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A parasite uses vesicles with proteins to invade host cells

EMBRAER

A company invests in partnerships to develop innovations

COLONIZATION

The Portuguese Empire shared power to keep power

INTERVIEWS

MARCO ANTONIO ZAGO

USP combines large size with high quality

RONALDO PILLI

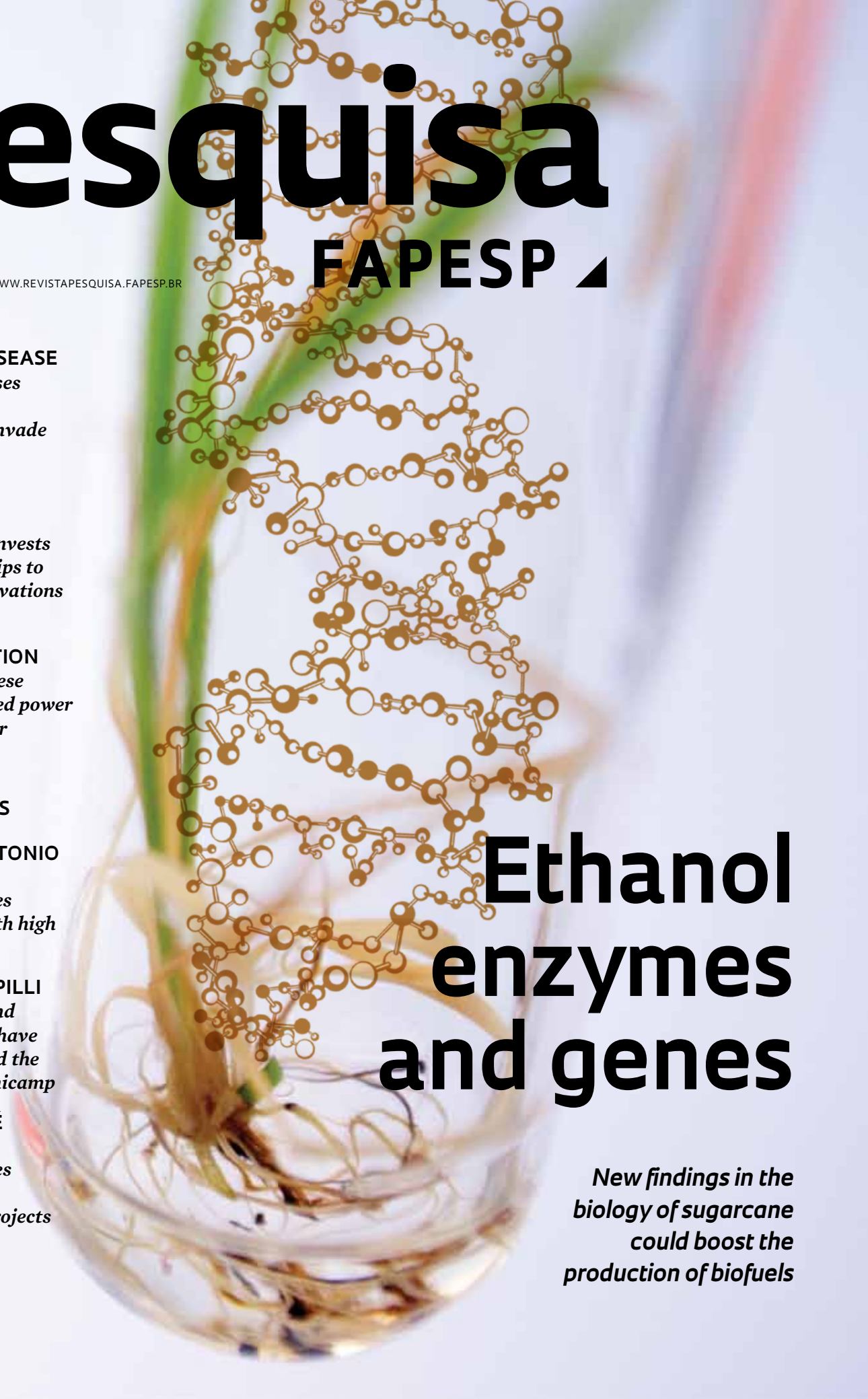
Bold ideas and innovations have characterized the history of Unicamp

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New findings in the biology of sugarcane could boost the production of biofuels



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FAPESP
ISSN 1519-8774

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LETTER FROM THE EDITOR

The sustainable future

Mariluce Moura

EDITOR IN CHIEF

The cover story for this second 2013 international issue of the magazine *Pesquisa FAPESP* reports on the wide variety of sugarcane studies that are currently being carried out by researchers from institutions in the state of São Paulo. Special emphasis is given to genetic research on bagasse and to investigations into the enzymes that are capable of boosting the hydrolysis of bagasse. As technology editor Marcos de Oliveira reports in an article beginning on page 5, the ultimate goal of these efforts is to produce more ethanol per hectare of land. Although this biofuel is quite clean compared to petroleum and comes from a renewable source, it still needs to be made more economically viable. With its long and successful tradition of research on sugarcane, Brazil can make a significant contribution to the development of second-generation ethanol.

In the first generation of production, sugarcane broth is converted by fermentation into biofuel. In the second generation, powerful enzymes break down the molecules of the bagasse and sugarcane leaves, allowing hydrolysis to extract additional sugar from the biomass. Genetics has been and remains a vital tool for advancing these protocols, and the launching in 1999 of the Sugarcane Genome Project (which was financed by FAPESP) was a decisive first step toward a more complete understanding of the important genes in sugarcane. New findings are now likely to encourage the use of hydrolysis and lead to an estimated increase of at least five billion liters in the ethanol production of Brazil, which is currently running at approximately 25 billion liters per year. Brazil is not alone in this race. In the United States, England, and Sweden, many laboratories are pursuing the same objectives, engaged in a scientific competition in which the big winner will be the environment.

We would also like to highlight from this issue a new study on Chagas disease that was conducted by researchers from the University of São Paulo (USP) and the Federal University of São Paulo (Unifesp). Since the discovery in 1909 of the disease and its causative agent, *Trypanosoma cruzi*, by the physician and scientist Carlos Chagas, unceasing efforts have been made to understand the mechanisms by which that parasite acts on the human body, as well as ways to prevent it. As the report by special editor Carlos Fioravanti (*page 34*) describes, the route that *T. cruzi* uses to

R&D Investment

Expenditures in research and development using state resources (DEPD) and Gross Domestic Product (GDP)

STATES	DEPD 2010 (in millions of US\$)*	GDP 2008 (in billions of US\$)**	DEPD (en %)	GDP (en %)
Acre	2.1	2,888	0.1%	0.2%
Alagoas	5.5	8,359	0.1%	0.6%
Amapá	2.6	2,903	0.1%	0.2%
Amazonas	27.4	20,095	0.7%	1.5%
Bahía	72.5	52,149	1.7%	4.0%
Ceará	38.2	25,793	0.9%	2.0%
Distrito Federal	42.3	50,460	1.0%	3.9%
Espírito Santo	9.7	29,987	0.2%	2.3%
Goiás	13.9	32,306	0.3%	2.5%
Maranhão	9.9	16,518	0.2%	1.3%
Mato Grosso	20.3	22,756	0.5%	1.7%
Mato Grosso do Sul	7.1	14,225	0.2%	1.1%
Minas Gerais	128.8	121,254	3.1%	9.3%
Pará	12.8	25,115	0.3%	1.9%
Paraíba	19	11,028	0.5%	0.8%
Paraná	249	76,939	5.9%	5.9%
Pernambuco	35	30,232	0.8%	2.3%
Piauí	1.1	7,193	0.0%	0.6%
Río de Janeiro	294.5	147,288	7.0%	11.3%
Rio Grande do Norte	11.4	10,936	0.3%	0.8%
Rio Grande do Sul	55.9	85,621	1.3%	6.6%
Rondônia	0.1	7,677	0.0%	0.6%
Roraima	1	2,098	0.0%	0.2%
Santa Catarina	126.4	52,911	3.0%	4.1%
São Paulo	3,019.3	430,478	71.6%	33.1%
Sergipe	8	8,391	0.2%	0.6%
Tocantins	1,5	5,618	0.0%	0.4%
Total	4,216.6	1,301,229	100%	100%

* Exchange rate in December 2010

** Exchange rate in December 2008

Source: DEPD - Ministry of Science and Technology, S&T Indicators. http://www.mct.gov.br/index.php/content/view/317045Brasil_Dispendios_dos_governos_estaduais_em_pesquisa_e_desenvolvimento_P_D_por_execucao_segundo_regioes_e_unidades_da_federacao.html


take up residence in a single cell and to differentiate, divide, and invade other cells has now been mapped out. This discovery opens up possibilities for developing new ways to combat and diagnose tropical diseases. Furthermore, these diseases have now also been observed in countries within temperate regions. Medical authorities in the United States, for example, have warned of the rise of Chagas disease in their region, especially among immigrants in states that are situated along the border with Mexico.

In the section on Technology, the example set by Embraer, the third largest manufacturer of jet planes worldwide—behind Boeing (United States) and Airbus (European Union)—provides evidence that companies should leave the confines of the research and development center and pursue partners in other places to add value to the manufactured product. Embraer has forged partnerships with universities, research institutes, and other companies in the aviation industry to develop new technologies for manufacturing composite materials, metallic structures, and on-board systems. One of the projects under way is examining biofuels based on sugarcane ethanol. This work is being carried out in cooperation with Boeing and a number of São Paulo research institutions, and it has received funding from FAPESP.

...

The three articles highlighted here represent research projects that were carried out in São Paulo and serve as examples of the importance of science and technology to this state. From the supplied chart, we can see that in 2010, São Paulo invested more than \$3 billion, which represented 71.6% of expenditures by all Brazilian states on R&D. São Paulo, meanwhile, produced 33.1% of the GDP of Brazil in 2008, the equivalent of \$430 billion.

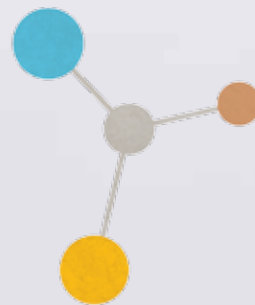
Between sugars and genes



Applied scientific knowledge of sugarcane
may prove useful in developing new
methods for ethanol production

Marcos de Oliveira

PUBLISHED IN OCTOBER 2012



Following a large number of genetic, physiological and agronomic studies of sugarcane conducted in recent years, our older colleagues might say that the plant is being turned on its head. Sugarcane is a member of the grass family and was brought to Brazil by the Portuguese in the 16th century. Today, scientists hope to gain a deeper understanding of sugarcane and its peculiarities with a view towards increasing its productivity. The ultimate goal is to produce more ethanol per hectare of land.

Efforts to achieve this increase have included research aimed at making sugarcane better adapted to the so-called second generation of alcohol production. In this technology, enzymes use the sugars recovered from crushed sugarcane, or bagasse, to form a type of broth, which is then used to produce more biofuel. For this reason, researchers from several Brazilian institutions are keeping one eye on basic research and the other eye on the future of industrial ethanol production processes. The first scientific advance came in 1999 with the launch of the Sugarcane Genome Project, financed by FAPESP. The most recent findings from that project confirm that sugarcane stalks and leaves have more sugars (the basic substances for creating ethanol) in the hemicellulose fraction than in the cellulose fraction. These findings could change the course of second-generation ethanol production in the future.

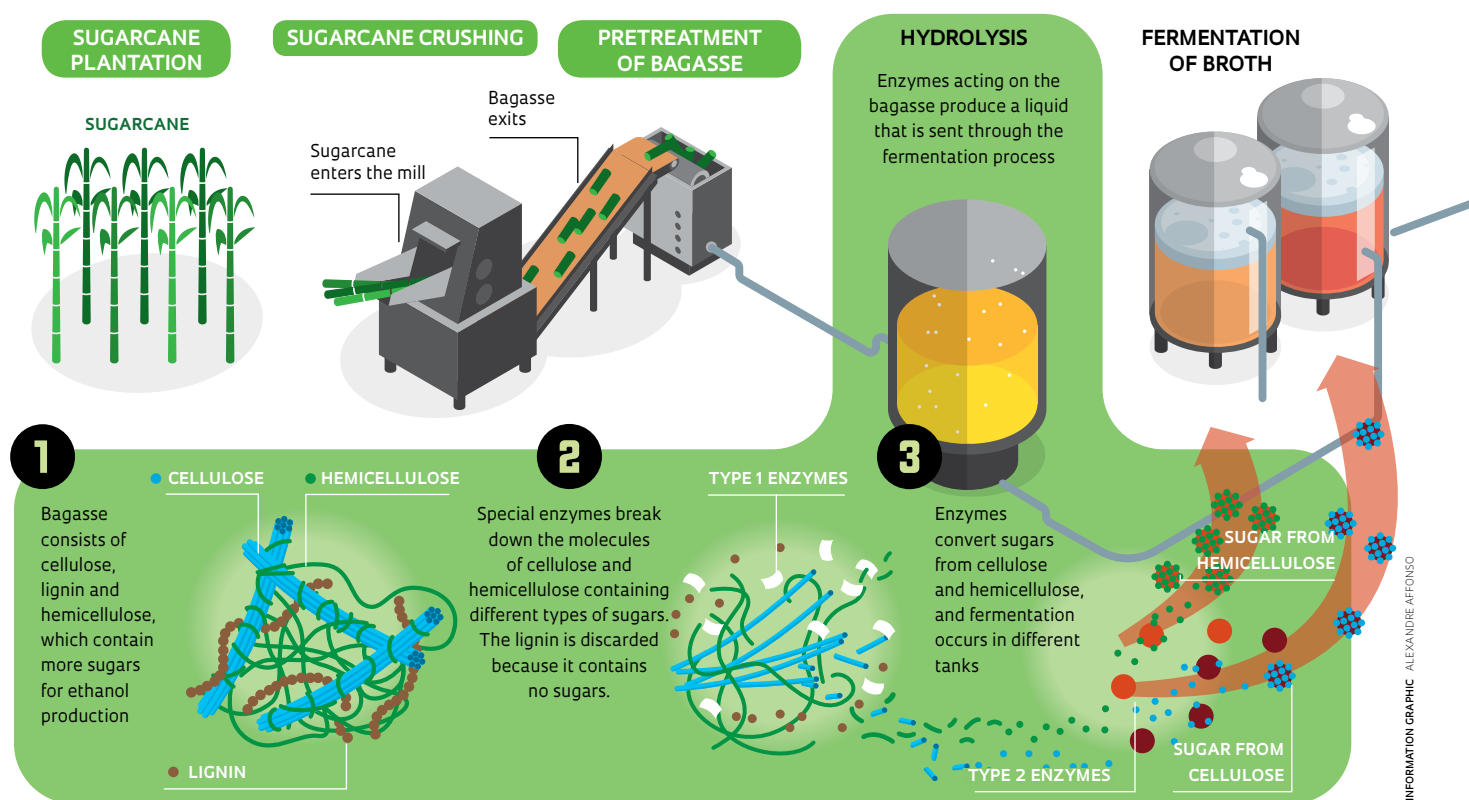
“Our studies of the cell walls of both the stalk and the leaves of sugarcane plants showed that about 30% of the sugars are present in the cellulose, 50% are in the hemicellulose, and 10% reside in the pectins. The technology now being designed for future second-generation ethanol was based only on cellulose, while the sugar polymers of hemicelluloses – which contain complex sugars such as arabinoxylans, beta-glucans and xyloglucans – are being ignored, as are the pectins, and together these represent 70% of the sugars in sugarcane cell walls,” says Marcos Buckeridge, a professor at the Biosciences Institute at the University of São Paulo and coordina-



Transgenic sugarcane seedlings at the Chemistry Institute of USP

The future of second-generation ethanol processes

After the sugarcane broth is used in the first-generation process, the bagasse and leaves are utilized in the hydrolysis process. The final stage involves traditional fermentation by yeasts that convert the sugars into ethanol



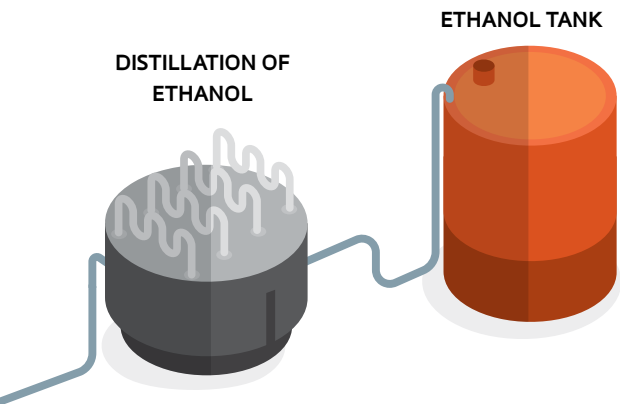
tor of Brazil's National Institute of Science and Technology (INCT) of Bioethanol, which encompasses 31 laboratories in five Brazilian states. In sugarcane cell walls, the hemicelluloses and pectins are located between the microfibrils, which are agglomerates of cellulose molecules. These microfibrils have many five-carbon sugars and are therefore not digestible by the yeasts (*Saccharomyces cerevisiae*) that are used to ferment sugarcane broth. These yeasts are accustomed either to sucrose (which is composed of glucose and fructose and found in sugarcane juice) or to glucose from cellulose or certain hemicelluloses that have six carbon atoms.

The future utilization, via hydrolysis, of pentoses (five-carbon sugars) from bagasse could drive up Brazilian ethanol production by an estimated minimum of five billion liters (see *Pesquisa FAPESP* No. 192) over the current output of 25 billion liters. Pentoses could also be utilized in biotechnology applications, thereby increasing the commercial value of bagasse. In second-generation processes, the enzymes form a liquid that also serves as food for the yeasts.

An estimated 5 billion more liters of ethanol can be produced using sugars from hemicellulose

“There have been attempts to produce *Saccharomyces* lineages capable of utilizing five-carbon sugars, including at the Brazilian Bioethanol Science and Technology Laboratory (CTBE) and at other institutions and companies in Brazil and abroad. In England and Sweden, scientists have already successfully shown that this is possible, although the work was done entirely in a sterile laboratory environment. For Brazilian production plants, however, that is not yet sufficient. The yeasts must be robust enough to survive in the presence of other microorganisms, such as bacteria, that exist in an unsterilized environment,” says Buckeridge, who is also the scientific director of the CTBE in Campinas, São Paulo.

Experiments on the most advanced stage, cellulose hydrolysis, show that many uncertainties still linger. “We now have a good understanding of the pretreatment process, but we still need to investigate the various options for performing hydrolysis in a way that the industry can quickly absorb, both economically and sustainably,” says Professor Rubens Maciel Filho of the University of Campinas (Unicamp), one of the coordinators of FAPESP's Program for Research on Bioenergy



(BIOEN), in which INCT Bioethanol also participates. “Techno-economic and sustainability assessments are needed – in this case, in analyses of water consumption and in the use of chemicals in the hydrolysis process,” Maciel Filho notes.

“In the current second-generation experiments, after the bagasse is discarded after the first generation when the sugarcane broth is extracted to make ethanol, it goes through a process of rupturing the cell walls to obtain the cellulose surrounded by hemicellulose and lignin, a polymer that has no sugar,” says Buckeridge. This rupturing is currently performed using a high-pressure steam process. During this process, the cell walls of the bagasse are relaxed, and solvents, acids and enzymes are used to separate the components. “It’s the use of force, in an effort to get rid of everything you have around the cellulose,” he adds. “Our idea is to start the hydrolysis process in the field. To produce sugarcane that is more second-generation-ready, that makes hydrolysis easier and eliminates the need to wash the bagasse, which removes many sugars from the material.”

In an article to be published in the journal *BioEnergy Research*, Buckeridge and two other researchers from his group at USP, along with two researchers from the University of Georgia Complex Carbohydrate Research Center in the U.S., present their work in identifying the fractions of each sugar polymer in sugarcane. They also make observations about the complexity of the cell walls and the difficulty of finding chemical keys or codes that could better utilize the network of polysaccharides. These researchers also believe that new knowledge of the sugar composition of sugarcane could lead to modifications in the second-generation process. Buck-

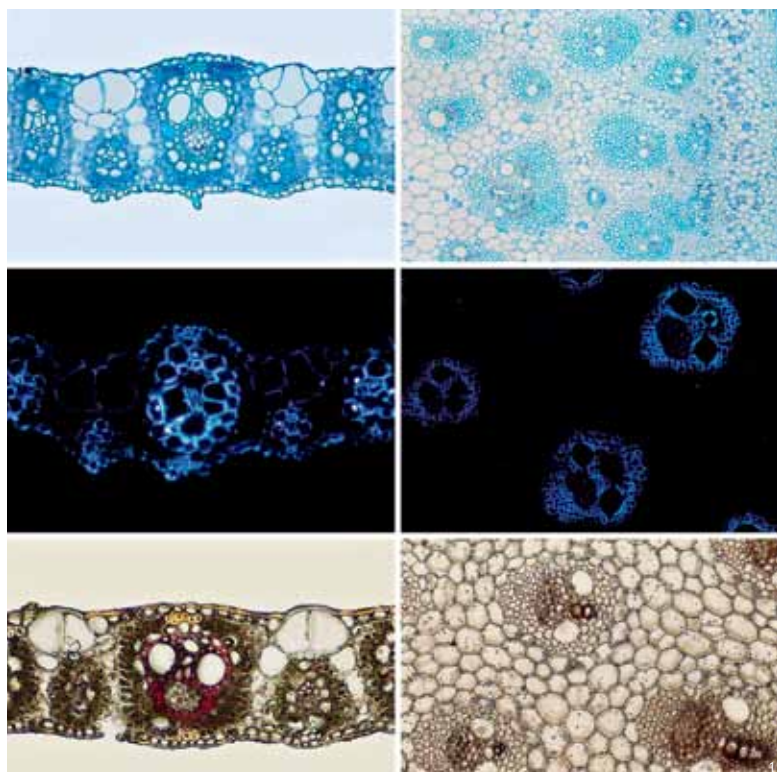
The sugarcane of the future would have some characteristics of the papaya, which is sweeter and softer after ripening and harvesting

eridge envisions a best-case scenario in which the sugarcane would be brought in whole for the hydrolysis process after the broth is extracted for the first generation process.

“The biology of the cell walls is the essence of these advances, and it is essential for technological progress to be made in the area of sustainable biofuels and biomaterials,” says Professor Leonardo Gomez of the York University Department of Biology in England. Gomez, who is Argentinian, spent time in Brazil in 2010 working with the CTBE. “In the opinion of many specialists, the development of second-generation biofuels has been made easier by the presence of a well-established first-generation industry. As a result, Brazil has the best environment for this to occur. But we are only talking about potential. Someone has to assume the risk and invest in biofuels on an industrial scale,” Gomez notes.

In the interest of advancing the process of obtaining second-generation ethanol, Buckeridge draws attention to a physiological pretreatment that leaves the plant more malleable and better-suited for processing by hydrolysis. “When this substance is applied in plantations while the plant is still very small, it inhibits an enzyme in the sugarcane that makes phenylpropanoids, which are the precursors of lignin, the substance that binds the sugars to the cell wall and gives the plant mechanical strength. We do not yet know for sure what happens, but with this compound, we were able to process 30% more xylans, which make up 50% of hemicelluloses,” Buckeridge says. The use of this substance, comprised of piperolylic acid in sugarcane, is the subject of a patent filed with the Brazilian Industrial Property Institute (INPI) by Buckeridge and his former post-doc Wanderley dos Santos. Santos is now a professor at the Federal University of Paraná (UFPR), and he is testing the product in the field. “We still have to improve it and try to reduce the cost,” Buckeridge notes.

Another solution for the second generation is being developed under BIOEN, a collaboration of 13 research groups. Their goal is to develop one or more agronomic and genetic varieties of sugarcane with high-quality characteristics for the first and second generations. One such characteristic is a greater capacity for photosynthesis. The researchers have already identified at least four genes that are responsible for capturing sunlight. These genes may be related to higher cellular growth and a consequent increase in sucrose production. The development of transgenic plants is one of the biotechnological tools being used to produce this supercane. In this case, transgenic methods would include not only introducing foreign genes into the plant but



Microscopic images for the analysis of sugarcane leaves (left column) and stalks (right). Fluorescence applied in cells (middle row) and the presence of lignin (in red, bottom row), where several intact circular-shaped cells full of juice can be identified

also activating or reversing the silencing of native sugarcane genes. “We could also develop plants with cell walls that are better accommodated to the second generation,” says Buckeridge. “These concepts might seem futuristic, but BIOEN has genes related to the modified cell wall of which we are thinking of making ‘sugarcane papaya,’ for example.” This proposed transgenic sugarcane would have some characteristics similar to papaya, which is sweeter and softer after ripening and harvesting.

