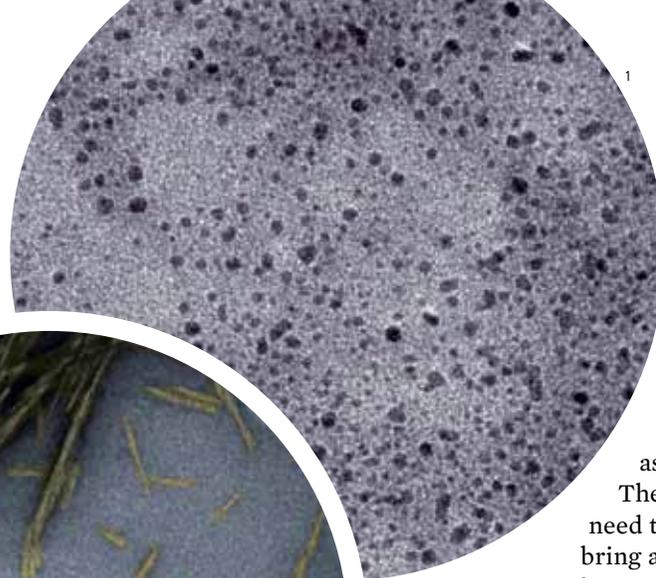
PUBLISHED IN MARCH 2017

The decline of the paper industry, which has been associated with progress in materials technology, has drawn attention to cellulose, a new player that has kindled entrepreneurial interest. At the nanometric scale (in which at least one dimension must be less than 100 nanometers, or nm), cellulose can take the form of nanofibrils or nanocrystals. Nanofibrils are spaghetti shaped, can be easily interwoven, and are used mainly to strengthen plastic packaging. Cellulose nanocrystals, with dimensions of 5 to 20 nm in width and 100 to 500 nm in length, resemble rice and are regarded as a more useful material because they can have an electrically charged surface as well as chemical, optical and electronic properties. This new material is characterized by a nanometric crystalline structure found within any plant fiber.

Nanocrystals, which are extracted from cellulose, the raw material in paper-making, can be sourced from reforested wood as well as from waste wood, sugarcane bagasse, coconut husks, rice husks, and waste from the production of soybean and palm oils. Nanocrystals come from a renewable source and are lightweight and biodegradable, lending them an advantage over other synthetic materials—often sourced from petroleum by-products. They have several potential applications, including for the reinforcement of plastic materials and cement, in sensors for the oil and gas industry, in specialized wound dressings, and in inks, coatings, cosmetics and, when combined with other substances, in the electrical and electronics industry. At present, there are no commercial products made with nanocrystals: the global production of this material, still in the early stages, is targeted to customers who can develop applications and create markets.

Brazil has invested in this promising material by acquiring equity in foreign companies that produce nanocrystals. In 2013,

Small spheres of carbon dots can be used in electronic equipment screens

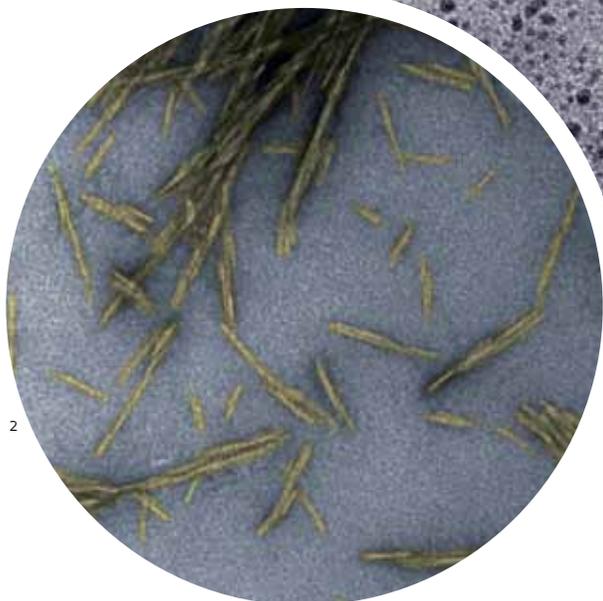


manufacturer of systems and equipment for the oil industry. Established in 2010, CelluForce launched its pilot plant in Montreal, Quebec, in 2012. With an annual production capacity of 300 tons, the company also offers its product as samples to potential customers.

According to Vinicius Nonino, director of new business at Fibria and now a board member of CelluForce, nanocrystals have potential uses in such industries as paper, cement and medicinal products.

These applications, which Nonino says still need to be developed for each industry, could bring about a major diversification of Fibria's business. The company holds production rights in Brazil and distribution rights for nanocrystals throughout Latin America. Both CelluForce and Fibria will be initial suppliers of raw material. Fibria plans to set up a pilot plant to produce cellulose nanocrystals at its Technology Center in Aracruz, in the state of Espírito Santo, in 2017.

The new material has awakened interest as a substitute for previously used raw materials and as a basis for developing new products. Estimates indicate that the price of nanocellulose crystals could run more than 20 times higher than that of cellulose. According to a study by the American consulting firm Market Research Store, the nanocellulose market was \$65 million in 2015. The company estimates that this figure could climb to \$530 million in 2021—a 30% annual increase.



Nanocrystals used to reinforce cement

Granbio, a Brazilian industrial biotechnology company, acquired 25% of American Process Inc. (API), a U.S. company. In 2015, API announced a new low-cost technology for extracting nanocellulose from biomass and began pre-commercial production. Granbio, one of two Brazilian companies that has the technology to make second-generation ethanol from sugarcane bagasse (see *Pesquisa FAPESP Issue No. 235*), invested in API to gain access to biomass pretreatment technology. In a press release, the Brazilian firm said it has been investing in nanocellulose research and development (R&D) for four years and operates at a plant in the United States through its API affiliate. The nanocellulose samples it produces are offered to potential customers.

In November 2016, Fibria, Brazil's global leader in commercial cellulose sales, became a shareholder in CelluForce, a Canadian company that is the leading producer of cellulose nanocrystals. Fibria invested about \$4 million to acquire an 8.3% equity interest in the company, which is a startup from FPIInnovations, a research center in the Canadian forest products industry. FPIInnovations (formerly Pulp and Paper Research Institute of Canada) holds the first patent on the production of cellulose nanocrystals, granted in 1997. In addition to FPIInnovations, the other shareholders of CelluForce are Domtar, a Canadian cellulose and paper-manufacturing company, and Schlumberger, a French company that is the leading

INTEREST FROM INDUSTRY

The first scientific paper on the production of nanocellulose crystals was published in the early 1950s by Swedish chemist Bengt Rånby of the Royal Institute of Technology (KTH). Having established a strong tradition in the paper and cellulose industry, in 2011, the Swedes inaugurated the world's first pilot plant that extracted cellulose nanofibrils, operated by the Innventia research institute. The use of nanocellulose to reinforce materials such as paper, composites and plastics was already awakening interest on the part of industry, but the extraction process required much energy and rendered the process unviable.

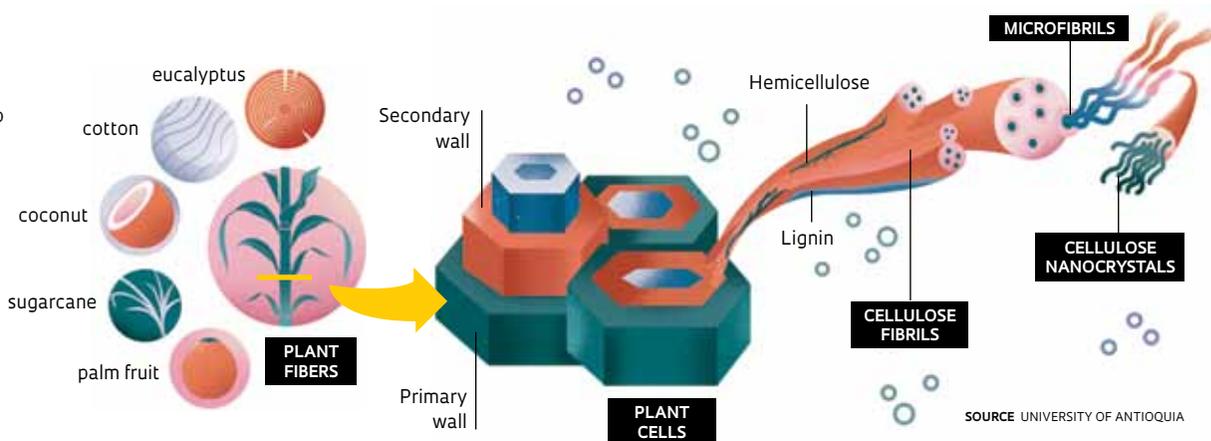
Holmen AB, a Swedish paper and cellulose company, became the principal shareholder in the Israeli firm Melodea, developer of an industrial process for extracting cellulose nanocrystals from paper manufacturing slurry. The company conducts research on the use of this material in foams without any type of plastic component and as a way to increase the strength of packaging, paper, acrylic adhesives and inks. In a partnership between Melodea and Holmen AB, the RISE Research Institutes (a Swedish government

Raw material extracted from inside plants

New material is created from the cellulose found in many plants

EXTRACTION OF CELLULOSE NANOCRYSTALS

The first step is to separate cellulose from hemicellulose and lignin. Smaller cellulose fibers are produced until they become nanocrystals. All the processes use chemicals, usually acids



initiative in the field of innovation that encompasses Innventia and other institutes) and MoRe Research (a Swedish R&D company in the forest products industry) are building the first cellulose nanocrystals pilot plant in Europe, 500 kilometers from Stockholm.

In Canada, another country with a strong tradition in the paper and cellulose industry, both CelluForce and Blue Goose Biorefineries sell nanocrystals in the form of a clear, nearly transparent gel, for \$1,000 per kilogram (kg). The buyers are companies and research institutions that test the raw material in various situations and products. The company's plant, in the Canadian city of Saskatoon, produces 35 kg of nanocrystals per week, sourced from products with a high cellulose content, such as tree pulp, recycled paper, cotton linter (fuzz that clings to cottonseed hulls), and flax fibers.

Blue Goose has developed an oxidative, nanocatalytic process that requires fewer chemicals and would therefore be more environmentally friendly for converting biomass into a nanometric-scale crystal. Nanocrystals are currently produced by acid hydrolysis (separation of wood fibers until the cellulose can be extracted in nanocrystalline form), in most cases using sulfuric acid but also using phosphoric acid or hydrochloric acid.

