S. Ranganathan: an organic chemist and an artist by nature

N. Sathyamurthy

Professor Subramanian Ranganathan, affectionately called Ranga, is an organic chemist extraordinary, an artist by nature, who sees art in organic synthesis, art in biosynthesis and art in everything around him. As a modeller, Ranga specializes in origami and can make out of paper a flying bird, a flying horse, a jumping frog, a double-helical DNA and a buckyball with equal ease. A forerunner of bioorganic chemistry in the country, he continues to solve challenging problems in organic chemistry and bioorganic chemistry, trying to understand how silica (the insoluble sand) gets solubilized in nature and yet gets crystallized in rice husk, for example. A scientist with a human touch, Ranga is known to not only train his students, but also launch them into their careers. He is a passionate teacher, who is ready to explain almost anything, with a twinkle in his eyes!

I still remember vividly Ranga standing with a pipe in his mouth in platform no. 1 in Kanpur railway station at 6 am on 5 July 1978 to receive me, a new faculty member and my wife Suguna. That was the beginning of our relationship with Ranganathan. Soon after we reached the Indian Institute of Technology Kanpur (IITK) campus, we were taken to the department, where we were given a cup of tea that was the trademark of the Ranganathans – Darshan and Ranga. Anybody who came to their lab was invariably given a cup of tea and often some goodies to go with it. Our first meal at IITK was with the Ranganathans and when they found out that Suguna was not well, they helped us move into a temporary accommodation and made sure that we were taken care of. We were advised to buy a ladies bicycle, which Suguna and I ride till this date, copying the Ranganathans! When Suguna was expecting our first daughter Aruna, the Ranganathans were there to provide full support – moral and physical. They would often invite us to their house for dinner and they were at home in our place too. They mentored us all the way until Darshan breathed her last. It is difficult to think of Ranga without Darshan, but he had to learn to cope with life without her.

Ranga, born in 1934, received his B Sc and M Sc (research) degrees from Madras University. As a student of S. Swaminathan, he worked on indoles which led to *inter alia N*-iso tryptophan and other novel systems. He had a brief stint at the Central Leather Research Institute, Madras (now Chennai), working under the supervision of Y. Nayudamma. He explored the mechanism of vegetable tannins that cross link the collagen of skin to hide, resulting in several publications. Ranga went on to do his Ph D under the guidance of Harold Schechter in the Ohio State University, USA, where he explored several aspects of the nitro group. As a postdoctoral fellow in the research group of R. B. Woodward (1962–1964), Ranga developed the isoxazole route to vitamin B_{12}, where the entire synthetic plan was pledged on the last step involving a stereochemically predicted *trans* cyclization of a triene. In the event, the reaction took an exactly opposite course (*cis* cyclization)! The perturbation cost by this disaster led fortunately to the development of the now famous Woodward–Hoffmann rules bringing in the principle of quantum chemistry to the domain of organic chemistry. From 1964 to 1966, Ranga continued to be with Woodward at the Woodward Research Institute (WRI), Basel, Switzerland, where he was instrumental in accomplishing the reaction cascade that transformed the protected cystine nucleus to that of Cephalosporin C in a single step (Figure 1). He went along with Woodward to Stockholm, where the latter received the Nobel Prize in Chemistry in 1965 and the Nobel lecture[1] focused on the synthesis of Cephalosporin C (ref. 2).

Figure 1. Ranga at Woodward Research Institute, Basel.

Ranga started his independent academic career at IITK in 1966, where he rose to the rank of a Professor and served as the Head of the Department of Chemistry and Professor-in-charge, Faculty Affairs. Those were difficult days. There was hardly any infrastructure and funds were limited. Ranga wrote his first book, *Fascinating Problems in Organic Reaction Mechanisms*[3]. It was an unusual book that showcased the challenges in organic synthesis over three decades preceding the publication. The book received rave reviews in international journals. It was followed by the books, *Challenging Problems in Organic Reaction Mechanisms*[4] and *Further Challenging Problems in Organic Reaction Mechanisms*', both of them co-authored by Darshan Ranganathan. It was difficult to get journals and keep up with the literature those days. The couple published *Current Organic Chemistry Highlights*, a newsletter that was produced the hard way by typing, cyclostyling (before the xerox machines appeared in the market), stapling and mailing it month after month without fail for eight years (1971–1979)! The chemical structures were drawn by hand by Darshan. It was clearly a labour of love.