“We now have 380 genes linked to sucrose and over a thousand related to drought resistance,” says Professor Glaucia Mendes Souza of the Chemistry Institute of USP (IQUSP), who will jointly head the sugarcane genome research at BIOEN with Professor Marie Anne van Sluys of the Biosciences Institute of USP. Also participating in the research will be Professor Marcelo Menossi of the Biology Institute of Unicamp. Of those 380 genes, 250 are now being tested in sugarcane seedlings placed in test tubes, tubs and pots at IQUSP or in greenhouses at the Luiz de Queiroz School of Agriculture at USP in Piracicaba. These experiments are being coordinated by Professor Helaine Carrer, who is studying gene expression. Also being tested is the expression of sugarcane genes in tobacco, a plant that is easy to manipulate in the laboratory and that serves as a model for this type of experiment. Two sugarcane genes linked to drought resistance have already been expressed in tobacco, and a patent for their use has been filed with the INPI.

Modifying a plant with genes of interest requires promoters, which are biotechnological tools in the form of the DNA sequences in which the gene will be expressed. It is in these molecules that researchers will modulate the superexpression or silencing of genes. “We filed a patent this year for 10 sugarcane promoters that will enable the genes to be expressed differently,” says Souza. In regard to sugarcane cell walls, she notes that she has already developed plants in which the genes for lignin production have been silenced. “Lignin upsets second-generation execution because it makes it difficult to extract polysaccharides, but switching off its production caused the plant to fall over in some experiments. We need to come up with varieties in which we can try for a midway point, reducing the presence of lignin but still keeping the plant upright,” explains Souza.

Academic research is also trying to improve hydrolysis through the use of enzymes that are more effective in breaking down sugarcane cell walls, extracting the sugars and preparing the material for ethanol production. However, which enzymes should be used to process the different polysaccharides that are present in the plants’ cell walls? Some enzymes used by the food industry, for example, are being tested with sugarcane, but in themselves they do not present a full solution. “These industrial enzymes are produced mainly by fungi,” says Professor Richard Ward of the Chemistry Department in the Ribeirão Preto School of Philosophy, Science and Letters at USP, and of the CTBE, who has successfully designed two multifunctional enzymes that act on hemicelluloses. Known as chimeric enzymes, these enzymes are produced by bacteria.

“We know that cellulose is more hidden than the other polysaccharides present in sugarcane cell walls, and our challenge is to create enzymes that are programmed to destroy and degrade the other components that are also important sources of sugar, until we get to the cellulose,” Ward explains. “It is important to develop the enzymes most appropriate for each polysaccharide. But it is still difficult to find good enzymes at a low cost. They are currently being marketed for tens of dollars per kilo. That may seem inexpensive, but we have to think about in-plant processing of hundreds or even thousands of tons of lignocellulosic material per day.” Ward says that the goal is to build chimeric enzymes such that each enzyme attacks more than one polymer of sugarcane bagasse. “That is especially important for hemicelluloses, which have a heterogeneous set of polysaccharides.”

While some of the enzyme research may seem unconventional, it is based on simple natural phenomena. In the search for enzymes that digest

The digestive tracts of cockroaches are being studied to find enzymes for second-generation ethanol processes

cellulose and lignocellulosic material, Professor Ednildo Machado of the Biophysics Institute of the Federal University of Rio de Janeiro (UFRJ) is studying the enzymatic composition of the digestive tract of two cockroaches. He has focused on two species: *Periplaneta americana*, which is common in large cities, and *Nauphoeta cinerea*, which was created to feed reptiles raised in captivity. “In lab experiments, I was only able to provide sugarcane bagasse to the cockroaches, and they fed on it. In other words, they were able to digest the cell walls of this material to survive very favorably,” Machado says. Consequently, he began to think about which enzymes in the digestive tracts of these insects could be useful in second-generation ethanol production.

Machado was introduced to Buckeridge during the Brazilian Conference on Biochemistry in 2010, and they formed a close collaboration. Buckeridge was at the CTBE, where a number of experiments were conducted. “We were able to identify a few enzymes that are produced by bacteria inside the digestive tract of cockroaches. We don’t yet know if these bacteria were already there, or if the insect acquired them from the material, in the case of bagasse.” The cockroach can also produce these enzymes through fungi and protozoa, can very easily feed on a wide variety of waste matter and can adapt easily to such diversity. “That characteristic enabled us to identify a number of enzymes in the insects that are excellent for various technological processes,” Machado says. The next step is to confirm the identity of the microorganisms that produce the enzymes. To do this, it will be necessary to sequence all of the DNA present in the cockroach intestines using a process called metagenomics. Metagenomics will allow researchers to identify the species and genes involved in the production of enzymes that specialize in breaking down cellulose and hemicellulose from sugarcane bagasse. Identifying these genes makes it possible to clone them into bacteria such as *Escherichia coli* and even facilitate the production of these enzymes on an industrial scale. Professor Ward is starting to use the same process in a laboratory to produce the enzymes that attack sugarcane cell walls.



Transgenic seedlings: biotechnological tools for testing strategies to silence or activate sugarcane genes

Such efforts are increasing the number of tools that could aid in producing more ethanol from sugarcane within a few years. “In the past 10 years, there has been an exponential increase in the amount of research and technological investment aimed at utilizing biomass as a renewable, sustainable substitute for oil,” says Professor Gomez of York University. “The current research in the field of biomass composition offers new potential for biorenewable energy.” With that goal in mind, the production of ethanol and high-performance chemicals from biomass is possible only with a detailed, multidisciplinary understanding of the biology and biochemistry of biomass. ■

Projects

1. National Institute of Science and Technology (INCT) of Bioethanol (nº 2008/57908-6); Thematic project of the FAPESP Program for Research on Bioenergy (BIOEN); **Coord.** Marcos Silveira Buckeridge/USP; **Investment** R\$2,896,588.59 and US\$303,342.92 (FAPESP);
2. Sugarcane signaling and regulatory networks (nº 2008/52146-0); Thematic project of the FAPESP Program for Research on Bioenergy (BIOEN); **Coord.** Glauca Mendes Souza/USP; **Investment** R\$3,390,743.73 and US\$1,174,768.67 (FAPESP)
3. Identification, characterization and engineering of enzymes that degrade plant cell walls (nº 2010/18850); Thematic project; **Coord.** Richard John Ward/USP; **Investment** R\$491,952.05 and US\$313,495.03 (FAPESP).

Scientific articles

- DE SOUZA, A.P. *et al.* Composition and structure of sugarcane cell walls: implications for cell wall hydrolysis and second generation bioethanol. **BioEnergy Research**. In press. Sept. 2012.
- BEGCY, K. *et al.* A novel stress-induced sugarcane gene confers tolerance to drought, salt and oxidative stress in transgenic tobacco plants. **Plos One**. Vol. 7, No. 9, e44697. Sept. 2012.
- FURTADO, G.P. *et al.* A designed bifunctional laccase /b-1,31,4-glucanase enzyme shows synergistic sugar release from milled sugarcane bagasse. **Protein Engineering, Design & Selection**. In press. Sept. 2012.

Connecting to society

Mariluce Moura and Neldson Marcolin

PUBLISHED IN OCTOBER 2012

Accustomed to both genetic and hematological studies and the twists and turns of political science, Marco Antonio Zago assumed the position of Dean of Research at the University of São Paulo (USP) in 2010 and soon faced a challenge. How do you inspire the most successful researchers to become more interested in the university that is responsible for their training?

Zago identified in many USP scientists a certain disconnect from the institution. To Zago, it is important to establish ways to strengthen everyone's connection to the university and thus to society itself. «You have to provide some coherence to the research within the university,» he believes.

The measures that the dean adopted apparently followed his desired course. The creation of multidisciplinary Research Support Centers (NAPs), for example, modeled after the Research, Innovation and Dissemination Centers (RIDCs) – a program created by FAPESP in 2000 – have attracted 118 groups of researchers since 2010. The USP Innovation Agency is closer to researchers and assists them with patent-related issues. New professors who join the university are encouraged to seek outside resources and join research teams. “Undoubtedly, we were able to improve the university in many respects,” says Zago. This assessment has been confirmed by the favorable position achieved in all of the rankings that evaluate universities – strong rankings despite the enormous size of USP, which is unusual in the best institutions that invest in scientific research.

Marco Antonio Zago graduated from the University of São Paulo (USP) School of Medicine of Ribeirão Preto. He spent part of his career as a researcher and also worked as a physician. He was the clinical director of the Hospital das Clíni-

cas and the scientific director of the Fundação Hemocentro, both of Ribeirão Preto. In 2007, he chaired the National Council on Scientific and Technological Development (CNPq) and created the National Institutes of Science and Technology (INCTs), which was an attempt to change the scientific production model in Brazil.

As a researcher, he contributed to the study of sickle cell anemia and thalassemia, fighting to establish methods to diagnose and treat these diseases. He went on to study population genetics and was able to identify the regions of Africa that had been home to the slaves brought to Brazil. He also performed outstanding work on the genomic sequencing of the bacterium *Xylella fastidiosa* and on the cancer genome. As the leader of the Cell-Based Therapy RIDC2, he has focused its efforts in recent years on studying stem cells. Below are the main excerpts from the interview.

What is the role of the Dean of Research at a university the size of USP?

I believe my role is to provide a certain direction and unity to the research performed by the university. And when I say a certain direction, it is not to perform or promote targeted research, in the traditional sense of the word, by defining lines of research; this is not possible at a university like USP. In terms of size and range of areas covered, we are one of the largest universities in the world. It is hard to find an area or sub-area of knowledge in which USP does not have qualified specialists. And, therefore, the research activity is very heterogeneous and takes various forms.

What exactly is that “certain direction”?

Perhaps to lend coherence and synergy to the university's research. When I arrived here, I realized that the sense of unity at USP was low. The

AGE 65

SPECIALTY
Hematology and genetics

EDUCATION
University of São Paulo (undergraduate and PhD)
Oxford University (post doctorate)

INSTITUTION
University of São Paulo



most successful groups were those that were less tied to the university, that were independent and that claimed that their resources came from outside, and not from USP.

There was a certain amount of detachment...

Yes, a detachment from the university, which leads to a degree of separation.

Where does USP stand among the world's largest universities?

UNAM [the National Autonomous University of Mexico] has 270,000 students, and the University of Buenos Aires around that number; they are institutions that have no *numerus clausus* and therefore any student who wishes to enroll may do so. On the other hand, when we look at the best universities in the world – those that everyone cites as examples of universities that we want to emulate – the most important universities of the United States, England, Japan and South Korea have an average of 17,000 students. And many of them have more than 60% of their students in graduate school.

And USP?

We have 91,000 students, 30% of whom are in graduate school. One of the common characteristics of universities with a strong commitment to research, in addition to teaching, is a mission to produce scientific research and transfer knowledge. USP fits that description. We must emphasize a commitment to teaching. This commitment is important because many are of the opinion that I am monomaniacal at times in thinking that the university should only do research. I do not think so. I understand that the basic role of the university is education, to train qualified people at a higher level.

Does USP fit that description and rank high among research universities?

USP ranks high in all types of rankings. There is unanimous agreement that USP is Latin America's premier university. There are other good universities in Brazil, but they are few in number. The club of research universities in Brazil is very small.

How do you take this diverse university and make the research activity developed by so many groups with different goals coherent?

First, you need to draw these groups' attention once again to the center, which is the university. And, through the university, these groups resume their relationship with society. We do not perform superficial research because we are seeking new knowledge, which may or may not have an immediate application. Research is not just a laboratory activity but also a creative activity in every respect, including the development of culture, which is the responsibility of the university.

Including art?

Arts and humanities represent a very important contribution for USP. If we look at some rankings that sub-

divide the university's performance, USP ranks high in the humanities. We must promote a more intense dialogue among these academic cultures.. When I speak of providing unity or coherence, it is to get the attention of researchers, especially the most successful ones, and to get them to return to the university and through the university, to society. One of the ways that we found to do this was to provide our own resources to support research; this has never been done at such an intense level at any Brazilian university. This level of commitment to research started here, although the amount of resources is not very large compared to what USP already applies to research. We invest approximately R\$2 billion per year in research, although this is not apparent to people.

Does this account include resources from FAPESP and CNPq?

No. The R\$2 billion refers to the budgeted resources that USP distributes to its activities. A considerable portion goes to pay technicians, laboratory infrastructure, improvements, water, electricity, and the share for full-time research activity. The university pays for everything. In American universities, these funds come from the researcher's grants, which pay for scholarships, technicians, the telephone bill and laboratory improvements, everything. This budgeted money is used for various purposes. We provide the basic infrastructure and some resources that go unnoticed on the pay slip. In addition to this, there is money from FAPESP that is distributed on the basis of proposals submitted for external review based on the merits of the project. This introduces a quality-control component to the distribution of money.

How is the research support program you created going?

In two successive internal requests for proposals, we placed R\$73 million in the first administrative year, which was 2010/2011, and then an additional R\$73 million in 2011/2012. To make these investments, we invited the researchers to submit research proposals, whose merit would be analyzed; the proposals were to envision the formation of a group of limited duration that was required to have a multidisciplinary aspect. The proposals also had to focus on a problem that was important to society, for immediate application or theoretical analysis. With that, from the two requests for proposals, we selected 43 in the first year and 75 in the second, for a total of 118 cores, or research centers. We called them NAPs, Research Support Centers.

Is there any overlap between the NAPs, the RIDCs and the INCTs?

You are always talking to the same individuals. Of course, the idea of people coming together around a subject arose there. I have been coordinating an RIDC since 2000. When I was chairman of the CNPq, we also had the idea of trying to do something that involved forming groups. I used the RIDC model and, considering what could be done with it on a national scale, we designed the INCTs,

which were and still are the largest science and technology programs that the CNPq has coordinated to date.

Do the NAPs then have the clear objective of bringing together more groups of researchers at the university?

Yes. Another complementary measure comes from the USP Innovation Agency, which is today linked to the Office of the Dean of Research. This agency has been completely transformed and plays an important role in solving the problems of the various research lecturers, for example, writing patents, treating this from a legal standpoint, and negotiating with companies that want to license patents, in addition to other tasks. Researchers today recognize that the landscape has changed to such a degree that USP is the Brazilian university that files the highest number of patents with the Brazilian Industrial Property Institute (INPI).

This piece of information is interesting because when it comes to university patents, Unicamp stands out.

That is a tradition because Unicamp was actually organized long before USP. Unicamp is extremely competitive in this regard. From 2000 to 2006, USP filed, on average, 29 new patents per year, which increased to 81 new patents per year between 2007 and 2011. Between 2009 and 2011, the three-year accumulated data are USP 231, UFMG 178 and Unicamp 170. In addition, the Innovation Agency acquired other functions, such as acting decisively in the education area. If the university's main contribution is education, we must also train people to have an innovative way of thinking. It is not the number of patents filed by researchers that will change the landscape of Brazil. What will change the landscape is training the young people who are about to graduate from the university to make things happen. This year, we created an entrepreneurship course, and there are 200 undergraduate students taking it.

In 2009, you said that the INCTs could change the scientific production model in Brazil. Have you come close?

I think that the INCT's wide scope and some of the goals have been abandoned. Today, the national science and technology plan is to send students abroad. When we created the INCTs, we had a program that involved many components, not only providing sources of funding but also planning and performing the follow-up. We convinced the FAPs [foundations that support research] to participate. The first to join was FAPESP, and then others followed. We had a great initial program with a single objective in which CNPq, Capes, the major FAPs, Petrobras, and BNDES were involved. If the program had continued along that initial path, we would have had an increasing role for the Ministry of Science, Technology and Innovation, not just as a source of funding. We would have been able to attract significantly more money than the ministry is able to distribute and we would have encouraged everyone to talk to each other and settle their differences, with the influence of the Southeast acting as a counterweight in relation to the Northeast and the North, and so on.

What other projects could encourage the USP researchers to congregate more around the university?

All of the newly hired professors receive resources to meet their basic needs as an instructor as long as they provide evidence of having submitted a request for research assistance to FAPESP. The success of this program since 2010 has resulted in a seven-fold increase in terms of what we are investing and how much research support has been brought in.

Let's talk about rankings. Is USP going up in all of the rankings because the university has, in fact, improved, or because you are doing a better job of promoting this improvement?

I think the rankings are a result of both. The university has improved in some respects and in others, it has been better promoted. There are extremely objective rankings that do not depend on analyzing opinions, such as the Webometrics Ranking of World Universities. This ranking works with Internet traffic measurements and the quantity of documents available. We improved enormously in this ranking – USP ranks 15th. This improvement occurred partly because the university is better organized and partly because as the university becomes more well-known, Internet traffic increases.

And the other rankings?

Other rankings are based on performance. In an important ranking such as Shanghai, which places a high value on research, when we look at the scores, we see that USP has performed exceptionally well. Nevertheless, Shanghai uses additional important criteria when deciding which universities to place first and in these, we do not perform as well. They take into account the number of Nobel prize winners who teach at the university, the number of alumni who have been awarded the Nobel Prize and the Fields Medal, etc. These factors are important in the decision concerning Cambridge, Harvard, or MIT, but they can cause a huge imbalance when an institution has only one winner. For example, if a university that is previously ranked unfavorably hires a Nobel Prize winner, it will soar. Does that mean that the university has shown enormous improvement? No.

And the rankings that measure opinion?

Some rankings are undoubtedly more influenced by factors such as opinion. To evaluate research, good or bad, we look at data, the number of papers published, the number of citations and the impact of the journals. An evaluation is a combination of information that gives us

Research is not just a laboratory activity, it is a creative activity in every respect

an idea of how the research is going, at least for the experimental areas. Other evaluation tools have recently begun to emerge for the purpose of improving this process. There is Google Scholar, which is now having a greater impact on the social sciences. Sometimes, they resort to expert opinion.

It's just another criterion...

Subjective, but it is a criterion. The most valued ranking, whose results should come out in a few weeks, is the Times Higher Education (THE) ranking. The so-called prestige ranking makes up 30% of the overall ranking. That is, the THE ask a large number of people around the world what their evaluation is of the different universities. And this weighs in the final ranking. This aspect, the fact that USP has had more exposure, or better exposure, is perhaps what was most influential. What does someone in Paris or Hong Kong think of USP or other universities? This opinion may be influenced by knowing people from here, by visiting, or by having people from here visiting their university.

Do these opinions impact the Times Higher Education (THE) ranking?

They have a very positive impact. In the prestige ranking that THE published earlier this year, USP was ranked among the world's top 70. And it will certainly influence the ranking that is about to come out because 70% is an objective evaluation, which is indicators, and 30% is opinion.

What has been done at USP about the need to internationalize Brazilian research?

The road to more productive internationalization is to establish partnerships with a select group of universities. We chose some of them here at the Office of the Dean of Research and try to enter into agreements, set up joint seminars and then propose bilateral research projects. We are currently finalizing an agreement with the University of Toronto, Canada, one of the 15 or 20 best in the world, which includes joint conferences and public notices for collaborative research. The same is happening with other major universities.

Let's jump ahead here. We would like to know how your own research is going since you became dean?

It would be unrealistic to think that since I left to become chairman of the CNPq in 2007 and then went on to become Dean, I have kept up the same level of activity in the laboratory. The intense and personal involvement of daily checking the method, of personally seeing a result, redoing, setting up bench experiments, this I don't do anymore. On the other hand, there is a group of researchers who has been working with me for a long time, and I have discussions with them almost every week.

From your point of view, what is your greatest contribution to knowledge at USP?

I would divide my contribution into three fundamental

periods. In the initial phase, I went to Oxford University for a post-doctorate and returned able to perform basic biochemistry research involving hemoglobins. At Oxford, I worked with David Weatherall, one of the pioneers in the field of hemoglobinopathies. Working as a physician in Southeast Asia, he saw a large number of children with thalassemia, a very special form of the disease, and along with biochemist John Clegg, he investigated the basic mechanism of the disease. There was evidence that this disease was caused by an imbalance in the synthesis of the two chains of hemoglobin: alpha and beta. These chains are very similar, synthesized under the control of different genes. In normal individuals, there is a balance: two alphas and two betas form a chain of hemoglobin. These two scientists developed a method to measure the synthesis of these chains. With this measurement, they proved that there is an imbalance in thalassemia. When I returned to Brazil, I knew that these diseases were common here, and I began to study them. I found a large number of patients and was able to establish methods to diagnose and treat these diseases.

Was there any way to treat them back then?

There was not. It was very disorganized; there were no segment protocols, no treatment protocols... I became involved not only with research but also in organizing activities as well as treatment. I persuaded the Ministry of Health to establish a program to treat patients with sickle cell anemia. The program still exists today and has evolved to include neonatal diagnosis.

So it was a contribution both in terms of basic research and direct intervention in the application.

Exactly. There was another component of these diseases, such as in the case of thalassemia, which is a complex disease in terms of its treatment because it requires that the patient receive regular blood transfusions. There must be a place to take in and follow these patients on a monthly basis. One of the complications is the accumulation of iron in the body. At that time, there was only one drug that could eliminate this element, which had to be given by injection – an injection that took a long time. An infusion pump is normally used to do this, but there was no such thing in Brazil, nor was there any way to import it. A colleague, Sebastião Ismael, and I designed one of these pumps, which were fabricated back in the time of Ibec (the Brazilian Institute of Education, Science and Culture) with Isaias Raw.

Is thalassemia less prevalent than sickle cell anemia?

It is roughly half as prevalent. The severe form of sickle cell anemia is due to the homozygous hemoglobin S gene. The prevalence of the heterozygote is approximately 2% of the population here in the state of São Paulo – it varies from place to place in Brazil because it was brought with the slave trade. The frequency is greater where you have a population with a higher incidence of African genes. Thalassemia is another type of change of the same beta gene so that when an individual is homozygous, s/he

has a very serious illness. This mutation came from the Mediterranean region, primarily Italy, Portugal, and Spain and, to some extent, from Lebanon.

Did these studies lead to another field of research, population genetics?

That is what happened. The world changed, and everyone began to study DNA. And in Ribeirão Preto in the 1980s, my group began to examine DNA related to some diseases, and then to population genetics. Our first study focused on the sickle cell anemia gene (beta S). In regions near the gene, there are elements, which we call polymorphisms, that define haplotypes. In the sickle cell anemia gene, depending on the location in Africa, the beta S gene is always the same, but the haplotype with which it is associated is different. When we look at blacks in the Brazilian population who have sickle cell anemia, we look at the gene and what is around it. This examination enables us to determine which part of Africa their ancestors came from and to reconstruct the history of the slave trade in Brazil. Once we performed this reconstruction, we were in for a surprise. The pattern of Africans who were brought to Brazil is very different from those who were taken to the United States. We were the first to demonstrate this difference.

And did this work demonstrate which region of Africa they came from?

Yes, it did. Approximately 60% came from regions with the Bantu haplotype, that is, Mozambique, the Central African Republic, Angola and South Africa; 30% to 35% came from the Benin region; and 1% to 2% came from the region of Gambia and Senegal. In the United States, the prevalence is approximately 60% from Benin, 15% from Senegal, and 15% from Gambia. After we performed this study, I found a book called *The Atlantic Slave Traffic* by Philip Curtin, who on the basis of working with primary source documents from the ports of departure and arrival, showed numbers that were identical to ours.

And did your third phase involve genomic contributions?

Yes, at that time I was out of medicine, and I had a group that addressed issues of molecular genetics and population genetics, when it began sequencing the bacterium *Xylella fastidiosa*, in 1998, which was an important milestone for Brazilian science.

Did your laboratory own any of this technology?

Yes, but the genome program focused attention on the work, and this has helped us significantly. After *Xylella*, we spliced into the cancer genome with Ricardo Brentani of the Cancer Hospital and Andrew Simpson of the Ludwig Institute. At the same time, the opportunity arose in 2000 to organize ourselves around an RIDC, and we decided to invest in cell therapy and stem cells. We were very successful, and we made progress on things that were not known at the time. Mesenchymal cells, for example, were regarded as exclusively deriving from bone

marrow. We were the ones who showed that these cells are found in the umbilical vein, in the saphenous artery, and then we described how they are found in virtually all fetal and adult tissues because the cells are present on the outside of the small vessels known as pericytes. We made an important contribution to this type of knowledge.

Is your work cited more often?

The most cited is the sequencing of the *Xylella*, for which there are more than 100 authors. The second is the world's first analysis conducted on the gene expression pattern of mesenchymal cells in 2003. And, the third is the work showing that mesenchymal cells, obtained from very different sources, have a pattern and property that are very similar to fibroblasts and pericytes.

You lived through a phase of genomic euphoria and live in the current phase, where it's clear that there is still a long way to go. How do you see this issue today?

That is the way it always is in science. I wrote a book with Covas Dimas called *Stem Cells, the New Frontier of Medicine*, about cell therapy. I say in the preface that exaggerated enthusiasm, largely inflated by the press, occurs repeatedly. I warned that there was, at that time in 2006, an expectation that was absolutely unrealistic regarding stem cells, as if they were going to save humanity over the course of just a few days. The technique of producing strains of embryonic stem cells is very difficult. It was the same thing with genomics. It is hard to see a work of molecular cell biology today that does not involve gene sequencing. And to think that gene sequencing will solve the entire question of knowledge with regard to biology would be very naive.