One bottleneck in R&D lies in the production of pieces of nanocellulose in larger dimensions. The challenge is to begin to efficiently produce the material in meters rather than in centimeters so that scientists can analyze its mechanical and functional characteristics and assess its benefits and uses as an end product. Melodea and MoRe Research are collaborating on a project to convert prototypes of films, papers and foams made in small dimensions in the laboratory us-

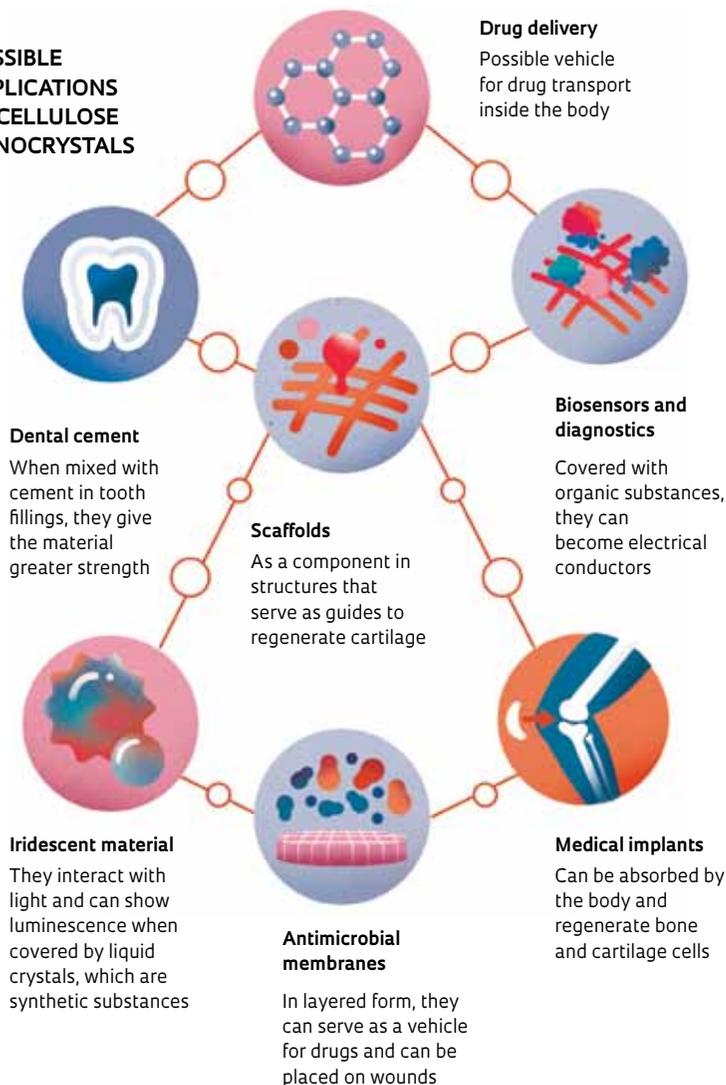
ing cellulose nanocrystals and nanofibrils into market-ready products. Under the leadership of KTH in Stockholm with participating Swedish universities and Processum, a biorefinery R&D company, the pilot plant now under construction in Sweden is expected to produce nanocrystals, nanofibrils and derivative products.

The project research team includes Daniele Oliveira de Castro, a Brazilian chemist who has an undergraduate degree from the Federal University of São Carlos (UFSCar), and a master's and sandwich doctorate from the Grenoble Institute of Technology in France, defended at the University of São Paulo (USP) under the advisorship of chemist Elisabete Frollini. In Sweden, Castro is developing processes to produce stronger paper with nanocellulose. "I'm also involved in creating foams made from nanocellulose that have fire retardant properties," she says. She has been at MoRe Research since September 2016, and her project ends in 2018.

Chemist Juliana Bernardes of the Brazilian National Nanotechnology Laboratory (LNNano) at the Center for Research in Energy and Materials (CNPEM) is coordinating a line of research using cellulose nanocrystals and nanofibrils extracted from sugarcane bagasse as thickeners in fluids. "These nanomaterials in small quantities can, for example, convert water into gel—an important feature in cosmetics," she explains. Bernardes will receive FAPESP funding for a three-month stint at Stockholm University to develop a dressing in gel form made of cellulose and wound-healing drugs.

One attention-grabbing use of cellulose is its application to reinforce cement. In a paper in the journal *Cement and Concrete Composites*, from February 2015, this use was evidenced by a study conducted at Purdue University. Researchers led

POSSIBLE APPLICATIONS OF CELLULOSE NANOCRYSTALS



Drug delivery
Possible vehicle for drug transport inside the body

Biosensors and diagnostics
Covered with organic substances, they can become electrical conductors

Medical implants
Can be absorbed by the body and regenerate bone and cartilage cells

Scaffolds
As a component in structures that serve as guides to regenerate cartilage

Antimicrobial membranes
In layered form, they can serve as a vehicle for drugs and can be placed on wounds

Dental cement
When mixed with cement in tooth fillings, they give the material greater strength

Iridescent material
They interact with light and can show luminescence when covered by liquid crystals, which are synthetic substances

by engineer Pablo Zavattieri demonstrated that cellulose nanocrystals can increase the traction strength of concrete by up to 30%. The results indicated that the biomaterial increases concrete hydration, which strengthens the material. This would make it possible to use less cement in the mixture. These findings led the Purdue group to set up a partnership with P3Nano, a public-private organization created to conduct research using nanomaterials sourced from wood. The initiative is being funded by the Silviculture Office of the United States Department of Agriculture (USDA). P3Nano intends to advance the technology and commercialize it. To that end, it will continue to engage with the Purdue researchers, who are now conducting large-scale testing. ■

Project

Cellulose nanoparticles as rheology modifiers for complex fluids (No. 16/04514-7); **Grant Mechanism** Regular Research Grant; **Principal Investigator** Juliana da Silva Bernardes (CNPEM); **Investment** R\$115,773.36.

Research in Brazil

Several research groups are studying the production and functionality of cellulose nanocrystals

Several research groups at Brazilian institutes and universities are studying ways to extract and purify cellulose nanocrystals, along with the applications of this material. Two recent studies have focused on light reflection, a feature of nanocrystals. One of these studies was the cover story of *Advanced Materials*, a scientific journal in the field of materials. “The innovation was in placing liquid crystals onto cellulose nanocrystals to produce iridescent films that absorb light and reflect only a few colors,” says Antônio Figueiredo Neto, a professor at the USP Physics Institute. He heads the group that is partnered with researchers from Portuguese institutions. “With cellulose, we obtained greater color versatility than we can with films made from synthetic material,” Figueiredo reports.

A project by a group of researchers from the Federal University of Minas Gerais (UFMG) in Belo Horizonte and the Federal University of Jequitinhonha and Mucuri Valleys (UFVJM) in Diamantina demonstrated that cellulose nanocrystals can be precursors for carbon nanomaterials known as carbon dots. They can be used as a substitute for quantum dots made from semiconductor materials in nanometric dimensions. Possible applications include solar cells, medical image-capturing devices and displays. Quantum dots are currently found in TVs that use this material to improve visibility and resolution on LED screens—known as QLED TVs.

“We developed a way to pyrolyze cellulose nanocrystals that result in spherical carbon dots from 4 nm to 8 nm in circumference, which show photoluminescence in green and blue. Carbon dots have been a known entity since 2004, and in this paper, we demonstrated that they can be made from cellulose—an abundant renewal source,” explains chemist Fabiano Pereira, a professor at UFMG. “Another advantage of carbon dots is the fact that they present no toxicity.”

Project

Optical and structural properties of elastomers and complex fluids of biological interest (No. 11/13616-4); **Grant Mechanism** Thematic Project; **Principal Investigator** Antônio Martins Figueiredo Neto (USP); **Investment** R\$2,519,727.73.

Biological control against citrus greening

Companies invest in small wasps produced in the lab to combat insects that spread diseases to orange groves

Domingos Zaparoli

PUBLISHED IN APRIL 2017

An orange farm without citrus greening disease



Citrus farmers in the state of São Paulo have successfully implemented biological control technology developed by the Luiz de Queiroz College of Agriculture of the University of São Paulo (ESALQ-USP) to combat citrus greening, one of the most devastating citrus grove diseases in history. Also known as

HLB, which refers to its original

name in Chinese (*Huanglongbing*, or yellow dragon disease), citrus greening disease turns leaves a yellowish color and leaves the fruit unripe and deformed. The solution is to remove the sick tree from the root. In the state of São Paulo alone, the pathogen has already prompted the removal of approximately fifty million orange trees covering an area of 100,000 hectares (ha) since 2004, an amount that represents one-fourth of the state's citrus orchards. Citrus greening is caused by the bacteria *Candidatus Liberibacter asiaticus* and *Candidatus Liberibacter americanus*, which are transmitted to citrus plants by a small insect, the psyllid *Diaphorina citri*.

The researchers led by agricultural engineer José Roberto Postali Parra, a professor from the Department of Entomology and Acarology at the Luiz de Queiroz College of Agriculture of the University of São Paulo (ESALQ-USP), have developed a method to raise the wasp species *Tamarixia radiata*—a natural enemy of the psyllid—in the lab. The wasps act as parasites to immature psyllids (those still in the nymph stage and therefore unable to fly) by laying eggs inside the insects. When wasps hatch from these eggs, the insects are killed. However, a significant problem is associated with this process. Namely, the insecticides used by farmers against psyllids are also fatal to their natural enemies.

The team from ESALQ-USP found that areas surrounding commercial farms could host wasp populations. These wasps could then serve as parasites against psyllids before they reach the groves and contaminate the trees. Thus, the researchers have found that *T. radiata* can eliminate over 80% of the vector population surrounding the crops. The 2014 experiment was performed in the city of Itapetininga, São Paulo in a three-kilometer radius around an orange grove managed by Citrosuco, one of the world's largest orange juice producers. To measure results, the researchers used sticky yellow cards as traps. Attracted to the color, the psyllids became stuck

to the glue-coated cards. Thus, the trap served to indicate the insects' arrival at the farms. The fewer psyllids stuck to the trap, the more effective the wasps. "Now, our priorities are to measure the impact of the reduction in this vector's population on the spread of the disease and to determine how many parasite release campaigns are necessary to increase efficacy in combating the psyllid," explains Parra.

