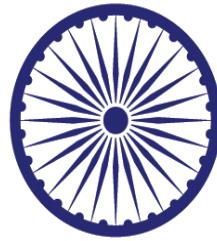


The biological sciences in India



Aiming high for the future

BY RONALD D. VALE¹ AND KAREN DELL²

India is gearing up to become an international player in the life sciences, powered by its recent economic growth and a desire to add biotechnology to its portfolio. In this article, we present the history, current state, and projected future growth of biological research in India. To fulfill its aspirations, India's greatest challenge will be in educating, recruiting, and supporting its next generation of scientists. Such challenges are faced by the US/Europe, but are particularly acute in developing countries that are racing to achieve scientific excellence, perhaps faster than their present educational and faculty support systems will allow.

India, like China, has been riding a rising economic wave. At the time of writing this article, four Indians rank among the ten wealthiest individuals in the world, and the middle class is projected to rise to 40% of the population by 2025 (Farrell and Beinhocker, 2007). Even with the present global economic setbacks, India's economy is expected to grow to become the third largest in the world. India's recent economic boom has been driven largely by its service and information technology industries, fueled to a large extent by jobs provided by multinational companies.

However, this "outsourcing" model is unlikely to persist indefinitely. India's future must rely upon its own capacity for innovation, which will require considerable investment in education and research.

Biotechnology represents a potential sector of economic growth and an important component in India's national health agenda. Appreciating the important role that biology will play in this century, the Indian government is expanding as well as starting several new biological research institutes, which will open up many new positions for life science researchers. Funds also are becoming available for state-of-the-art equipment, thus decreasing the earlier large disparity in support facilities between the top research institutes in India and the US/Europe. India is becoming an increasingly viable location to conduct biological research and a fertile ground for new biotechnology companies. However,

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success need not rise in proportion to money invested, unless India attracts and supports its best young people to do research.

Many academic centers and industries in the US/Europe are beginning to have an eye on India, the world's largest democratic country, for possible collaborations. Western institutions have long benefited from having Indian scientists on their faculty or postdoctoral fellows/graduate students in their laboratories (perhaps benefitting more than India itself). However, Western scientists, by and large, know very little about the scientific and educational systems in India. (As was true of authors of this article before we began our 8-month sabbatical at the National Center for Biological Sciences in Bangalore). The goal of this article is to provide a brief historical and contemporary view of the biological sciences in India. We also provide an editorial perspective on the upcoming challenges for the Indian life sciences, with a particular emphasis on how India will grow and support its next generation of scientific leaders.

The Past and Present: An Overview of Biological Research in India

"It is science alone that can solve the problems of hunger and poverty, of insanitation and illiteracy, of superstition and deadening of custom and tradition, of vast resources running to waste, or a rich country inhabited by starving poor... Who indeed could afford to ignore science today? At every turn we have to seek its aid... The future belongs to science and those who make friends with science."

—Jawaharlal Nehru (Independent India's first Prime Minister)

India's footprint in the biological sciences is relatively small, especially considering its population. Much of India's high-level biology research is pursued at ~15 Institutes and a few Universities with good biology departments, each of which houses ~10–80 faculty (Table I) (see Fig. 1 for an overview of the Institute, University, and College systems). The relatively small size of India's life science enterprise is hardly surprising given that the country began much of its own national scientific agenda after achiev-

ing independence in 1947 (with more pressing needs occupying the nation at the start). In addition, physics, math, and engineering in India have been considered as higher scientific endeavors than biology and have produced more internationally recognized scientists. Thus, it is useful to look at how biology in India developed in the last century, to provide a historical backdrop for its current situation and a perspective for how it might develop in the future.

In the middle of the 19th century, the British East India Company established Universities in the three Presidency towns of Calcutta, Madras, and Bombay (now known as Kolkata, Chennai, and Mumbai) with the objective of training native Indians in liberal arts and sciences, medicine, law, and engineering (see perspective from VijayRaghavan [2008]). Just before Independence, India had ~20 Central (Federal)- and State (Provincial)-run Universities, in addition to the original Presidency Universities. These Universities provided a solid basic education, but did not conduct any significant amount of research. The first Institute with a mandate to pursue scientific research was the Indian Association for the Cultivation of Science (IACS), which was established in Calcutta in 1876 and focused on chemistry and physics (as a note for newcomers, a daunting aspect to the Indian scientific scene is the lettered acronyms by which Indians refer to their numerous research Institutes, Universities, and funding agencies [see Table I as a guide]). The IACS spawned a number of intellectual giants, including Sir CV Raman who conducted his Nobel Prize-winning research there. A second prominent research Institute was the Indian Institute of Science (IISc) in Bangalore, which was conceived of in 1896 and launched in 1909. These two Institutes continued to dominate basic scientific research in the physical sciences for the first half of the 20th century.

At the end of World War II, a committee was convened to establish higher technical institutes for the industrial development of an independent India. This committee envisioned these institutes as engaging in world-class engineering training and research, following Western examples such as the Massachusetts Institute of Technology. The first Indian Institute of Technology (IIT), as these schools came to be known, was inaugurated near Kolkata in

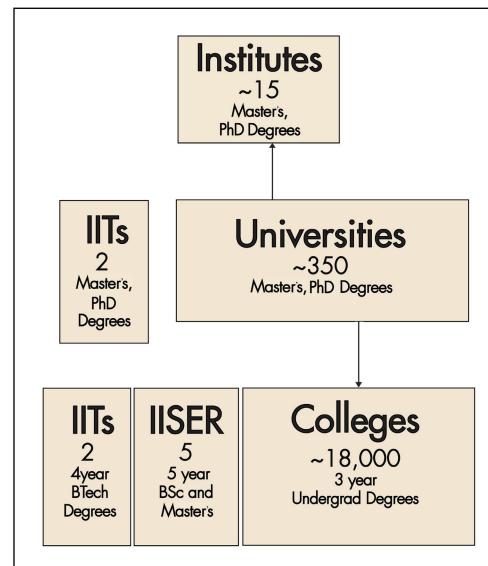


Fig. 1. Educational and research Institutes in biology in India, including Indian Institutes for Science Education and Research (IISERs) and Indian Institutes of Technology (IITs). (Note—only two of the seven IITs currently offer degrees in biology). Arrows indicate that Universities oversee the degree grants from the majority of the undergraduate Colleges and Institutes. Medical colleges and postgraduate institutes are not included in this diagram.