But there has been progress.

History shows that no scientific question can be answered with one technique or a single discovery. We take one step forward and we increase our knowledge. However, today, we already have a drug sold in pharmacies that was developed because they took a neoplastic gene, sequenced it and discovered that it was a hybrid gene that altered the synthesis of a particular protein. The pharmaceutical industry has produced an inhibitor that is used orally that impedes the gene function – and the individual recovers from the disease. So yes, genomics has produced results and will continue to do so. The yellowing disease caused by *Xylella* has not yet been cured, but that is minor compared to the benefits we have already achieved. ■

USP has performed exceptionally well in the Shanghai ranking of scores



From bold ideas to innovation

Fabrício Marques

PUBLISHED IN DECEMBER 2012

AGE 57

SPECIALTY

Organic chemistry

EDUCATION

University of Campinas (undergraduate and PhD)
University of California at Berkeley (post-doctoral studies)

INSTITUTION

University of Campinas

The academic career of Ronaldo Aloise Pilli, Dean of Research at the University of Campinas (Unicamp), is tangentially associated with the history of that educational and research institution, which has become one of Brazil's most important. According to the Times Higher Education World University Rankings, Unicamp stands between 251st and 275th place. In Brazil, only the University of São Paulo (USP) ranks higher, in 158th place. Pilli entered Unicamp in 1973 as a member of the seventh undergraduate class to enter the Chemistry Institute (IQ). He earned his doctoral degree in short order. His advisor was Albert Kascheres, an American who was one of the many foreign professors who helped found the university. Pilli became a full professor at the IQ in 2000 after doing post-doctoral work at the University of California at Berkeley. Specializing in organic chemistry, with an emphasis on the synthesis of drugs and natural products, he has been granted many patents – not surprising at a university that is second only to Petrobras in the number of patent applications filed with the National Industrial Property Institute (INPI)

between 2004 and 2008. His innovative work has not overshadowed his career as a professor: Pilli has trained 40 master's and doctoral degree holders in the field of organic chemistry.

As head of the Office of the Dean (a post he has held since 2009), Pilli led a group engaged in strategic actions intended to further globalize the university's research. One of these elements was a program that aimed to attract foreign visiting professors who were interested in spending two years at Unicamp, with the added incentive of being able to participate in a competition for a position on the teaching staff at the end of the period. Announcements in international scientific journals attracted applications from dozens of interested parties; 11 professors were chosen and are now in Campinas. Pilli also helped reorganize the institution's research infrastructure, increasing the assistance to professors and teaching staff who were just beginning their careers and coordinating the establishment of laboratories in preparation for multidisciplinary research. Married, a father of two children and about to become a grandfather, Pilli summed up the evolution of research at Unicamp in an interview he gave to *Pesquisa FAPESP*.

Transferring our academic skills to innovation has been part of life at Unicamp since the very beginning

You entered Unicamp as an undergraduate in 1973. What has changed in the research done by the institution over the course of nearly four decades?

Unicamp was born of a bold idea: it was established on the premise that education and research are inseparable. Gradually, extension services were also established as an end-activity. In those days, that was not the standard, at least not for Brazilian universities. Unicamp recruited its staff of professors by taking a serious look at their ability to carry out research and to teach at the undergraduate and post-graduate levels – another feature that is rather recent. This enabled the institution to distinguish itself quickly in certain fields because it was able to bring foreign and Brazilian researchers together within a relatively short space of time. In 1966, the university started implementing this system. I arrived here in 1973, and by 1976, when I finished my undergraduate work, Unicamp was already very strong in engineering, physics, and the humanities. Chemistry was beginning to develop.

There were a lot of foreign professors. More than half of them came from outside when the university was founded.

There were also a lot of Brazilians who had experience abroad. At the Chemistry Institute, with which I am affiliated, there were professors who had graduated from USP, recent PhDs who came here to accept the challenge of building a university in the interior of the state, an idea that few believed would succeed. I remember that there were professors

who refused the invitation to teach at Unicamp on a part-time basis even though they would not be required to give up their affiliation with their university of origin. It was a bold experiment. The kind of tenured professor who dictated all the rules never existed at Unicamp. Every young professor had total freedom to pursue his or her area of research. This was important in order to allow the free flow of skills and talent. Unicamp set up its post-graduate program at almost the same time as the undergraduate program, linking research, instruction, and innovation. Another feature is that the artificial dilemma – basic science vs. applied sciences – never divided our university environment. Some people had reservations against partnerships with companies, but those were neutralized once many of our best academicians had demonstrated that it was possible to reconcile a solid reputation with an eye to innovation. The issue that today is on Brazil's agenda – that we must transfer

our academic skills to innovation – has been part of life at Unicamp since the very beginning.

How big is Unicamp's contribution to Brazilian research?

If we were to add up all the production that has come out of this university, it would represent 15% of all the research done in Brazil. If we are talking about articles that have been indexed in databases, such as the Web of Science, the number is a little smaller. Unicamp is responsible for about 12% of the scientific production of this country. In 2011, we had 4,000 publications indexed in periodicals, written by a contingent of approximately 1,800 professors. This represents more than two publications per researcher, which is the highest ratio among Brazilian universities.

In what fields does Unicamp most often make headlines?

Unicamp has a long, well-consolidated presence in the natural sciences. The fields of physics, chemistry, mathematics and biology are recognized as very strong. This is clearly shown in the assessment of its post-graduate programs done by the Coordinating Agency for the Improvement of Higher Education Personnel (Capes). Many programs were given a score of 7. We see excellence in engineering and in medicine. The School of Medical Sciences has earned distinction thanks to its policy of being very selective in recruiting new professors. It is a large school, but its teaching staff is heavily involved in research. In the humanities, the Institute of Language Studies is prominent, as is the Institute of Philosophy and Human Sciences. We also offer a curriculum at the Art Institute that is playing an important role in both art production and on the academic side. Unicamp has been expanding its leadership in some other areas. This is reflected in the National Institutes of Science and Technology. We have nine such institutes – not coincidentally in medicine, physics, chemistry, and engineering.

One notable characteristic of Unicamp is its devotion to innovation. In terms of number of patents, only Petrobras ranks higher. What is the recipe for maintaining a group of researchers who are open to innovation?

When the teaching corps was recruited at the end of the 1960s, some people came from corporate research laboratories. Several instructors from the Physics Institute had spent time at Bell Labs, a world reference point at that time, and their minds were already open to the relationship between academic research in both basic knowledge and applied knowledge. We never had a system of academic chairs, and this factor allowed personal initiatives to flow. If you have complete freedom to direct your research toward an application or a deepening of basic knowledge, it is much more likely that further innovations will emerge than if you are subject to decisions from on high. Also important is the fact that professors are achieving success in the true sense of the word when their works appear in noted magazines and

journals, their contributions are recognized in other countries, they are quoted, and they receive awards. We have proved that there is no incompatibility between developing knowledge, applying it to an innovation, and obtaining a patent. The university has maintained an annual volume of about 50 patent applications filed with the INPI. We also have licensing, which is more important than patents in that licensing recognizes the utility of an invention. All this explains our second place rank with the INPI, right behind Petrobrás. It's unusual, because this is not what happens in most other countries. It is a peculiar feature of the system of innovation in Brazil that a university can be one of the most important actors on the technological innovation scene. Now we need to develop the ability to deposit more patents and technologies in other countries so that we can become international players.

How are Unicamp's relationships with companies?

INOVA, our innovation agency, was established in 2003, but long before then we had an active innovation office. In recent years we have received visits and held discussions with a great number of companies. The idea is to strengthen that relationship within the context of the university's mission, which is to prepare the most well-qualified human resources and advance knowledge. Without neglecting our mission, we are willing to enter into dialogue with any agent, public or private. The funds for research come from contracts, from formal agreements we establish and sign with both state-owned and private companies. FAPESP funds cover about 40% of our research budget. Capes and the National Council for Scientific and Technological Development (CNPq) also contribute important sums. But about one-fourth of the funds for research come from agreements and contracts signed with public and private companies. Companies seek us out because they know that the university is interested in studying their proposals.

Can you mention some of the main examples?

Petrobras, Braskem, Shell, CPFL, Repsol and Microsoft are some of the companies involved in recent partnerships. There's a lot of collaboration with companies in the medical field that are interested in establishing partnerships, both for clinical trials and for basic research.

Why encourage entrepreneurial capacity even in the areas of music and dance by offering courses that prepare students to win grants under the 1991 Federal Law on Incentives to Culture (Lei Rouanet)?

Our innovation agency engages in cross-cutting activities, and that is one of them; the university not only provides our students with a good technical education but also gives them tools so that they can form their own companies, obtain financing available under the law, or become future entrepreneurs. It is a way to prepare them for the labor market, which has different configurations today. We have records of more than 200 companies having been created that have some connection with the university

– either owned by former students or incubated here. Many are doing well on the Brazilian market and others even have representatives in other countries.

During your administration, the Office of the Dean has sought to further globalize the research done at Unicamp. What have been your results?

In the first place, we have tried to convey, through very specific initiatives, the idea that the teaching staff should balance their activities of instruction, research, and extension. Of course not everyone is able to achieve a level of excellence according to the three pillars of the university, but we need to be alert to this need. With regard to support, we have detected a demand for continued institutional support to cover certain needs that the financing agencies don't cover.

For example....?

Construction of new laboratories. The current administration is responsible for three major projects. One is a highly developed central technology laboratory that would provide services to the fields of genomics and proteomics, bioinformatics and cellular biology. We received support from FAPESP through a request for proposals issued under the Multiuser Equipment Program, and the university is investing R\$6 million in construction of the building. Another initiative is the São Paulo Bioenergy Research Center, which involves all three São Paulo state universities. FAPESP participates in this program by financing research projects. We received R\$15 million from the state government and are using it to renovate an area of 4,000 square meters to house laboratories. We are building a headquarters building measuring more than 1,000 square meters and finalizing contracts with five instructors who will work in the field of bioenergy. Our budget for 2013 calls for hiring five more instructors. Added to the number of researchers now on staff, there would be 50 staffers working in bioenergy. Through an internal request for proposals that recruited outside consultants to evaluate the proposals, we offered the possibility for contracting senior technical personnel to assist research groups that have solid reputations in their specialty fields and recognized fund-raising ability. Forty-five hires were authorized for groups that are supported by thematic projects, National Institutes of Science and Technology (INCT), multiusers, and international collaborations. Lastly, we established the Integrated Research

More than 200 companies have been created by former students or incubated within the university

Laboratories (ILP) to accommodate interdisciplinary research projects. That structure will house researchers for specific periods of time so that they can carry out projects financed by foreign sponsoring agencies. We also issued two requests for proposals on infrastructure, to renovate certain research laboratories. Unicamp was a pioneer in setting up a researcher support unit whose primary intent is to help researchers in preparing progress and project outcome reports, and free them from some administrative obligations. Today there are five employees working locally, and two others in units where there is a high demand for those services and, because the units have obtained funds under FAPESP thematic projects, they have qualified to have one staff member to manage those projects.

Is the support tied to the ability to raise funds?

Once they are working on three thematic projects, a unit may ask the Office of the Dean of Research to assign it an employee who will provide administrative project management services. This is tied to fundraising. We have to have a counterpart to the investment that the university will make via payment of salaries and other benefits. We hope that this trend continues and that the units will increasingly be able to justify the hiring of that kind of professional to assist them in managing their activities.

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How has the university been able to renew its corps of researchers?

We have experienced a strong increase in the hiring of teaching staff. For

the coming year, we expect to hire 75 new instructors, lecturers, etc. We need to offer them the conditions for beginning their work so that they can assemble their groups, raise funds, and attract students. We give them a modest initial assistance package that amounts to almost R\$50,000 each. An individual can request R\$15,000 of that total as soon as he or she submits an application for research assistance to some Brazilian or international sponsoring agency. The money is used to adapt a workspace, purchase equipment, reagents, and so on. Then, if that aid is approved, the individual is entitled to a grant to fund a master's degree. Young instructors frequently have trouble finding advisees because they are still building their academic reputations. This allowance helps ensure that they will have a master's degree candidate to advise. Today, we also have about 1,500 grant recipients in the area of undergraduate research. If that young instructor can couple that initial aid package with some grant

recipients working on undergraduate research projects, in one or two years he or she will have assembled a small group of researchers that will be able to consolidate itself and attract other researchers in the future.

How is the effort to bring in foreign professors going?

Although Unicamp was born with hefty support from international experience, over the years, for various reasons, that component ceased to be as strong as it originally was – a trend that portrays the Brazilian post-graduate education system. One of the initiatives we established seeks to attract teaching staff from abroad. A Brazilian who has settled abroad, or a foreigner who wants to come to Unicamp can be appointed to staff a unit of instruction and research under the visiting professor program. The only obligation such a unit has is that by the end of the second year, a competitive examination will be opened in the area in which that instructor specializes, since the invitation for him or her to come means that he or she works in a field of strategic importance. If the unit needs an expert in numeric systems, it may invite a well-qualified researcher in that field to stay here for as long as two years. And so that person becomes familiar with our university system and enables us to get to know him or her well, and, at the end of the period, that individual can take part in the competitive exam. We now have 11 professors in this program. Seven are foreigners and four are Brazilians who had gone abroad and have returned. We also make funds available from our budget to support short-term visits of between 15 to 60 days by foreign researchers who are distinguished in their fields, in order to accelerate the process of getting our younger teaching staff involved in international collaboration. Instructors who have approved proposals receive funds to enable them to visit the partner laboratory outside Brazil for the same period of time. Under both kinds of visits, there was provision for a doctoral or post-doctoral student to visit the partner laboratory.

Why are rankings of academic performance important to the universities? What has Unicamp been doing to improve performance?

Unicamp is a medium-sized university whose mission is to achieve quality. We have about 30,000 students. It's not likely that we'll eventually have more than 40 or 50 thousand students. Scientific production is increasing in a natural way, but there are no indications that the university will ever be numerically bigger than it is now. When we look at the ranking, we ask ourselves whether it is measuring the quality of production by the university, or the quantity. By any standard of measurement, Unicamp is one of the best in Brazil – for example, when you compare the numbers of post-graduate courses scored at 6 to 7 in the Capes ratings, or academic production per professor, or number of applications for admission to the post-graduate program or to undergraduate courses. We are encouraging our units to enter into a dialogue with noted foreign institutions. Several workshops have been and will be held with universi-

Unicamp's mission is to achieve quality. We're not likely to have more than 40,000 or 50,000 students

ties of international renown. The expectation is that this will create more lasting ties. We are not interested in sending students abroad for six months and getting them back. That doesn't change the perception that the world scientific community has of Unicamp. We have to engage in major projects and collaborative efforts and see that our work obtains greater visibility.

I would like you to talk about your personal experiences – the three periods you spent outside Brazil.

I did post-doctoral work for two years at the University of California at Berkeley and then I had two short stays as a visiting professor in Germany and England. I'm from a generation that believed that post-doctoral work abroad was mandatory. The entire academic community used to expect that after earning a PhD, one would go to a famous university in another country, then return and establish one's own line of research. I was helped by my doctoral advisor, Albert Kascheres, an American, in making a choice from among competent groups that I could join abroad. I had the good fortune of going to the group that was prominent in my field, which is organic synthesis. I was able to learn, come back to Brazil, and establish a laboratory for asymmetric synthesis and natural products. Until then there had been no concentration of efforts in that area, which was growing in importance in the synthesis of medications, in agriculture, and in foods. My career began in 1973. After four years of undergraduate work and four more years of doctoral studies, I went to the University of California at Berkeley. I returned at the end of 1984; 1985 was my first year as an independent researcher here. I have done 27 years of work in organic chemistry and have trained more than 40 post-graduate students plus 20 students in undergraduate research. Currently I am gaining administrative experience as director of the Chemistry Institute and as dean of research.

I would like you to talk about your contributions as researcher. Your field is organic chemistry. How did you happen to become interested in it?

My training is as a chemist, and my specialization is organic chemistry, which deals with the transformation of simple organic matter into more complex products. I began my doctorate by studying some cycloaddition reactions, which is an important family of organic reactions – studying them from the methodological standpoint, i.e., looking to see in which situations the reaction might occur and how it would occur. In my post-doctoral work, I went on to study synthesis, the laboratory preparation of natural products, of chemical substances found in nature and that have some practical use but cannot be extracted from nature in sufficient quantity. Drugs are an example of this. Many drugs were inspired by natural products, but nature cannot supply the quantity required in order to treat great masses of people. This is where organic synthesis comes in, because it produces in a laboratory that which nature took billions of years to develop and in quantities that permit access by a large number of

people. I went to do that post-doctoral study in an area of synthesis of the antibiotic erythromycin, which at the time was the holy grail of organic synthesis, one of the most complex structures that could be synthesized and produced in a laboratory. When I returned to Brazil, I applied the same methodology to a different area, which is pheromones, substances that insects use to communicate. Many pheromones have direct and important applications in agriculture. At that time, the substances were not as complex as those I had studied during my post-doctoral years. The structural conditions available to us enabled me to apply that knowledge in a domain that was less complex – but not for that reason less important, because those substances are used to control pests. As the conditions for research improved, I began to get involved in the synthesis of more complex drugs and natural products, as well as catalytic methods for synthesizing natural products. Today my focus is on linking my skills in organic synthesis with the field of medicinal chemistry. I work with various groups so that what I produce in the laboratory can be tested with respect to different biological activities, such as anti-cancer activity.

You have two projects involving cancer, don't you?

I have a thematic project under way that attempts to combine different areas of knowledge in a search for new structures that might be able to interfere with cancer cell metabolism. We have several colleagues who are working on the new molecules synthesis part; we have groups that are handling the structural biology part, enzymatic activity, pharmacological studies, etc. In short, we have put different skills to work together so that we don't have to end our work only with the production of a new molecule; instead, we can evaluate its potential and from that point redesign new substances that may have even more interesting properties than those we have observed. It's an interface between organic chemistry, medicinal chemistry, and an area known as chemical biology, which is the use of chemical tools to understand biological processes. It's a natural evolution for someone who began by studying rather basic processes and gradually moved on to the synthesis of more complex natural products. That in turn led to the application of that expertise in collaboration with groups that are able to evaluate the biological activity of that compound. These days, you can't just consider developing new molecules without evaluating their implications, whether as new materials with pharmaceutical potential, pest control agents, or something else. ■

Organic synthesis produces in large quantity that which nature took billions of years to develop

The art of taking shortcuts

Fabrcio Marques

PUBLISHED IN MARCH 2013

Since 2009, microbiologist Maria José Soares Mendes Giannini has coordinated a series of endeavors with the aim of enhancing research quality at the young Universidade Estadual Paulista (Unesp). As head of the university's Office of the Dean of Research for the past four years, she has organized initiatives that have boosted the number of thematic projects at Unesp by 130%, taken fundraising to unprecedented heights, and increased the scientific article output by 42%. She has relied on an assortment of strategies to address the natural imbalances in an institution with campuses spread across 24 cities. One of her goals has been to coordinate the efforts of different researchers in order to generate research that is more robust. Another has been to increase the international visibility of the university's scientific studies by encouraging faculty members to publish in high-impact journals and by bringing in scientists from abroad. She has also established support offices for researchers at each of Unesp's academic units, thereby relieving faculty members of the bureaucratic tasks associated with progress and project outcome reports. These successes earned her the right to continue leading the Office of the Dean for the next four years, under the administration of the new president, Julio Cezar Durigan.

Born in Portugal, Giannini has lived in Brazil since she was three. She completed all of her studies in microbiology and immunology at the University of São Paulo (USP), in the city of São Paulo, complemented by short-term internships abroad. In 1983, she moved to the interior of the state, accepting an invitation to work at Unesp's Araraquara campus with the School of Pharmaceutical Sciences, an institution that recently celebrated its 90th anniversary. She was one of the forces behind the introduction of the graduate program in clinical analysis in the late 1990s. "In less than 10 years, we managed to go from a course that was not recognized to a course that the Coordinating

Agency for the Improvement of Higher Education Personnel (Capes) has given a rating of 6 [out of a potential top score of 7]. This was a huge effort," she recalls. Married and the mother of an adult son and a teenage boy, Giannini divides her time between her office in São Paulo, where she spends Mondays through Thursdays, and Araraquara, where she has her laboratory and lives with her family on Fridays through Sundays. She visits every Unesp academic unit once a year – "It's important so that researchers feel supported and we can listen to them" – and she maintains frequent contact with researchers via a videoconferencing device located next to her desk. Since 2010, she has been a member of FAPESP's Board of Trustees.

How do you coordinate research efforts at a university that has campuses spread across 24 cities?

The Office of the Dean of Research is new at Unesp. It began under the administration of Prof. Marcos Macari [president from 2005 to 2008]. Prof. José Arana Varela was the first Dean of Research, and then I took over. We're heading into our third administration. Unesp is a research university, although it is also strong in teaching and extension work. However, it has a special feature: it's a university that covers the entire state of São Paulo. We are the largest multi-campus university in the country, perhaps in the world. If you draw a sixty-mile circle around each of these 24 cities, you'll fill in the map of São Paulo state. Today, quality science is being produced in the farthest corners of the state; it's essential that the state derives benefits from this research. Of course, we have our imbalances, and the Unesp Dean of Research must try to overcome them.

Research at Unesp got off to a stronger start in the more traditional academic units, such as the Araraquara campus. How do you extend one standard to all units?

SPECIALTY

Mycology

EDUCATION

University of São Paulo (USP)

INSTITUTE

Araraquara School of Pharmaceutical Sciences, Universidade Estadual Paulista (Unesp)

SCIENTIFIC PRODUCTION

117 scientific articles, 10 book chapters. Served as an advisor to 27 Masters and 15 doctoral candidates and 26 undergraduate students. Supervised 7 post-doctoral internships



Our schools of Pharmacy and Dentistry will turn 90 this year, and they have been involved in research for some time. This is likewise true of the former Araraquara School of Philosophy, Science, and Language and Literature (FFCLA), now called the Chemistry Institute and the School of Science and Language and Literature. However, it was not only there that we started out strong. In Jaboticabal, the agrarian areas started out strong as well. If you look at the percentage of all published research studies in the field of agrarian sciences that are conducted at our university, you'll see that the number is quite substantial, with research coming from other units as well. Our institutes of Chemistry and of Theoretical Physics, along with the Bioscience Institute in Botucatu and the one in Rio Claro, are among the units whose research is the most international. In the beginning, back in 1976, 14 campuses were incorporated, 10 fewer than today. The university is now 36 years old, and as time has gone by, new academic units have been added. Even the newest ones are conducting quality research and offer graduate programs. We have foreign professors working at Ilha Solteira, São José do Rio Preto, and various other units. If we didn't have a quality public university, how would we be able to attract foreigners to perform top-level research? This history has sustained a process of steady growth, and in 2005 we reached a watershed

moment. We charted out research groups and the types of publications and periodicals where we'd been publishing, and we identified many imbalances. Not today. Our research work has been strengthened, and it is growing and improving in quality, making an extraordinary contribution to the development of science and technology in Brazil. Over the past four years, we've hired nearly 1,000 faculty members, over 60 researchers, and over 30 higher-level

staff who maintain major pieces of equipment, and this contingent of highly qualified personnel will entrench research efforts at Unesp. Today, our focus is to increasingly internationalize our research so that it becomes more relevant in today's world and has an impact in Brazil and abroad. We are playing our part as active agents in the promotion of the scientific and technological development of our state and Brazil and in transferring such developments to society.

Could you cite some figures to illustrate this growth?

I'll compare 2007 and 2011 because the numbers for 2012 haven't been fully processed. If we compare these two periods, our scientific production climbed 42% in the Thomson Reuters database. This is a substantial increase. When I assumed my post, one of the goals of the Office of the Dean was to add and merge expertise so that we could achieve quality science by strengthening our institutional capabilities through a focus on innovative proposals. And so we held a

series of seminars and of thematic workshops. These were attended by invitees from several universities in Brazil and abroad. Discussions were aimed at fostering progress in topics related to the frontiers of knowledge, in alignment with our national agenda. Research groups from a variety of areas took part in the discussions at these events. This has given us science with a more cross-sectional nature that is more inter-, multi-, and trans-disciplinary. These diverse perspectives generate quality, as well as an advantage that groups with a single discipline focus fail to develop. This is what we're trying to do here at Unesp. The major challenge presented by the distance between our campuses is how to transform isolated groups into groups that have a more active presence both inside and outside Unesp. We have very strong groups that do magnificent international work and that serve the university as well – such as ceramic materials and nanotechnology, natural products, and the computational science group, which is responsible for Unesp's grid. We have groups that coordinate Research, Innovation and Dissemination Centers (RIDC) of the São Paulo Research Foundation (FAPESP); the National Science and Technology Institutes (such as the one connected with international relations); one on nanotechnology; and another on comparative physiology. We have the Confucius Institute, considered the finest in the world. We have consolidated groups, and the Unesp Dean of Research must ensure that more groups distinguish themselves in their fields of knowledge.

