



IN FROM THE COLD

After keeping science alive during decades of scarcity, Cuba's "guerrilla scientists" are ready to rejoin the world

By Richard Stone, in Havana

Ernesto Altshuler has a principle for doing science in one of the world's more challenging settings, Cuba. Faced with scant resources and a persistent brain drain, the University of Havana physicist says he became a "guerrilla scientist."

That didn't mean toting a Kalashnikov. "My strategy to survive as an

experimental physicist was to violate the boundaries of safe science," Altshuler says, "invading zones where I was not a specialist, looking around for new phenomena with wider eyes, seeing scientific instruments in daily life objects, attacking and retreating from serendipitous findings like a guerrilla." He has used ants to model how panicked people behave, for example, and has studied

how bits of tea leaves seem to defy gravity by climbing a stream of tea into a pot's spout. In his studies of granular materials, Altshuler spent about \$100 "to obtain the same quality of data" as other researchers who spend millions of dollars on microgravity experiments, says Thorsten Pöschel, a physicist at the Friedrich-Alexander University Erlangen-Nürnberg in Germany. "This should have



At the University of Havana, Ernesto Altshuler spends pennies on his microgravity experiments—and gets million-dollar results.

embarrassed some of our colleagues.”

If Che Guevara were alive today, the iconic guerrilla leader of the Cuban revolution surely would applaud how Altshuler and a handful of comrades have kept science alive by cunning and daring in an isolated nation trapped in a time warp. Here in Havana, '50s Chevrolets and Soviet sidecar motorcycles share the rutted roads with sleek Chinese limousine buses whisking tourists to beachside resorts. On a manicured bluff overlooking Havana Harbor behind the Hotel Nacional de Cuba, foreigners and well-heeled Cubans sip mojitos and puff cigars next to Bay of Pigs-era cannon emplacements.

For every expansive mind like Altshuler's, there are scores of researchers working with blinders to the outside world, producing little while being paid less. Cubans blame their penury on “the blockade”: the U.S. embargo in place for a half-century. “The embargo is like God. It affects every aspect of life,” says Sergio Jorge-Pastrana, foreign secretary of the Academy of Sciences of Cuba (ACC). It

stymies the import of equipment and supplies made in the United States or with U.S. components, and it has turned Cuba into a cyber-backwater with excruciatingly slow Internet speeds. Meanwhile, U.S. travel restrictions hampered academic exchange between the two countries.

But at long last, Cuban science is poised to join the modern world. In a historic rapprochement, Cuban President Raúl Castro and U.S. President Barack Obama announced last December that their nations would strive to overcome mutual hostility and normalize relations. The overtone stunned Americans and Cubans alike. “I almost fainted,” says ACC President Ismael Clark-Arrex. The pace of détente picked up in April, when Obama struck Cuba from the list of states that sponsor terrorism, paving the way for the two nations to reopen embassies as early as summer. Revised travel rules ease visits to Cuba for U.S. scientists, and the U.S. Commerce Department now allows scientific equipment to be freely donated to Cuba, so long as it does not have potential military applications.

Reforms are taking root on Cuban soil as well. In early 2013, Cuba abolished exit visas and now permits citizens to spend 2 years overseas—up from 11 months—without losing residency rights at home. And in a critical way, Cuba is about to join the scientific mainstream. In the coming months, the government is expected to establish an agency akin to the U.S. National Science Foundation (NSF) that will distribute research funds through competitive, peer-reviewed grants.

Few on either side of the Cuba-U.S. ideological divide anticipate a quick end to a rift that has lasted more than 50 years. Yet Cuba and the United States have shown that they can overcome political differences for the sake of science. A U.S. State Department official says that the United States will not link science engagement with Cuba to progress on human rights, such as free expression, that are still curtailed in Cuba. Already, joint efforts to assess Cuba's coral reefs (see p. 751) and to combat Ebola in West Africa are under way. Science diplomacy, Jorge-Pastrana says, could help Cuba

and the United States lay the foundation of a new relationship.

At the very least, says Luis Montero-Cabrera, a computational chemist at the University of Havana, “we don't want to be a pariah anymore.”