1951. Jawaharlal Nehru, the first Prime Minister of India, was a key force in establishing four additional IITs in other regions of the country in the ensuing decade. Currently, India has seven highly regarded IITs that attract top students in a highly competitive admissions process. The IITs and other research institutes such as the IISc and the Bose Institute were focused primarily on mathematics, physics, and engineering. The legacy of this early investment carries through to the present; India now trains over 400,000 engineers per year (National Knowledge Commission [2006]) and has a strong international reputation in physics, math, and engineering.

In contrast, modern biological research came into being much later in India. Until the 1960s, biological research was largely directed toward pragmatic applications in agriculture, nutrition, and public health. For example, the IISc in Bangalore started laboratory groups involved in fermentation, pharmacology, and silkworm biology in 1941. The first truly modern "molecular biology research unit" began in 1962 as a branch of the Tata Institute of Fundamental Research (TIFR) in Mumbai, an institute originally devoted solely to physics and mathematics. (As an aside, TIFR's current Department of Biological Sciences faculty is still small (16 faculty)

in comparison to mathematics [~ 40] and physical sciences [>100]). Similarly, new biological research units formed within traditional physical science institutes in other locations. G.N. Ramachandran (trained as physicist and inventor of the “Ramachandran plot” widely used in protein structural studies) founded the Molecular Biophysics Unit at the IISc in 1970. The Center for Cellular and Molecular Biology (CCMB) in Hyderabad also began as a semi-autonomous branch of a regional Indian Institute of Chemical Technology in 1977 and became a National Laboratory in 1981. Other biology institutes started with very pragmatic goals and then broadened their scope. The National Institute of Immunology (NII) began in 1986 with the focused goal of developing vaccines but broadened several years later and is now conducting a wide range of basic biological research. The Center for Biochemical Technology began as a producer of biochemical reagents for India in 1977 but changed its name (Institute of Genomics and Integrative Biology) and mission (basic scientific research) in 2002. In a somewhat analogous path, the National Center for Cell Science (NCCS) started in 1988 as a repository and distribution center for tissue culture cell lines (then known as the National Facility for Animal Tissue and Cell Culture) but became a broad, basic biological science institute and was rechristened with its current name in 1995 (Table I).

More recently, research Institutes have seeded new Institutes. Obaid Siddiqi, who started the molecular biology unit at TIFR, Mumbai, went on to found the National Center for Biological Sciences (NCBS) in Bangalore in 1992, which has developed into India’s premier biological institute (Fig. 2). NCBS’s current institute

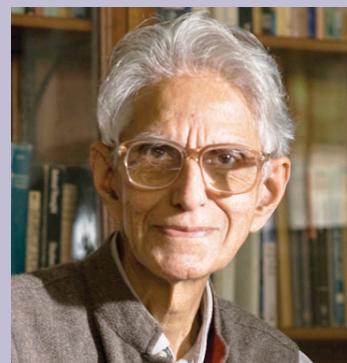
director K. VijayRaghavan now has been instrumental in launching a nearby Stem Cell Institute (discussed later). In recent years, the government has invested heavily in the infrastructure of its research institutes, and some of their facilities are on par with those in the US and Europe (e.g., state-of-the-art microscope and fluorescence-activated cell sorter facilities).

Prior to the formation of biology research Institutes, the top Universities were home to much of India’s best biology research. However, since the 1990s the research Institutes have been heavily favored in research funding and faculty recruitment, which has contributed to a two-decade decline in the stature of the Universities. Currently, there are more than 350 Indian Universities, a spectacular rise since Independence. Most are operated by State governments along with a smaller number of Central, and, more recently, private Universities. The Universities are primarily dedicated to graduate training (master’s, PhD, and postgraduate training after a medical college degree).

They also serve as official degree-granting entities for the graduate students at most research Institutes. Universities also oversee the curricula, textbooks, and exams of the vast majority of India’s $>18,000$ undergraduate colleges; >100 colleges are often affiliated with a single University, thus creating a complex administrative system (Fig. 1). Most of the Colleges are physically separated from the Universities, a trend that was initiated at least four decades ago (a few exceptions exist such as Benares Hindu University, which has retained undergraduate colleges on its campus). A few medical schools also have basic science departments, most notably the All Indian Institute of Medical Sciences (AIIMS) in New Delhi. While there are examples of fine biologists at the Universities, financial constraints and substantial demands on faculty for teaching and administrative duties have made it difficult for biological research to thrive in the current University system, as will be discussed later in the article.

In summary, biological research in India has progressed mostly through the formation of independent, free-standing research Institutes, rather than through the University system. The founding of these Institutes is relatively recent, and the fac-

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OBAID SIDDIQI founded the molecular biology unit at the Tata Institute in Fundamental Research (TIFR) in Mumbai in 1962 and was the key figure in founding the National Center for Biological Sciences (NCBS) in Bangalore in 1992. Siddiqi is a *Drosophila* geneticist and studies olfaction and is a foreign member of the US National Academy of Sciences.

ulty numbers are still relatively small. For example, the total number of biology faculty at the Institutes listed in Table I is less than the number of faculty holding NIH grants at the University of California, San Francisco (720). Thus, India has yet to achieve a much-needed critical mass in biology. However, as described in the next section, plans are underway to expand the life sciences in India substantially.

Plans for Expanding Biology in India

“Five years ago, I would have not gone back to India. But with new initiatives and more funding, there is a chance to do serious research and I decided to come back.”