One of your concerns has been increasing production in the engineering sciences and the humanities to bring them in line with the life sciences. How is this endeavor coming along?

Our participation in the life sciences is strong, accounting for nearly 70% of what Unesp produces. Two areas where we had noted significant imbalances were the engineering fields and the humanities, so we established Project Renew – Renewing Engineering and Renewing the Humanities. Our focus was not only to provide financing through a funding opportunity announcement but also to facilitate projects that required a merger of expertise in these areas. I feel we've already achieved some positive results. We also launched our human sciences forums, and now we have them in the engineering sciences as well; these are meant to form cooperative ties and now innovative ties as well. We have established 11 engineering degree courses at our university. Three have already opened their doors – environmental engineering at São José dos Campos and bioprocesses and chemical engineering at Araraquara's School of Pharmacy and its Chemistry Institute, respectively.

Have researchers responded well to these initiatives?

Yes, they have. Attendance was very high at the forums, which were held precisely to pinpoint and recognize the academic talents already here at our university, especially in key fields of knowledge. As part of the Contemporary Challenges series, these initiatives led to the introduction of incentives and sponsorships for publishing e-books in the fields of the human sciences and those on the cutting edge and in areas of knowledge that are of national interest, such

If we didn't have a quality public university, how would we attract foreigners to perform top-level research?

as nanotechnology, bioenergy, natural products, biotechnology, food and food security, and others, which provides a more effective way of disseminating the findings of large research groups. However, we observed that other initiatives were needed, and so we expanded the Renew program to encompass more university groups that had been shut out of the research process. There is a contingent of faculty members who went into administrative roles early on and never developed a career in research, so we decided to launch the General Renewal program, which is for all areas and seeks to attract staff who currently don't have access to funding mechanisms. We evaluate their processes and, in addition to funds, we include a research grant. All of this is done so that they'll return to researching and publishing and engage with a line of research and graduate programs.

The approval of thematic projects has risen. At what rate?

The number of thematic projects has climbed nearly 130%, and in monetary terms, we've enjoyed growth of almost 340%. We know that research requires skilled human resources and a good research infrastructure. We've received very substantial funds for these purposes from FAPESP, under its Multi-User Equipment Program; from the Brazilian Innovation Agency (Finep), under an infrastructure funding opportunity (up 340%); and from both Capes and the National Council for Scientific and Technological Development (CNPq). Our research infrastructure has seen great improvements, and today we have many facilities, many new buildings, and new laboratories. In order for research to grow, we had to open up new spaces and merge expertise; to this end, special institutes have been formally established, bringing together researchers from different campuses. Four such institutes have been approved by collegiate bodies. One is the Bioenergy Institute, headquartered in Rio Claro but with eight associate laboratories; it was created in conjunction with the other São Paulo state universities and is linked to the São Paulo Bioenergy Research Center. A joint graduate program was designed among the three universities. A Marine Institute was inaugurated in São Vicente, merging expertise from various campuses. There's a strong group in Rio Claro that works with geology; we have the Center for Geosciences Applied to Petroleum (Unespetro) there, which has close ties to Petrobras. And we have the Biotechnology Institute in Botucatu, which is also home to our central vivarium; many other groups that address different topics and come from a variety of campuses also participate there. The Institute of Public Policy and International Relations was also established. It currently operates on the university grounds in downtown São Paulo and offers graduate courses. Our outlook for the future is to have a space that can meet the needs of current agendas and of new trends and eventually serve as a center of dissemination for the university, broadening discussions. The funds for setting up these institutes – which were quite substantial – came from project grants approved by the Ministry of Science, Technology and Innovation; the São Paulo State Secretariat of Economic Development, Science and Technology; Banco Santander; Finep; and the university itself, which has invested heavily in tailoring its facilities to the new demands of a contemporary teaching and research university.

The number of doctorates awarded is an important factor.

We rank second among universities worldwide in the number of doctorates awarded – almost 1,000 a year. First comes the University of São Paulo and then us, followed by the University of Campinas (Unicamp) and universities in the United States.

Graduate programs usually have strong ties to research. What is the status of this interaction at Unesp?

The number of courses has grown. We offer more than 90 doctoral programs and over 100 masters programs, totaling 122 graduate programs. Unesp ranks second in the number of courses offered in Brazil. The number of programs receiving Capes ratings of 5, 6, and 7 has been rising steadily. We want more, and that will occur naturally as research by different groups advances.

What impact does Unesp research have on the development of rural São Paulo?

Years ago, a group in the field of economics did a survey that showed that Unesp contributes enormously to the local economy in cities where we have academic units. However, I believe we can contribute much more, and the Dean of Extension, the vice-president, and I will be working to see that Unesp becomes more integrated with these cities and forges partnerships with local governments involving the extension programs we already have in place; this may also have the added advantage of fostering truly innovative research. Our academic units are located in places ranging from extremely wealthy cities, such as Araraquara, to places where we know that the Human Development Index is very low, such as Vale do Ribeira, where we are introducing a course in aquacultural engineering in partnership with the city. In other cities as well, local governments do important work alongside Unesp to deliver science to these locations.

How does Unesp place in international rankings?

We've been focusing on our ranking, which has been an important topic of discussion since the implementation of the Institutional Development Plan under President Herman Voorwald in 2009. In its strategic plan, the university announced the goal of ranking among the top 200 universities in the world. This gave us a target, and our initiatives provide support towards this end.

What's the value of having a goal like this?

Without a doubt, it helps a great deal. In my talks, I jokingly say that we've already made it there in some rankings. For example, we're 174 on SCImago, and we're the

There are faculty members who went into administrative roles early on. We launched a funding opportunity announcement so they would return to engaging in a line of research

third university in Brazil and the fifth in Ibero-America. In terms of some other classifications, we need to make further improvements. One ranking that says a lot about Unesp in its youth – we're only 36 years old – is the *Times Higher Education's* list of the best universities under 50 years of age; there are over 2,000, and we're among the top 100 in the world. On the QS University Ranking, we hold quite an attractive position: 17th in Latin America; and, if you break down the research, 7th place. We've grown a lot and taken shortcuts; that isn't easy in science.

How do you take shortcuts? By bringing in people from abroad?

Yes. This is what we had in mind by creating special research institutes. We're in the phase of hiring researchers because we have career tracks for professors and for researchers. Our research institutes will basically have researchers working alongside professors and students. The researchers' responsibilities encompass research and training students at the graduate level. The idea is to invite foreigners to these spots. We've worked at the Marine Institute, the Biotechnology Institute, and the Bioenergy Institute; we have collaboration agreements in place with international groups. The Marine Institute, for instance, has close ties with Germany

– universities such as Heidelberg and Kiel – and also with the Universidade do Porto, as well as a partnership with South Africa. We have a cooperation agreement with KU Leuven University in Belgium, under which we co-fund the arrival and return of researchers. We have highly internationalized groups. The Institute for Theoretical Physics (IFT) is the only one in Latin America that houses a unit of UNESCO's International Centre for Theoretical

Physics (ICTP). Last year, they brought in more than 80 highly eminent foreigners. In the physical sciences, and the biological sciences as well, Unesp is becoming increasingly internationalized. Even an area that hadn't appeared in international publications, that is, the humanities, is now beginning to do so. This is a sign that we're turning Unesp into what is called a world-class university.

Unesp has created offices at all of its academic units to help researchers deal with the bureaucratic administration of their projects. What was this process like?

It was a lengthy discussion; it wasn't easy. The original idea was to put an office on every campus, but we saw that the results wouldn't be consistent because each unit on each campus has a different way of functioning. Therefore, we established a research office within each unit, and now we've hired a staff member for each unit to relieve researchers of tasks related to progress and project outcome reports. In

some units, we've hired a second person, based on a number of considerations – mainly related to internationalization – and this person serves researchers involved in international cooperation, thematic projects, and international workshops. We'll have a third staff member, as well, who will be hired to work with innovation. The idea is to forge a link between researchers and businesses right inside the office itself.

How will that work?

There will be a place where we will be able to invite business to come in and become involved. That way, we'll be doing all that I think we should be doing to achieve what I consider to be the responsibilities of an office of the dean of research by serving the areas of research, internationalization, and innovation; helping researchers; and working to secure funds.

You're beginning a new four-year term now. What are your goals and the new demands of the role?

We're already working on a number of points, but we'll be expanding initiatives to foster greater inclusion of newly hired professors, who are the university's future. We're working hard so that they'll find a support system here, integrate themselves into strong research groups, and devise innovative lines of research. We have a special funding opportunity for first-time projects, and now we intend to expand it. We're going to work with areas that are not very internationalized even though their output is high. Therefore, we'll be providing incentives for them to make this a major focal point. Another issue is innovation: that is, university-business interactions. Because we already have this type of link in a number of cities in the state of São Paulo, where there are high-tech hubs, we're going to move toward increasing the involvement of city governments so that more such technological hubs are set up and consolidated.

With regard to your own career, all of your training was at USP.

Yes. I specialized in pharmacy and biochemistry and started working when I was in my first year of undergraduate studies. My first job was at a City of São Paulo laboratory; then I went to Fleury laboratory – I learned a lot there, but I didn't want to do routine types of work. Starting in my fourth year as an undergraduate, I went to USP's School of Medicine and worked there for 10 years in medical mycology, which involves the study of fungi of medical interest, a subject that hadn't been included in my coursework. I worked with Carlos da Silva Lacaz, a leading scholar on fungi and a great teacher and humanist. I discovered that I liked research and teaching, as well as having a new challenge every day. I think that's what research is all about: seeing a new path within each finding. There were a number of people who were very important to me, great teachers of mycology and immunology, such as Prof. Antônio Walter Ferreira, my masters and doctoral advisor; Mario Camargo, with the Institute of Tropical Medicine; and Vera Calich, with the Institute of Biomedical Sciences (ICB), who gave me enormous encouragement. When it came time to choose a topic for my work, I realized I didn't want to do classic mycol-

The goal is to be among the top 200 universities in the world. Of the newer ones, we're already among the top 100

ogy; I was already starting to fall in love with immunology. I began conducting research on the serological diagnosis of paracoccidiodomycosis, which is an immensely important disease in Latin America. I developed markers, reagents, and methods that hadn't been applied to this disease, such as carrying out research into antigen circulation in patients. This made it possible to make a diagnosis and initiate treatment earlier. My co-advisor was Prof. Aoi Massuda and, together with Prof. Maria Aparecida Shikanai Yasuda, we published two articles as a product of my doctorate that were extremely important at that time. When I finished my doctorate, I was invited to join the School of Pharmacy in Araraquara, and that proved to be a great challenge. That's because when I was in São Paulo, I moved quite freely between the School of Medicine and the Institute of Tropical Medicine; I did part of my dissertation at the Institute of Biomedical Sciences, where Prof. Erney Camargo had just arrived. I had access to a number of laboratories that had fantastic equipment for that epoch. The School of Pharmacy in Araraquara already offered a class in clinical mycology, but there was no established research area. I had been following the development of research work at Unesp since 1983. Prof. Deise Falcão, from microbiology, knew about my specialization and, although she was a bacteriologist, she invited me to work on a broad-scope project funded by Finep. This experience with bacteriology showed me that I didn't want to continue doing research on diagnostics. I did some short-term internships abroad and in Brazil and began studying models of host-fungus interactions. I began implementing *in vitro* models, which I still use today, and I made my way to the discovery of the molecules that mediate interactions between the fungus and the host. I started working with adhesins, which are the molecules involved in that interaction, and now we are studying invasins.

You had a FAPESP project about this model...

I had a number of them. I coordinated a thematic project that is already finished, together with Prof. Gil Benard – it was an effort to combine knowledge from the *in vitro* model with the human one – and another project with Prof. Célia Maria Soares of the University of Goiás. I later joined her in a funding opportunity from Finep's Genoprot Network [which provides funding for genomic and proteomic research]; more recently, with financing through a Finep infrastructure funding opportunity, we are implementing 'omic' platforms in our laboratory. Along the way, I had a remarkable professor who unfortunately passed away last year: Henrique Lenzi, from the Oswaldo Cruz Institute's pathology sector. He was a wonderful person, as a human being, and a great humanist and specialist in science. He was of tremendous help in discussing and implementing these new technologies. Today, because of a shift in the teaching project in the pharmacy course, another line of research has been implemented, with a more technological foundation. We're creating a platform for developing antifungal agents and bioreagents. This platform was only feasible through the support of FAPESP programs, such as Biota-FAPESP's subprogram BIOprospecTA (São Paulo State Bioprospecting Network),

in conjunction with groups from chemistry and with Prof. Vanderlan Bolzani, Maysa Furlan, and Prof. Ana Marisa Fusco Almeida, who is my assistant – along with other researchers. It was arduous work to make the advances that I did but because I endeavored to work in collaboration with others, I didn't find it so hard. I'd like to stress that it was only one year prior to my coming to the Office of the Dean that I was assigned an assistant, Prof. Almeida. Without her help, this antifungal platform would not have been developed. We're working on a prototype.

What's the prototype?

Some of the substances we've been working with showed potential during *in vitro* assays, and now we're progressing to *in vivo* assays and also using new formulations to ascertain their potential applicability as antifungal agents. I hope this joint work will yield an innovative product. We're also looking at microbial antibiofilm and antifungal agents because these microorganisms are more resistant in this form. Biofilm formation is a classic model in some diseases, especially in the case of pathologies where some fungi and bacteria are associated with a complex multicellular structure, which leads to points of ongoing contamination. A matrix is formed, and the antifungal and antibacterial agents cannot reach the sites of action. We're studying biofilm formation in endemic diseases, and we've already described this both in histoplasmosis, in a study by an advisee of Prof. Almeida's, and also in paracoccidiodomycosis, the disease I've worked with the most since starting my studies at the School of Medicine. It's a neglected disease among the fungal diseases and resembles tuberculosis.

Research by pharmaceutical companies doesn't come into play?

Diseases caused by fungi generally fall into the neglected disease category. Mycology is considered microbiology's poor cousin. You've got bacteriology, virology, and then mycology. However, it's grown because of a higher prevalence of fungal diseases among some groups of patients because of people's increased longevity and because of immunosuppressive diseases. You improve living conditions, but this opens the door to so-called opportunistic agents. Today we have a rising number of diseases caused by fungi that hadn't even been described as pathogens – unlike *Paracoccidioides*, which was always considered a primary pathogen. It was described by Adolfo Lutz in 1908 and is one of the fungal diseases of greatest concern in Brazil. At first, I contributed to its diagnosis, and now I'm working mainly with adhesins, using them as targets in the search for new drugs. ■

It was arduous work to make the advances that I did, but because I endeavored to work in collaboration with others, I didn't find it so hard

High-level partnerships

Pilot program draws scientists from abroad to form new research groups in São Paulo

Fabrício Marques

PUBLISHED IN NOVEMBER 2012

Two thematic projects have now been approved under a FAPESP pilot program known as the São Paulo Excellence Chairs (SPEC), which seeks to establish collaborations between institutions from São Paulo State and high-level researchers abroad. One such project will bring to Brazil a husband-and-wife team of Brazilian scientists, Victor and Ruth Nussenzweig, both 84, who have lived in the United States since the 1960s. Their work has become the international benchmark in the search for vaccines and treatments against malaria. Andréa Dessen de Souza e Silva, a Brazilian who lives in France, also had a project selected under the program and will lead a research group at the Biosciences National Laboratory (LNBio) in the city of Campinas. Since 2000, Souza e Silva has led a bacterial pathogenesis research group at the Institute of Structural Biology in Grenoble, France.

The goal of the SPEC program is to attract renowned scientists to Brazil to coordinate thematic projects in their areas of expertise at universities and laboratories in São Paulo. The researchers continue to be affiliated with their home institutions but are required to spend at least 12 weeks of each year of the project's five-year duration in Brazil while coordinating a group of FAPESP grant recipients, including post-doctoral associates, PhDs and even under-

graduate students. "The goal is to attract highly qualified researchers and establish core research groups in areas where we want to excel and to enable these groups to advance more quickly," says Hernan Chaimovich, special advisor to the FAPESP scientific director. The initiative, he says, is part of the organization's strategy to stimulate the internationalization of science in the state of São Paulo. "FAPESP's mission is to improve the quality of science, technology and innovation in São Paulo State and that is why we are seeking to internationalize. We want the groups formed by initiatives such as SPEC to be able to obtain support from international research-sponsoring agencies," he says. The program is offered to institutions and highly qualified researchers interested in establishing partnerships.

Research conducted in the United States by the Nussenzweigs led to prototype vaccines tested in the 1980s, which were only able to guarantee immunity for very short periods. Since 1960, the Nussenzweigs have been affiliated with New York University, where they both work today, in the field of malaria parasites. The couple is currently engaged on two fronts: the search for a vaccine against malaria caused by the *Plasmodium vivax* parasite and techniques to destroy proteins essential for development of the parasite.



Two projects have been approved for the program, and two others are being evaluated

Ruth and Victor Nussenzweig, in São Paulo: thematic project and core research training at UNIFESP

NEW INHIBITORS

The thematic project that the Nussenzweigs will coordinate at the Federal University of São Paulo (UNIFESP) seeks to characterize enzymes essential to plasmodium development and find new inhibitors, with the potential to develop drugs against malaria. “I’ll bring a Chinese researcher who has worked with me in New York for four years, and we will also recruit other PhDs and post-doctorates,” says Victor Nussenzweig. They will work at UNIFESP with researchers that have been accepted at New York University as doctoral or post-doctoral students, such as professors Mauricio Martins Rodrigues, Sergio Shenkman and Nobuko Yoshida. The terms of the project grant will be signed in the next few weeks.

Last July, Souza e Silva became the first researcher selected under the pilot program. She graduated from Rio de Janeiro State University (UERJ) in 1987 with a chemical engineering degree and moved to the United States 25 years ago. Before settling in France, she received her PhD from New York University and did postdoctoral work at Albert Einstein College of Medicine and Harvard University. She specialized in the study of protein structures, using biochemical and crystallographic techniques. “I’ve always studied protein structures associated with medicine. I’ve been working with HIV and with inflammation,” she says. She is currently focusing on the viru-

lence of bacteria by studying the three-dimensional structure of proteins that form the bacterial wall. The goal is to understand the structures for the synthesis and repair of the bacterial wall and to try to block the infectious process. “One target is the structures that lead to antibiotic resistance,” she says. That is the focus of the work to be conducted in Campinas.

Souza e Silva has long wanted to return to Brazil. “However, I have a position in Grenoble and two small children, and I did not want to return permanently. The SPEC program format was perfect,” she says. After lecturing last year at LNBio, she initiated talks with the laboratory director, Kleber Franchini, to collaborate with the institution. In addition to LNBio hiring David Neves, a research assistant who did post-doctoral research with Souza e Silva in France, the group will also have two PhD research grant recipients and one post-doctoral research grant recipient. “I have a person I can trust coordinating the group in Campinas,” she says. The arrangement will allow an intense exchange between Campinas and Grenoble, with researchers going back and forth between the two institutions. Two other projects are being evaluated by FAPESP under SPEC, one in the area of climate change and another in materials science. “Proposals can be made in any field of knowledge, as long as they involve high-level researchers,” says Chaimovich. ■

Postdoc and research opportunities in Brazil

Fifty percent of all science created in Brazil is produced in the State of São Paulo. The state hosts three of the most important Latin American universities: USP, UNICAMP and UNESP. Other universities and 19 research institutes are also located in São Paulo, among them the renowned Instituto Tecnológico de Aeronáutica (ITA), Instituto Nacional de Pesquisas Espaciais (INPE) and Laboratório Nacional de Luz Síncrotron, besides most of Brazilian Industrial P&D.

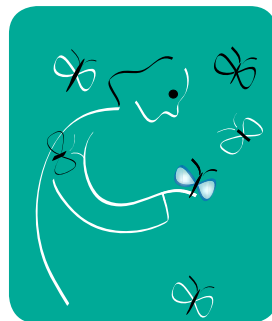
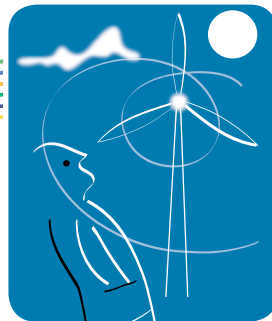
The São Paulo Research Foundation (FAPESP), one of the leading Brazilian agencies dedicated to the support of research, has ongoing programs and support mechanisms to bring researchers from abroad to excellence centers in São Paulo.

The **Young Investigators Awards** is part of FAPESP's strategy to strengthen the State research institutions, favoring the creation of new research groups. See more about it at www.fapesp.br/en/yia

FAPESP **Post-Doctoral Scholarship** is aimed at distinguished researchers with a recent doctorate degree and a successful research track record. The fellowship enables the development of research within higher education and research institutions in São Paulo. Postdoc fellowships are available when calls for applications are issued internationally, or as individual scholarships requested on demand.

In the first case, positions are advertised at www.fapesp.br/opportunidades and candidates are selected through international competition. In the second, the proposal must represent an addition to a pre-existent research group and should be developed in association with faculty in higher education and research institutions in São Paulo.

More information at www.fapesp.br/en/postdoc



www.fapesp.br/en

Organized diversity

Center creates a database of chemical compounds that have potential use in the development of pharmaceuticals

PUBLISHED IN OCTOBER 2012

Detailed information on 640 chemical compounds extracted during studies of Brazilian biodiversity is available on the Internet at www.nubbe.iq.unesp.br/nubbeDB.html. This database contains knowledge generated over 15 years of research by the Center for Natural Products Bioassays, Biosynthesis and Eco-physiology (NuBBE) at São Paulo State University (UNESP) in Araraquara. “We realized that our research results, which have been published in more than 170 articles, could be more useful if they were organized into a database than if they remained dispersed. We have valuable information on the chemical diversity of the species studied, and we decided to make this information available so that other researchers could use it in further studies,” says Vanderlan Bolzani, professor at the Institute of Chemistry (IQ) of UNESP in Araraquara and member of the group coordinating the Biota-FAPESP program. The database was designed in collaboration with Professor Adriano D. Andricopulo of the Medicinal and Computational Chemistry Laboratory (LQMC) of the Physics Institute (USP - São Carlos) and his doctoral student, Ricardo N. Santos, a FAPESP scholarship recipient.

PROPERTIES IDENTIFIED

This resource assembles a variety of types of information, such as the origin of the compound, the species from



Studies on research to develop medicine from *Rubiaceae* species, such as the coffee tree, are part of this online tool

which it was isolated, its chemical properties and its identified biological activities. The results of online research enable users to view the chemical structure and a table with information on the compound, and also to download the three-dimensional structure. The NuBBE database is composed of isolated plant compounds (80%), fungi or microorganisms (6%), synthetic compounds inspired by natural products (7%), semi-synthetic compounds (5%) and biotransformation products (modified by enzymes) (2%). A set of properties helps to define whether a given compound has the potential to be used in the development of new medicines. “The database is chemically diversified and rich. It is an interesting source for identifying bioactive compounds for testing in other, more sophisticated assays,” says Bolzani. His study on the search for cancer-fighting substances in the medicinal shrub *Rubiaceae brasiliensis*, conducted during the 1990s, is one of the oldest accessions in the database.

The data were compiled over a period of two years by a six-person team that included technicians and researchers. The database web site was designed by Leandro Figueira, who holds a Master’s

degree in computer science. “An undergraduate research internship student helped us to analyze all the NuBBE papers and to obtain information on the compounds,” says Marília Valli, a doctoral student at the UNESP Chemistry Institute and FAPESP scholarship recipient who is working on a project that studies the potential of NuBBE natural products as a resource for the rational planning of new anti-tumor agents. Valli’s dissertation, under the guidance of her advisor Bolzani, should be concluded in 2013.

One of the ambitions of the project participants is to cross the NuBBE database with information in the Environmental Information System (SinBIOTA), which links information generated by projects in the Biota-FAPESP program with a cartographic database. “This is not yet available, but we want to show the species to which the compounds are related and the habitats in which these species live. We hope this database will be the starting point for a national database on all the substances that have already been isolated from Brazilian biomes. We need to make our colleagues more aware of the value that such work would represent,” says Bolzani. ■

Fabrcio Marques

A scanning electron micrograph (SEM) showing a large, complex, and somewhat spherical structure of a parasite, likely Trypanosoma cruzi. The structure is composed of numerous small, interconnected components, possibly vesicles or filaments, creating a dense, textured surface. The background is dark and granular. A yellow triangle is in the top-left corner.