PEDRO VALDÉS-SOSA was a 9-year-old Cuban expatriate living in Chicago when Fidel Castro seized power in his homeland in 1959. The ferment filled him with pride. The next year, when his fifth-grade teacher explained that U.S. Army physician Walter Reed first hypothesized that mosquitoes transmit yellow fever, Valdés-Sosa could not contain himself. “I stood up and objected,” he says. “The true discoverer, of course, was Carlos Finlay,”

a Cuban doctor. (Reed himself credited Finlay with discovering the vector.) In 1961, Valdés-Sosa's parents moved the family to Cuba to take part in the socialist experiment. Pedro and his fraternal twin brother, Mitchell, would both become influential neuroscientists here, while remaining lifelong White Sox fans.

Finlay is the founding father of Cuban science. A white marble bust of the epidemiologist sporting a bushy mustache and muttonchops sits on a 3-meter-tall pedestal in a garden across from ACC's headquarters in Old Havana. Finlay's key insight into yellow fever came in 1881, when Cuba still belonged to Spain.

After Cuban independence in 1898, however, intellectual life withered, and the island became known as a winter playground for fast-living U.S. celebrities like Ernest Hemingway, Ava Gardner, and Marlon Brando. A team from the International Bank for Reconstruction and Development that visited Cuba in 1950 reported, “In the field of applied research and labs, there was no development at all in Cuba.” The country possessed just three agricultural research stations specializing in sugarcane and tobacco and a single higher education institution, the University of Havana.

Science became a priority again after Cuba's 1959 revolution. In a speech in January 1960, Castro declared, “The future of our country has to be necessarily a future of men of science, of men of thought.” Cubans were gobsmacked. “One-fifth of the

Meager resources

\$4
million

Science ministry's R&D budget in 2015

\$2
million

GDP per peer-reviewed scientific paper, about 3% of U.S. figure

6000

Number of scientists in Cuba

559

Number of Cubans who earned a B.S. in natural sciences or mathematics in 2007–08

\$36

How much most scientists in Cuba earn each month

population was illiterate. Everybody thought he was dreaming,” Jorge-Pastrana says.

In 1965, the government established the National Center for Scientific Research here, for applied science and engineering. Later that year, ACC, quiescent for decades, began opening institutes in natural sciences. Guevara, as industry minister, launched research centers in mining and metallurgy and in sugarcane byproducts. A stream of students headed overseas, mainly to Eastern bloc countries, for graduate studies.

In 1973, the first Ph.D. was awarded in Cuba, in neuroscience. Cuba now has 63 universities, and roughly one scientist for every 1800 people. Salaries have always been a pittance, but in the heyday of the Soviet bloc they came with scientific perks. High-powered specialists in geology, marine biology, and other fields beat a path to Cuba from the Soviet Union and other communist redoubts with robust scientific traditions. The visitors took aspiring Cuban scientists like Manuel Iturralde-Vinent under their wing.

As a youngster, Iturralde-Vinent loved to explore caves near his hometown of



Manuel Iturralde-Vinent's geological research flourished when a strong Soviet Union aided Cuban science.

Cienfuegos, on Cuba's southern coast. In 1964, when he was 18, the high school dropout parlayed his amateur prowess in speleology into a job as a technician at the newly formed National Institute of Hydraulic Resources. After becoming a department head at the tender age of 22, Iturralde-Vinent turned to mapping water basins with a Russian field geologist. "I treasured him as a father I didn't have. We were speaking in my poor Russian, I was writing in Spanish about karst geology,

and we were drinking vodka all the time."

Iturralde-Vinent joined the Institute of Geology and Paleontology in Havana just as it was gearing up for a massive Eastern bloc effort to map Cuba's geology. Once that was complete, Comecon, the Soviet-led economic assistance body, poured millions of dollars into an effort in the early 1980s to translate the newly acquired geological knowledge on Cuba into data on mineral resources, such as the country's prodigious nickel reserves. "We drilled like crazy," says Iturralde-Vinent, president of the Cuban Geological Society. "For any other country at that time, it would have been impossible."

In many fields Cuba was the junior partner to its socialist big brothers. But in one risky new field it set out to be a pioneer.

BIOTECH BEWITCHED FIDEL CASTRO.