—recent faculty recruit

Just like its cities, economy, and social structure, times are changing rapidly for the biological sciences in India. The country now has the ambition and better financial backing to begin to become competitive internationally in basic biological research. While biology still does not have the same prestige afforded to physics/mathematics, interest in biology is growing rapidly and eventually will hold an equal footing with the physical sciences.

At the time of writing this article,



Fig. 2. The National Center for the Biological Sciences, a center of research excellence and a green oasis in crowded Bangalore.

Table I. Major Institutes and Universities conducting life science research in India

Institutes	Location & Year Institute Opened	Faculty Number	Junior Faculty	Women Faculty	PhD Students	Postdocs
All-Indian Institute of Medical Sciences (AIIMS), Basic Science Depts.	New Delhi, 1956	85	39	42	278	~40
Anna University, Center for Biotechnology	Chennai, 1993	12	5	5	100	5
Bose Institute, Dept. of Biochemistry	Kolkata, 1974	7	0	2	19	5
Centre for Cellular and Molecular Biology (CCMB)	Hyderabad, 1977	53	10	9	150	20
Central Drug Research Institute (CDRI)	Lucknow, 1951	156	43	31	297	5
Delhi University, South Campus	New Delhi, 1988	33	12	9	137	26
Indian Institute of Chemical Biology (IICB)	Kolkata, 1935	75	12	20	190	21
Institute of Genomics and Integrative Biology (IGIB)	New Delhi, 2002 (1977)	49	15	14	100	1
Indian Institute of Science (IISc), Division of Biological Sciences	Bangalore, 1941	57	12	15	305	55
Indian Institute of Science Education & Research (IISER), Biology, Kolkata	Kolkata, 2006	9	9	2	11	2
Indian Institute of Science Education & Research (IISER), Biology, Pune	Pune, 2006	9	8	3	11	1
Indian Institutes of Technology (IIT), Biosciences & Bioengineering, Bombay	Mumbai, 1990	12	2	2	96	2
Indian Institutes of Technology (IIT), Biosciences & Bioengineering, Kanpur	Kanpur, 2001	10	9	1	65	2
International Centre for Genetic Engineering and Biotechnology (ICGEB)	New Delhi, 1988	34	8	5	101	44
Jawaharlal Nehru University (JNU), Life Sciences	New Delhi, 1970	68	38	21	250	25
National Center for Biological Sciences (NCBS)	Bangalore, 1992	25	8	8	110	14
National Brain Research Center (NBRC)	Manesar, 2003	16	10	6	62	2
National Center for Cell Science (NCCS)	Pune, 1995 (1988)	29	7	7	137	3
National Institute of Immunology (NII)	New Delhi, 1986	47	13	11	130	30
Tata Inst. of Fundamental Research, Dept. of Biological Sciences (TIFR-DBS)	Mumbai, 1962	16	6	5	46	5

Several departments contribute to the numbers shown for AIIMS, Delhi University, JNU, and IISc. Junior faculty are considered as seven years or less on the faculty. Information for this Table was obtained from directors or faculty at the Institute or University. NCCS was originally the National Facility for Animal Tissue and Cell Culture (its founding year, 1988). IGIB was originally the Center for Biochemical Technology (its founding year, 1977).

many new initiatives have begun or are in the planning stage. Several of the premier research institutes (e.g., NCBS, CCMB, and TIFR [Dept. of Biological Sciences]) are or will soon be constructing new buildings on their campuses, which will result in a doubling of their faculty. Several new research Institutes also are being planned. Notably, a new Stem Cell Institute has been approved recently by the Central government. Located adjacent to the NCBS in Bangalore, this new research facility is expected to hire 40 faculty and will interface in clinical translation projects with the Christian Medical College in nearby Vellore. The Stem Cell Institute is the first of what may become a very exciting and collaborative campus of several adjacent research institutes. The other institutes, which are in an early planning phase, include (1) a center for platform technologies (e.g., imaging, mass spectrometry, etc.), which is provisionally called the Bangalore BioCluster; (2) an institute focused on problems at the interface of biology and material sciences; and (3) a plant genomics center. In the national capital territory around New Delhi, a new Translational Health Science Technology Institute (THSTI) is being planned, as well as a UNESCO center for biotechnology research and education, which together might add over a hundred faculty. The National Institute of Immunology also has long-range plans to expand its ac-

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M.K. BHAN is the Secretary of the Department of Biotechnology (DBT), a Central government department agency based in New Delhi that functions as a major funding agency for biology. Dr. Bhan has been instrumental in developing the Wellcome-DBT India Alliance and the founding of the Stem Cell Institute.

tivities adjacent to the THSTI/UNESCO campus. A National Center for Translational Science is being planned in Pune, which will have three units that study different complex diseases and will emphasize stem cell and regenerative biology. Each unit will have ~20 translational faculty, an associated hospital, and a training program for MD/PhD students. In Kolkata, an Institute for Human Genetics and Medicine is in the proposal stage.

Biology also has come to the Indian Institutes of Technology. The IITs at Kanpur and Mumbai have started biotechnology departments, and several new IITs are being established, some of which are likely to have biotechnology/bioengineering departments. The Indian government also has launched five Indian Institutes for Science Education and Research (called IISERs), which are new campuses devoted to undergraduate/master's science education and research (Fig. 3; discussed later). Each IISER is expected to hire ~30 biology faculty, with additional physical science faculty working on problems that interface with biology. In addition, the Indian National Science Academy, New Delhi and Indian Academy of Sciences, Bangalore (2006) have recommended establishing 10 Universities as premier internationally recognized centers for research as well as higher education. Other proposals have called for the building of >1,000 new Universities (National Knowledge Commission [2006]).

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K. VIJAYRAGHAVAN is the Director of the National Center for Biological Sciences (NCBS) and a key figure in launching the new Stem Cell Institute in Bangalore. His group studies the wiring of nerves with muscles during development and how this results in specific locomotory behavior in *Drosophila*.