SCIENCE


In search
of new spaces:
T. cruzi (in wine)
with vesicles
(in yellow) on its
body, next to
a host cell

Parasite poised for the attack

Vesicles with proteins help *Trypanosoma cruzi*
invade host cells

Carlos Fioravanti

PUBLISHED IN OCTOBER 2012



By examining their own data and that of other groups from the past 40 years, researchers in São Paulo have identified a potential mechanism that may help the protozoa that causes Chagas disease invade host cells. As soon as it settles into a single cell, *Trypanosoma cruzi* differentiates, divides violently enough to rupture the cell and release vesicles with proteins and lipids (fats) that facilitate the establishment of the parasite in other cells.

“It seems to be a wide-ranging phenomenon,” says Walter Colli, professor of chemistry at the University of São Paulo (USP) and supervisor of this study, which was carried out by Ana Cláudia Torrecilhas of the Federal University of São Paulo (UNIFESP) in the city of Diadema in collaboration with Robert Schumacher and Maria Júlia Manso Alves of USP. “Other parasite groups and tumor cells also release vesicles that operate in a similar fashion and facilitate the infection of host cells.”

Experts in this area, in both Brazil and other countries, are excited about the possibility of using this information to develop new ways to combat or diagnose tropical diseases on a broad global scope. Such is the case with Chagas disease, which affects approximately 10 million people in South America and is becoming a public health problem in the United States.

In an editorial published in May of this year in *PLoS Neglected Diseases*, researchers from the United States and Mexico warned about the advancement of Chagas disease in the United States, mostly among immigrants in the states closest to the Mexican border; an estimated 1 million people are infected. This study refers to Chagas disease as “the new AIDS of the Americas,” and although one is caused by a protozoa transmitted by an insect and the other by a virus that is primarily transmitted through sexual contact, both can be passed on through blood transfusions, are more common among the poor and require prolonged treatment. Moreover, Chagas disease has become an important opportunistic infection among people living with HIV / AIDS, and as in the first two decades of the AIDS epi-

dem, most people with Chagas disease have no access to medical care.

In August, Peter Hotez, a professor at Baylor Medical School, director of the Sabin Vaccine Institute in Houston, Texas, and principal author of the *PLoS* editorial, wrote an article in the *New York Times* arguing that tropical diseases such as Chagas, leishmaniasis, dengue, and cysticercosis were the “new plagues of poverty.” He said that 20 million people in the U.S. live in extreme poverty. “Without new interventions,” he said, “these diseases are here to stay and will keep people in poverty for decades to come.”

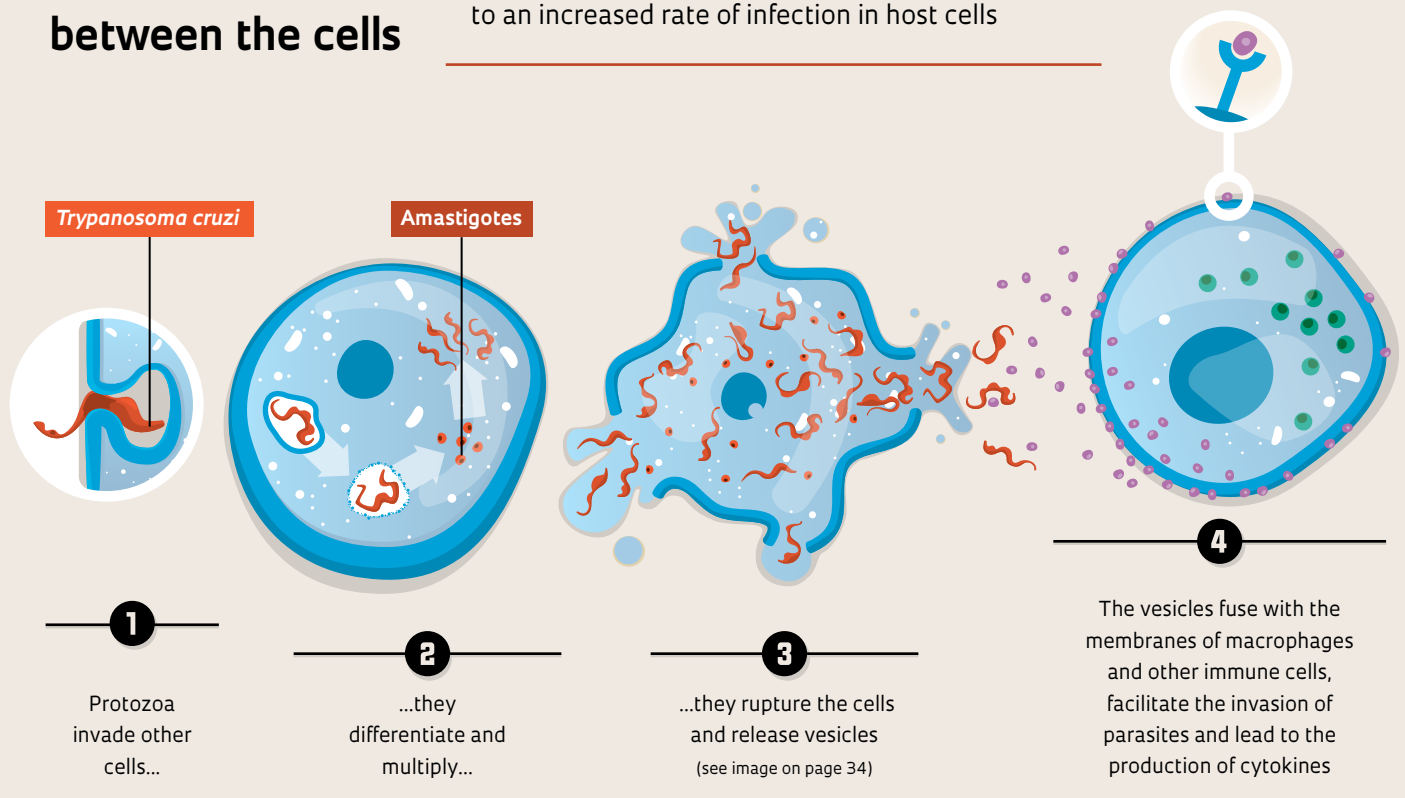
VARIOUS SIZES

There has been a vast amount of scientific literature about these vesicles – approximately 3,500 articles on these structures have been published over the last five years – but many questions remain unanswered. The first question to be answered: what should these compartments full of protein be called? In an article published in February of this year in *Proteomics and Bioinformatics*, two researchers from La Trobe University, Australia observed that the so-called extracellular microvesicles were given different names based on their size, composition and origin. One type of vesicle, the exosome, which measures 30 to 100 nanometers in diameter, proved significant because of its multiple functions, which include transferring the HIV virus to target cells; the exosome now has its own website, www.exocarta.org, with almost 150 studies and 4,563 identified proteins by early September. There are also other types of vesicles, which for now are less important, such as the ectosome (a large membrane vesicle and apoptotic bubble that may be as large as 5,000 nanometers wide and is released by dying cells).

The *T. cruzi* vesicles are smaller, measuring 20 to 80 nanometers in diameter, and initially attracted little attention. In the late 1980s, upon identifying the vesicles, Marinei Gonçalves, Maria Júlia Manso Alves, Bianca Zingales and other researchers from Colli’s team thought, along with others in this area, that the vesicles were just discarded material, although it had already

Battle between the cells

Trypanosoma cruzi releases vesicles that lead to an increased rate of infection in host cells



been observed that the more virulent varieties of *T. cruzi* released more vesicles than the less virulent ones.

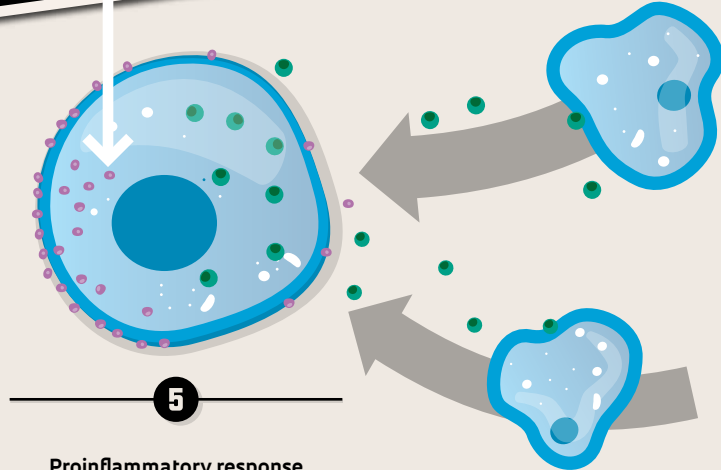
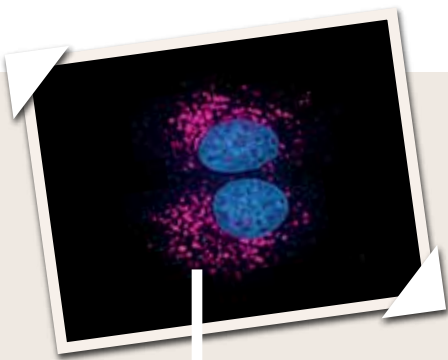
In subsequent years, other studies and more sensitive equipment showed that vesicle proteins and lipids could facilitate host cell infection by the parasite. In her doctoral and post-doctoral work, performed under the direct supervision of Alves, Ana Claudia Torrecilhas found that vesicle proteins increased the amount and the activity of the parasites in the tissues and induced an inflammatory response in the host. In a study using mice, she observed that the vesicles facilitated the entry of the parasite into the heart cells and hastened the death of the animals.

Now, in a study to be published in October in *Microbes and Infection*, researchers from USP and UNIFESP note that nearly half of the vesicle content is made up of glycoproteins (proteins with sugars attached). One of these is trans-sialidase, an enzyme specific to this parasite, as well as others encoded

The parasites that cause sleeping sickness and leishmaniasis also release vesicles

by a super-family of genes called gp85 that contains approximately 700 active genes and 700 pseudogenes, also discovered in Colli's laboratory.

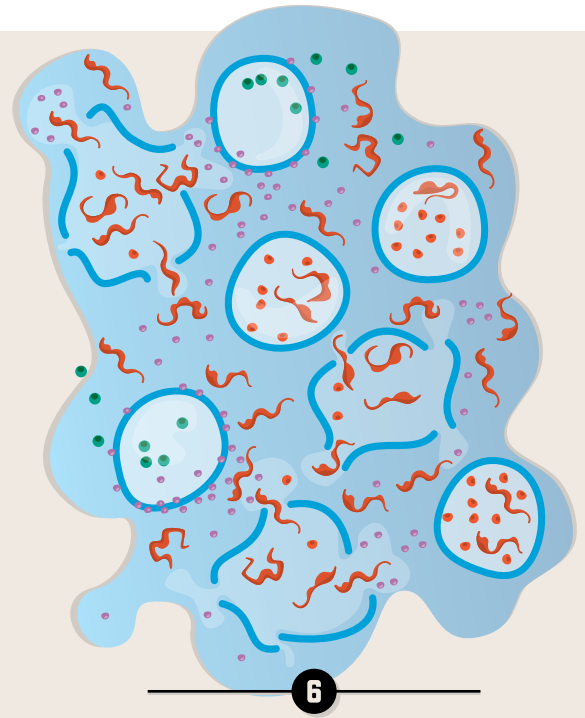
These molecules are able to activate receptors from the outer membrane of immune cells such as macrophages, dendritic cells and lymphocytes. In turn, these receptors stimulate the production of nitric oxide and other molecules such as interferon-gamma, tumor necrosis factor and interleukin-12. These molecules increase the inflammatory response of the host cells and attract more cells, which destroy the parasites but also damage the organism's cells, thus facilitating invasion by the parasites that survived the battle or that quickly follow. After *T. cruzi* invades a cell, one thing it will never lack is a parasite. According to Colli, a single *T. cruzi* parasite divides rapidly. Within hours it can multiply 500-fold, causing the host cell to explode and releasing the parasites into the extracellular environment and the bloodstream, allowing them to reach other cells.



5

Proinflammatory response

The cytokines activate other immune cells that can eliminate the parasites



6

More parasites arrive, releasing more vesicles, and, by still unknown mechanisms, alter the response of the organism to the benefit of the parasites

OTHER PARASITES

“The *T. cruzi* vesicles can fuse with macrophages within 15 minutes,” says Torrecilhas. Other researchers have found that two other groups of protozoa also release vesicles with similar functionality, although the content is most likely distinct. The first group contains the protozoa of the genus *Leishmania*, which causes leishmaniasis, a disease that has spread to 98 countries and registers 2 million new cases per year. The second group is *Trypanosoma brucei*, with subspecies (*T. b. gambiense* and *T. b. rhodesiense*) that cause sleeping sickness, a disease that affects approximately 70 million people in sub-Saharan Africa.

Two other parasites, *Plasmodium falciparum*, which causes malaria and is responsible for approximately 1 million deaths per year in Africa, and *Toxoplasma gondii*, which causes toxoplasmosis, act in a different manner: they invade host cells and quickly produce vesicles with proteins of the invading microor-

ganisms, which are then released to alert other immune cells.

The researchers are attempting to learn as quickly as possible which protein vesicles from *T. cruzi* and other protozoa activate inflammatory responses in the host cells and how the organism’s response is altered to benefit the parasites. It is now clear, however, that the vesicles function as a means of signaling or communicating the distance between the parasites and the host cells.

In recent years, several cellular structures have been recognized as being able to destroy or, conversely, benefit other cells. Other studies have shown that cells can produce structures called tunneling nanotubes, which measure from 50 to 200 nanometers in diameter and can have a length equivalent to the diameter of several cells. Through these tubes, a lymphocyte can bind to another lymphocyte and send nutrients or cellular components that, in the case of immune cells, help prolong – and usually win – the battle against parasites and tumor cells. ■

Projects

1. Interaction between *Trypanosoma cruzi* and host: ligands, receptors and determinants of intracellular development (nº 4/03303-5); Thematic project; **Coord.** Maria Júlia Manso Alves/IQ-USP; **Investment** 1,248,031.59
2. Vesicles released by *T. cruzi*: role of their components in infection (nº 4/08487-7); PhD scholarship; **Grant recipient** Ana Claudia Torrecilhas/IQ-USP; **Investment** R\$ 204,190.40 (FAPESP)

Scientific articles

- GONÇALVES, M.F. *et al.* *Trypanosoma cruzi*: Shedding of surface antigens as membrane vesicles. **Experimental Parasitology**. v. 72, n. 1, p. 43-53. 1999.
- TORRECILHAS A.C. *et al.* Vesicles as carriers of virulence factors in parasitic protozoan diseases. **Microbes and Infection** (in press). 2012.
- TORRECILHAS A.C. *et al.* *Trypanosoma cruzi*: parasite shed vesicles increase heart parasitism and generate an intense inflammatory response. **Microbes and Infection**. v. 11, p. 29-39. 2009.
- SIMPSON, R. J. and MATHIVANAN, S. Extracellular microvesicles: the need for internationally recognized nomenclature and stringent purification Criteria. **Proteomics & Bioinformatics**. v. 5, n. 2, p. ii. 2012.
- HOTEZ P.J. *et al.* Chagas Disease: the new HIV/AIDS of the Americas. **PLoS Neglected Tropical Diseases**. v. 6, n. 5, p. e1498. 2012.

Evolution written in lianas

Botanists use climbing plants to understand the origin
of Brazilian forests | **Ricardo Zorzetto** | PUBLISHED IN OCTOBER 2012

No challenge appears to be too intimidating for botanist Lúcia Garcez Lohmann, a specialist in plant systematics at the University of São Paulo. Upon completing her studies in biology in 1995 at the age of 22, she took on a task that would strike fear into the heart of any experienced researcher. She decided to seek a definitive answer to a question that had occupied botanists for two centuries: understanding the kinship and the evolutionary and biogeographic history of the 382 species of lianas that are scattered across a vast swath of the Americas, from southern Mexico to northern Argentina and Chile, and that help make tropical forests so different from temperate forests.

After visiting museum collections around the world and spending months collecting new specimens in Central and South American forests, Lohmann set up a classification system based on the kinship relationship between the species using the genetic and morphological characteristics of these plants. Now, as she is beginning to understand when, where and how these lianas—species representing nearly half of the Bignoniaceae, a family of plants with bell-shaped flowers that includes trees such as *ipês* and rosewoods—developed such variety, Lohmann is ready to begin an even more ambitious project. She now wants to understand what led the Amazon forest to host the world's largest variety of plants

and animals—in other words, how the Amazon became the Amazon.

Over the next five years, in collaboration with Joel Cracraft, a U.S. ornithologist, Lohmann will coordinate approximately 30 researchers—half in Brazil and half in the United States—who will analyze data on plants, animals and the environment as they seek an explanation for the biodiversity of the world's largest tropical forest. The project, approved in September, is the result of a collaboration between FAPESP and the U.S. National Science Foundation. Through the Biota-FAPESP and Dimensions of Biodiversity programs, the two foundations will devote US\$ 2 million to this research. “I know of no other project that proposes to produce such a comprehensive, integrated view of the Amazon,” Lohmann says. “The idea is to do a synthesis of everything we know about the region and build a theoretical model to better explain the origin of its biodiversity.”

Approximately 40 years ago, the emergence of the abundant variety of plants and animals in the Amazon was viewed in the light of the refuge theory, which was proposed in the late 1960s by German geologist Jürgen Haffer and was tested by zoologist Paulo Vanzolini. According to this model, climate change left the region dryer than in the past, and the forest shrank down to narrow, isolated areas. These areas, known as refuges, were thought to have



Lianas in the Atlantic Forest in Itatiaia, State of Rio de Janeiro: Lianas of the group Bignoniaceae can help determine the evolutionary history of several ecosystems

enabled the survival of many species and promoted the emergence of others that later spread out when the climate again became humid and the forest expanded. Having been put to the test a number of times, the refuge theory no longer seems sufficient to explain the biodiversity of the Amazon.

One reason for the debate is the idea that refuges, as centers of species diversity, may be the result of a distortion, because in many cases, the refuges coincide with the areas where the most specimens of plants and animals have been collected. Therefore, more species may have been found in the refuges because more searches have been conducted in those areas and not because these areas necessarily have a richer variety of species. “People who study biodiversity test the refuge theory because no other alternatives exist,” Lohmann comments.

With this new project, Lohmann and Cracraft hope to create a more comprehensive theoretical model to explain Amazonian biodiversity. “By the end of the five years, we hope to understand in detail the patterns of biodiversity that occur in the Amazon and to be able to resolve some controversies about the environmental history of the region,” says Cracraft, who conducts his research at the American Museum of Natural History in New York. He, Lohmann and other researchers began planning this study nearly four years ago. “We had a scien-

tific interest in the Amazon, and many of us had already published papers on the region,” Cracraft notes. “But understanding the biotic and environmental history of the Amazon is too big and complex an undertaking to be resolved by a few researchers, so it made sense to think about a larger-scale project.”

The first step will be to gather all the available information about certain groups of Amazon flora and fauna. Using these data, the researchers hope to identify the location where the greatest number of species is concentrated and whether that concentration is associated with some environmental charac-

teristic, whether geological or climatic. Then, the researchers plan to uncover the evolutionary history of all the species of plants, butterflies, birds and mammals they have been able to sample. Using genetic information and fossil dating, they want to identify the principal events that gave rise to species diversification and where each group’s ancestors were. They also plan to investigate whether the diversification events were associated with geological or climatic phenomena or with other past environmental characteristics, such as variations in the availability of carbon and nitrogen. “We want to reconstruct what happened in the last 20 million years, since that is when many of the species living there are thought to have emerged,” Lohmann says.

Much of what is to be performed in the Amazon is no different from her work with the 382 species of lianas of the group Bignoniaceae, the largest of the groups or tribes of the family Bignoniaceae. Using the genealogy she constructed, she and her team began to uncover the evolutionary history of these plants, which are the largest group of lianas—climbing plants with a woody stem—in the Americas. These plants have so many variations in shape, are spread over so many environments and are so abundant in tropical forests that, botanists say, they serve as a model for understanding what is happening with other species of flowering plants.

ORIGIN

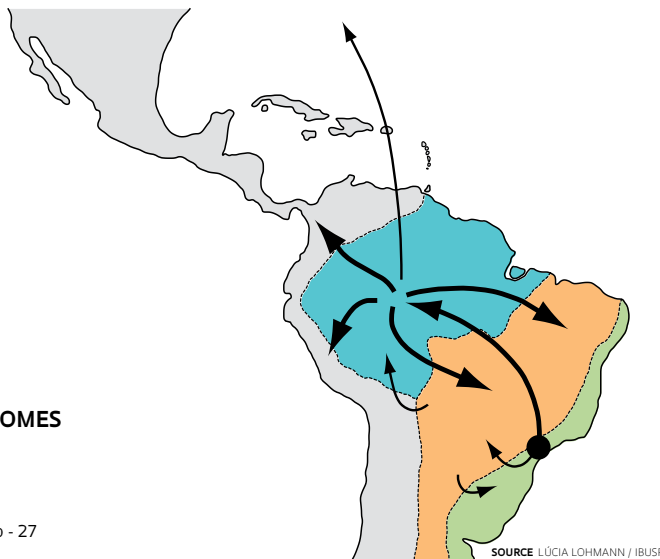
On the basis of molecular data and the new genealogy, Lohmann can say with more assurance that lianas of the group Bignoniaceae appeared approximately 50 million years ago in the region that is now the Brazilian coast occupied by the Atlantic Forest, according to an article to be published in the *Botanical Journal of the Linnean Society*. At that time, South America had already separated from Africa. The climate was hot and humid, dinosaurs were extinct, and a large variety of mammals had begun to occupy the planet.

The ancestor of these 382 species of lianas was most likely a tree, not a climbing plant. The flowers of the Bignoniaceae ancestor had five petals that formed an elongated tube, with internal sexual organs and a nectar-producing region at the bottom. These flowers were similar to the flowers of species of the genus *An-*

“We want to reconstruct what happened in the Amazon in the last 20 million years,” Lohmann says

Conquest of a continent

Native to the South American coast, lianas of the group Bignoniaceae spread to the humid regions of the continental interior before reaching dryer climates and Central and North America



OCCUPATION OF BIOMES

(*in millions of years ago)

- Atlantic Forest - 50
- Amazon - 39
- Cerrado, Caatinga, Chaco - 27

SOURCE LÚCIA LOHMANN / IBUSP



Clockwise from left: *Dolichandra unguis-cati*, *Martinella obovata*, *Pyrostegia venusta*, native lianas of the Amazon found nearly throughout the Americas



emopaegma, which are purple, white or yellow, concluded Lohmann and botanist Suzana Alcantara after analyzing the evolution of 12 anatomical characteristics of Bignoniaceae flowers. “The flowers of the first Bignoniaceae were probably purple and pollinated by small bees,” Alcantara says.

The external morphology of the flowers, however, appears to be the characteristic most subject to change. Although most of these flowers are pollinated by bees, those with more vivid colors (reds and yellows) and a shape that facilitates pollination by hummingbirds appeared 11 times among the 104 species analyzed by Alcantara and Lohmann. Flowers that were generally white, had a narrow elongated tube, and released an intense perfume attractive to butterflies appeared five additional times. However, what actually appears to have influenced the spread of these plants are environmental characteristics such as the availability of water and light and temperature variations.

NEW FRONTIERS

From the coast, the Bignoniaceae traversed a long path through the Americas. They

arrived in the region that is now the Amazon, home to the world’s greatest species diversity, 39 million years ago. From there, they spread to the Andes and to Central and North America. Then, 27 million years ago, they spread into the Cerrado, the Caatinga and the Chaco.

Whenever these plants migrated to these dryer ecosystems, they underwent drastic changes in morphology: climbing plants gave way to shrubs, with a variety of probable adaptations to the new environment where there was greater luminosity and the plants did not need to climb a tree to receive light.

During this migration, these plants lost their tendrils, which are the filaments that spiral up the trunks of trees and enable the plants to reach the forest canopy. At the same time, small nectar-producing structures on the stem and leaves—the extrafloral nectaries—appear to have stopped performing a protective function. In the forest, they exist in greater quantity and attract ants, which in turn drive away herbivorous insects. “At each transition of humid forests to dryer areas, the number of nectaries decreased, altering the interactions of these nectaries with ants and herbivores,” explains ecologist Anselmo Nogueira, a member of Lohmann’s team. “These

morphological transitions opened the door to other environments for the Bignoniaceae and probably enabled them to diversify so much,” he says.