The release of *Tamarixia radiata* in the vicinities of sprayed orchards is an important tool for controlling the disease in abandoned areas, on family farms, and at households with citrus trees in the yard or with decorative plants identified as *Murraya spp.* The latter are remote citroid fruit trees common in cemeteries and other public areas in Brazil, and these trees attract psyllids. "The release of the wasps into these areas was found to be effective at reducing the incidence of the disease on commercial farms," explains Parra.

Biological pest control has been a focus of studies in Brazil since the 1950s. In the 1960s, the United States and Europe developed the concept of integrated pest management as an alternative to the application of extensive chemical controls against pests on farms, including bacteria and viruses. In Brazil, some companies currently raise insects to combat other insects on farmlands. One example is the *Trichogramma* genus of wasps, which are used to combat various moth species



PHOTOS 1 HENRIQUE SANTOS / FUNDECITRUS 2 FUNDECITRUS



Deformed oranges on a tree infected by the disease

on cotton, sugarcane, soy, tomato, and cabbage crops (see Pesquisa FAPESP, issue No. 195).

There have been records of psyllids in São Paulo's orange groves since the 1940s, but the first report of citrus greening disease did not occur until 2004. The cities of Matão and Araraquara, two large orange-producing regions in the state, were the epicenters of the infestation that devastated long-standing orchards. The entomology team from ESALQ-USP immediately began to study the possibility of introducing a natural parasite against psyllids in the orange groves. They found information on the efficacy of *T. radiata*-based pest control in French territories in the Indian Ocean. In addition, one of Parra's students working toward a PhD in entomology, Ecuadorian Mariuxi Gomes Torres, detected specimens from this wasp species in Brazil. The ESALQ-USP team needed to study both the wasp's and the psyllid's reproductive cycle before developing the technology to raise the insect in the lab. These tasks were completed in 2011 with the financial support of FAPESP and the Brazilian Fund for Citrus Protection (FUNDECITRUS).

The success with *T. radiata* led Citrosuco to build four biofactories insect breeding laboratories. The first biofactory was established in Itapetininga in 2014 followed by the labs in Boa Esperança do Sul, Onda Verde, and São Manoel, all located in São Paulo State. The company has released a total of 3.9 million wasps into nature, which has resulted in a significant reduction in psyllid capture on the edges (the first 300 meters) of their commercial orchards, the most vulnerable areas. "It's an effective and sustainable way to respond to the disease," says Helton Leão, general manager of the Agricultural Department of Citrosuco. The company plans to build three more biofactories by 2018, which will result in a total production capacity of approximately 600,000 wasps per month. These specimens will be sent to the company's 26 orange groves.

In 2015, FUNDECITRUS, which is maintained by citrus farmers, invested R\$400,000 to build a *T. radiata* biofactory in Araraquara, São Paulo with the support of Bayer CropScience, the agriculture research division of the German chemical company. The laboratory can produce 100,000 wasps per month. Each insect can eliminate up to 500 psyllid nymphs. In December 2016, FUNDECITRUS surpassed the one-million mark for the number of wasps produced. The wasps are distributed free of charge to citrus farmers, who release them within an area that totals 2,420 ha. Parra estimates that there are 12,000 ha surrounding the commercial orchards that should be the target of biological control, with continuous wasp release campaigns.



The small wasp species *Tamarixia radiata* (above) and orchard release (right)



Citrosuco and FUNDECITRUS have been working hard to spread the word about the techniques to combat citrus greening. Citrosuco has organized workshops emphasizing the use of the wasps in order to promote these practices among independent orange producers who supply Citrosuco and even Citrosuco's competitors. "It is not one isolated measure or another that's going to beat citrus greening; a combination of efforts is needed," says Leão from Citrosuco. According to Antônio Juliano Ayres, general manager of FUNDECITRUS, the current idea is for citrus farmers to invest in their own wasp production efforts.

Biofactories require many rooms for the different stages of growth to be housed at controlled temperatures. The cost of a small biofactory capable of producing approximately 100,000 wasps per month can range from R\$40,000 to R\$200,000 depending on the infrastructure that the institution in question has for the project. According to Parra, two or three employees are typically sufficient to raise the wasps. The wasps may be raised by people with a secondary-school education as long as the employees are trained and assisted regularly by entomologists.

With headquarters located in the Netherlands and activities in Brazil since 1942, the Louis Drey-



Adult and immature psyllids; the latter are known as nymphs

fus Company (LDC) uses FUNDECITRUS wasps. Jorge Costa, director of operations at the Plataforma Sucos juice company, reports that they periodically release wasps on the farms and in surrounding areas to complement the integrated management program currently in place for HLB. Recommended by FUNDECITRUS itself, the measures include monitoring the presence of the vector and planting seedlings obtained from nurseries protected against psyllids. “This management plan has kept HLB infestation low in the orchards we oversee and has therefore kept productivity levels consistent on the farms,” Costa says.

Citrus farmer Janderson Bortolan, who owns two farms in the São Paulo countryside (located in the cities of Guaraci and Cajobi) with a total of 40,000 plants, also uses FUNDECITRUS wasps. Bortolan utilizes intense chemical pest control campaigns with complete orchard spraying one week and spraying specific to the edges of the properties the next week. Using this method, he keeps the rate of infection below 0.5% in his trees. Since 2015, he has performed five wasp release campaigns around his property, all of which were performed three days after chemical spraying.

Citrus greening has spread worldwide. The disease affects farms in Asia, Africa, and the Americas. Recently, one of the psyllid vectors of the bacterium *Trioza erytreae* was detected on citrus trees in the Mediterranean region, placing Italian and Spanish farmers on alert. Currently, Australia is the only region with no signs of infection or vector insects. In addition to orange trees, lime and tangerine trees are the main victims of the disease. According to agricultural engineer Antônio Juliano Ayres, general manager of FUNDECITRUS, fruit production in an infected plant is reduced to only 25% of its potential. Fruit quality is also compromised; the fruit becomes bitter and more acidic. The plant must be pulled out at the root because the bacteria travel through the sap to infect the entire plant, including the roots, which renders pruning useless. The shoots and buds that form after pruning are the source of new infections.

In 2005, citrus greening disease was identified in Florida, the United States’ main orange-producing state. Prior to that date, annual production remained steady at approximately 220 million crates, each containing 40.8 kilograms of fruit. As a consequence of the disease, the 2016 harvest produced 67 million crates, which was the smallest harvest in 70 years. “American farmers have been reluctant to remove infected plants, and greening has spread. Now, it will be very difficult to undo this drop in production,” explains the general manager of FUNDECITRUS.

Ayres argues that Brazilian farmers who have already addressed other threats to orchards (such as citrus canker and citrus variegated chlorosis) are more open to adopting radical strategies that may include the destruction of contaminated fruit trees. Even so, the damage is extensive. FUNDECITRUS estimates that 16.9% of orange tree farms in the state of São Paulo and in the country’s Triângulo Mineiro region have experienced some degree of HLB infection to date. “In 2016, the country’s orange production was 244 million crates. It could have been five percent higher without the disease,” Ayres notes. Brazil is the world’s largest orange producer, and the state of São Paulo is responsible for 80% of the country’s production. Orange juice is the third most commonly exported product in the state. In 2016, sales from exports generated US\$1.78 billion in revenue. ■

Projects

1. Biotechnological strategies for HLB control through transgenics (No. 15/07011-3); **Grant Mechanism** Thematic Project; **Principal Investigator** Leandro Antônio Peña Garcia (FUNDECITRUS); **Investment** R\$1,169,211.09.
2. Bioecology and establishing control strategies against *Diaphorine citri* Kuwayama (Hemiptera: Psyllidae), vector of the bacteria responsible for citrus greening (No. 04/14215-0); **Grant Mechanism** Thematic Project; **Principal Investigator** José Roberto Parra (USP); **Investment** R\$701,840.94.

Cattle genes

Knowledge of bovine genetics could help farmers select Nelore cattle with tender meat



PUBLISHED IN APRIL 2017

Studies of selective breeding based on the identification and manipulation of genes and proteins are currently underway in Brazil with the aim of improving the quality of beef cattle. The goal is to develop cattle with a greater feeding efficiency—the ability to transform what they eat into meat and fat—as well as cattle that exhibit faster weight gain, resistance to parasites and diseases, and more tender meat. This selective breeding was initially performed using only animals' visible features, but the information encoded in their genes has been found to aid in the selection of

cattle with desired qualities for meat production. Most studies have been performed on the Nelore breed of the zebu subspecies (*Bos taurus indicus*), which originated in India and composes 80% of Brazil's cattle herds.

An analysis of the structural and functional variations in the Nelore genome and their associations with production-related traits, such as meat quality and breed feeding efficiency, has been carried out by the veterinarian Luciana Correia de Almeida Regitano, an animal genetics researcher from EMBRAPA Livestock Southeast, one of the branches of the Brazilian Agricultural Research Corpo-

ration (EMBRAPA) located in the city of São Carlos, São Paulo. "The goal is to understand the molecular mechanisms that contribute to genetic variation and that affect the animal's phenotype [an individual's set of observable characteristics]." Using this information, farmers can select animals that exhibit favorable characteristics or can even induce mutations in the animal's genome, thereby improving the breed's traits.

One of these studies, conducted by Regitano's group, examines the KCNJ11 gene. In mice, a lack of expression of this gene led to low food use and muscle weakness. "When we investigated the



Nelore cattle herds on the Brazilian Agricultural Research Corporation (EMBRAPA) farm in São Carlos: complete gene and protein sequencing to determine individual differences

function of this gene in cattle, we found it to be associated with meat tenderness,” Regitano explained. “Animals with reduced expression of this gene were found to have more tender meat, but they also exhibited lower hay consumption, lower daily weight gain, and lower growth rates. These results indicate how interfering in the expression of a single gene can have both positive and negative results from a farmer’s point of view.”

In Brazil, these studies have become particularly important: the country is the second largest cattle producer in the world, with 215.2 million head of cattle in 2015, and is second only to India, which

had 330 million head in 2014. Zebu cattle, which are the dominant subspecies in Brazil, are adapted to tropical climates, in that they are more resistant to diseases and weaker pastures. Good, tender meat is associated with a higher fat content, which occurs in the subspecies *Bos Taurus taurus*, of European origin.