The pharmaceutical and biotechnology businesses also are likely to grow considerably in the coming decade. Big pharmaceutical companies already have a presence in India (e.g., AstraZeneca). However, with the increasing cost of drug discovery and the high cost/enrollment problems of clinical trials, it seems likely that US/European/Japanese pharmaceutical companies will eventually outsource more of their trials to India, which has many talented, English-speaking physicians. In addition, home-spun Indian drug discovery, genetic/bioinformatics, and bio-engineering companies have emerged in the last few years and entrepreneurship in biotechnology is likely to grow. Given the difficulty/expense in obtaining supplies and reagents from Western companies, there also is a clear niche for more Indian "Invitrogenes."

Even if all of the plans mentioned above do not come to fruition, the scope and output of the biological sciences in India is destined to increase considerably. But a substantial increase in output cannot be realized by just giving more support to its existing life science faculty. Rather, the future of Indian biology must be built by a new generation: junior faculty who will be recruited back to India from their studies abroad and, further down the road, by high school students who will become inspired to become scientists. In the next sections, we consider what it is like to be a faculty member or a student in India today, which provides a perspective of where scientific research and education in India will have to go in order to fill their new institutes with capable scientists.

Life as a Faculty Member

"When I was at Columbia, for instance, I could simply pick up the phone and have reagents instantly delivered to my bench. Here (in India), it can take up to four weeks depending on where the manufacturer is located."

—Satyajit Mayor (Nature, 2005)

Like the broader social structure of India itself, opportunities for research vary tremendously at different institutions within India. At the top end, faculty members at the Research Institutes possess, by and large, the necessary equipment to perform high quality research and have access to central staff that take care of needs such

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SATYAJIT MAYOR is the Dean of Research at the National Center for Biological Sciences (NCBS, Bangalore) who studies the properties of microdomains (e.g., lipid rafts) on plasma membranes and mechanisms of endocytosis.

as autoclaving and media preparation. The Internet and electricity mostly work (generators providing back-up during inevitable city outages). The faculty feel reasonably well supported financially. Individual grants are usually relatively modest, but the “pay line” is not highly competitive, so faculty spend less time writing for grant support than most US scientists. On the negative side, the reviewing process is often long, qualified reviewers are hard to find, and grant outcomes are generally not accompanied by critical feedback. Also, the time from grant review to receiving money can be long. (An overview of grants and granting agencies is provided in a review of Indian biology by Dhawan et al. [2005]). Institutes also provide faculty/graduate housing, crèche services, and low-cost cafeterias. Many Institutes have achieved a reasonable balance of female and male faculty (Table I; many in the range of 25–35% women faculty; for comparison, 17–25% of the life science faculty are women at UCSF and Harvard). However, as is true in the US as well, Indian women face greater challenges in their academic jobs and relatively few have risen to leadership positions (Bal, 2004).

Institute faculty cite several impediments in their professional work and personal lives. Many procedures that are relatively simple in the US/Europe can be slow and arduous in India. Waiting a month (indeed, sometimes up to four months) for a key reagent from an international vendor

in India is not unusual, the delay coming both from administrative paperwork (often very laborious in India) and shipping, if the item is not stocked in India. Because of such delays, reagents are sometimes purchased in anticipation of experiments that might never be performed. Reagents and equipment also are generally more expensive for Indian than US scientists. This can be particularly problematic, since Indian grants, which provide adequate support for salaries (much lower than the US/Europe), are often insufficient for purchasing equipment from foreign-based companies. Furthermore, after succeeding in purchasing an expensive instrument, company support/repair can be slow or inadequate, again delaying scientific progress. As one faculty with former training in the US stated, “When things proceed without a glitch, our research can go well. However, when there is a problem, then you know that you are in India.”

A second challenge cited by faculty is finding good people to perform research in their laboratories. Indian research is almost entirely performed by graduate students, since the vast majority of the better Indian PhD graduates go abroad for postdoctoral training and the influx of foreign postdocs is very limited (see Table I for numbers; for comparison, the University of California, San Francisco alone has ~1,100 postdoctoral fellows). Although Indian graduate students at the research Institutes are smart and hardworking, many are unprepared for research from their college undergraduate experience and often even after a master’s

degree. Without postdoctoral fellows and lack of adequate prior training, faculty must invest considerable effort in preparing/training new graduate students (especially challenging for junior faculty who do not yet have senior graduate students to help). But many faculty feel that the biggest problem is that the brightest students in India are simply not coming to graduate school. As one junior faculty said, “We are not getting the best students. We are losing at every stage. The brains are going elsewhere.”

A third, and perhaps greatest challenge is the lack of a critical mass of life science researchers in India. New Indian faculty members, who performed their postdoctoral training in well-established academic centers in the West, face a difficult transition of working in greater isolation without nearby collaborators and resources (e.g., mouse facilities, proteomics, genomics). As shown in Table I, most institutes are relatively small and the faculty work on very diverse topics, as a result of their bringing back different research problems from their postdoctoral studies in the US and Europe. Many faculty also feel removed from the rest of the world, due to the great travel distances and costs; some faculty feel that their research does not receive proper recognition because of infrequent opportunities to present their work at international meetings. However, more international collaborations are beginning to take place, being facilitated by organizations like the Wellcome Trust (discussed later), and the critical mass situation will improve.

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At the Tata Institute for Fundamental Research (TIFR, Mumbai) Dept. of Biological Sciences, **VERONICA RODRIGUES** (Professor, left) studies how sensory neurons form and make connections in the *Drosophila* olfactory nervous system. **SHUBHA TOLE** (Associate Professor, right) is studying the role of transcription factors in the development of the mouse cortex and amygdala.



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RAJENDRA PRASAD is a Professor and ex-Dean of the School of Life Sciences at Jawaharlal Nehru University (JNU) who studies multi-drug resistance in pathogenic fungi.