Lohmann and her team are currently compiling data on the timing of the appearance and disappearance of these and other characteristics of the Bignoniaceae. It is an attempt to understand whether the changes are innovations that enabled these plants to occupy new environments, or whether they occurred after the arrival of new biomes as an adaptation to different environmental conditions. “The evolutionary history of the Bignoniaceae,” Lohmann believes, “can help us explain the origins and evolution of tropical ecosystems in general.” ■

Projects

1. Systematics of the tribe Bignoniaceae (Bignoniaceae) (nº 2011/50859-2); Regular Line of Research Project Award; Coord. Lúcia Garcez Lohmann –IB/USP; Investment R\$721,836.88 (FAPESP)

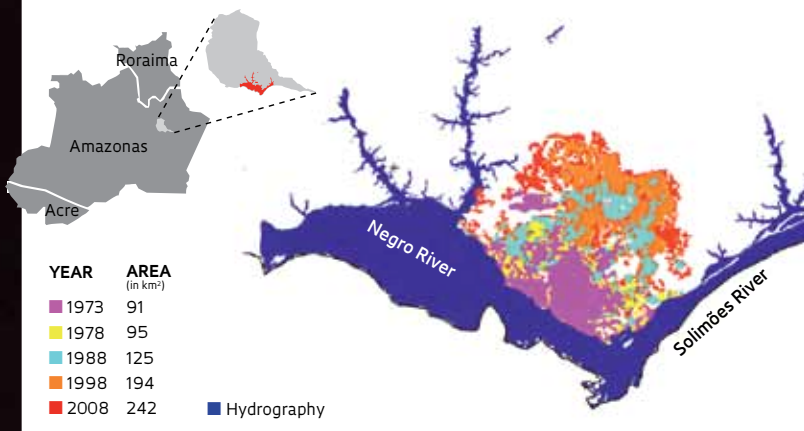
2. Structure and evolution of the Amazonian biota and its environment: An integrative approach (nº 2012/50260-6); Biota Program –Thematic project; Coord. Lúcia Garcez Lohmann –IB/USP; Investment R\$2,974,606.54 / US\$461,132.00 (FAPESP).

Scientific articles

LOHMANN, L. G. *et al.* Pattern and timing of biogeographic history in the neotropical tribe Bignoniaceae. *Botanical Journal of the Linnean Society*. 2012.

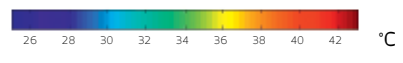
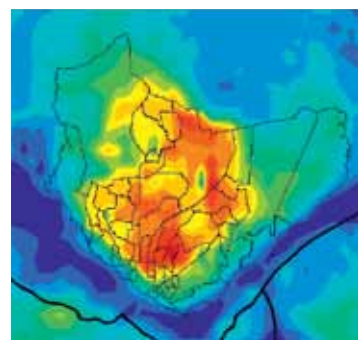


Growth of the urban area of Manaus



Average surface temperature

(Aug–Sept 2009)



A heat island in the Amazon

The urban area of the city of Manaus is 3°C warmer than the surrounding forest

Marcos Pivetta

PUBLISHED IN OCTOBER 2012

The cities of Manaus and Belém, centers of development in the immense, hot, humid tropical forest of the Brazilian Amazon, are beginning to manifest the climate changes typical of large cities. From 1961 to 2010, the average temperature in Manaus rose by 0.7 degrees Celsius (°C) to 26.5°C, according to data from the National Institute for Space Research (INPE). During the same period, the average temperature in Belém rose by 1.51°C to 26.3°C. In both cases, the increase was due principally to the growth of urban areas in the cities, a process that has intensified in recent decades, although aggregate effects related to climate changes on a larger scale may also have had some impact. In 1973, the urban areas of the Manaus and Belém metropolitan regions covered 91 and 76 square kilometers, respectively. By 2008, these numbers had risen to 242 and 270 square kilometers, respectively (see the charts on pages 42 and 45).

With more buildings and concrete and asphalt taking the place of native vegetation, what is known as the urban heat island effect – a phenomenon long known to the residents of São Paulo and Rio de Janeiro – has also taken hold in the two main cities of Brazil's north. At any time of day, the temperature in the most densely populated areas of these cities is consistently

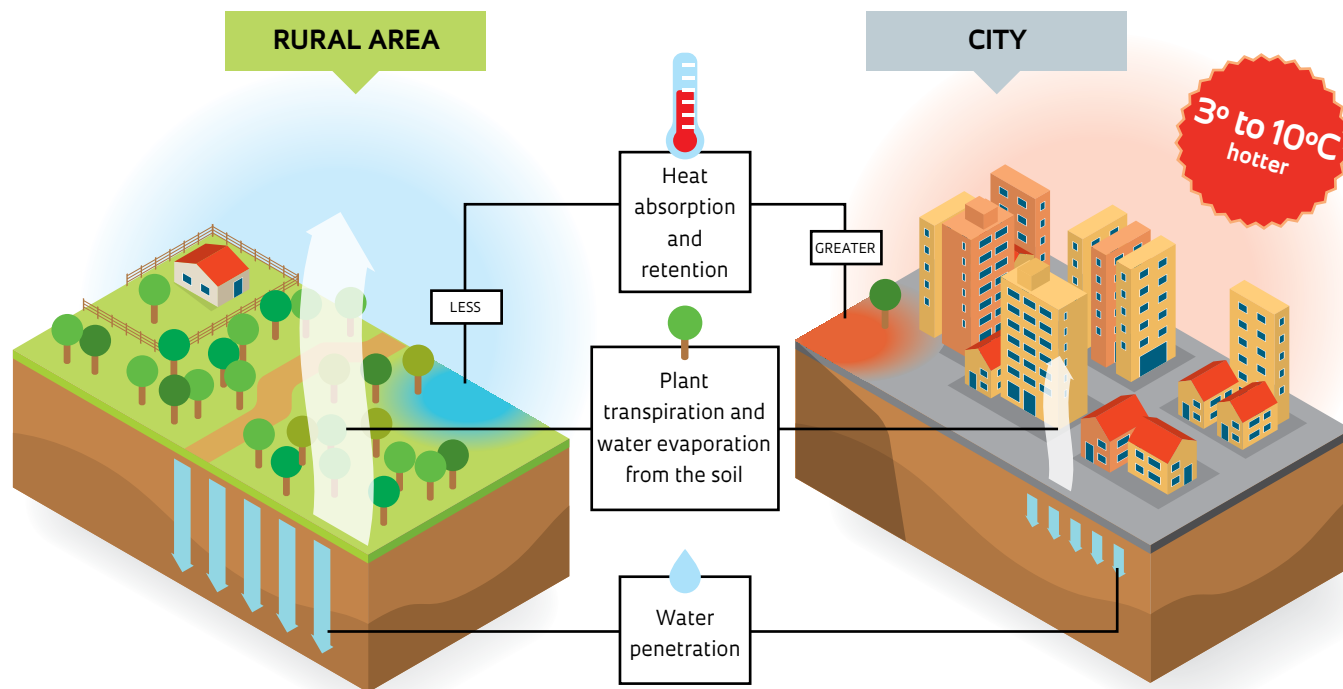
higher than that in nearby rural areas, where forest remains. Heat island data are clearer in the case of Manaus, today the seventh most populous Brazilian city, with over 1.8 million residents. Its population has surpassed those of northeastern state capitals such as Recife and major cities in the south such as Porto Alegre and Curitiba. The temperature difference between the more urbanized parts of the Amazon metropolis of Manaus and an area of Amazon forest approximately 30 kilometers away, the Cuieiras Biological Reserve, peaks at more than 3°C in five of the twelve months of the year.

These results are based on data collected hourly at four weather stations from 2000 to 2008 and reported in an article by Diego Souza and Regina Alvalá, former INPE researchers currently at the National Center for Natural Disaster Monitoring and Alerts (CEMADEN), in the city of Cachoeira Paulista, published on August 8 in the journal *Meteorological Applications*.

The study by Souza and Alvalá also indicates that the atmosphere of the urban areas of Manaus has become drier than that of the surrounding forests. During the period studied, the relative air humidity in the central areas of Manaus was, on average, 1.7% lower than that in the adjacent forest. The difference in relative humidity is greatest in February, in the middle of the rainy season,

The capital of the state of Amazonas: increases in concrete and asphalt make the city warmer

Why the urban heat island effect occurs



when the relative humidity is 3.5% lower in the city than in the forest. “This data clearly shows the heat island effect in Manaus,” according to Regina Alvalá, a cartographic engineer specializing in the mapping of land use and cover that is used in weather modeling.

The CEMADEN researchers were unable to determine the extent of the urban heat island effect in Belém due to the absence of long-term historical records containing daily averages based on hourly data for different parts of the city and its surrounding forested areas. However, there is evidence that the heat island phenomenon in Belém – the eleventh most populous Brazilian city, with just over 1.4 million people – is most prominent during the night.

Although they may seem small to the millions of residents of Brazil’s two megacities (São Paulo and Rio de Janeiro), Manaus and Belém have become large urban metropolitan areas by world standards. If they were, for example, French or Italian cities, they would be behind only Paris and Rome in terms of population.

TWO PEAKS

A unique and controversial point noted in the article by Souza and Alvalá was the identification of two daily peaks during which the heat island effect is exacerbated in Manaus: the first at approximately 8 am and the second between 3 pm and 5 pm. As the meteorologist Souza stated, “most cities have only one daily peak of the heat island effect, and it usually occurs at night or in the early morning.” The researchers are not sure why the peaks in Manaus occur at these two times of day, but they speculate that they may be associated with rush hour traffic. The heat generated by fuel combustion is one of the factors that contribute to local warming of the atmosphere.

A study undertaken by Francis Wagner and Rodrigo Augusto de Souza, physicists at the Amazonas State University (UEA), also evaluated the heat island effect in Manaus. Not all of their findings concerning the characteristics of the phenomenon are consistent with the information in the CEMADEN article. However, in addition to methodological differences, the UEA researchers’ work

From 1961 to 2010, the average temperature in Belém increased by 1.51°C to 26.3°C

covered another time period. Between May 2010 and April 2011, air temperature data from four stations – two in urban areas and two in rural areas – were analyzed. Wagner and Rodrigo Souza found two peaks in the heat island effect, one at 7 am and another at 8 pm. The largest temperature difference between the urban and rural areas was on the order of 3.5°C.

Based on data from the environmental satellite Aqua, which scans the area with a spatial resolution of 1 x 1 km, UEA scientists estimated temperature variations on the ground in Manaus from August to September 2009, typically the driest months. The hottest areas were precisely the most urbanized, and the coolest were those with the largest quantity of preserved vegetation. On the ground, the temperature differences between areas covered by concrete and asphalt – such as the downtown area and the Cidade Nova and Petrópolis neighborhoods – and forested areas reached 10°C. “We’re doing a study of the microclimate in the urban areas of Manaus to aid in creating a master plan for forestation and ecological zoning,” stated Wagner, whose project is financed by the Manaus Municipal Development and Environment Fund.

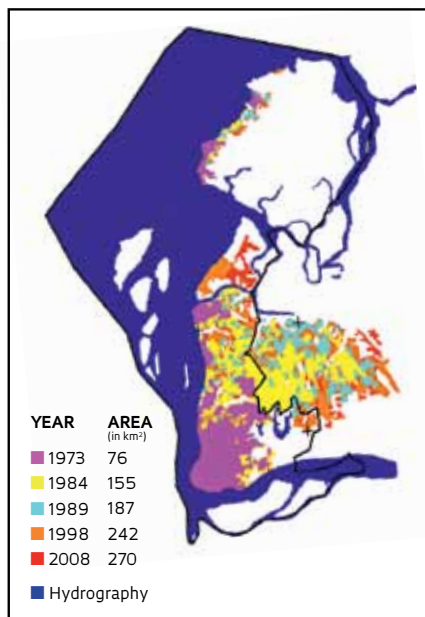
A possible result of the heat island effect is the alteration of rainfall patterns over the two Amazonian cities. For example, in São Paulo, the largest city in Brazil, the average annual rainfall has increased 30% over the past 80 years, and part of this increased rainfall, particularly in spring and summer, is attributed in some studies to increased urbanization. The results of high-resolution atmospheric modeling studies carried out by Souza and Alvalá indicate that if the urban areas of the two capitals continue to grow, there will be a downward trend in rainfall in Manaus, whereas Belém is expected to experience a slight increase in rainfall. “However, the changes in rainfall patterns do not seem to be very significant,” according to Alvalá.

LONDON HEAT IN THE NINETEENTH CENTURY

Although it was not then known by that name, the urban heat island phenomenon has been studied since the early nineteenth century, when British scientist Luke Howard measured differences of almost 2°C at night between London, then the largest metropolis in the world, with more than 1 million inhabitants, and three rural locations nearby. Since then, the analysis of city climates has become an increasingly important research topic, especially in the twenty-first century, when, for the first time in history, more people are living in urban centers than are living in rural areas.

Enlargement of Belém

In 35 years, the size of the urban area of the metropolitan region has tripled



The building of cities radically alters patterns of land use and creates microclimates where heat islands almost become a natural law. Instead of exposed soil, grass and trees, which are rural features that mitigate high temperatures both at the ground level and in the air, the urban landscape is dominated by impermeable and heat-trapping materials that retain heat differently than vegetation. In the countryside, the presence of woody vegetation and scrub creates shadow zones that reduce soil temperature and subsequently reduce the atmospheric temperature. Green areas also contribute to the cooling of a locale’s climate through evapotranspiration. This is the mechanism by which plants and soil release water to the air, dissipating heat from the environment.

In the most urbanized parts of a city, everything that makes the climate of the countryside milder is either scarce or absent. Rainwater barely penetrates the soil, there is less local moisture and the evapotranspiration process is less intense. In general, a city of concrete, asphalt, glass and metal tends to absorb and store twice as much heat as a neighboring rural area. Urban architecture,

with its tall buildings and structures with surface textures different from those of the countryside, can also change wind patterns and intensify the sensation of heat. In megacities such as São Paulo or New York, the heat island effect may result in a difference of up to 12°C in air temperature between a densely urbanized area and a rural area or forest. If the comparison is made with ground temperatures, the differences tend to be even larger.

In Brazil, the effect of urban heat islands has been studied in many state capitals for some time. In the state of São Paulo, small and medium cities have also become the target of research on the phenomenon. A team of geographers from the Presidente Prudente campus of São Paulo State University (UNESP), led by João Lima Sant’Anna Neto and Margarete Amorim, measured the heat island effect in six municipalities in the inland regions of São Paulo state: Teodoro Sampaio, Euclides da Cunha, Jales, Rosana, and Birigui, and Presidente Prudente. They used data from the Landsat satellite thermal channel and from fixed and mobile weather stations to measure the phenomenon.

In Presidente Prudente, a city with 207,000 inhabitants, there were differences of up to 8°C between the more urbanized and rural areas, especially at night. The hottest areas in the city were the neighborhoods where government-built housing projects were located. Sant’Anna Neto notes that “in these places, the use of inappropriate building materials, such as fiber cement tiles, the high density of built area and the scarcity of green space is intensifying heat islands, since there are no large pollutant emissions from industry and vehicles.” Even tiny towns, such as Alfredo Marcondes, a city with 3,800 inhabitants adjacent to Presidente Prudente, has suffered climate change. Differences of 2.5°C were measured between its urban and rural areas. “Heat islands are also a public health problem and predispose the elderly and children to respiratory and circulatory diseases,” according to Sant’Anna Neto. ■

Scientific article

OLIVEIRA, D.O. and ALVALÁ, R.C.S. Observational evidence of the urban heat island effect in Manaus City, Brazil. *Meteorological Applications*. Published online. Aug. 3, 2012.

The heart of the Milky Way

Largest survey of stars ever performed
reconstitutes the central region of the galaxy

Igor Zolnerkevic

PUBLISHED IN OCTOBER 2012

Astronomers' demands for high-definition images far surpass those of any movie aficionado. To determine the maximum number of visible stars in what is known as the galactic bulge – the inner portion of our galaxy, the Milky Way, and the location of the greatest concentration of stars – an international team of 12 researchers, led by Brazilian Roberto Saito and Argentinian Dante Minniti, both from the Pontifical Catholic University (PUC) of Chile, analyzed the 190,000 by 170,000 pixel picture of this region shown on these pages. The image, produced by Chilean astronomer Ignacio Toledo of the Alma Observatory, is so large that it would take 6,000 HDTVs to display it at full resolution.

This photograph of the heart of the Milky Way reveals a population of stars in which planets similar to Earth can be found and promises to help us understand how the galaxy was born. It also strengthens the hypothesis that there are two large regions with a high density of stars in the form of a large X in the galactic bulge, the central region that is shaped like a football. The analysis of the new image produced a catalog of information on the position and brightness of 84 million stars. Larger surveys have been carried out, but according to Saito, no one has ever before analyzed such a large number of stars at one time.

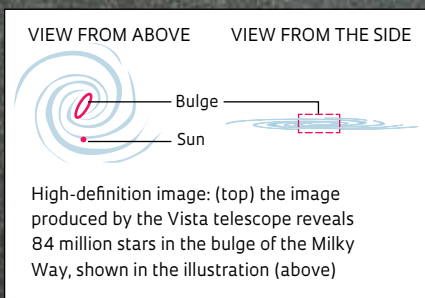
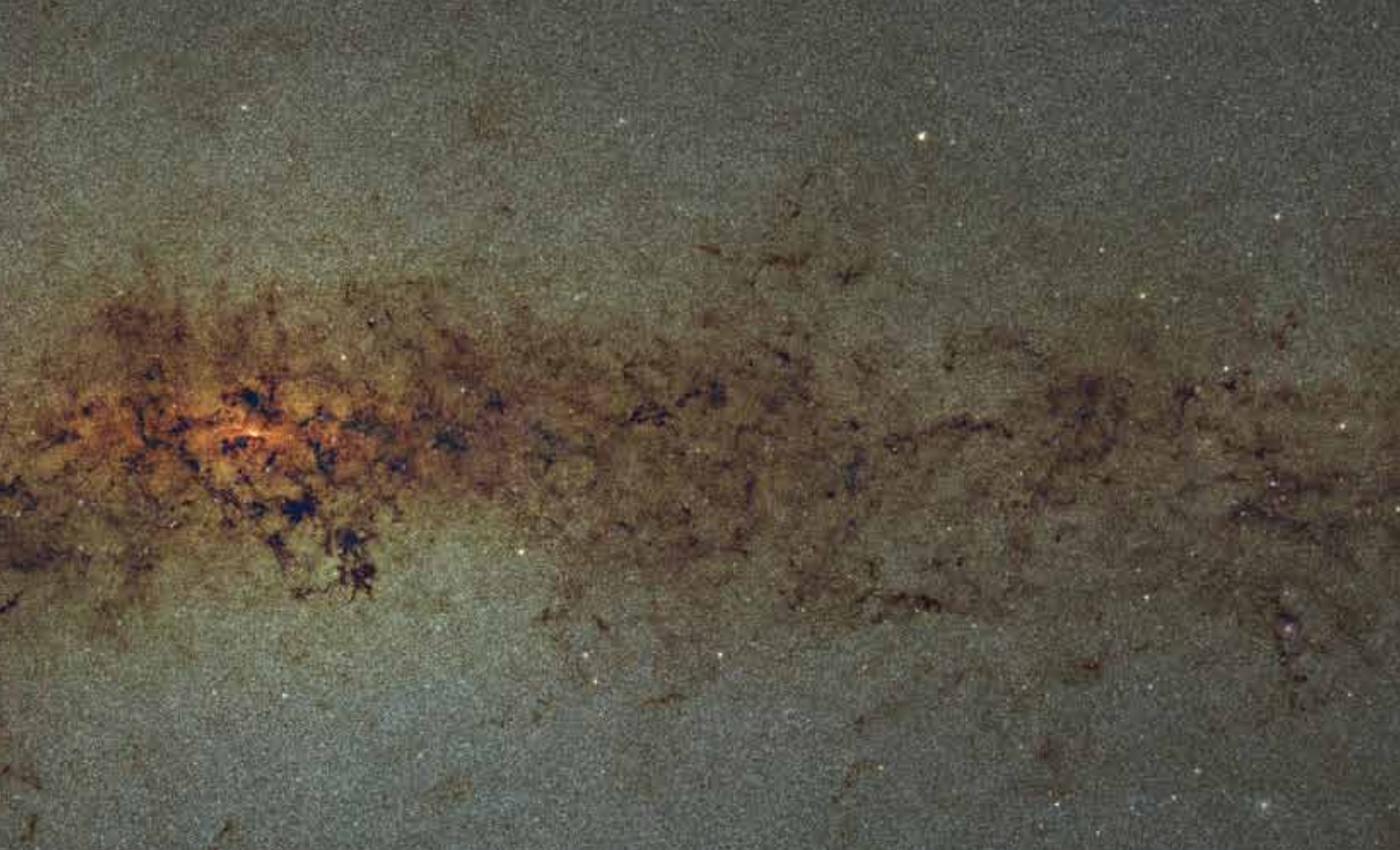
At maximum resolution, the new image occupies 200 gigabytes of computer memory. Because

of the amount of data, no Internet connection was large enough to transfer it error-free from Chile – where it was obtained over the course of more than a year of observation by the four-meter telescope Vista at the European Southern Observatory (ESO) – to the UK, where it was synthesized by researchers at the University of Cambridge. Therefore, it had to be transported there and back by plane.

From the new catalog of stars in the bulge, the research team – which includes Brazilian astronomers Márcio Catelan, from PUC Chile, and Beatriz Barbuy and Bruno Dias, from the University of São Paulo – has produced a graph called a color-magnitude diagram that correlates the intensity of star brightness with the color of its light. This graph was published in *Astronomy & Astrophysics* in August of this year. By studying the distribution of the stars in this diagram, astronomers are able to infer the mass, age and location of the stars in the galaxy and describe the population of stars in the bulge.

The 84 million stars in the catalog are a tiny fraction of the hundreds of billions of stars in the Milky Way. More than a third of them are clustered in the bulge, while the rest, including our Sun, are located in the spiral arms that form the outer part of the galactic disk.

It was not easy to see the stars in the bulge. They are not very bright, they are highly concentrated, and the light they emit is blocked by an enormous amount of gas and dust. The Vis-



ta telescope was only able to detect so many because it can capture the infrared radiation emitted by the stars that manages to penetrate the fog of gas and dust. “Only infrared surveys can see the bulge, and therefore, they are fundamental to understanding how the Milky Way formed,” says Kátia Cunha, an astronomer at the National Observatory and an expert on the subject.

A STAR CENSUS

The researchers confirmed that most of the bulge stars are *red giants*, elderly stars in the last stages of their lives, which is consistent with the widely accepted idea that the bulge was the first region of the galaxy to form. The *red clump giants*, a type of star with well-known color and brightness, stand out among these red giants. “That means

they can be used as distance indicators,” says Saito. “If they are not very bright, this indicates that they are far, and if they are bright, it is because they are close.”

Using the red clump giants, Saito and his colleagues mapped the bulge and confirmed the findings of previous surveys: the center of the galaxy contains two regions in which there is a higher concentration of stars. Each of these regions is shaped like a bar, and they cross in the form of an X. However, the researchers found something new: the extremities of the X are much longer than previously thought.

The astronomers also identified a series of red dwarf stars that were beyond the detection limits of previous surveys because of their faint brightness. “They are small, one tenth the size of the Sun and are believed to be the most common stars in the galaxy,” says Saito. According to the researcher, the red dwarfs are currently of interest because it is easy to detect small, rocky planets similar to Earth around them. Through 2014, the Vista telescope itself will look for changes in the brightness of these stars caused by planets crossing in front of them.

“Today, there are at least two scenarios that explain the formation of the

bulge, which, in turn, may provide an explanation for the formation of other parts of the galaxy,” says Brazilian astronomer Cristina Chiappini of the Leibniz Astrophysics Institute in Potsdam, Germany. One view is that the bulge may have formed by clumping together smaller galaxies in the first billion years of the universe. The alternative explanation is that the formation of the bulge was slower because of instabilities in the rotation of the galactic disc, where there are more gas, dust and young stars. “The important thing is that the different scenarios suggest the emergence of stars with different chemical and physical properties,” says Chiappini.

She and Cunha emphasize that the catalog produced by Saito and his colleagues paves the way for large-scale spectroscopic surveys of the chemical composition of a large number of stars simultaneously, thus providing data to test theories about how the Milky Way may have formed. ■

Scientific article

SAITO, R. K. *et al.* Milky Way demographics with the VVV survey I. The 84-million-star color-magnitude diagram of the galactic bulge. *Astronomy & Astrophysics*. Aug. 28, 2012.

Flights of the future

Embraer is investing in partnerships to develop biofuels and cabin innovations

Dinorah Ereno

PUBLISHED IN NOVEMBER 2012

Embraer is the world's third-largest manufacturer of commercial jets, ranking behind only giants Boeing of the United States and Airbus of the European Union. Embraer was founded to transform science and research projects into technology products. "Knowledge is in the company's DNA," said Mauro Kern, vice president for engineering and technology at Embraer, where he started 30 years ago. According to Kern, a mechanical engineer who graduated from the Federal University of Rio Grande do Sul (UFRGS), "in the post-war period there was a vision that the aviation industry could serve as a major driver of technology in Brazil," he says.