Comparisons between Angus (the most common European breed raised in Brazil, particularly in the south of the country) and Nelore meat are one way to understand that factors that distinguish them beyond the higher fat content in the European breed. This was the focus of a doctoral dissertation by

the veterinarian Rafael Torres de Souza Rodrigues from the Federal University of Lavras (UFLA) in Minas Gerais State. “We wanted to know why European cattle meat is tenderer and has more intramuscular fat than zebu cattle meat.” The researcher, now working on his PhD at the Federal University of Vale do São Francisco (UNIVASF) in the city of Petrolina, Pernambuco State, compared the proteomes (sets of proteins) from the muscles of these breeds soon after slaughter. “Because proteins make up most of the muscle tissue, and because they are responsible for tenderizing the meat after slaughter, the difference in the

abundance of specific proteins between the two breeds may explain why one is tenderer than the other,” Rodrigues explains. He found evidence that the difference in meat tenderness is associated with the same mechanisms that guide apoptosis, or programmed cell death. This mechanism is triggered by cellular stress, which itself is caused by factors such as a lack of oxygen or glucose and a drop in pH, all of which occur after the animal dies.

“In recent years, this biochemical process has been found to be responsible for coordinating meat tenderizing after slaughter,” Rodrigues said. Currently, the difference in meat tenderness between zebu and taurus cattle has been largely attributed to the zebu subspecies’ higher activity of a protein known as calpastatin. “This protein inhibits calpain activity. Calpains are the main enzymes responsible for meat tenderness after slaughter.” In his study, Rodrigues established a correlation between these two mechanisms: his hypothesis was that the increased activity of this protein in zebus occurs because the muscle cells of these animals are more resistant to apoptosis. “The most interesting thing is that caspases, the main enzymes that perform apoptosis, have been associated with calpastatin degradation.” If his hypothesis is proven true, Rodrigues says, researchers will be able to consider developing techniques and procedures to stimulate apoptosis in Nelore muscles soon after slaughter, thereby decreasing the negative effect of calpastatin on zebu meat quality. “This could be achieved through selective breeding using animals that better express genes that codify proteins and stimulate apoptosis, or through treatment that accelerates this biological process.”

DNA CHIPS

Studies in molecular biology involving bovine proteomics and genomics are being conducted in many other countries, including the United States, France, Italy, and Australia.

An important milestone in genetic studies on cattle was the complete sequencing of the bovine genome in 2009, a project that involved 25 countries, including Brazil. This success was followed by the development of methods to analyze and understand how this ge-



The bovine DNA chip is a blade with sensors used to determine familial relationships within a group of animals, as well as to identify genetic defects

nome works. One of the new technologies uses molecular markers known as single nucleotide polymorphisms, or SNPs. These are variations in DNA sequences that allow for differentiation between the individuals of a single species (or breed) and may be associated with certain characteristics, such as meat tenderness, for example.

The first Brazilian SNP chip for cattle was created by a research group led by the veterinarian José Fernando Garcia, a professor at the School of Veterinary Medicine of São Paulo State University (UNESP) at Araçatuba. “It’s a test that brings together all of the conditions necessary to identify, with certainty and in a way that can be repeated, a large amount of specific DNA markers associated with information that we hope to investigate in the animals,” the professor explains. Garcia also explains that because the first SNP chips developed in the world were based on the genomes of taurus breeds, it was difficult to use them in improvement studies of zebu breeds, which are common in Brazil.

Garcia then partnered with selective breeding and genome analysis companies, such as Illumina in the United States, which creates technology for this type of chip. With the support of these companies and FAPESP, Garcia developed an SNP chip containing 30,000 markers for use in zebu cattle, and this chip has now been on the market for a few years. The chips were analyzed by the Araçatuba-based company De-oxi Biotecnologia, which was acquired by the American company Neogen last year. For these devices, a blood, hair, or muscle sample from the cow or bull is enough to generate the amount of DNA necessary to be placed on the chip a slide with nanotechnological sensors which is then used in laboratory analysis. The price of each test ranges from R\$100 to R\$180, depending on the number of SNPs. “This technology may also be used to determine familial relationships between animals,” Garcia notes. It may also be employed for genomic selection, inbreeding control, genetic defect detection, and product certification. The test may also be applied to research projects to discover genes that may be candidates for explaining phenotypes of interest, such as meat tenderness, milk production, and disease resistance.

This new knowledge of DNA and SNPs has led to the discovery of genome editing, which is performed using biotechnological techniques. These techniques include a relatively new tool that involves regularly interspaced short palindromic repeats (CRISPR), a system that relies on the Cas9 protein to introduce targeted mutations into the genome of a living being. “With this technique, if a bull with exceptional production traits was identified as the carrier of a hereditary disease, it would be possible to easily produce a clone of this animal with corrections to the gene sequence associated with the disease,” explains Regitano from EMBRAPA. Genome editing techniques also make it possible for beneficial gene mutations from one animal to be induced in the DNA of another. Another example of this application comes from the United States, where researchers have produced hornless calves from a Dutch breed by inducing the mutation in the gene that controls horn development.

Regitano’s group also discovered differences in the genetic profiles of ani-

2
mals with better or worse performance of 10 production traits and detected both genes and metabolic pathways that may control differences between individuals, as well as copy number variations (CNVs) in genome regions that affect meat tenderness. In a former project, 800 steers were monitored from conception to slaughter (*see* Pesquisa FAPESP, issue No. 179), and their DNA was analyzed to investigate more than 700,000 SNP markers. The result was the identification of genome regions that influence the manifestation of ten attributes.

For her most recent study, Regitano used one of EMBRAPA's own Nelore herds with 200 animals selected from the former group of steers. All of the steers underwent complete gene and protein sequencing to determine what genes and proteins influenced muscle tissue at the time of slaughtering. "Our studies have identified various genes that may be targets for gene editing," Regitano explains. EMBRAPA Livestock South has conducted these studies in partnership with EMBRAPA Informatics in Campinas, with the University of São Paulo (USP), and with American universities in Iowa and Missouri, as well as with the Commonwealth Scientific and Industrial Research Organisation (CSIRO) of Australia. Regitano reports that other applications are possible, such as the use of nutrients or drug products to activate or inhibit genetic processes. ■

Projects

1. Molecular bases for the quality of meat in bovines of the Nelore breed (No. 12/23638-8); **Grant Mechanism** Thematic Project; **Principal Investigator** Luciana Correia de Almeida Regitano (EMBRAPA); **Investment** R\$2,688,295.06.

2. Studies of genomic associations of the reproductive traits of zebu steers (*Bos indicus*) using a high-density SNP chip (No. 10/52030-2); **Grant Mechanism** Regular Research Grant; **Principal Investigator** José Fernando Garcia (UNESP); **Investment** R\$338,482.64.

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SILVA, V. H., *et al.* Genome-wide detection of CNVs and their association with meat tenderness in Nelore cattle. **PLOS ONE**. v. 11, i. 6. 27 Jun. 2016.

TIZIOTO, P. C., *et al.* Gene expression differences in longissimus muscle of Nelore steers genetically divergent for residual feed intake. **Scientific Reports**. v. 6. 22 Dec. 2016.

ZHOU, Y., *et al.* Genome-wide CNV analysis reveals variants associated with growth traits in *Bos indicus*. **BMC Genomics**. v. 17, 419. 1 Jun. 2016.

Angus cattle of European origin: gene and protein analyses to determine why Angus meat is tenderer than Nelore cattle





Electrical steel coils at Companhia Siderúrgica Nacional (CSN), in Volta Redonda, Rio de Janeiro State

More efficient metals

Technological innovations enhance
performance of steel used in
electric motors and power transformers

PUBLISHED IN JANUARY 2017

The global demand for more efficient consumption of electrical energy is driving the evolution of steel used in the manufacture of refrigerator compressors, air conditioners, generators, and transformers. In production since the early 20th century, a magnetizable metal called electrical steel, composed basically of iron and silicon, can transform electrical energy into mechanical energy. A steady push is underway to improve the performance of this material and meet the needs of conventional manufacturing industries, such as the home appliance sector, and more state-of-the-art technologies, including electric car design. In the 1990s, Brazilian steelmaker Companhia Siderúrgica Nacional (CSN) and a team of researchers from the São Paulo Institute for Technological Research (IPT) collaborated to develop a project under a FAPESP program called Research Partnership for Technological Innovation (PITE). The company's electrical steel production system was successfully overhauled as a result, bringing a 30% increase in product efficiency. The latest innovation comes from Minas Gerais-based steelmaker Aperam (formerly Acesita). In the closing quarter of 2016, the enterprise completed a series of improvements to its production processes, enabling it to begin manufacturing an even more energy-efficient material: high-permeability grain-oriented (HGO) steel.

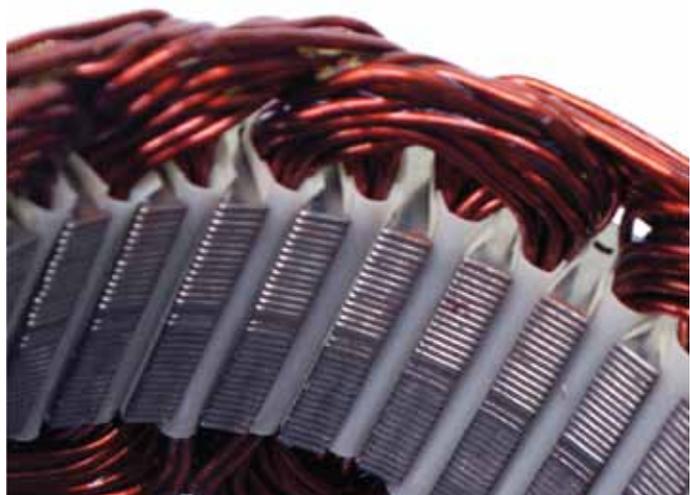


Motors consume half of all electrical energy worldwide

“This technology lowers core loss during the energy transformation process by as much as 30% in the metals,” says Aperam engineer Rubens Takanohashi. Core loss refers to the energy dissipated as heat during alternating magnetization and demagnetization of the metal. HGO steel is an outgrowth of one of two other types: grain-oriented (GO) electrical steel, a high-performance metal used in transformers, which change and adapt the voltage in alternating current electrical circuits, and non-grain-oriented (NGO) electrical steel, used in motors, compressors, and generators. GO steel displays a core loss of approximately 1.25 watts per kilogram of material, a figure that drops to approximately 0.95 watts with HGO. The difference may seem minor, but it is quite significant given that the loss occurs across all transformers in Brazil. “The Brazilian market was demanding it,” says Takanohashi. “This material makes it possible to produce more efficient transformers that are 10% to 15% smaller, while taking less feedstock to manufacture and facilitating transportation of the equipment.”