Being a science faculty member at a University is even more challenging than at a research Institute. Even at the very top Central Universities, a typical start-up package is \$4–10,000 compared with \$150,000 at a nearby research Institute (although reasonable core facilities are available for young investigators at some Universities). Most Universities also lack or have minimal internal discretionary research funds that many research Institutes possess. Isolation becomes more of a concern, since even the best University faculty generally only have sufficient funds to attend an international meeting once every 2–3 years. At many State-run Universities, faculty also must combat crumbling infrastructure, such as lack of reliable electricity, Internet, and running water. University faculty typically teach 15 hours per week and have many administrative duties. Since there is insufficient incentive/reward for mounting a successful research program on top of the mandatory teaching/administrative duties, most faculty either do not perform research or settle for a nonambitious research program (10–25% of University professors hold a grant). As one faculty said, “There is no recognition for my research in the University system.” University-driven research also has been steadily getting worse, as Universities find themselves at a disadvantage in recruiting new faculty, since most good postdoctoral fellows are eyeing positions at research Institutes. However, despite many of these difficulties, there are many examples of remarkable University faculty who have retained their passion for

research and have developed successful laboratories. The Indian government also recognizes the profound need to reverse the current slump of University research.

The salary and promotion systems for faculty (at both Institutes and Universities) also lack strong incentives for performance. In the Universities, faculty have secure positions from hiring until retirement. In the research Institutes, formal evaluation takes place within the first 5 years, but few have been denied tenure (only single instances at NII and NCBS in the past 21 and 16 years, respectively). Frustrating to many hard-working faculty, promotions and salary increases tend to be driven by years of service, and scientists are often evaluated by the same procedures as administrative and support staff.

Faculty salaries also are generally lower (perhaps 2–5 times) compared with jobs in the private sector. At the time of writing this article, a junior faculty might earn \$8,500/year and a senior faculty approximately double that (salaries are slightly higher at research Institutes than state Universities but marginally so). A competitive Ramalingaswami fellowship or a Wellcome Trust grant for a junior faculty, however, would double their salary. While these salaries allow a decent standard of living in University- or Institute-sponsored housing, it is difficult if not impossible for new faculty (without a spouse working in industry) to buy or even rent modern condominiums/homes in cities such as Bangalore, Mumbai, and New Delhi. We note, however, that a considerable faculty salary increase (~50%) is working its way through an approval process in the Central government. While likely falling short of catching up with the rapidly rising costs of living in the major urban cities, this measure should improve the situation for faculty considerably.

Being a Student in India

“When I was young, money was not that important. The current India is about making money.”

—senior faculty member

Education in science and math in India is excellent from elementary to high school, perhaps taught at a higher level than in the US. The Central government sponsors outstanding public schools (Kendriya

Vidyalaya, “central school”) for the best students. Good private schools abound; they encompass a wide range of admission fees, making many of these schools more affordable to the middle class than is true in the US. During our stay in India, we witnessed impressive elementary school science fairs and interacted with very scientifically astute high school students. Much of the instruction focuses on performing well for exams rather than emphasizing curiosity and scientific inquiry, but the same criticism can be levied against US K–12 education. Educated people in India also are generally interested in science and technology. As an example, a traveling science exhibit (the Science Express) sponsored by the German government drew large crowds in Bangalore, with families waiting up to several hours in line to gain admission.

With such a strong early educational system and a large population base, why has it been so difficult for India to populate its biology institutions with the very top investigators in the world? The answer is that the pipeline from student to faculty investigator has many leaks (see also article by Desiraju [2008]). The first and perhaps greatest leak in the pipeline occurs during high school, the turning point taking place in the 11th and 12th grades (ages 16–18). At this time, the academically strongest students are directed to careers in medicine and engineering by their families and teachers, and, in many cases, are actively discouraged from pursuing

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scientific research. The deciding factor is money. Young people are assaulted daily with symbols of India's emerging middle and upper class wealth—advertisements of luxury condominiums, fashionable shopping malls, new automobiles, friends telling of vacations abroad. Young people and their families want to be part of this new economic prosperity, and the surest path for a bright student to achieve a comfortable life style is to enter the medical profession or obtain a job in the engineering or IT sectors. As a result, entrance to the IITs and medical colleges is fiercely competitive. Study of the pure sciences is usually a second choice, if one does not gain admission to these training schools. As one young (and successful) biology faculty member said somewhat tongue-in-cheek, "We are all failures in the college exam system." This problem also is true in the US and elsewhere, although it is more exaggerated in present day India.

Given the large population (and inherent inaccuracies of large-scale entrance exams), there are still many very bright students who pursue undergraduate biology degrees (three year). Here, another opportunity is missed to entice and train students for careers in the sciences, since college biology teachers have little, if any, experience in scientific research. As a result, college undergraduates learn facts from textbooks and do not understand the excitement of research and are not taught the latest scientific developments (see also discussion of this issue by Sur [2005]). Being physically separated from research Institutes and Universities, college students also are not exposed to the leading scientists in India. The separation of teaching and research contrasts the situation at top US universities, where undergraduates are taught by and can do research internships with the best scientists in the world. As one Indian University faculty stated, "Colleges have become mass teaching shops. How can you train students if you yourself do not do good research? They need to be exposed to role models of scientists who are excited about their work."

A growing and increasingly popular track in colleges is a BSc Biotechnology degree, but sadly, most graduating students are ill prepared for jobs in the biotechnology industry or for graduate-level education (a default for many who cannot

find a job). Many colleges have started to encourage or require their students to obtain research internships, but most provide little help in facilitating these arrangements (a few good exceptions exist, however, such as programs run by IIT, Kanpur and the Vellore Institute of Technology, a private college). As a result of inadequate college education/training, many students take private commercial courses in running electrophoretic gels, basic DNA cloning, etc., in the hope of being better positioned to obtain a job in industry.