The first move in this direction was the creation of the Technological Institute of Aeronautics (ITA), in partnership with the Massachusetts Institute of Technology (MIT) of the United States, to train aeronautical engineers. Then

came the Aerospace Technical Center (CTA), which, in the 1950s and '60s, carried out projects to create a technological knowledge base. One of these projects paved the way for the aviation industry in 1969. "Embraer was established to produce the Bandeirante airplane," according to Kern. New projects followed on the heels of this one, such as the Ipanema single-engine agricultural aircraft in the late 1960s that was mass-produced beginning in 1972. "This was the world's first aircraft certified to fly with biofuel, and it is still being manufactured today", Kern said.

Between 1983 and 1984, Kern spent six months in Italy working on the AMX program, a line of military aircraft developed in cooperation with two Italian companies to build Brazilian industrial capacity in systems integration. Andrea Barp, an electronics engineer who graduated from ITA and works in systems simulation and modeling for Embraer, also spent some time in





Left to right:
Alexandre Filogonio,
Paulo Anchieta,
Fernando Fernandez,
Allan Pereira, Mauro
Kern and Andrea
Barp, at the Embraer
headquarters in São
José dos Campos

Italy in 1983, along with other young researchers. “The degree of integration and the complexity of onboard aircraft systems was considered advanced for the time, mainly because of onboard software,” he says. Embraer’s challenges were overcome with a substantial amount of research, and five years later, the knowledge acquired during this period enabled Embraer to produce the onboard software for the AMX aircraft.

Embraer’s true goal was to acquire autonomy at every stage of aircraft development and construction. For example, when Kern returned to Brazil, he was assigned to an Embraer subsidiary created to develop skills in landing gear and fine hydraulics. “I was the first engineer in the technical unit of this subsidiary,” Kern said. There were several cooperation and development programs between then and 1996, when Embraer certified the landing gear for the ERJ 145, a 50-seat regional jet. This was the first re-

gional jet that Embraer developed entirely on its own. In 1999, Kern transferred to Embraer’s headquarters, where he focused on the Embraer 170 and 190 projects. These are commercial jets with capacities of between 70 and 120 seats. Initially, he worked as chief engineer on the 190 project; next, he was transferred to manage the 170 and 190 series programs. He then became vice president for commercial aviation. Eighteen months ago, Kern was named vice president of engineering and technology, a position that encompasses all of Embraer’s aviation programs.

Barp was working with aircraft for military defense use and was also called upon to join the Embraer 170 and 190 regional jet programs in 2000. Barp noted: “My job was to assist in integrating the simulation models with the testing devices, an activity which to that point had been nearly stagnant.” A realistic simulation of flight conditions is necessary to prepare the



Commercial jet assembly line

aircraft for its first test in the air. At that time, Embraer had delegated the responsibility of integrating and developing the onboard software for the jets to vendors, whose task was to link everything together in the airplane and to put in place a series of functionalities important for the competitiveness of the product and the services associated with it. This, however, created development issues. In 2005, Barp began to study the basic reasons for these obstacles. To turn this situation around, he focused on methods, procedures, tools and environments, including testing, certification and customer support, that extended the use of mathematical modeling and system simulation throughout the aircraft manufacturing value chain.

At Embraer, the research and development (R&D) area is divided into competitive research and pre-competitive research. Beginning in the year 2000, the competitive research division was responsible for the 170, 175, 190 and 195 family of commercial jetliners, known as E-Jets, with capacities between 70 and 120 seats, as well as the Legacy 600, which heralded Embraer's breakthrough into the executive aviation market, the Phenom 100s and 300s, which are small executive jets that seat as many as 11 passengers, and the Lineage 100, an executive jet whose interior measures 120 square meters and is offered with a choice of several passenger environments. Now under development are the Legacy 450 and 500 and the KC 390. The KC 390 is a military cargo plane that is the "the biggest in its category and the largest ever designed by Embraer," according to Kern. "This jet has very interesting per-

formance features, such as the ability to land on very short runways and in-flight refueling capability," he said. In selecting the portfolio of technology development projects, the interaction between commercial aviation, executive aviation, and defense and security aviation is very intense. In 2011, Embraer's net revenue was R\$9.8 billion, 63.6% of which came from the commercial aviation segment.

There is no product currently in the pre-competitive development pipeline, but there are technologies that could be used in future projects, such as friction welding, a solid-state process for producing welds by rotating or moving compressed parts. "This welding permits a reduction in weight that is of interest to the aviation industry," said Fernando Fernandez, a mechanical engineer who graduated from the São José dos Campos School of Industrial Engineering and who holds a Master's degree from the ITA. Fernandez worked on this technology from 2003 to 2011. For now, friction welding will be used only for a small dashboard on the Legacy 500 aircraft, which will be in the air by the end of the year. For the last year, Fernandez has been analyzing technologies "looking out to 15 or 20 years from now."

Embraer has a number of projects under way in cooperation with research institutes, universities and other companies. One example is the Comfort Engineering Center, a project being

There is an interaction between commercial aviation, executive aviation, and defense and security aviation

conducted in partnership with the University of São Paulo (USP), the Federal University of Santa Catarina (UFSC) and the Federal University of São Carlos (UFSCar), with support from FAPESP and the Brazilian Innovation Agency (Finep). The purpose of research being conducted in the nearly 300-square-meter comfort laboratory is to upgrade aircraft interiors and increase passenger comfort.

Under the project funded by FAPESP titled *Silent aircraft: an investigation of aeroacoustics*, a group of 70 researchers from Embraer, USP, the University of Brasília, UFSC and the Federal University of Uberlândia (UFU), is developing noise-reduction methods and equipment. The first discussions that led to the project began in 2003, with Allan Kardec Pereira, 47, an aeronautical engineer who graduated from the Federal University of Minas Gerais (UFMG). Pereira's post-doctoral studies in mechanical engineering at the University of Campinas (Unicamp) addressed the link between vibration and internal noise in airplanes. Pereira worked at Embraer at two different times, the first of which was in 1989, in the area of product development.

R\$9.8
billion

The company's
net revenue
in 2011

In the early 1990s, Pereira returned to Minas Gerais, where he obtained a Master's degree in the area of optimization at the UFMG and then a PhD in vibration control at Unicamp. When he returned to Embraer in 2001, he worked in the area of product development and drafted a proposal for a project in which he would be in charge of developing the preliminary design for a new product. "I worked on the first Phenom 100 and 300 and Legacy 500 projects," Pereira said.

In April of this year, an Embraer project conducted in partnership with a consortium of Portuguese companies and the Institute of Industrial Engineering (Inegi), affiliated with the University of Porto Engineering School, won the Crystal Cabin Award in the Visionary Designs category. This is an international award for innovation in airplane interiors. Known as "Life," this project introduces a new design for the executive aircraft of the future, with materials such as cork and leather, optical fibers and light-emitting diodes (LEDs).

LESS CARBON

Embraer is also a participant in consortiums with other companies in the sector as well as research institutions for the purpose of developing new manufacturing technologies, composite materials, metal structures and onboard systems. "We have different types of projects under way on several fronts," Kern said. Among these are biofuel development projects, one of which is being conducted in partnership with two US firms, Amyris and GE, as well as Azul Linhas Aéreas, and is focused on producing jet biofuels made from ethanol and sugar cane. Another such project, being conducted in cooperation with Boeing with funding from FAPESP, seeks to identify sustainable alternatives for developing and producing biofuels for commercial aviation in Brazil.



Technicians working on various stages of manufacturing, such as the installation of the acoustics (below)





Testing laboratory and materials checking (left) and the Legacy 450 dashboard (above)

Monitoring serves as a preventive tool for analyzing airplane components

“Biofuels made from renewable sources are not just an alternative to kerosene-type jet fuels made from petroleum, but they also contribute to reducing carbon emissions,” said Alexandre Tonelli Filogonio, who graduated in mechanical engineering from UFMG and did post-graduate work in economic engineering at the Dom Cabral Foundation, where he heads a group that focuses on alternative fuels in the area of pre-competitive technological development. According to data from the Intergovernmental Panel on Climate Change (IPCC), commercial aviation accounts for 2% of all carbon dioxide (CO₂) emissions generated by human activities. The challenge is to curb emissions so that by 2050 they are half of what the sector emitted in 2005, in accordance with the commitment the industry made in April 2008 and ratified in March 2012.

One noteworthy area for Embraer is aircraft health monitoring. The coordinator of Embraer’s

efforts in this area is Paulo Anchieta, 46, who has had a unique career path. He began working at Embraer at age 26 as a mechanic and then transferred to the engineering department, where he prepared mathematical data that engineers used to evaluate aircraft structures. A graduate of a trade school, Anchieta then decided to study mathematics at Salesian University in Lorena, located in the interior of São Paulo State. “Because of those courses, I had the opportunity to assist engineers in areas in which they were not proficient,” he said.

Monitoring serves as a preventive tool for analyzing aircraft components so that future problems are averted. The technology of managing the health of systems, known as PHM (prognostics and health management), was tapped in 2009 as one of the 10 most promising technologies for aviation by the American Institute of Aeronautics and Astronautics (AIAA).

Anchieta’s experience with military aircraft was his passport to receiving an invitation to work on a project to monitor the health of commercial airplanes. Anchieta drew the comparison that “the structure of a military airplane is monitored in the same way as a medical check-up for humans.” Anchieta studied mechanical engineering in night classes at the Engineering School of São Paulo State University (Unesp) in Guaratinguetá so that he would be able to work in areas that were more in line with his knowledge and experience.

NAMES OF INSTITUTIONS FROM WHICH EMBRAER RESEARCHERS GRADUATED

Mauro Kern , Vice President of Engineering and Technology	UFRGS – undergraduate degree
Andrea Barp , systems modeling and simulation	ITA – undergraduate degree
Fernando Fernandez , materials and processes development	School of Industrial Engineering undergraduate degree; ITA – Master’s
Allan Kardec Pereira , technology development	UFMG – undergraduate and Master’s degrees Unicamp – doctorate and post-doctorate
Alexandre Tonelli Filogonio , alternative fuels	UFMG – undergraduate degree Dom Cabral Foundation – post-graduate studies
Paulo Anchieta , aircraft health monitoring	Salesian University of Lorena and Unesp of Guaratinguetá – undergraduate studies



The financial crisis of the early 1990s, which brought about drastic layoffs at Embraer, turned into an apprenticeship for Anchieta. “I had to wear several hats,” Anchieta said. At the time, just 30 people were responsible for all the engineering tasks related to structural analysis. Today, there are more than 17,000 employees, with 4,000 in engineering, including engineers and aeronautical design technicians. In the 1990s, with incentives from the company, Anchieta took several post-graduate courses at the ITA. These studies considerably improved the range of his theoretical knowledge.

When he took over the leadership of the aircraft health monitoring team, he looked for partners to develop innovations for commercial aviation. He began by contacting the Mechanical Engineering School at the UFU and the Unesp Engineering School at Ilha Solteira. These cooperative efforts were expanded to include the Pontifical Catholic University of Rio de Janeiro, the Polytechnical School of the Federal University of Rio de Janeiro, and researchers from UFMG and the Campinas Telecommunications Research and Development Center (CPqD). Some projects have already been completed and produced encouraging results.

EARLY DETECTION

The research partnership with the Federal University of Uberlândia produced a new project to develop a mass-produced structural monitoring system. “We are developing a software and hardware system, based on what is termed electro-mechanical impedance technology, to perform the work of sensors in airplanes,” Anchieta said.

Phenom 100 executive jets (left) and Lineage 100 (above) and an artist's rendering of the KC 390 military cargo jet (right) under development

Based on vibration results, the sensors will detect the locations and severities of faults. The system will be used first for testing aircraft fatigue. “The gains will be tremendous, because a crack detected in its initial phase will prevent future damage that would occur if it gets bigger.” The next step is to qualify the sensor system for in-flight use, for military as well as commercial and executive aircraft.

In July of this year, a technology conference was held at the European Structural Health Monitoring (SHM) Workshop in Dresden, Germany, and Anchieta won the annual award established by Stanford University astrophysics professor Fu-Kuo Chang. Anchieta was selected as the winner of this award by an international committee consisting of 120 people from academia, the government, industry organizations such as NASA (the US space agency), and US, European, Australian and Japanese research centers, in addition to professionals from Airbus, Boeing and Bombardier. ■

Research as a basis for policy

Academic studies on the public's needs increasingly help governments adopt solutions

Claudia Izique

PUBLISHED IN OCTOBER 2012

The Audit Court of the State of Mato Grosso (TCE/MT) monitors spending on education and health in 141 municipalities and the impact of these policies on the quality of services rendered to citizens through georeferenced databases developed by the Center for Metropolitan Studies (CEM). “This model allows us not only to assess whether municipalities are spending what the constitution requires, but also whether their performance has been improving,” says Marta Arretche, a professor in the Political Science Department of the University of São Paulo (USP) and director of the CEM.

The methodology, created five years ago at the request of the TCE/MT, was transferred to the state and began to be used as a tool for evaluating the performance of municipal administrations. The information resulting from the application of the model, the *Health and Education Performance Index* for the cities of Mato Grosso, is available on the TCE/MT web site and can be accessed by any citizen interested in obtaining information about spending and services in these areas in their municipality.

Communicating the results of policy assessments is the primary mission of the CMS, one

of the Research, Innovation and Dissemination Centers (RIDCs) supported by FAPESP (São Paulo Research Foundation) and established by the Brazilian Center for Analysis and Planning (CEBRAP) and the USP School of Philosophy, Letters and Humanities (FFLCH) and School of Communication and Arts (ECA). Since its inception in 2003, over 30 research projects have been implemented that involve methodology transfer to the public sector.

The partnership between the TCE/MT and the CEM began in 2007, when the court decided to conduct an investigation that went beyond checking the appropriateness of public spending, including analyses of legality, legitimacy and economic viability. “The court also felt that we needed to assess whether spending had a positive impact on society,” says Volmar Bucco Jr., a public auditor at the TCE/MT. This investigation gave rise to the notion of evaluating public policies using performance indicators, and the court signed a partnership agreement with the CEM. “This is a valuable tool. Through the portrayal of the results of public policies on health and education in the state and its municipalities, the efficient management of public resources can be evaluated through external control,” he



explains. Thus, the government can assess its own performance by evaluating progress and results compared to the Brazilian average. This facilitates decision making, and citizens can monitor the performance of public officials and demand improved services.

The *Health and Education Performance Index* is actually a georeferenced database with information provided by the ministries of education and health and permits a comparison of the performance levels of different Brazilian municipalities. The assessment matrix considers 10 items for each of the areas in question. The analysis of health systems, for example, tallies neonatal mortality, health coverage for pregnant women, children's health indicators, deaths from infectious contagious diseases (such as dengue fever and tuberculosis) and the number of women's health visits. The data are collected by the Unified Health Care System database (Datasus). The information used to analyze the education system was collected on grade repetition rates up to the 4th grade and for the 5th to 8th grades, among other data. The National Institute for Educational Studies and Research (INEP) and the School Census (systems for evaluation of basic education in Brazil) provided this information.

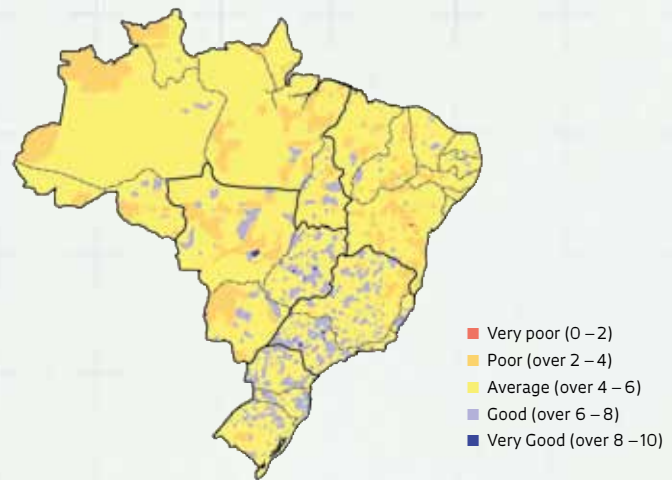
NATIONAL DATA

The maps on the right and on page 113, for example, allow us to compare the performance of the health and educational systems in different municipalities throughout the country. The reddish areas indicate situations that are classified as "very bad." Dark blue areas represent circumstances rated as "very good." These two tones and the color gradient between them consolidate data collected at the municipal level from across the country.

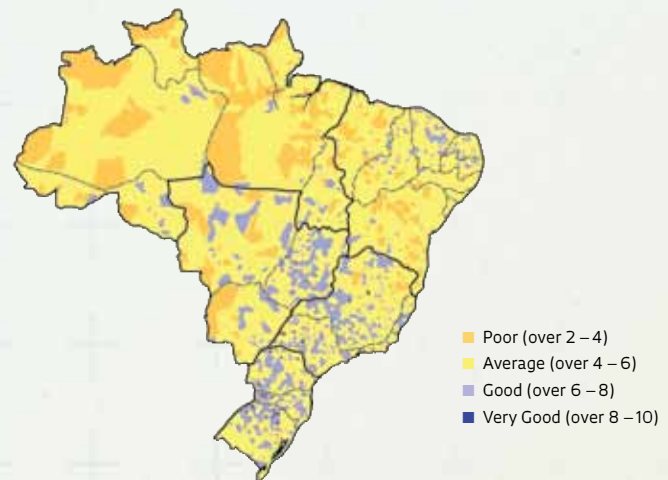
According to Marta Arretche, this type of analysis was only possible because the country has comprehensive and free public information systems. "To learn how the municipal or state governments are spending, you need to build a reliable system. And this information already exists. Only Japan compares to Brazil in terms of the availability of information on public systems. "In the United States," she adds, "there are no national information systems containing city data. There, to assemble a similar system one

MAP OF DEFICIENCIES

Inequality in health (2004 – 2006)



Inequality in health (2007 – 2009)



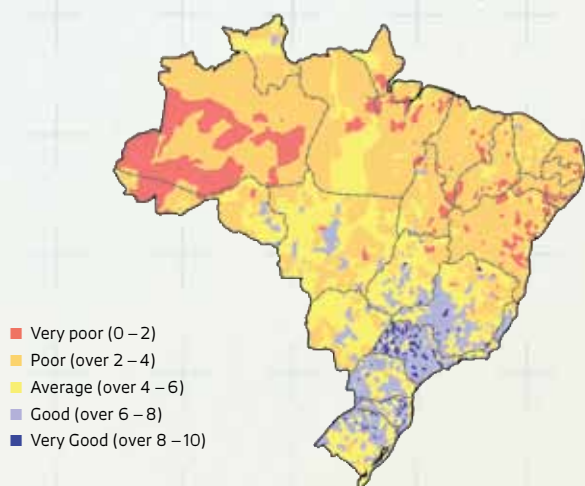
would need to go city by city, collect the desired information, then standardize it. Here we have the School Census, the Brazil Exam, Datasus, and the Brazilian Institute of Geography and Statistics (IBGE) municipal information surveys."

This information must be standardized to permit comparisons. For each indicator, the municipality receives a score from 0 to 1. The indicator scores are summed to obtain the total score. The conditions are always analyzed for three-year periods (the maps are for the periods 2004–2006 and 2007–2009).

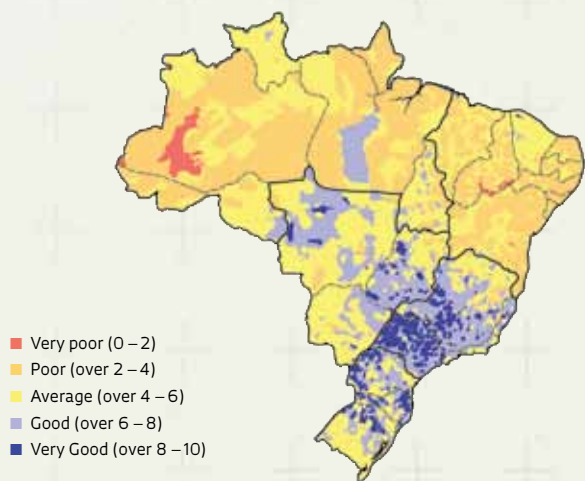
"We work with a three year average because, if an extreme event were to occur in a city in a given year, for example, distortions could be corrected."

The result of the comparative analyses for the period reveals that, in education, a substantial number of municipalities exhibited extremely poor performance at the beginning of the decade, while a small number of cities represented "islands of excellence" that have increased in size over the decade. Conversely, the Brazilian health sector does not exhibit these contrasts. "There is less inequality

Inequality in education (2003 – 2005)



Inequality in education (2007 – 2009)



SOURCE: CENTER FOR THE STUDY OF MUNICIPALITIES

between municipalities, but we have no points of excellence, even though significant improvements have been seen over the years,” says Arretche.

THE QUALITY OF LIFE INDICATOR

The expectation of the TCE/MT’s public auditor is that this analytical methodology should be made available to any public agency in Brazil, or even to private ones. According to Marta Arretche, the study may help measure the degree of economic development and quality of life provided to the population of a

country the size of Brazil. In her opinion, the Human Development Index (HDI) does not represent a good tool for the assessment of decentralized public service delivery systems. Because the CEM methodology permits much more comprehensive and realistic evaluations of the performance of health and education policies, it supports the development of more precisely targeted public policies that will have more substantial effects on the affected population.

Mato Grosso, for example, is beginning to see results. The diagnostic in-

dicators consolidated by this system have already resulted in improvements statewide. “Since the TCE/MT began using this methodology to assess the accounts of public administrative officials as well, societal control has intensified and the tool has begun to show the status of each municipality compared with others,” he explains. “Government officials then had to take steps to improve their indices.”

The successful implementation of the methodology had other outcomes: the CEM was asked to develop a panel for monitoring the number of homicides for the state Secretary of Public Safety, based on a set of indicators that measure the performance of security actions and also allow comparisons among different regions in the state. The panel serves as a sort of alarm whenever it registers negative changes in the average indicators.

“This information methodology has become an important tool for assessing and supporting the formulation of public policy,” said Eduardo Marques, a CEM researcher and professor in the USP Political Science Department. The CEM has conducted over 30 studies focused on providing support the formulation and implementation of public policies. Among these are a *Map of Social Vulnerability*, which allowed deficiencies to be detected by analyzing the distribution of socioeconomic structures, and *Environmental indicators and urban management: sustainability challenges in the city of São Paulo*, which enabled the administration to identify the substantial variability in environmental problems and pressures in different urban spaces; both of these studies concerned the City of São Paulo. Two other studies conducted for São Paulo concerned housing vulnerability, which were used to develop the city’s Housing Plan. This last experience led the Ministry of Cities to commission the development of a methodology for the analysis of shantytowns, which generated information about the housing needs of a selected group in 560 municipalities.

Partnerships with public agencies developed gradually through contacts between managers. “The CEM was one of the first to digitalize databases,” says Marques. “We started with the city of Mauá in 2003. The information circulates, and demands arise.” ■



Monument to
the Discoveries,
Lisbon, Portugal



An immense Portugal

The Lusitanian Empire knew how to use freedom granted the local elites and missionary religious fervor to maintain its standing for five centuries

Carlos Haag

PUBLISHED IN NOVEMBER 2012

How did a small country of less than 90,000 square kilometers establish a presence on five continents in regions such as Africa, Japan, China, India and Brazil? No modern colonial European empire was as lasting and/or as broad in scope. Portugal was the first global empire-builder (although the Portuguese refer to themselves as a kingdom, not an empire, as the Spanish do) whose holdings survived pretty much as a whole until the mid-1970s. It was not until 1999 that Macau was given back to China. “Portugal’s success was due to innovations that exceeded the bounds of any known model. The pioneering relationship between center and periphery was marked by the flexibilization of the power held by the local elites, without Lisbon ceasing to be the pole from which authority radiated. Also fairly new was the use of religion to create imperial unity,” explains historian Laura de Mello e Souza, of the University of São Paulo (USP). She coordinated the research project *Dimensions of the Portuguese Empire*, a thematic project begun in 2004 and recently completed with FAPESP support.

The objective of the research, which has already given rise to books such as *O governo dos Povos* (The government of the people) (Alameda), *Contextos missionários: religião e política no Império Português* (Missionary contexts: religion and politics in the Portuguese empire) (Hucitec/FAPESP), and *O império por escrito* (The empire in writing) (Alameda), was to revisit the concept of the “old colonial system” and to see whether it was still workable, given the innovations that historical

research had brought to light. The study generated about approximately 30 academic papers, among masters' theses and doctoral dissertations, and was divided among groups of researchers for a better analysis of the political, economic, cultural, and religious dimensions of the Portuguese Empire. The result was a complex picture full of diversity in which de Mello e Souza says, "the multiple is visible in the one."

"Long-accepted views of a chaotic colonial administration, a monstrous bureaucratic regime that was sluggish and inefficient with an authoritarian center and submissive colonies cannot account for the ability of this immense empire to maintain itself over such a long period. The fact is that Lisbon used its power intelligently in overcoming the separation, of oceanic proportions, between the capital and its colonies," the professor explains.