On a visit here in 1981, R. Lee Clark, president of the MD Anderson Cancer Center in Houston, Texas, met the fatigue-clad leader and bent his ear about the potential of interferon, an immune-modulating compound, to subdue cancer. Castro dispatched two

Fidel Castro's first-born son fomenting a nanotech revolution

By Richard Stone

The father took care of the politics. The son shepherded some of Cuba's biggest science dreams. In the 1980s, Fidel Castro tapped his eldest son, Fidel Castro Díaz-Balart, to bring nuclear power to Cuba. Fidelito, who had earned a Ph.D. in 1978 from Moscow's Kurchatov Institute, took the reins of a new Cuban Atomic Energy Commission and oversaw the creation of a nuclear research center at Juragua. Construction of the first of two Soviet VVER pressurized-water nuclear power reactors began in 1983.

The reactors were never finished. In 1992, after the collapse of the Soviet Union, Fidel Castro pulled the plug on the project. Castro Díaz-Balart's influence in Cuba waned and he reinvented himself as a science statesman, representing the nation at international forums. When Raúl Castro took power in 2008, Castro Díaz-Balart, who has always been close to his uncle, saw his stock rise. Now, he has discovered a new passion, nanotechnology, and has spent several years laying the groundwork for a nanotech R&D center slated to open later this year in south Havana.

A demicelebrity, Castro Díaz-Balart, 65, landed in

the gossip columns in March when heiress Paris Hilton snapped selfies of herself and a bemused Fidelito during a cigar festival in Havana. The soft-spoken science adviser to Cuba's powerful Council of State and vice president of the Academy of Sciences of Cuba sat down with *Science* in February in the towering José Martí monument, a short walk from his office in the main government complex in Havana. This transcript was edited for clarity and brevity.

Q: Growing up, were you sheltered from politics?

A: The early years were very intense. Due to the aggression and continuous sabotage,

our government policy was oriented to the survival of the revolution. In those years, I was concerned only with science. I was very interested in relativity theory, and how the nucleus worked. When I was a teenager, some of my classmates called me the atomic engineer.

Q: As a student in Moscow, you went by the pseudonym José Raúl Fernandez. Would the Castro name have brought unwanted attention?

A: Due to the conditions, I had that name from high school. Some people saw that as an order from above. It was because I loved chess. I took that name from José Raúl

PHOTO: LISETTE POOLE

bright young biologists to Houston in 1981 for a weeklong crash course on interferon in Clark's lab. The duo next did a stint at the State Serum Institute in Helsinki with Kari Cantell, who in the 1970s had been the first to isolate interferon from human white blood cells. Back in Havana, the government gave them a two-building compound to use for lab space; it had been expropriated from a Cuban family that had fled after the revolution. In short order "they isolated the first Cuban interferon," Jorge-Pastrana says. "Within 2 years, they could produce interferon by genetic engineering." Cuba used its interferon widely in the early 1980s to stem internal bleeding in dengue patients.

Emboldened by that success, Cuba decided to get into genetic engineering on the ground floor. "We were not going to miss the biology revolution," Clark-Arrex says. The country spent about \$1 billion on biotech in the 1980s and 1990s, he says. Cuba's state-owned biotech industry now employs more than 21,000 people at 32 institutes and enterprises managed by BioCubaFarma, a holding company. Biotech is now the country's second biggest source of revenue, after tourism, earning several hundred million dollars each year from exports of products such as recombinant epidermal growth factor for diabetic ulcers; recombinant erythropoietin for anemia; and a pentavalent vaccine against diphtheria, tetanus, whooping cough, hepatitis B, and *Haemophilus influenzae* B.

Biotech was one of the few areas of Cuban science to survive "the special period," Cuba's existential crisis after the collapse of the Soviet Union, its main financial backer, in 1991. Within 4 years, Cuba's gross domestic product contracted 40%, sinking from third in Latin America to 23rd. "There was no petrol, so there were almost no cars on the streets. And there were food shortages," even malnutrition, Jorge-Pastrana says. Outside of biotechnology, most scientists fell into indigent hibernation. "There was almost no research," says Iturralde-Vinent, who in 1988 had moved to the Museum of Natural History, where he pillaged old data for insights into Caribbean plate tectonics.