Following college, the most highly motivated students seek graduate degrees in the US/Europe or at one of the Indian research Institutes. However, given the shortcomings of the three-year college training discussed earlier, students are usually not competitive for admission to a PhD program immediately. Thus, many students often pursue a two-year master's degree before applying for a PhD program overseas or within India. For students who wish to apply to an integrated master's/PhD program at a top research Institute, many students first pursue a one-year "Junior Research Fellowship" (JRF), a paid research apprenticeship. Admission to the best master's or PhD training programs in India is competitive. Students take one or more national exams, the results of which determine whether they will receive a post-graduate fellowship that will make them also more attractive for admission to an Institute or top University. Approximately

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100,000 students sit exams for 4,000 scholarships in the life sciences through various funding mechanisms. Many research institutes also impose their own exam and interviews. At NCBS, 5,000 students take an NCBS-specific written exam. Based upon these results, 500 students are invited to submit full applications and 200 are interviewed for 20–25 slots. The training period for a PhD is 5–6 years at research Institutes (following a 2-year master's), thus representing a relatively long training program. An integrated master's/PhD program offered at several Institutes typically shortens the total training time by a year.

Students who fail to achieve high marks in the national or institute exam or are geographically constrained might enroll in a University to obtain a master's and then a PhD (the Central Universities being more prestigious than State Universities). The time to achieve a PhD at a State University might be ~4 years, generally less than at a research Institute. The majority of State University master's or PhD students hope to find jobs in industry or as teachers. As one University faculty member stated, "If we do not provide job placement for students, there is no way to motivate them."

A third leak in the pipeline occurs at postdoctoral training. Virtually all good Indian graduate students seek postdoctoral training in the US or Europe. Many students see a foreign postdoc as a first step in obtaining a permanent job overseas, but obtaining a good academic faculty position

Highlights from Indian Life Sciences in 2008

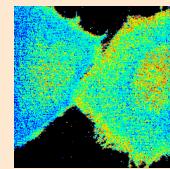


Chopra, T., Banerjee, S., Gupta, S., Yadav, G., Anand, S., Surolia, A., Roy, R. P., Mohanty, D., and Gohkale, R. S. 2008. Novel intermolecular iterative mechanism for biosynthesis of mycokeptide catalyzed by a bimodular polyketide synthase. *PLoS Biol.* 6:1584–1598.

The pathogen *Mycobacterium tuberculosis* uses polyketide synthase enzymes to produce complex lipids that are essential to its virulence. This study uncovered a novel mechanism for catalysis, which they term “modular iterative biosynthesis” (previously not discovered for polyketide synthases). The results have implications for engineering polyketide synthases to produce novel metabolites and in drug discovery for tuberculosis.

Goswami, D., K.S. Gowrishankar, S. Bilgrami, S. Ghosh, R. Raghupathy, R. Chadda, R. Vishwakarma, M. Rao, and S. Mayor. 2008. Nanoclusters of GPI-anchored proteins are formed by cortical actin-driven activity. *Cell.* 135:1085–1097.

Several years ago, the Mayor laboratory developed a novel microscopy method (homo-FRET) that can detect the clustering of a few proteins in the plasma membrane, thereby providing an important tool in understanding membrane organization and lipid rafts. In this study, the authors show that a dynamic cortical actin network is needed to form nanoscale clusters of GPI-anchored proteins. This work provides a new perspective on how actin can contribute to membrane organization, revealing that actin can actively drive membrane protein clustering and does not just act by forming “static corrals.”



Khan, A.G., M. Thattai, and U.S. Bhalla. 2008. Odor representations in the rat olfactory bulb change smoothly with morphing stimuli. *Neuron.* 57:571–585.

This paper addresses the question of how the mammalian central nervous system decodes combinations of odors. This experimental and theoretical study examines how the output neurons of the rat olfactory bulb (mitral/tufted cells) respond to varying the mixture of a pair of odorants. Their data are inconsistent with an “attractor network” model, which is widely used to describe many neural networks. Rather, their results are best explained by a model in which the inputs of different odorants act additively upon the mitral/tufted cell.

Mangale, V.S., K.E. Hirokawa, P.R.V. Satyaki, N. Gokulchandran, S. Chikire, L. Subramanian, A.S. Shetty, B. Martynoga, J. Paul, M.V. Mai, et al. 2008. Lhx2 selector activity specifies cortical identity and suppresses hippocampal organizer fate. *Science.* 319:304–309.

This paper reports a key finding on how the hippocampus, a critical structure in the brain for learning and memory, is formed during development. A region of the cortex called the “hem” was previously proposed to induce hippocampus formation. By using genetic tricks to control a key homeobox protein called Lhx2, the authors were able to produce multiple hems in the cortex, each of which was found to be capable of inducing the formation of ectopic hippocampal tissue. This study clearly defines the role of Lhx2 in specifying cortical cells to adopt a “hem fate” as well as the hem’s role as an organizer of the hippocampus.



Ravi, M., M.P.A. Marimuthu, and I. Siddiqi. 2008. Gamete formation without meiosis in *Arabidopsis*. *Nature.* 451:1121–1124.

Certain native plants can produce seeds without undergoing genetic shuffling that normally occurs during meiosis, resulting in offspring that are identical clones of their mother. This process of clonal reproduction (termed apomixis) could be advantageous for plant breeders who wish to fix a collection of desirable traits in crops. In this study, the authors have found that mutation of a gene called dyad (which encodes a protein involved in controlling chromosome organization during meiosis) enables the normally sexually reproducing plant *Arabidopsis* to undergo an apomixis-like development. The study opens up the possibility of engineering a more efficient apomixis process into crop plants in the future. **JCB**

within India also requires international training. A second reason for the exodus is that postdoctoral salaries in India (~\$5,000/year) have been only nominally higher than that of a graduate student. Thus, postdoctoral work abroad is economically as well as scientifically attractive. However, postdoctoral salaries will be increased by nearly twofold in the near future, which will make it more attractive for many to pursue postdoctoral training in India.

Changes on the Horizon

“We should not be in a rush to hire faculty. We must seek out the brightest and the most competent.”

—Obaid Siddiqi, NCBS

India’s biomedical enterprise is poised at a critical juncture. As discussed above, scientists in India have and still face many more challenges than investigators in the

US and Europe. However, interesting biological research is emerging from India (for recent examples, see above “Highlights from Indian Life Sciences in 2008”). Furthermore, new initiatives being set in motion will make it more attractive to pursue scientific careers in India. Below, we briefly discuss some of these new programs and possible developments that might occur in the coming decade.