Ranga had met Darshan for the first time for a few minutes on the sidelines of the Indo-Soviet symposium on natural products at Delhi in early 1971. Few months later, he wrote her an Inland letter which concluded after all the banalities with the postscript: 'If you are not married, will you marry me?' To Ranga's delight, the offer was accepted and they were married on 4 June 1971.

Darshan resigned from her job in Delhi University and started working on her own problems in Ranga's lab. Ranga and Darshan were made for each other (Figure 2). They were so much involved in their work that Darshan left her newborn with her mother. The boy Anand would come to live with the parents only when he entered class six! The couple was inseparable. They would ride a

bicycle together to work and live in the lab until they had to go home to sleep for the night. Ranga always arrived in the lab at 7:30 am, day after day. There were no holidays for him or his wife or his students. His son Anand, literally, grew up in the lab. One of Anand's early accomplishments was to memorize the periodic table and recite in front of many of us.

Darshan was not formally a faculty member at IITK, but she worked in Ranga's lab by taking up the position of a Research Associate or a UGC Scientist, working on her own problems. Later she took up the position of an independent scientist in the Regional Research Laboratory (now, called CSIR-NIIST), Thiruvananthapuram. Ranga decided to move with Darshan, initially as a Visiting Scientist to the same lab. Subsequently, both of them moved to the Regional Research Laboratory (now called CSIR-IICT), Hyderabad. While Darshan published on her own profusely in the area of supramolecular chemistry, Ranga chartered his own path.

The dream like Darshan–Ranga combination was shattered with the passing away of Darshan on 4 June 2001 (Darshan was born on 4 June 1941). As a tribute to Darshan's genius, Ranga edited and published a book entitled *Patterns for Supramolecular Design*[6], wrote the INSA Memoirs on Darshan[7] and contributed a chapter in her honour in the book *Leelavathi's Daughters*[8]. He established endowment lectures in her name in The Andhra Pradesh Academy of Sciences, Hyderabad, the Chemical Research Society of India, Bangalore, and the Indian National Science Academy, New Delhi. At this critical stage, Ranga's very survival was of concern. K. V. Raghavan, Director, IICT and his wife Chandrika constantly visited him. Raghavan found for Ranga a place to stay and asked him to take over the guidance of all of Darshn's students so that he would remain preoccupied. The subsequent Directors J. S. Yadav and Lakshmi Kantam have continued to support Ranga during his trials and tribulations.

Figure 2. Ranga and Darshan with items of art behind them in their office.

Ranga started guiding Ph D students at IITK and he continues to do so at IICT Hyderabad. The list of Ph D students guided by him is given in Box 1. Ranga did not believe in routine synthesis. He had participated in the synthesis of vitamin B_{12}. So, he knew the challenges in organic synthesis. He also knew the importance of biochemistry. He was perhaps the first organic chemist in India to start working at the interface of chemistry and biology. He undertook the synthesis of prostaglandins starting from castor oil and started working on peptides before many others in the country. He suggested challenging problems to his students and guided them *en route*. Often, the expected results were not achieved, but he spent time in understanding why the reactions did not succeed. Soon after I joined IITK, my wife and I were invited for dinner to his house. The dinner was followed by a long discussion on symmetry allowed reactions that were not taking place. I had to learn Woodward–Hoffmann rules and thermodynamic and kinetic stability to make sense out of what he was saying. My participation in the discussions was acknowledged in his paper dedicated to Woodward[9].