The Aperam factory in Timóteo, Minas Gerais, has the only GO steel plant in Latin America and now boasts the only HGO plant as well. The new facility is one of 15 operating in 10 countries. The startup of HGO production required an investment of \$19 million over two years. Rather than purchasing a technological package, the company opted to devise an in-house solution; this demanded eight

Aperam steel plant in Timóteo, Minas Gerais (above). IPT experiment: steel sheet wrapped in copper wire (right)



years of investigations at the Aperam Research Center in Timóteo, where six researchers are assigned to developing electrical steels.

Brazil consumes approximately 45,000 metric tons (mt) of GO electrical steel every year. The world steel market is estimated to consume nearly 12.5 million mt per year of electrical steel, divided into 2.5 million mt of GO and 10 million mt of NGO. In Brazil, the total consumption of both types of finished products plus semi-finished products stands at approximately 400,000 mt per year. The Aperam plant has an annual production capacity of 60,000 mt of GO steel and a current yearly output of 55,000 mt, which supplies the domestic market and other countries in Latin America. Making the new HGO steel will not boost the company’s capacity but will shift its prod-

uct profile. According to Takanohashi, Aperam currently has no projections about the future proportion of HGO in its product mix. He states that “It will depend on demand.”

ECO-EFFICIENT MOTORS

Steel sheets are composed of billions of crystals. While the crystal grains vary in size, their diameter averages approximately 100 μm (1/10 of a millimeter). In electrical steel, the crystals are cube-shaped, and the greater the number of crystals oriented with one side of the cube parallel to the direction in which the sheet is rolled, the better its magnetic property. “Although technological advances have yielded ‘recipes’ that afford good control over crystal orientation on a steel sheet, science hasn’t yet been able to explain how this occurs,”



Aperam manufactures new electrical steel products that are used to make smaller, more efficient transformers

says metallurgical engineer Fernando Landgraf, CEO of IPT.

Landgraf leads an electrical steel research group at the Department of Metallurgical and Materials Engineering of the University of São Paulo's Polytechnic School (Poli-USP), where he is a professor. The group evaluates crystal size, spatial orientation, impurities, and crystal defects. Both the IPT and the Polytechnic School have been researching magnetic materials since 1982. In the 1990s, a team of researchers led by Landgraf applied its experience in magnetic research to designing solutions for the electrical steel market.

According to Landgraf, research into more efficient electrical steel is currently a global concern and an integral part of the drive for energy savings. He states that "It is estimated that 50% of the electric power produced worldwide every year is consumed by motors. Approximately 3% of this energy is dissipated through core losses. These numbers can be reduced by developing more efficient electrical steel."

SECOND FAMILY

In the early 1990s, CSN began making NGO electrical steel to supply manufacturers of motors used in low-efficiency electrical equipment such as car parts and in kitchen appliances including blenders

and microwave ovens. The company's next challenge was to design a second family of electrical steel to enter markets that demand greater energy yield, including makers of refrigerator compressors, air conditioners, and industrial motors.

Nilza Cristina Sabioni Boechat Zwirman, manager of specifications and product systems with CSN's division of Research, Development, and Innovation, says that the company was then working on research that explored the possibility of adding chemical elements such as silicon, phosphorous, and aluminum to electrical steel to enhance its magnetic properties. The IPT began collaborating with CSN in 1994, when institute researchers attempted to bring steelmakers, stampers, and motor manufacturers together to form a technological consortium. The group never materialized, but CSN took an interest in the research and proposed an exchange effort. The partnership was born as a project under PITE, a program launched by FAPESP in 1994 to fund initiatives developed jointly by research institutes and businesses.

At that point, the IPT team was already aware that controlling grain orientation is important when producing NGO steel; they also knew that certain impurities, such as exceedingly tiny crystals, impair the magnetic properties of the steel. "CSN had previously focused on

making chemical improvements to electrical steel and had tried to link the microstructure of the metal and the control of impurities to core losses. Our studies helped them rethink their production processes," says Landgraf. According to Zwirman, by adjusting production processes, CSN could manufacture a steel product that displays a 30% lower electrical energy loss than the product line previously offered in its catalog.

Zwirman explains that developing a line of electrical steel of medium efficiency allowed CSN to keep pace with a robust market trend in recent years: energy efficiency labeling for electrical equipment. In Brazil, the National Institute of Metrology, Quality, and Technology grants the National Energy Conservation Seal, while the National Program for Electrical Energy Conservation (PROCEL) offers the PROCEL Seal. The IPT-CSN contract was one of the first signed under the PITE program. "PITE was really important. If the costs of innovation hadn't been shared, it's unlikely the research would have moved forward," states Landgraf. The joint IPT-CSN efforts took nearly four years. Since project completion, the company has produced over 500,000 mt of electrical steel, mainly for the Brazilian market.

Zwirman believes the partnership extends beyond financial investment in the project. "It afforded a valuable opportunity to share skills," she says. According to her, CSN contributed by opening the doors to its industrial park and providing steelmaking experience, while the IPT chipped in with technical know-how, laboratories, and ties to other institutions. In addition, the Nuclear and Energy Research Institute (IPEN) furnished its knowledge on how to measure the distribution of grain orientation, and the Center for the Characterization and Development of Materials (CCDM), at the Federal University of São Carlos (UFSCar), offered assistance in the realm of transmission electron microscopy (TEM) of steel structure. ■ Domingos Zapparoli

Project

Development of electric steels (No. 95/03988-7); Grant Mechanism Research Partnership for Technological Innovation (PITE); Principal Investigator Fernando Landgraf (IPT); Investment R\$137,096.77 (FAPESP) and R\$154,500.00 (CSN).

Settlers and farmers

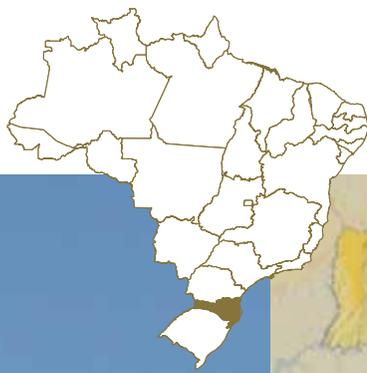
Ancestors of the Jê group lived in pit houses and cultivated cassava and beans in the Santa Catarina highlands a thousand years ago

Marcos Pivetta

PUBLISHED IN FEBRUARY 2017

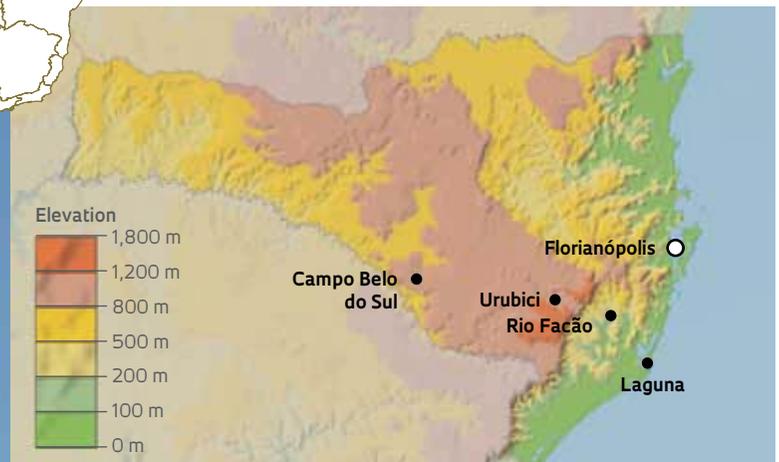
New archaeological studies have put to the test the traditional view concerning the indigenous peoples of the Jê linguistic branch who lived between present-day southern São Paulo State and northern Rio Grande do Sul state in the first half of the previous millennium. Recent excavations at sites in the highlands of Santa Catarina state indicate that these groups—ancestors of Indians of the present-day Kaingang and Laklãnô/Xokleng ethnic groups—were more than simply hunter-gatherers who led a nomadic life with a well-defined social hierarchy and no fixed residence. They practiced agriculture and were able to live for long periods in pit houses, most likely for protection from the cold climate of that region. A series of studies further suggests that the proto-Jê, as experts now call these pre-Colombian peoples, had considerable knowledge of their natural surroundings, knew to some extent how to manage the *araucária* (Brazilian pine) forest, and were capable of shaping the local landscape. The *araucária* tree, for example, supplied them with pine nuts, an important part of their diet.