Bringing Research to College Undergraduates

Improving the educational pipeline for attracting and training students to become life science researchers is essential. No single measure will suffice. The physical separation of undergraduate Colleges from research Institutes and Universities stands out as a particular weakness in the educational system (Fig. 1). However, an important new educational initiative has

been established in the form of the Indian Institutes of Science Education and Research (known by the acronym IISER), which have been or are being established in five cities (Fig. 3). The IISERs are five-year combined bachelor’s/master’s programs for training in science education and research, admitting a relatively small, select class (targeted at ~150 students per year when the IISERs are in full operation). In their first two years, students are exposed to an integrated curriculum in physics, chemistry, math, biology, history of science, and science writing, thus requiring collaborative teaching and curriculum development between faculty in different departments. The third and fourth years are devoted to specialized didactic and laboratory training, and year five consists of a research thesis. Importantly, the faculty who are joining the IISERs are establishing internationally

competitive research programs and will train undergraduates to perform research in their laboratories. While the IISERs will not provide an education in the humanities, they have the potential to train students broadly within the sciences and produce graduates who will be competitive for admission to PhD programs or to obtain jobs in industry.

While the IISERs represent an important educational advance, other programs are needed for talented undergraduates at the numerous Indian Colleges that lack on-site research. Consolidation of some Colleges into new or existing University campuses might be one route. Active partnerships between the research Institutes and Colleges represent another avenue for exposing undergraduates to active scientists and modern research. The numerous commitments of Institute faculty may preclude more than an occasional lecture or sponsoring a student in their laboratories. However, Institute graduate students (perhaps with a small financial incentive) could partner with willing College teachers, allowing graduate students to offer their knowledge of research but also gain a valuable teaching experience.

Reversing the Brain Drain: Bringing Talent Back to India

India's greatest challenge in the coming decade will be to recruit talented scientists to the many life science Assistant Professor faculty positions that are becoming available and to establish an active postdoctoral training program and culture within India. A recently announced \$120 million/five-year training program

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jointly sponsored by the Wellcome Trust (Great Britain) and the Department of Biotechnology (India) represents an important step forward in stimulating a career path for both postdoctoral fellows and junior faculty in the life sciences. The Wellcome Trust/DBT India Alliance announced generous four-year postdoctoral fellowships (up to 40 per year, starting in 2009), which will allow Indians to pursue foreign postdoctoral training but require that at least one fellowship year be spent in an Indian laboratory. This interesting program allows for valuable international training, but also cements a strong connection and possible international collaboration with an Indian laboratory. The India Alliance also will support 20 five-year fellowships for senior postdocs, providing transition funds that will allow them to start laboratories in India. Finally, the India Alliance will fund 10 renewable grants per year for young investigators who have already started laboratories in India, providing them with salary, research, and travel support. These grants should make a substantial difference for stimulating young scientists to return to and be successful in India.

In addition to new funding mechanisms, India must improve its recruiting process and mentoring of young faculty. In the past, Indian Institutes and Universities had a significant amount of in-breeding, with former students returning to their prior establishments as faculty members, in sometimes less than fully open searches.

While this practice is diminishing, Institutes/Universities must continue to improve their searching/hiring strategies to bring in the best candidates. In addition, newly hired faculty must learn the necessary skills to become successful, such as choosing good research problems and managing their laboratories. As a step toward helping young scientists, a "Young Investigator" meeting is taking place in February, 2009, which will bring together 40 junior faculty from throughout India and 20 Indian postdoctoral fellows (mostly working overseas) to meet each other as well as meet and obtain advice from well-established senior Indian scientists, directors of Indian and international funding agencies, Indian biotechnology entrepreneurs, and nine well-known international scientists. This meeting, which may become an annual or biannual event, could serve as a model for recruiting and assisting junior scientists in other countries.

Involving Senior Scientists in the Development of Indian Biology

China and Singapore, by providing very substantial financial resources, have been successful in attracting well-known senior scientists from the US/Europe to set up laboratories in their countries. Such a model is less likely to work in India, as Institutes/Universities tend to operate more by equality rather than by setting up a few individuals with much greater salaries and laboratory resources than their colleagues. However, a growing number of senior international scientists are becoming actively involved in the Indian life sciences, through collaborations and scientific advisory boards. In addition, an interesting new program (with modest financial incentives) will seek senior international scientists who are interested in spending a minimum of two months per year in India to run a small laboratory.

Instead of relying upon foreign recruitment, India must look to its own mid-level and senior scientists to invest their time in leadership positions, especially as new institutes and programs are being launched. However, this is easier said than done, since many of the very best senior scientists are working hard to run their laboratories and maintain/improve their international standing in research. Perhaps some type of incentive might entice India's best researchers to invest more of their time in the "big picture" of building science in India.



Fig. 3. An architectural drawing of the future Indian Institute of Science Education and Research (IISER) in Pune (state of Maharashtra). The current IISER at Pune is housed in a modern and well-outfitted rental building near the future campus. IISERs offer a science education and research training curriculum as a five-year combined bachelor's/master's program.

New Institutes vs. Improving Existing Institutes and Universities

Perhaps the greatest juggling act for the Indian government will be balancing its investment in starting new life science Institutes versus improving the infrastructure and culture of its older Universities and Institutes. Starting new Institutes has advantages, since its members are freed from the inertia of a preexisting faculty/administration. Indeed, many of the premier life science research centers in India were built on new land, rather than from within the confines of existing Universities/Institutes (see Table I). As discussed earlier, building of new Institutes is likely to continue and indeed accelerate in the coming decade. However, the Indian government and its advisory panels realize that leaving behind its Universities will ultimately have disastrous consequences on science and education. However, the path is not simple. There are many Universities that need saving and recommendations have called for the building of many more Universities to educate and prepare Indians for jobs in the 21st century (National Knowledge Commission [2006]). A recommendation by the Indian National Science Academy (New Delhi) and Indian Academy of Sciences (Bangalore) (2006) was to upgrade ten Universities in India to high international standards in research as well as education and promote the development of one University in each Indian State to the caliber of a Central University. These will be important steps in improving the status of Universities and increasing their role in India's research enterprise.