Cuba began pulling out of its nosedive around 1996. But the isolation of Cuban science has continued. "The miracle is that we are still competent in some important fields," Clark-Arrex says. One standout is the Cuban Neuroscience Center. In the dark days of the early 1990s, "it didn't have money for toilet paper," says Mark Rasenick, a neuroscientist at the University of Illinois, Chicago, who collaborates with Valdés-Sosa. But the center kept its research going at a slow burn and today, Rasenick says, its brain mapping studies "are really among the best in the world." Adrian Raine, a neuropsychologist at the University of Pennsylvania, agrees. Research in his area, the biological roots of violence, "is being largely transported to countries like Cuba," he says. "They seem to

be well ahead of the United States."

Another miracle is that there's anyone left in Cuba to do good science. "Our biggest problem is a massive emigration of young professionals," Altshuler says. "We could be sucked dry." The country's crumbling buildings and infrastructure tell young scientists that the odds are against a research career. Bright young science students decamp to universities from Argentina to Arkansas. And fewer go into science in the first place. Just 559 students in Cuba earned a B.S. degree in natural sciences and mathematics in 2007 to 2008: less than a sixth of the number who had enrolled in these areas 4 years earlier.

"Some people say the special period is still going on," Iturralde-Vinent says.

UNLIKE MANY OF HIS NEATLY COIFED countrymen, Altshuler wears his wavy gray hair hippie-long. Ingenuity borne of dire straits has, he says, given him "an immense feeling of freedom." A couple of years ago, he designed, for pennies, a system for studying how granular materials respond to different gravitational fields: a free-falling, sand-filled bucket. It plunges 15 meters while a Ping-Pong ball fitted with an accelerometer penetrates the sand. The out-of-this-world rationale, as described in *Geophysical Research Letters* online on 1 May 2014, was to test how spacecraft and other objects settle on granular surfaces in gravities different from Earth's. "In Cuba, we don't have much

Capablanca [the Cuban world chess champion from 1921 to 1927]. I have 30 scientific publications with that name.

Q: Considering the geopolitical reality, was Cuba's nuclear program doomed from the start?

A: I don't think so. When we were building the Jurgua power plant, we had to develop the nation's infrastructure. It was called the investment of the century. We created an institute to train nuclear scientists and engineers. This effort boosted all of Cuban science and technology.

Q: Tell me about your nanotech ambitions. Can Cuba really compete in this area?

A: Cuba, like many countries, cannot replicate what you have in the United States. We

don't have to develop new materials for planes or rockets like big powers in the world. But we have a critical mass of people with knowledge in this sphere. We're not going to have a Caribbean, tropicalized nanotechnology. We're going to have state of the art.

Nanotechnology is a dis-



ruptive technology. In a small way, we want to take part in this new revolution, the most important in the last 200 years. To create this kind of oasis, we'll have to have good cooperation with first-world countries.

Q: That prospect seems brighter now that the United States and Cuba are normalizing relations.

A: I'm optimistic. We have a lot of common ground. However, a discouraging but a true reality is that most modern hardware and equipment for science and medicine has more than 10% American components. We cannot obtain it because it is subject to the embargo. That is a dark point.

It's true that almost any scientific materials can be put to military use. That is the yin

and yang of science. People raised those questions about our biotechnology in the early 2000s. Experts came to our P3 laboratory [for research on dangerous pathogens] and vaccine facilities to see if there was weaponization. They could understand perfectly well that our research is for the benefit of society.

I'm confident that as scientists, we can put aside differences. You don't have to agree to everything when you have relations with a friend. Healthy disagreement is good. It's time to get past poisoned disagreements.

Q: Do you have political aspirations?

A: [smiles] Maybe in my next life. In this one, I feel very good to be a scientist. ■

Graying Cuba strains socialist safety net

By Richard Stone

At Cuba's Center of Molecular Immunology (CIM), a biotechnology hub on Havana's western edge, Director Agustin Lage points to a country-by-country graph of life expectancy versus health care spending. Many dots are unsurprising: The United States spends a bundle and people tend to live long, whereas Sierra Leone lays out almost nothing and its citizens have an average life expectancy of 46. Then there's Cuba. The impoverished nation spends a pittance on health care, but with a life expectancy of 78 years for both sexes, it's neck and neck with its northern neighbor.

Two big reasons why Cubans live long without prospering are a raft of compulsory childhood immunizations—13, including eight vaccines produced in Havana—and an army of doctors, six per 1000 inhabitants, deployed across the nation. In 2013, Cuba's infant mortality rate was 4.76 per 1000 births—less than a third of Mexico's rate and even better than that of the United States, which recorded 5.9 deaths per 1000 births.