The chronological period selected for the project, between the 15th and 19th centuries, was chosen because it was the period of Lusitanian expansion. After 1822, there is no justification for treating formations as independent as the Brazilian and Portuguese empires as a group.

The project updates a debate that had arisen at the end of the 1970s as to how to interpret the economy and society of Portuguese America, reassessing both Caio Prado's idea of "the meaning of colonization" and the concept of the "old colonial

system" defined by Fernando Novais. The result, says de Mello e Souza, is a dialectic play between the parts and the whole, eliminating the mechanical opposition between capital and colony and going far beyond the Brazil-Portugal relationship. "In this rereading, the Portuguese Empire lacks homogeneity and has relatively autonomous political centers. The idea of a unitary imperial ideology needs to be challenged," says the researcher.

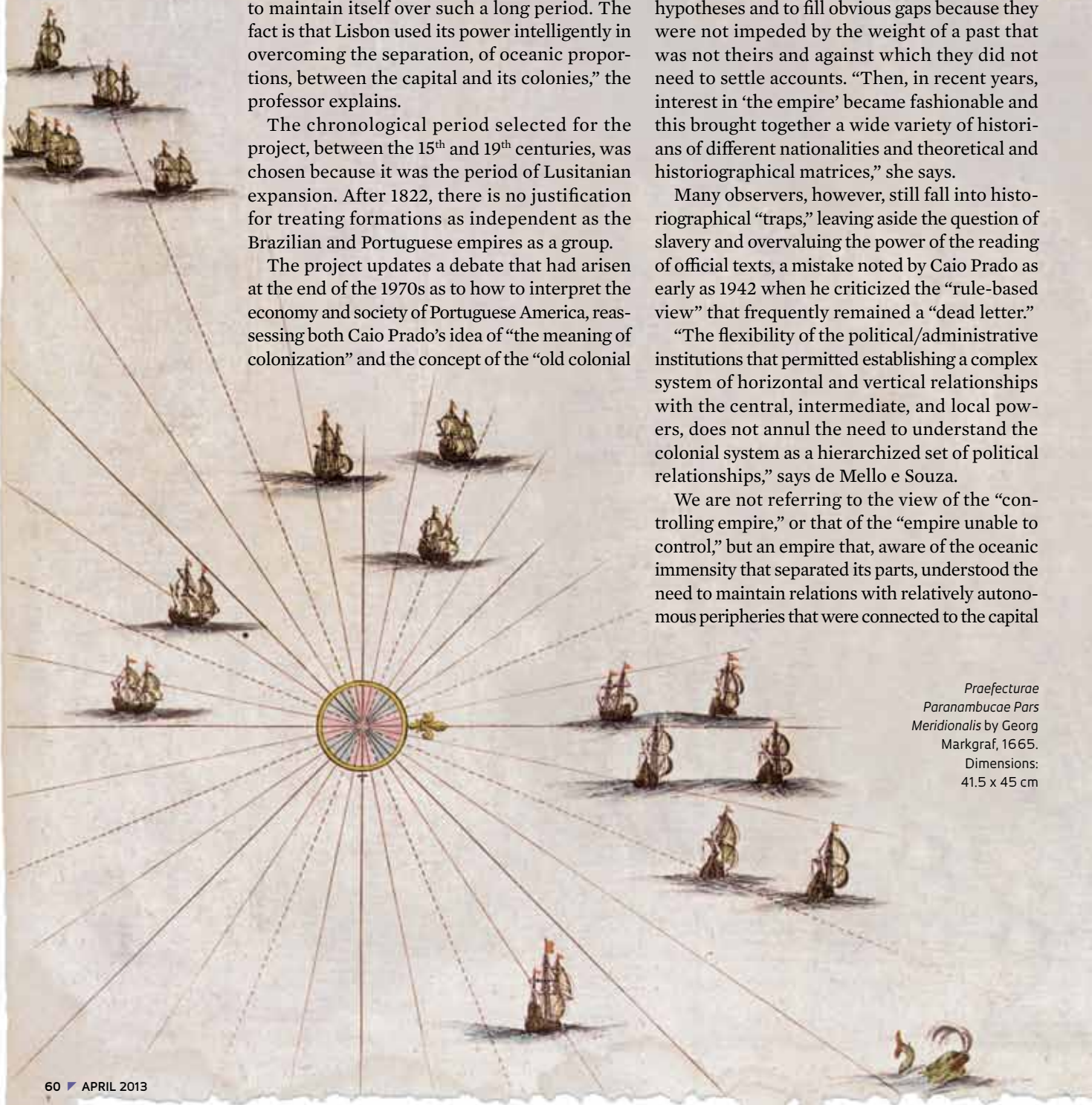
HYPOTHESES

To Professor de Mello e Souza, the post-colonial resentment of the Brazilians cleared the way, for many years, for foreign historians to trace their hypotheses and to fill obvious gaps because they were not impeded by the weight of a past that was not theirs and against which they did not need to settle accounts. "Then, in recent years, interest in 'the empire' became fashionable and this brought together a wide variety of historians of different nationalities and theoretical and historiographical matrices," she says.

Many observers, however, still fall into historiographical "traps," leaving aside the question of slavery and overvaluing the power of the reading of official texts, a mistake noted by Caio Prado as early as 1942 when he criticized the "rule-based view" that frequently remained a "dead letter."

"The flexibility of the political/administrative institutions that permitted establishing a complex system of horizontal and vertical relationships with the central, intermediate, and local powers, does not annul the need to understand the colonial system as a hierarchized set of political relationships," says de Mello e Souza.

We are not referring to the view of the "controlling empire," or that of the "empire unable to control," but an empire that, aware of the oceanic immensity that separated its parts, understood the need to maintain relations with relatively autonomous peripheries that were connected to the capital



*Praefecturae
Paranambucae Pars
Meridionalis* by Georg
Markgraf, 1665.
Dimensions:
41.5 x 45 cm

It was a highly rational empire that was aware that local problems required immediate solutions produced locally



Novissima et Acuratissima Totius Americae Descriptio, by John Ogilby, 1671. Dimensions: 43,5 x 54 cm

by ties that were more or less loose – without, however, Lisbon ceasing to be the center from which power emanated. The distance between king and subjects, which could appear to be a problem, reappears now as a “virtue” for purposes of governing.

“The colonies also, among other traits, mirrored the sociocultural values of the Iberian peninsula. To that end, the creation by the Portuguese of an almost universal system of political communication between the Court and the colonies was important. What might appear to be an institutional weakness became its strength, revealed in adaptability to different political and territorial situations and, at times, in a sort of administrative pluralism,” the researcher observes.

The originality of the foundations of the Portuguese Empire can be seen in its creation of new structures that served as intermediaries in the relationship between the local powers in the overseas territories and the powers of the center.

“For example, the Portuguese administrators who came to certain parts of what would eventually become Brazil did not match the stereotype of the “petty tyrant” who sought to seize the spoils from the Brazilians. Of course, there were unscrupulous people. But, in general, it was recognized that one couldn’t lean too hard on the colony. Exploitation very often took the form of intolerance, followed by flexibility in application of the laws,” de Mello e Souza notes. “Thus, to complain – as Tiradentes did – that the Portuguese administrators came to plunder our riches and suck our blood, does not explain much, and it entangles us in the wrong kind of discussion

of domination. In reality, the administration was able to function only because the local elites were participating in it,” she says.

THE CROWN

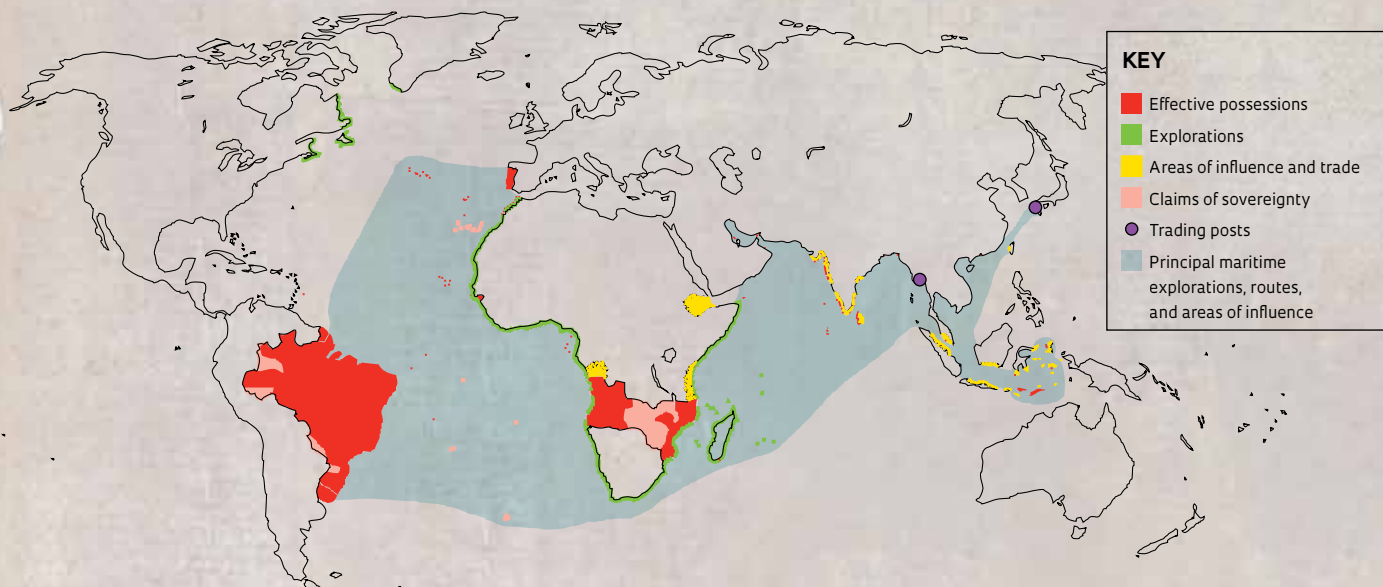
The researcher stresses that relationships within the empire cannot be understood merely by consulting legal documents. “The Crown knew that it could not impose control by insisting on the letter of the law. Until 1822, the ‘Brazilians’ saw themselves as Portuguese and not as a dominated people,” she explains. Thus, local episodes of revolt were not always synonymous with a “struggle for independence,” but rather were reactions to rearrangements. The definition de Tocqueville gave of the Old Regime is still valid: “Rigid rules but flaccid practice.”

However, we should not speak of a “tropicalized Old Regime.” If colonial society is viewed as the Old Regime in the strict sense, its particularities explode and corrode the basic principles because it was organized and stitched together by the practice of slavery, something that did not exist in the European environment,” de Mello e Souza remarks.

“The slave trade sullied the image of the local nobility, separating them from the monarchy. They chased after titles, honors, and indulgences, thereby increasing their dependence on the Portuguese king, a situation that was exacerbated over the years,” the historian says. The specificity of Portuguese America did not reside in the assimilation, pure and simple, of the world of the Old Regime, but in its perverse re-creation, fed by the slave traffic, by the labor of black slaves,

Map of the Portuguese Empire (1415-1999)

The development and decline of the Lusitanians, from glory until decolonization



by the introduction into the old society of a new element that was more structural than institutional: the practice of slavery.

Once again, the solution came through flexibilization. “According to the principles of the Old Regime, persons of “infected blood” were forbidden to hold administrative office. This would make it impossible to govern the colonial regions because most of the native elite was composed of mestizos. Regions such as São Paulo and Minas, for example, were almost entirely populated by half-breeds and mulattoes. Thus, a mulatto would be appointed to commander of the local militia and would then cease to be a mulatto and could rise in status,” the professor notes. Although officially subject to the rules of the old colonial system, the periphery of the empire used and abused the ability to “roll with the punches.”

“The project was innovative in that it discussed those peculiarities of the Portuguese Empire, making it more explicative. The discussion caused us to replace the concept of a colonial system with the idea that the colony was not a mere extension of the metropolis but a subordinated territory that played a vital role for the Empire by providing a considerable portion of the resources essential to its existence,” observes historian Jobson Arruda of USP, a member of the project team. “The Lusitanian imperial system was highly rational and featured an awareness that local problems required immediate solutions produced locally,” he continues.

This awareness was one of the principal reasons the Portuguese were more successful than their Spanish rivals. “The Spanish monarchy

was a variety of kingdoms, while Portugal was a unified monarchy. Great efforts were made to increase the power of the State at the expense of the nobility and the administrative districts. Those resources helped in the maritime expansion, which, in turn, left the monarchy less dependent on noblemen and the common people, thanks to the resources obtained. In exchange, those resources enabled the State to co-opt the nobility, which afforded the Portuguese king an astonishing consolidation of his power,” explains historian Ana Paula Megiani of USP, compiler of *O império por escrito* (Alameda) and also a researcher on the project team.

“That centrality gave the Portuguese monarchy a level of command over its empire that was greater than the Spanish had. The local authorities served as the means for exercising that power, expressions of centrality, rather than of dismemberment of the empire,” Megiani comments. Even so, Portugal was living with a contradiction that did not afflict the Spanish: it was an empire without an emperor.

“In that context, the religious face of the empire is the one that best expresses its universality. The Church offered a substrate suited to the practical implementation of a group of dogmas and principles. Its religious missions were its principal operational tool for cementing together the parts of the totality,” says historian Adone Agnolin of USP, a contributor to the research project unit titled Religion and Evangelization. “The religious perspective introduces the foundation of a *universalitas* (an empire-building principle inherited from the Romans) that was passed on,

from the political standpoint, to maintain those empires but that, in the last analysis, is grounded on the idea of a 'symbolic empire' uniting politics and religion," says Agnolin.

According to Agnolin, through its missionaries the Portuguese Empire reversed the historical formation process when it found its universal purpose in the figure of the monk. "Monks were its privileged instrument for the realization of the project and, from that starting point, Portugal introduces itself as a new and unprecedented imperial model," he says.

De Mello e Souza says that this view is one of the great novelties brought to light by the research project. "Missionaries are arms of the homogenization of the faith, making the Portuguese more adaptable in the face of religious and cultural confrontations," the historian says. The temptation to "demonize" the Church is great, but mistaken. "All the actions of the diplomatic, administrative, or commercial agents were backed by the missionaries, who lent legitimacy to the array of actions that were intended to advance the common good and, therefore, the salvation of men," she says.

WEALTH

In those days, the notion of "the common good" encompassed the colonial dimension alongside Christianity, albeit with tensions. Increasing the wealth of the king meant increasing the wealth of the monarchy and, thus, the wealth of its Christian vassals. The increase in trade and in the wealth of the kingdom was connected to and based on the function of the king in his expression of the exercise of the theological virtue of charity and of earthly virtues in distributive justice.

The unity of the monarchy as a unit of the community was directed toward both the common good and salvation. The ultimate purpose of the Empire was not restricted to colonization; that was seen only as a means. The purpose was salvation because it permitted conversion of the heathen and sustained the missionary, expansionist, and universalizing action of the Catholic Church.

"That specificity develops in the second half of the 15th century. At the foundation of colonial expansion we find theology and, in its wake, the results of a new colonial commerce. It is in that direction that Portugal builds, with an extraordinarily early start with respect to other European nations, the new perspective of universalization represented by the articulation among empire, theology, and trade," Agnolin explains. The missions, along with commerce, were one of the privileged channels for the first dialogues with the cultures that came in contact with the Iberian world. The empire of men was, first of all, the empire of God.

"In addition, while Europeans needed to understand the local cultures, it was also necessary

Colonial Possessions

From glory to decline, each century reveals the course of imperial development



to develop new cognitive tools to use in dealing with the new situations resulting from contact. It was a process of translation from one party to another in which the religious language functioned as a symbolic forum for mediation that was vital to the incorporation of the native people into the Portuguese monarchy," observes the historian. The missions made the necessary "accommodations" to the various local realities.

"While commercial interests were the starting point in the relations between empire and religion

The wisdom of the Lusitanian Empire was to govern each region in a specific way, flexibilizing the power according to local issues, handing down power depending on the needs

and between the administration of peoples and the Catholic missions, we cannot fail to consider how the 'dimensions of the Portuguese Empire' were sustained on the universalism that submits to the modern achievement of autonomy of natural law," says Agnolin. Thus, at the base of the tension between theology and empire, we find that notion of empire whose objective was to accomplish the imposition of a common government for the peoples, according to the varying modes of local interlocution, as in the political and cultural dimensions.

Another element of Lusitanian wisdom was to maintain specific governments for each part of the empire, adapting them to the local idiosyncrasies. One colonial region was not governed in the same way as another. In the fundamental case of religion, Christianity determined, starting from that context, a nexus between "things of faith" and "political life." It was from that standpoint, which sought the universal, that the practice of evangelization made the necessary "adjustments" in relation to the particular non-Western cultures.

The Portuguese Empire developed projects that sought to incorporate other peoples, with

catechesis as the central vehicle of this attempt. "Flexibility and adaptability, along with relative autonomy, were instruments of survival of that empire, with Lisbon at the center, although very often overloaded. The fundamental role was assigned to the Church and the religious orders, which were more important to the maintenance and defense of the Lusitanian territory than was the Portuguese State," says Brazilianist Kenneth Maxwell of Harvard University.

Within the empire, the Europeanizing culture, including religion, played a role in the maintenance of that empire. "It was a culture that was enraptured by the civilizing ideal but alert to recombinations and mechanisms capable of further extending its dominion. Hence the various forms of circulation of written materials or aids to representation such as cartography," adds historian Leila Algranti of the University of Campinas (Unicamp). This peculiarity made it possible, using the thematic project, to create the Digital Library of Historical Cartography (see "A mine of maps," issue 183 of *Pesquisa FAPESP*), the Laboratory of Historical Cartography Studies (LECH), and the Center for Documentation on the Atlantic (CENDA).

To de Mello e Souza, the consultation of previously ignored writings was another high point of the project in that it revealed how communication took place among the distant parts of the empire without relying on the invention of the printing press. "It was a process of intensification and diffusion of the methods of collecting, organizing, and preserving written information related to the formation of the bureaucracy and the modern State and associated with the sophistication of forms of knowledge and the new ways in which elements connected with writing ascended the social scale," Algranti states.

"In terms of Portugal and Brazil, it is obvious that without written communication it would have been practically impossible to administer the empire. In addition to the printed materials, handwritten records of every kind (letters, regulations, chronicles, grammar books) performed a vital role in the transmission of ideas, values, rules, customs, and wisdom between the metropolises and their colonies, as well as among the various overseas possessions that were part of those colonial empires," Algranti observes.

As it expanded, the Portuguese Empire felt the need to exchange information more rapidly. "Orders that until then were given orally began to be put in writing. The rules regulated not only administration but also other spheres, such as the political and judicial realms, involving complaints or accusations," Algranti continues.

According to Algranti, understanding the colonization of America means capturing the forms of communication between conquerors and the con-



Armillary sphere
Dimensions:
38.5 x 38.5 cm

quered, of integration and modification between the Old World and the New World. “Looking at the empire, those new analyses allowed us to see the ways in which the metropolitan presence came to be relative, the prominence of the role of the colonial elites, and the specificity and scope of the evangelizing processes,” de Mello e Souza observes.

“With that, the fundamental economic and social questions, i.e., the siphoning off of wealth and the establishment of compulsory systems of labor, especially slavery, assumed their relative positions. The meanings and contents of the Lusitanian empire gain a singularity that forces us to rethink its essence, particularly how it became part of the capitalist logic,” she says.

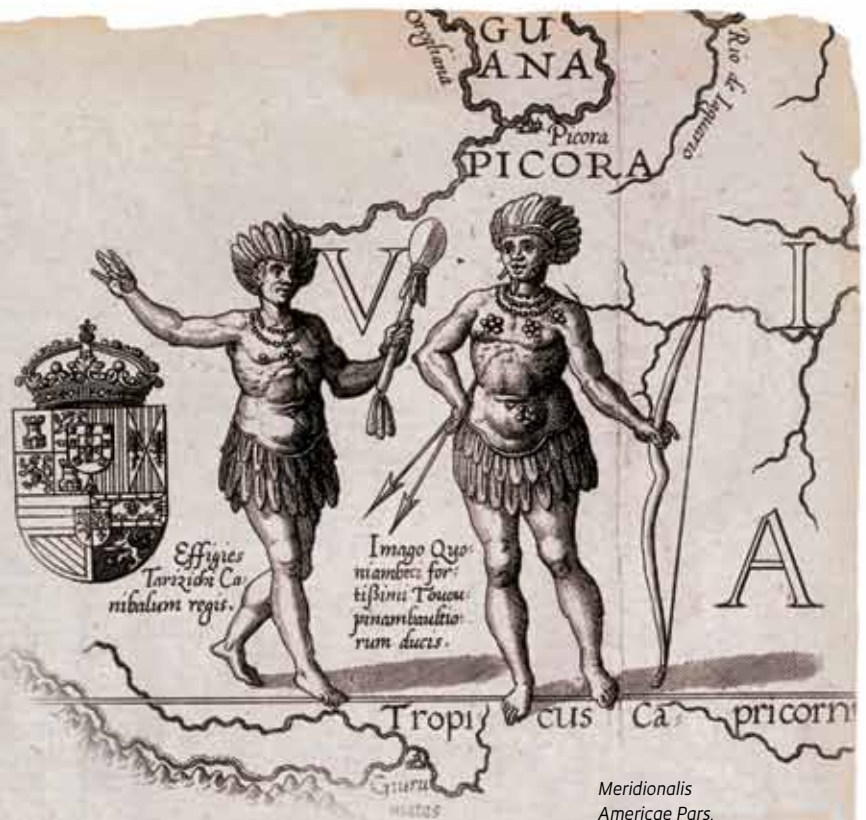
This colonial dynamic ultimately made the resident colonizers, previously connected to the metropolitan sovereignty, a force moving toward autonomy. “Their action made it feasible for capital to take root and for trade routes to be obtained, making them independent of the metropolis,” says Arruda.

One could not exploit the colony without making it grow, without developing it, thus leading to tensions whenever the central authority in Lisbon was unable to satisfy the new local necessities and when it may have been hindering growth.

DECLINE

The seeds of the empire’s decline were present in the very essence of its maintenance. “Portugal was an important cog in the gears of the construction of capitalism, especially during the mercantile stage. In capitalism, however, it is impossible to maintain hegemony forever because its logic is the dynamics of migration from the center of accumulation,” Ana Paula Megiani explains. During the 18th and 19th centuries, we no longer see in Europe the affluence of wealth among the Iberians. “The crisis in mercantile capitalism led to the crisis in the Portuguese Empire, but if we were to consider the cultural, religious, and political dimensions, we find a different duration,” she says. “The impact of Lusitanian colonization was much greater than its governmental structure,” Maxwell reports.

“The inflexion point of the Empire occurred during the Marquis de Pombal period, between 1750 and 1777. The marquis had given the local elites great authority, and whenever this was not the case, there was conflict,” de Mello e Souza observes. Increasingly, the old idea of the necessity and possibility of a Luso-Brazilian empire tears the notion of the old colonial system to shreds. “Many people wanted to decentralize the empire and make Brazil the center, which was beginning to destroy the relations between metropolis and colony to the point that one can no longer speak of center and periphery,” the researcher continues.



Meridionalis Americae Pars, Petrus Plancius c. 1592-1610 Dimensions: 39.5 x 55.5 cm

The local elites were gaining unprecedented status. The arrival of the royal family in 1808 hastened the trend by creating the strange situation of a colony that was also the seat of the empire.

“The fears expressed in light of the increased independence of the local groups only intensified with the French Revolution and the advances made by Napoleon. Some members of the Portuguese elite were starting to seriously consider that a change in roles was the only way to hold on to Brazil,” says de Mello e Souza.

In 1822, the process consolidated. “However, one part of the old empire was freed only after a painful process of civil wars, as in Africa, where external forces entered the field, due to the refusal of the Salazar regime to negotiate,” Maxwell recalls.

That intransigence, according to the Brazilianist, left few alternatives open, and in the 1970s, when the empire in Africa came to an end, there remained Cold War battles and the issue of South African apartheid, with Cuba, the United States, and the former Soviet Union extending their conflicts into the former Portuguese colonies.

No longer was there any way for “that land to pursue its ideal/to become an immense Portugal,” as boasted by songwriter Chico Buarque in *Fado Tropical* (A tropical fado). ■

Project

Dimensions of the Portuguese Empire (nº 2004/10367); Thematic Project; Coord. Laura de Mello e Souza/USP; Investment R\$578,580.17 (FAPESP)



Interventions on the street

PUBLISHED IN DECEMBER 2012

In 2011, São Paulo artist Eduardo Srur, 39, released 360 floats bearing the slogan "Art saves" onto the reflecting pools at Brazil's National Congress in Brasília. Srur was attempting to put into practice the idea that artistic initiatives can communicate messages about social issues. Srur is part of a long and fruitful line of avant-garde artists who have sought to use the tools of artistic creation in a manner that connects art with the everyday lives of individuals, transforming public spaces into a platform for experimentation.

Photo Fabio Rodrigues Pozzebom/ABR