Identifying and Supporting the Best Investigators and Teachers in India

Funding outstanding individuals, rather than institutions or departments, has been a very successful strategy for the Howard Hughes Medical Institute, the NIH (especially the new Pioneer Awards), and the Wellcome Trust. The new Wellcome Trust/DBT India Alliance described earlier is a positive step in this direction. However, India needs to put more programs in place to recognize and provide incentives for its scientists and teachers at all levels of the research/education system. Some type of

"Pioneer Award" could be used to reward the top scientists in the country. However, programs also are needed to reward researchers at Central and State Universities, who are performing at their best, given their level of support. Similarly, University and College faculty who demonstrate both excellence and extraordinary passion for teaching deserve national and/or state recognition as well as financial rewards. Such efforts can boost moral and foster improvement, even if large-scale improvements in infrastructure are not possible or slow in coming. Most importantly, recognition/reward systems must be seen as being fair and apolitical, thus requiring careful national and perhaps even international peer review.

Philanthropy and the Life Sciences

Science in the US and Europe has benefited enormously from philanthropy. In the life sciences, charitable foundations have impacted research and education (e.g., Howard Hughes Medical Institute, the Wellcome Trust, the Gates Foundation), junior faculty development (e.g., the Pew, Searle, and Burroughs Wellcome awards), postdoctoral training (e.g., Damon Runyon and Jane Coffin Child), and disease-oriented research (e.g., American Cancer Society, March of Dimes). We discussed earlier how the Wellcome Trust is promoting postdoctoral fellows and faculty in India. In contrast, Indian-based philanthropy or private sector funding of academic biomedical research is strik-

ingly absent or minimal at best. This was not the case historically. Mahendral Sircar garnered donations to start the Indian Association for the Cultivation of Science in the late 19th century; in the early 20th century, the industrialist Jamsetji Nusserwanji Tata founded the Indian Institute of Science and Acharya Jagadish Chandra Bose founded the Bose Institute. Later in 20th century, the Tata family helped to launch the Tata Institute of Fundamental Research (TIFR).

India's earlier philanthropists realized that research and innovation are an important part of a nation's identity. Even with India's many pressing social needs, philanthropy also needs to be directed toward India's research efforts. Yet, contemporary India, with more private wealth than ever, has surprisingly little philanthropy directed toward basic science. If such philanthropy were to surface, it could transform Indian biology, as it has elsewhere. Being less constrained, a private foundation (either as a stand-alone institute or as a granting agency) could operate using a different organizational system from government Universities/Institutes, provide new incentives to scientists, and take on different scientific challenges. 21st century billionaires will hopefully eventually realize the lasting impact that they could make on the Indian sciences, just as the Rockefellers are credited for in early days of American science and the Tata family has done in India.

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Conclusions

India is beginning its third epoch of “nation building” in the life sciences—the first being the construction of educational institutions at the inception of an independent India in the 1950s, the second being the launch of research Institutes devoted to modern biology in the 1980s, and now the investment to build a research/biotechnology enterprise that can compete internationally. Like many developing countries that are reevaluating their roles the 21st century, India is no longer content to be an “outsourcing center” for the West.

Without doubt, life science research in India will change dramatically by 2030, but what will it look like? Indians themselves debate the outcome, some being optimistic and others pessimistically projecting that India cannot rise above mediocrity in the life sciences. While pointing out weaknesses in this article, we stand on the side of optimism. The critical mass in biology will certainly increase, conditions for conducting research will improve, the life sciences will assume a more equal stature to physics, and even the launching of a few new programs for life science faculty will make a world of difference. But India’s success will not be measured solely by the money that it invests, the number of life scientists that it employs, and the number of papers that it publishes. It also must take advantage of this unique period of

growth to find opportunities for innovation. Will India try new experiments in academic research/biotechnology or continue to adopt Western models? Will India develop closer collaborations between biology and its extensive physical science enterprise (something that has been lacking in the past)? Will it formulate new models for translational research involving a strong connection between research institutes and medical centers (underdeveloped at present)? Will it develop a new culture for collaborations between academic centers and industry (currently minimal in the life sciences)? And will it tackle biological questions and diseases that are understudied in the West (particularly those that affect India)? While developing basic infrastructure for research and education is still of paramount concern, India also must think about these grander challenges. However, interesting new initiatives are sprouting in India, an example being a recently launched “Open Source drug discovery model” for tuberculosis. This initiative, launched by the Council for Scientific and Industrial Research (CSIR), will promote collaboration and open access/Internet sharing of data from drug screening, bioinformatics, and early-phase clinical trials.

One must keep in mind how far the life sciences in India have come in the past three decades. Many scientists have demonstrated their determination, resourcefulness, and intellect under less than optimal circumstances for scientific research. Thus, India’s journey in biology has involved courage and initiative as well as increased funding. Now, India must look to a new generation of pioneers—a successful postdoctoral fellow who turns down a job at Harvard to take a faculty position in India; a senior scientist who invests time to teach undergraduates, mentor young faculty members, or assume an important administrative responsibility and not just focus on his/her own research; a bright high school student who turns down an IIT to train in biological research at an IISER; a graduate student who takes time off from his/her thesis work to teach college undergraduates; or an American or European who comes to an Indian laboratory for their postdoctoral training. India’s future biology enterprise shall be built, brick by brick, from such rewarding individual success stories. **JCB**

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SAMIR BRAHMACHARI is the Director General of the Council of Scientific and Industrial Research (CSIR), an important research/development funding agency of the Central government (CCMB, CDRI, IICB, and IGIB [Table I] are operated by CSIR). Dr. Brahmachari developed the Open Source drug discovery initiative described in the article.