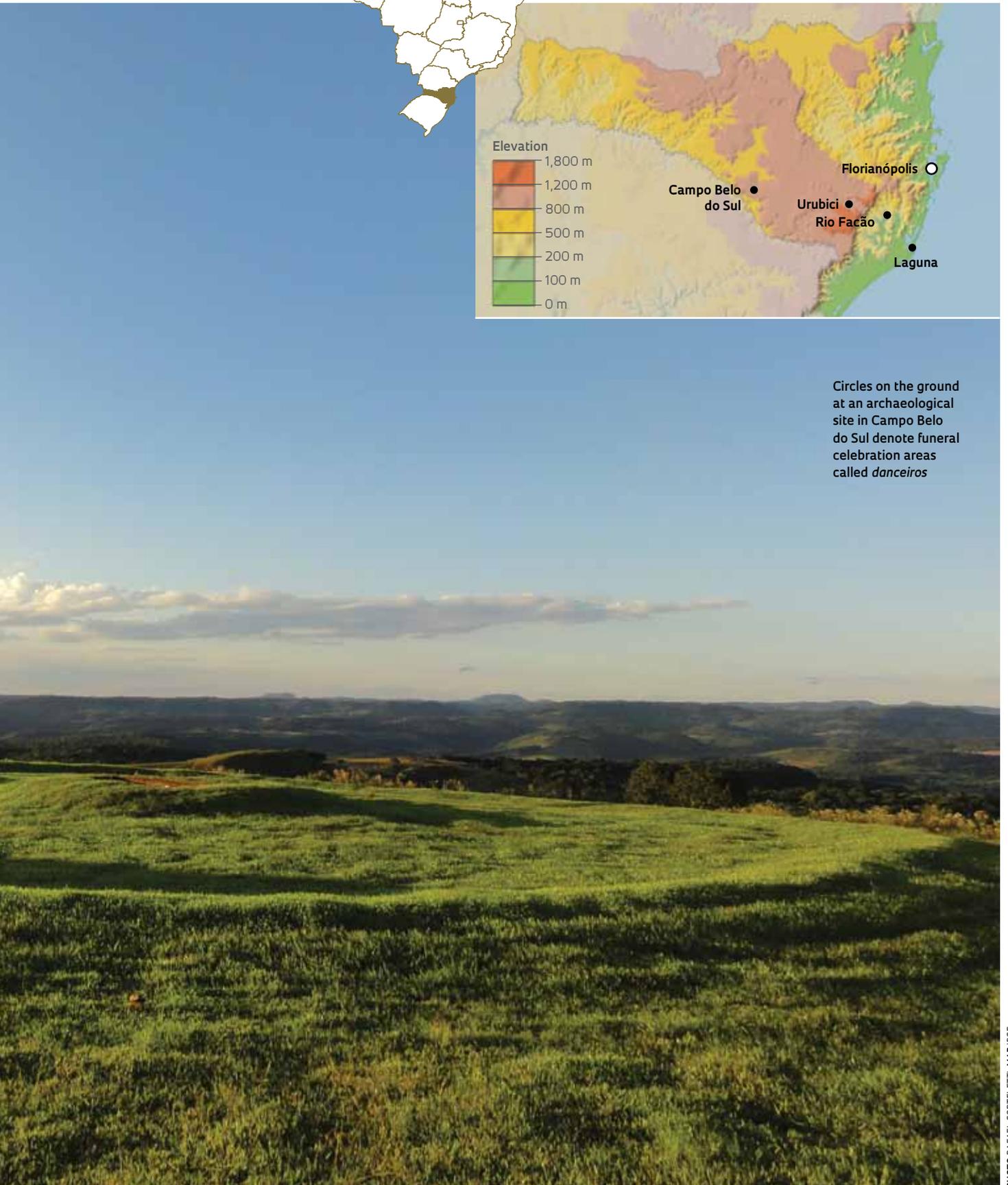


THE PROTO-JÊ CULTURE IN SANTA CATARINA

An international project excavates sites in four municipalities



Circles on the ground at an archaeological site in Campo Belo do Sul denote funeral celebration areas called *danceiros*





Remnants of plants that existed in the Santa Catarina highlands in the era of the proto-Jê, such as *araucária* pollen (at left), are studied for clues on forest expansion

Their extensive interaction with the southern highlands landscapes is an important indicator of the ancient way of life of the proto-Jê, who generally inhabited inland areas of Brazil and were adversaries of the peoples of the Tupi-Guarani linguistic family. The latter were a more populous group typically associated with coastal areas and the lowlands of the great fluvial plains. A paper describing an oversized pit house built by the proto-Jê, published in the scientific journal *PLOS ONE* in July 2016, illustrates some of the hypotheses concerning this new focus. In the paper, researchers from the Museum of Archaeology and Ethnology at the University of São Paulo (MAE-USP) as well as the University of Exeter and the University of Reading, both in the United Kingdom, describe a house with 12 archaeological layers of occupation at the Baggio I site in Campo Belo do Sul, in the highlands of Santa Catarina.

According to their analyses, the house was occupied continuously for approximately 250 years, between AD 1395 and 1650. The remains of the house occupy a circular area 16 meters (m) in diameter and up to 1.6 m in depth. “We have found no evidence that the house was abandoned for any lengthy amount of time,” comments MAE archaeologist Paulo DeBlasis, who heads an international project studying the southern proto-Jê,

in collaboration with the group headed by José Iriarte of the University of Exeter. “This fact contradicts the view that the proto-Jê had no fixed place of residence.” Construction of ancient pit houses of this type, also found at archaeological sites in other cold regions of the world, was begun by excavating a large rounded pit in the rocky ground. Large tree trunks inserted at different points on the excavated floor of the house functioned as pillars. With the help of these supports accompanied by wood framing, the Indians built a straw-covered roof that extended beyond the pit. An opening served as the entryway.

The international team used the carbon-14 method to date samples of charcoal found in each of the house’s 12 layers. Between the deepest, oldest layer and the shallowest, most recent layer of the site where the house was built, the chronology that they obtained is practically continuous. “The house shows evidence of periodic renovations, including roof-burning rituals,” says Brazilian archaeologist Jonas Gregório de Souza, who is pursuing his doctorate at the University of Exeter.

The deepest layer indicates an occupation that began in the late fourteenth century, and the twelfth layer provides evidence that the house was last used in the mid-seventeenth century, by which time European colonists had settled there. Remnants of five different collapsed and burned roofs made of plant fibers were found in the archaeological layers of sediments that contain the remains of the pit house. “It makes no sense to build a house with these features for a temporary home,” says archaeologist Rafael Corteletti of the Federal University of Pelotas (UFPel), who participated



Blackened fragments of ceramics indicate the use of containers for cooking food

in the project. “Additionally, an intervention of this size in the landscape indicates that the proto-Jê had a well-structured social organization after AD 1000.”

Surrounding the oversized house at the Baggio I site, which sits at the highest point in the area at an elevation of 1000 m, there are seven smaller pit houses between 2 m and 5 m in diameter. On the outskirts of this village are funeral sites, popularly known as *danceiros*, consisting of circular earthen structures and funeral mounds. The *danceiros* can exceed 150 m in diameter. In lower areas of the site, there is a group of eight houses with diameters of 2.5 m to 7 m.

In terms of artifacts, the site excavations corresponding to the period of the house’s early occupation reveal a large array of a type of ceramics that differs somewhat from the rustic Itararé-Taquara tradition, which features small, slender, dark-colored pieces typically associated with the proto-Jê groups. The greatest abundance of ceramic finds from the early decades of use are thicker and reddish. The interiors of many pieces are blackened and contain residues from burning—an indication that they were used to process foods. “Most of the pit houses were most likely used as residences but not necessarily by farmers. Hunter-gatherer societies also could

have occupied this type of house,” says archaeologist Silvia Copé of the Federal University of Rio Grande do Sul (UFRGS), one of the project’s collaborators, who has excavated nearly 60 proto-Jê sites in that state, located in Bom Jesus and Pinhal da Serra. “The pit houses also could have been used as silos.”

Another site in the Santa Catarina highlands that strengthens the hypothesis that the proto-Jê were not nomads and did not live from hunting and fishing alone is Bonin, in the municipality of Urubici, near Lages, which is currently one of the coldest places in Brazil. There, researchers found a village with 23 partially underground houses scattered across a 3-hectare area on the upper floodplain of the Canoas River. In a paper published in the *Journal of Archaeological Science* in June 2015, Corteletti, DeBlasis and their colleagues give the first report of the identification of remnants from the consumption of cassava, beans and perhaps yams at a proto-Jê site, in addition to the traditional maize and squash. They discovered residues of starch and phytoliths (microscopic particles of silica, formed in plants) associated with these plants in 14 ceramic fragments found in two underground structures that appear to have been used as “kitchens” at the Bonin site. According to the dating results obtained by the researchers, the site was occupied between AD 1300 and 1440. “These discoveries indicate that the southern proto-Jê had a diversified subsistence economy and that in addition to hunting, fishing and gathering, they produced their own food more than a century before the arrival of the Europeans,” Corteletti notes.

If they devoted time to some form of agriculture, the researchers say, then they most likely had settled in the region. When added to the evidence of a long, continuous occupation of some houses in the Santa Catarina highlands, as appears to be the case with the oversized house at the Baggio I site, the clues that the ancestors of the present-day Kaingang and Laklânõ/Xokleng cultivated the land are at odds with the more traditional idea that these native people remained nomads until they began to decline. That more widespread view holds that the proto-Jê had a seasonal economy, which forced them to alternate between the highlands and the coast to survive.

According to this model, the ancient Indian populations generally moved to escarpment areas and the coast in spring and summer due to the scarcity of natural resources in the highlands during the hotter seasons and returned to the mountainous areas in the fall, when pine nuts—their principal source of food—could be harvested. “However, our research indicates that the proto-Jê were also farmers and were able to

Discovery of the oldest archaeological site in São Paulo

Flakes indicate that Paleoindians inhabited the central part of the state, near São Carlos, 12,600 years ago

Identified two years ago on land in the municipality of Dourado, approximately 50 kilometers from São Carlos, the Bastos archaeological site holds remnants of humans' presence in the state of São Paulo that date back 12,600 years, according to a study published in the journal *Palaeoindian Archaeology* in December 2016. Researchers found 449 pieces forged by human hands, most of which were flakes of silicified sandstone. Six samples of charcoal and one of organic matter, removed from different geological layers associated with the lithic pieces, were dated using the carbon-14 method. "These data make Bastos the state's oldest site, equivalent to those in Lagoa Santa, Minas Gerais," explains Astolfo Araujo, the leader of the team that made the discovery and a researcher with the University of São Paulo's Museum of Archaeology and Ethnology (MAE-USP). "Little by little, we are showing that the state's interior contains important archaeological sites." A few other pieces are being analyzed using a different method, luminescence dating, but those results were not yet available. No human skeletons have been found in Bastos; thus, researchers still do not know whether Paleoindians settled in Dourado earlier than 10,000 years ago.

Since 2009, Araujo and his students from the MAE, such as master's candidate Letícia Correa, who participated in the excavations at Bastos, have been conducting systematic field trips to search for new evidence of the first human occupations in the state of São Paulo. The discovery of the site in Dourado, which is in an open-air location (and, therefore, lies outside of any cave or shelter), occurred almost by accident. Four years ago, the owner of a coffee plantation in that municipality contacted the researcher and offered his property to be used for excavations. "He had already found some archaeological material there, but he had no idea what it was," Araujo says.

The researchers made three trips to the area, identified the site and, upon dating the finds, were shocked at their antiquity. According to the data, Bastos was the locale of two different occupations in prehistory: an older occupation from approximately 12,500 years ago and another more recent occupation, no older than 9,000 years. In the 1980s, dating analysis of samples of charcoal from the Alice Boer site in Rio Claro yielded an age of 14,000 years, but those results are disputed by many archaeologists. In addition to Bastos, Araujo found another ancient site in Dourado: Lagoa do Camargo 1, also in Rio Claro, which dating analysis placed at 10,500 years old.