While Cubans live longer, young adults have left the country in droves, and those who stay aren't having babies: Cuba has one of the lowest fertility rates in the world, averaging 9.9 births per 1000 people. "There is no money to raise a family," explains Pedro Valdés-Sosa, research director at the Cuban Neuroscience Center in Havana. Cuba's median age is now 40—far senior to Mexico (27.3) and even older than the United States (37.6)—and continues to rise.

A graying population is straining Cuba's social safety net and its vaunted health system. Studies suggest that roughly 10% of Cuba's population has dementia to varying degrees, Valdés-Sosa says. "It's a huge social problem that we have to start attacking."

Cancer, another disease of the elderly, is also on the rise. CIM is trying to extend the lives of Cuba's cancer patients by broadening the use of therapeutic vaccines, designed to rouse the immune system so that it attacks the tumor, curtailing growth and metastasis. "The goal is to transform cancer into a chronic

disease," Lage says.

In the United States and other Western countries, cancer vaccines are still largely experimental. Cuba has been in the cancer vaccine business for nearly 15 years—longer than most countries, says Tania Ramos, director of CIM's clinical research division. "I have no doubt that the Cuban population has received more immunotherapy than any country in the world," she says.

Cuba's willingness to gamble on cancer vaccines is attracting foreign patients with late-stage cancer. Some health experts see parallels with the clinics in Mexico that dispensed dubious treatments with the drug laetrile. But such worries are off target, says Mark Rasenick, a neuroscientist at the University of Illinois, Chicago, because Cuba's cancer vaccines "are based on a solid scientific foundation."



Pedro Valdés-Sosa seeks ways to slow cognitive decline in the elderly.

A colleague with advanced lung cancer recently followed the well-trodden path to Havana for treatment, because, Rasenick says, patients know "you won't be in a control group" that is denied the vaccine.

Starting this year, Cuba is pushing cancer vaccines out of its oncology units and into the hands of primary care doctors. In a trial run, CIM last year began stocking 50 primary care units across the country with two lung cancer vaccines. The center hopes to have the vaccines in all clinics by the end of 2015. Vaccines against breast cancer and other tumor types are on the way. ■

fancy equipment," Altshuler says, "but we have tons of beautiful sand!"

Altshuler's observation of tea leaves flowing upstream into a teapot led to another case of bargain-basement physics. A few years ago, Troy Shinbrot, a physicist at Rutgers University, New Brunswick, in New Jersey, was intrigued by Altshuler's account of the phenomenon. They collaborated on experiments confirming that bits of matter could climb a 1-centimeter waterfall and move upstream in a meters-long channel—all thanks to surface tension. "It's a pretty cool phenomenon," says Shinbrot, who with Altshuler published their findings online on 3 July 2013 in the *Proceedings of the Royal Society A*.

For the vast majority of Cuban researchers, however, the embargo is a scientific straitjacket. Strolling through the verdant south Havana campus of the Higher Polytechnic Institute José Antonio Echeverría (CUJAE), Cuba's top technical university, research vice-rector Orestes Llanes-Santiago recounts the university's early travails in computing. Barred from buying U.S. computers, scientists with CUJAE—then the technology faculty at the University of Havana—and colleagues formed a crack team to design Cuba's first computer from scratch in the early 1970s.

Cuban industry produced the computer, similar to Digital Equipment Corp.'s PDP-8, until 1990. By then the archaic machines were almost useless, and CUJAE set out to obtain a Sun Microsystems workstation. They got one through a chain of contacts in "five or six countries," Llanes-Santiago says, "to erase the trace." But whenever they tried downloading software or upgrades over the Internet, their Cuban IP address betrayed them. A message would flash on the screen—"You are in a forbidden country"—and the updates were blocked.

Few pieces of Cuba's lab equipment are state of the art. "It's tremendously difficult" to buy genuine reagents and other supplies, says Agustin Lage, director of the Center of Molecular Immunology here. Montero-Cabrera chafes at not being allowed access in Cuba to computational chemistry software. "It's insulting and discriminatory," he fumes. "I'm treated as a terrorist."

The restrictions are maddening, agrees Rasenick, who failed a few years ago to send a functional magnetic resonance imaging machine to Cuba. U.S. officials deemed it to have potential military applications. "I guessed if you dropped it on someone you could hurt them," he says.

THE PROSPECT OF NORMALCY is intoxicating, even though Cuban scientists expect it will be slow in coming. "What Obama and

Castro did was very gutsy,” Valdés-Sosa says. “This is the beginning of the end of an absurd situation.”

Freer travel will aid the handful of U.S. researchers who have used private money in recent years to nurture collaborations in Cuba. Last year, ACC and AAAS (*Science*’s publisher) signed a memorandum of understanding seeking to expand such efforts in areas like neuroscience and infectious disease. One target is chikungunya, a mosquito-borne malady working its way through the Caribbean toward Cuba and the United States. “We have to face this virus together,” says Guadalupe Guzmán Tirado, an epidemiologist here at the Institute of Tropical Medicine.

As the awkward pas de deux takes shape, Cuba is seeking to bolster its own scientific capacity. Ever since the revolution, the government’s unwavering policy has been to yoke science to societal needs: girding for the consequences of climate change, for example, or bolstering energy supplies. Researchers not pursuing such national priorities have had to fend for themselves. “You can study mathematics or basic science, but there’s no money,” Llanes-Santiago says. “Everything is for applied science.”

That could change with the upcoming establishment of the Cuban NSF. Key details, including its budget and management structure, are still being worked out. But the science ministry has agreed that it will dole out a chunk of its R&D budget—a paltry 90 million pesos (\$4 million) in 2015—on competitive grants for basic research. “It’s essential to have this fund,” Valdés-Sosa says. While most of Cuba’s R&D budget will continue to go to “national needs,” Clark-Arxxer adds, “there must be space for creativity.”

Cuba remains a place of outsized ambitions. Castro’s eldest son, Fidel Castro Díaz-Balart, for example, is leading an initiative to build a nanotechnology research complex on Havana’s southern outskirts. The Center for Advanced Studies of Cuba hopes to carve niches in, for example, drug delivery and solar cells. “We will never be a power in nanoscience,” Clark-Arxxer acknowledges. “But we have to be proficient.” Seemingly defying poverty and the embargo, the center’s labs are billed as having “ultralow vibrations without electromagnetic interference,” a “powerful computational infrastructure,” and “world-class laboratories for nanocharacterization.” Work on a nanofabrication facility is slated to begin next year.

Cuba’s precision strike into a field dominated by the United States and other powers sounds a lot like guerrilla science. But until the embargo fades, that’s the way it has to be, Castro Díaz-Balart says. “This approach,” he says, “is consistent with the economy and possibility of Cuba.” ■



Elkhorn coral has vanished in much of the Caribbean but hangs on in Cuban waters.

CUBA’S CORAL EDEN

Scientists rush to study what may be some of the last healthy corals in the Caribbean

By **Elizabeth Pennisi**

Last month, Amy Apprill checked in for a 30-minute flight from Miami to Havana with 17 pieces of luggage stuffed with water filtration pumps, underwater cameras, an ocean acidity probe—even liquid nitrogen. To get anything done in Cuba, the marine microbiologist at Woods Hole Oceanographic Institution in Massachusetts had to bring everything with her. Cash, too: She had \$1500 stashed in her backpack to augment the \$15,000 that colleagues carried to Havana to pay for diesel fuel and the use of a research vessel.

Those hassles, Apprill hoped, were a small price to pay for an extraordinary opportunity. Thanks to limited development and extensive conservation efforts, Cuba has “the best

coral reefs of the region,” says Dan Whittle, an attorney in charge of the Cuba program for the Environmental Defense Fund in Raleigh. Many Caribbean reefs are dead or dying, he says, yet Cuba’s remain “stunningly beautiful.” Apprill wants to know why.

She’s not the only one. As Cuba-U.S. relations thaw, scientists are eager to size up the reefs before an anticipated economic boom has a chance to degrade them. “There’s a little bit of a stampede to get there,” says Clare Fieseler, a graduate student at the University of North Carolina (UNC), Chapel Hill, who made it to Cuba several years ago and hopes to return to visit underexplored reefs. Also fueling a sense of urgency: Cuba’s coral reefs may hold the cure for ailing reefs elsewhere in the Caribbean.