In the same issue of the journal *Palaeoindian Archaeology*, a team from the firm Zanettini Arqueologia reports the discovery of another locale with very old Paleoindian artifacts in inland São Paulo. The Caetetuba site in the municipality of São Manuel, 25 kilometers from Botucatu, yielded nearly 3,500 fragments and artifacts from a lithic industry of human origin that was established there nearly 11,000 years ago, according to dating analysis of charcoal samples taken from the site. Notable among the materials



Pieces from the lithic industry at the Bastos site in Dourado, now the oldest in the state



recovered are arrowheads made of silicite, in addition to plano-convex scrapers made of silicified sandstone, resembling snails.

"Despite all of the research already conducted, inland São Paulo has countless gaps that have sometimes been filled by preventive archaeology," says Paulo Zanettini, whose company specializes in developing programs designed to analyze and mitigate impacts on archaeological heritage as part of the environmental project permitting process. The Caetetuba site, for example, was located during excavations to calculate the effects of expanding a sugarcane plantation in the area.



Arrowheads found at the Caetetuba site in São Manuel, which were dated at nearly 11,000 years old

Project

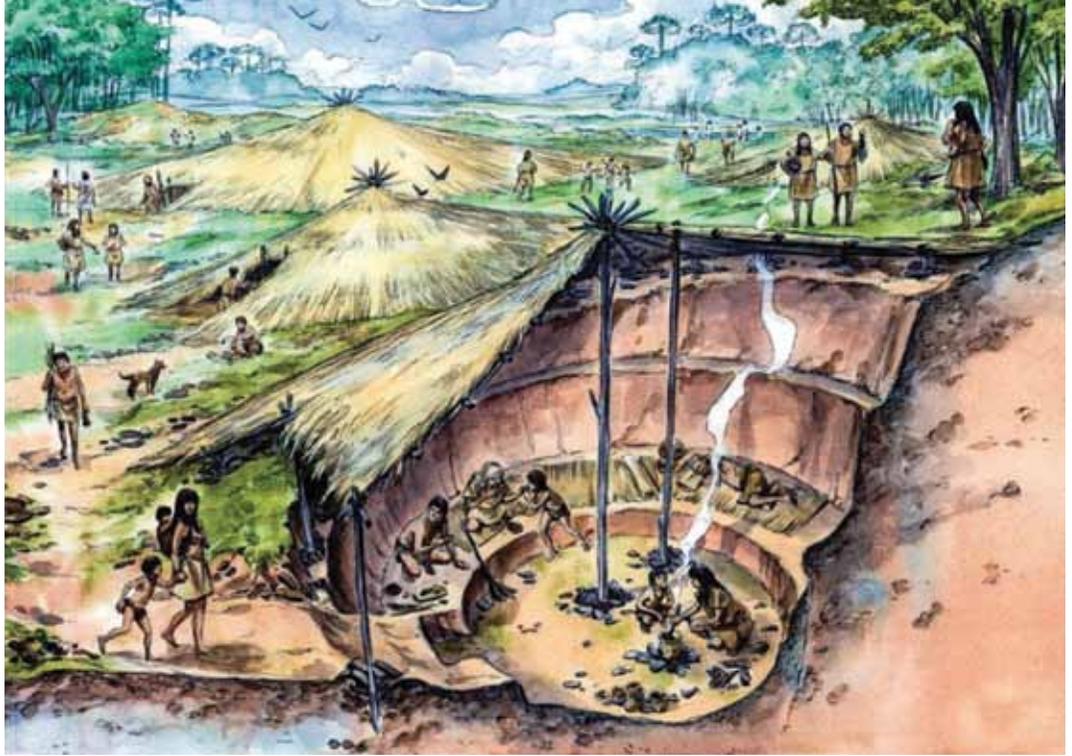
The Paleoindian occupation of São Paulo State: a geoarchaeological approach (No. 13/13794-5); Grant Mechanism Regular Research Grant; Principal Investigator Astolfo Araujo (USP); Investment R\$247,647.91.

Scientific articles

ARAUJO, A. G. M. & CORREA, L. First notice of a Paleoindian site in central São Paulo State, Brazil: Bastos site, Dourado County. *Palaeoindian Archaeology*, v. 1, i. 1, 2016.

TRONCOSO, L. P. S. *et al.* Paleoíndios em São Paulo: Nota a respeito do sítio Caetetuba, município de São Manuel, SP. *Palaeoindian Archaeology*, v. 1, i. 1, 2016.

Artistic rendering of the pit houses built by the proto-Jê



The present-day Kaingang and Laklãnõ/Xokleng ethnic groups descend from the ancient southern Jê peoples

establish residence in certain places,” DeBlasis suggests. Depending on when they are planted, cassava and beans—two of the plants found at the Bonin site—can be harvested in spring and summer, which in theory clashes with the idea that resources were scarce during the hot season in the highlands. To study how these ancient peoples occupied sections of the coast and the escarpments of the Santa Catarina mountains, the international project is also conducting excavations at archaeological sites in two additional low-lying areas, Laguna, on the coast, and Rio Facão, on the slope.

The relationship of the proto-Jê to the *araucária* forest and pine nuts is an intriguing subject in the minds of archaeologists. The first pit houses associated with these peoples date back to 300 BC. But the development of this type of construction, which is found at approximately a hundred archaeological sites in the states of Rio Grande do Sul, Santa Catarina and Paraná, occurred circa AD 1000—precisely when the *araucária* forest was greatly expanding, according to paleobotanical data. One possible interpretation for this coincidence is that the growth of the *araucária* forest, which provided food for the native peoples and attracted the animals that

they hunted, made it possible for the proto-Jê to disperse. Some researchers raise the possibility that the increased coverage of the *araucária* forest may have been stimulated, at least in part, by the ancient inhabitants of that region. The Indians likely used selective tree-cutting and thereby promoted *araucária* propagation.

The Chilean paleoecologist Macarena Cárdenas, a postdoctoral researcher at the University of Reading, is investigating this hypothesis. She has collected samples of sediments from depths of up to 2 m at sites in the four areas where the project is conducting excavations. Using this material, which can contain preserved remnants (pollen, seeds, charcoal) of the vegetation that occurred over the past 8,000 years, she is constructing models of the growth of the area occupied by *araucárias* in Santa Catarina. “We are going to study the vegetation in different areas over time and compare it with the distribution of the proto-Jê people,” the researcher explains. “In Amazonia, there are indications that the management of palm trees promoted the expansion of human occupation in the past. Perhaps *araucárias* played an important role in the South.” ■

Project

Jê landscapes of Southern Brazil (No. 12/51328-3); Grant Mechanism Thematic Project; (AHRC, RCUK Agreement); Principal Investigator Paulo DeBlasis (USP); Investment R\$897,654.12.

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Seeking freedom and survival

Slave women used strategies to purchase their liberation and obtain employment

Christina Queiroz

PUBLISHED IN MARCH 2017

Refusing to work, talking back to their masters and causing minor damage became strategies employed by enslaved black women to reduce their personal value and thus lower the price they would have to pay for freedom. Some even resorted to seeking protection from families who were enemies of the masters whom they served in order to obtain their freedom. Abolition did not occur until 1888, but after the enactment of the Law of Free Birth in 1871, which declared all children born of slaves to be free after the law was passed, slaves acquired the right to purchase their freedom. Saving money for that purpose required sacrifices beyond slavery, such as working on rare days off or negotiating the portion of their pay that would be passed on to their owners. Women were more successful than men in these strategies, primarily due to the demand for domestic services. Once freed, however, they had to overcome other obstacles

no less difficult than the previous ones: finding sufficient work to support themselves, assuming sole responsibility for their children, and gaining a place in local society.

In research that she began during her master's studies and continued during postdoctoral studies at New York University, historian Lúcia Helena Oliveira Silva, a professor at the São Paulo School of Sciences and Letters on the Assis campus of São Paulo State University (FCL-UNESP), examined how African and Afro-Brazilian female slaves used the courts to win emancipation. "Starting with a study of 157 lawsuits that were heard at the court in Campinas, I found that women were involved in more than half of the proceedings for the purchase of freedom," says the researcher, who is the assistant coordinator of the Negro Center for Research and Extension (NUPE-UNESP).

Slaves who wanted to purchase their freedom would petition for an audience



Quituteiras in Rio de Janeiro, in 1875: women had more employment options than men



with the local judge in order to establish the price to be paid. They had to be represented by a free man because, under the law, they were not considered persons but someone's property. According to Silva, in order to earn the sum stipulated for their release, slaves worked as laundresses and nannies, wet nurses, and embroiderers, as well as in starching and ironing clothes. They also sold homemade foods on the streets or grew vegetables in small gardens. The domestic market offered more opportunities for freed women than for the slaves.

To win their freedom more quickly, slave women took steps to reduce their

value, such as making repeated attempts to escape, the researcher found. The case of a slave, Cristina, serves as an example. Taken against her will from Rio de Janeiro to Campinas, she refused to remain in that city. Although frequently beaten, she would not obey the master's orders. He decided he had made a bad deal and got rid of her, sending her back to Rio de Janeiro. "Cristina was on the brink of death, but in the end, she got what she wanted," says Silva.

Another ruse was to take advantage of the close friendships between masters. Silva tells the story of a captive in the interior region of São Paulo who, after

being beaten, fled to the house of an enemy family. The patriarch of the family who accepted her was a judge. Later, she won her freedom with his help. "Stories like these enable us to break down the stereotype of the well-behaved female slave who earned her emancipation letter from the master as a reward," the historian argues. "Or even the image of the rebellious slave who was always trying to escape and was therefore condemned to be forever enslaved."

Once freedom was achieved, a slave's problems were far from over. Needing the intervention of third parties to make freedom feasible meant that relation-

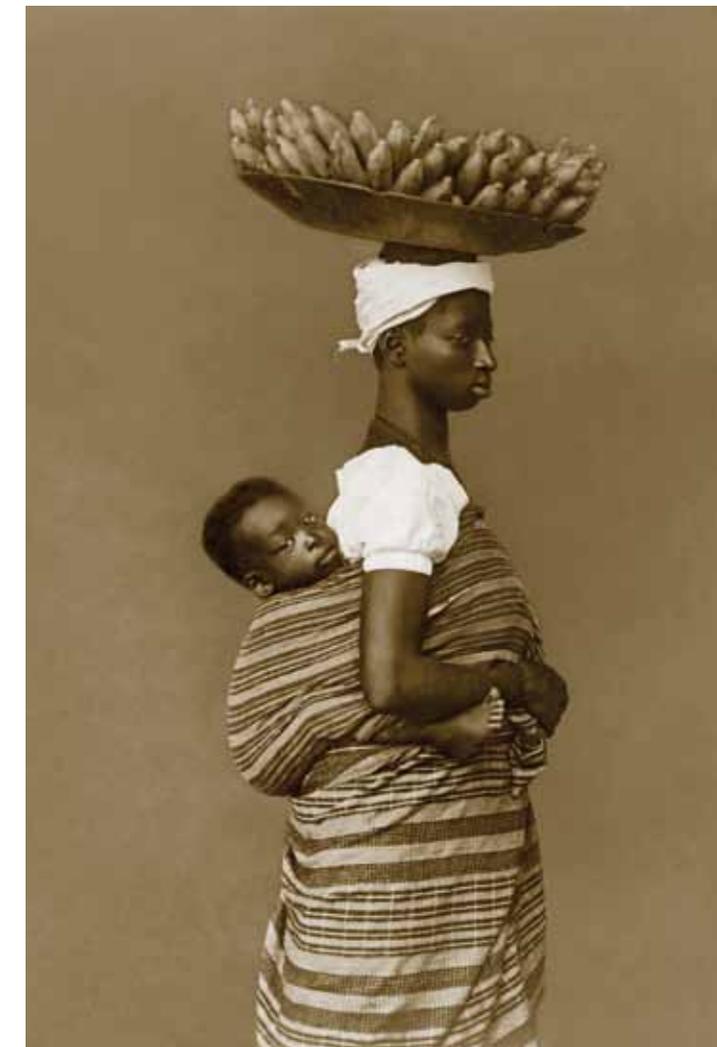
ships of dependency were often created. These might entail providing services, agreeing to sexual relationships, or making cash payments.

From 1888-1926, one of the survival strategies adopted by freed women in São Paulo was to move to Rio de Janeiro. Based on her analyses of census documents available in the records of proceedings of the São Paulo state legislature, Silva observed that, between 1888 and 1890, the state of São Paulo was home to the third largest contingent of slaves in Brazil. However, by 1892, blacks had become scarce in the region. “The experiences of freed people and Afro-descendants in São Paulo were permeated by expectations of winning a place in society, countered by attempts by the masters to maintain the socio-racial situation that prevailed before Abolition,” she says. With the arrival of European immigrants, entering the labor market became even more challenging because employers preferred to hire whites.

On the other hand, Rio de Janeiro served as a place for slaves and freedmen from all over Brazil to fraternize. “The docks at the port and the availability of urban odd jobs to be performed by the black community facilitated their absorption into local society,” she says. One hypothesis advanced by Silva for this migratory movement is that freed slaves wanted to escape the stigma of slavery, a mark usually more apparent in the context of smaller cities; São Paulo, in 1900, was a city of approximately 240,000 inhabitants, whereas the population of Rio de Janeiro had reached 811,000.

Historian Isabel Cristina Ferreira dos Reis, a professor at the Center for Arts, Humanities, and Letters of the Federal University of the Recôncavo of Bahia (UFRB), reports that, contrary to the movements of former slaves from São Paulo, those from the sugar mills in the Recôncavo region of the state of Bahia, the area with the highest concentration of slave labor, remained close to the places where they had lived. This was because of their desire to maintain family and community ties.

Additionally, in Recife, many freed female slaves preferred to remain in the region so that their status would not be questioned since not all emancipation letters had official value, and freed women could be pursued by the police, who



Mother and son in Salvador, photo from 1884

**In Recife,
many women
preferred to
remain in the
region so that
their free status
would not
be questioned**

might mistake them for fugitive slaves. “The women freed themselves of the stigmas of captivity by inventing strategies to guarantee their place in society through work, networks of *compadres*, or affiliation with the Catholic sisterhoods,” reports historian Valéria Costa, a member of the faculty of the Federal Institute of the Pernambuco Sertão. She describes how the streets were full of women, particularly because of the retail trade. As part of a public safety policy, which viewed the black population as a potential cause of disturbances, municipal patrols prohibited the circulation of slaves and freedmen after 8:00 p.m. in the center of Recife, especially in the heavily commercial Santo Antônio district.

In Rio de Janeiro, the freed female slaves arriving from São Paulo maintained the same occupations that they had before emancipation. “The *quituteiras*, for example, moved quite freely in the urban spaces and preserved the



Female workers with their children and other workers leave to harvest coffee in southern Rio de Janeiro State, in 1885: motherhood in a dramatic fashion

tradition of preparing sweets and savory tidbits, as well as popular foods such as *angu*, a kind of polenta with pieces of meat, just as in the days when they were slaves,” Silva explains. The researcher verified this migration process during her analysis of close to 300 copies of seven São Paulo periodicals read by the black community, covering the years from 1886 to 1926. Those newspapers described the frustration that slaves and freedmen experienced in looking for work and for recognition as citizens.

Silva also consulted criminal and civil court case records from the National Archives, as well as 310 inmate record cards from the Casa de Detenção in Rio de Janeiro, dating from 1888 to 1920. Of all the cases she studied, the researcher found 275 that involved problems of drunkenness and disorderly conduct. Black women spent more time in jail when they had been arrested at night, at a time when it was thought that only immoral women would be out.

The status of females helped emancipated women find work but also exposed them to violence. Unlike what occurred with most white women, blacks—whether slaves, free born, or emancipated—

had to face the problems associated with the streets, working for their masters or for their personal survival. “In Bahia, as in Rio de Janeiro, they encountered all sorts of harassment and aggression but defended themselves as best they could: they shouted and fought, and ended up getting a bad reputation,” noted Ferreira dos Reis, from the UFRB.

MOTHERHOOD

Although research has depicted female slaves as much less passive as was generally thought, Maria Helena Pereira Toledo Machado, a full professor in the History Department of the School of Philosophy, Literature and Human Sciences of the University of São Paulo (USP), reaffirms the precariousness of the emancipation process when it was based on domestic work. The employers exercised control over the autonomy of the freed female slaves, who were separated from their families and were given extremely few days off.

Toledo Machado described how those women experienced motherhood in dramatic fashion, whether as female slaves trying to build up savings to pay for freedom prior to 1888 or as freed-

women. In her research, she observed how frequently freedwomen lost custody of their children on the grounds that they were morally unfit to raise them. Because of that kind of situation, the historian argues that abolition should be thought of as a process marked by gender issues. “That suffering, however, does not invalidate the battle those women fought to reinvent their lives and reminds us how tough that battle was,” she concludes. ■

Project

Black diásporas in post-abolition: ex-slaves and African-Brazilians in São Paulo (1888-1930) (No. 09/14974-1); Grant Mechanism Fellowship abroad; Principal Investigator Lúcia Helena Oliveira da Silva (UNESP); Investment R\$ 15,951.30.

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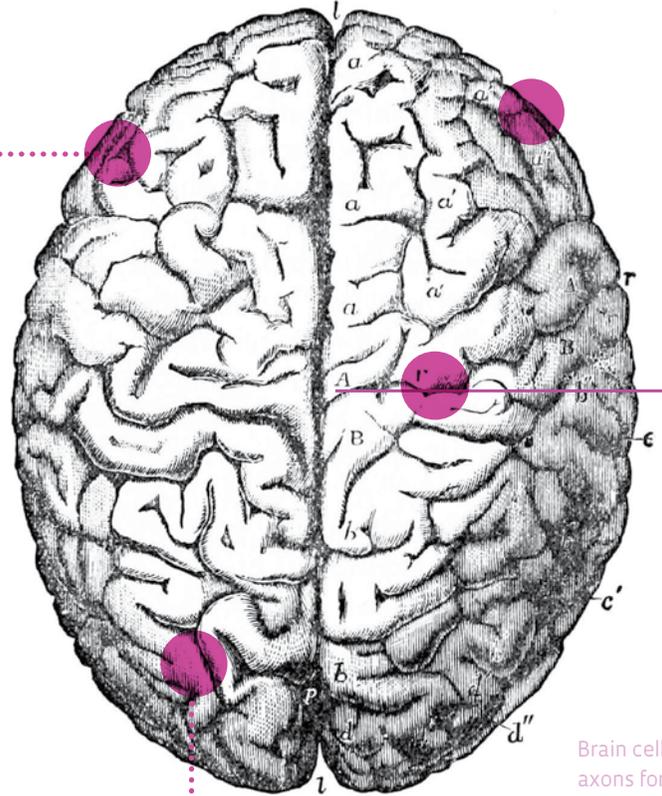
This is not a fried egg

Sun coral has a great ability to regenerate and a varied reproductive repertoire. These characteristics have enabled *Tubastraea coccinea*, a species that originated in the Indo-Pacific, to spread along the Brazilian coast, damaging native coral populations. Oceanographer Bruna Luz is studying the species from a genetic perspective, uncovering knowledge that may help us understand the organism and allow us to use it as a model in other research.

Image submitted by Bruna Luz, doctoral student at the Federal University of Paraná (UFPR)

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The behavior of blackouts

Physicist and leader of an international team succeeded in the local laboratory in electrical networks

Author: [Name], [Institution]

The childhood of physicist Yang Wang was marked by blackouts. He grew up in Beijing at the end of the 1940s, when the capital of China suffered from frequent blackouts. "The power plants could not meet the high demand for electricity in the summer," says the Chinese researcher. Last year Yang completed his doctorate in theoretical physics under the guidance of the American physicist, at Northwestern University in Evanston, Illinois. He has developed mathematical models that may help reduce the risk of blackouts in the electrical systems of large countries like China, the United States, and Brazil.

Using these models, Yang, Minner, and a colleague at Northwestern, the Japanese mathematician Takashi Minakawa, identified an algorithm (a sequence of procedures) that makes it possible to recognize the areas in an electrical network that are more likely to fail in a succession, causing a cascade effect that can leave states or even an entire country in the dark. This algorithm was described in an article published in