Box 1. List of Ph D students guided by Ranganathan

B. B. Singh (1969), H. Raman (1971), C. S. Panda (1972), S. K. Kar (1973), A. K. Mehrotra (1975), M. M. Mehrotra (1978), C. B. Rao (1980), Raaj Kumar (1981), V. Maniktala (1982), P. V. Ramachandran (1983), K. Keshavan (1983), S. Bamezai (1984), F. Farooqi (1985), S. K. Singh (1987), S. Mehrotra (1987), G. P. Singh (1988), W. P. Singh (1988), D. Bhattacharya (1988), R. C. Rathi (1989), N. Jayaraman (1993), N. K. Vaish (1993), B. K. Patel (1993), N. Tamilarasu (1994), K. S. George (1994), D. Kundu (1994), K. M. Muraleedharan (2000), C. Lakshmi (2001), M. P. Samant (2002), M. Gopi Kumar (2002), Ch. C. Rao (2002), P. Venkateshwarlu (2008), Y. B. R. D. Rajesh (2008) and S. M. Babu (2008).

Ranga has explored over 15 domains of carbon science ranging from organic chemistry, bio-organic chemistry, inorganic chemistry, bio-inorganic chemistry, DNA recognition, protein engineering, crystal engineering and chemical topology. Early on, his work on prostaglandins suggested possibilities in 'natural products engineering' that led to the transformation of readily available castor oil to PGF1, insect pheromones and a range of synthons. He explored a new dimension related to Woodward–Hoffmann rules, providing a link of these reactions with the energy of the transition state. He discovered several reactions, notable amongst which was the one-step transformation of the hydrophobic trindane to complex highly oxygenated structures having several chiral centres and with the potential as drug targets. He made novel contributions in the domain of protein evolution, the origin of the genetic code, and theoretical and experimental studies of peptide bond formation. He contributed greatly to the area of protein engineering and discovered a selective method for peptidation using reverse micellar systems. Ranga proved why amongst the coded amino acids, only lysine is four $-CH_2-$ groups away from the peptide backbone. He discovered a method for proteins to pick up Cu^{2+} ions by the attachment of a suitable linker. In collaboration with Balasubramanian, he found that in ageing cataract, the tyrosine group gets partially racemized. He showed that chemical mimicking of enzyme reactions is possible. For the first time, along with his student Jayaraman, he synthesized a minimalistic zinc-finger module, incorporating the thiol–disulphide exchange strategy, and extensively studied its interaction with calf thymus DNA.

With benzene hexacarboxylic acid (mellitic acid) as the anchor and in collaboration with the famous crystallographer, Isabella Karle, he explored extensively in the domain of crystal engineering leading to synthesis of mesoporous materials, composites having magnetic properties and supramolecular arrays.

There is a pressing need to solubilize sand (silica), not only to make its use environmentally compatible but also to

enhance the availability of silica to the soil, a substance essential for the growth of many plant species like rice, maize, sugarcane and several others. A decade of work by Ranga and his group has revealed a novel way to enhance the solubilization of silica through a shifting of the equilibrium $SiO_2 + 2\ H_2O = Si(OH)_4$ by capturing silicic acid in a carrier-mediated network of hydrogen bonds (Figure 3). Detailed studies have shown that the enhancement of silica in soil vastly reduces the biotic and aboitic stress in the rice plant. Ranga has found that silicic acid in tetrahydrofuran in the presence of carrier molecules can deposit silica in fractal forms (Figure 4).

What was remarkable about Ranga was that he never complained about the lack of facilities at IITK. On the days when there was no electricity, he would be sitting outside the lab in the corridor, reading something and writing something. He and Darshan would go to the Central Drug Research Institute, Lucknow to get NMR and mass spectra of compounds recorded. 'Beg, borrow or steal' was the *modus operandi* and the purpose was to do research, an outstanding one in that. The couple would spend summer months in IICT and CCMB in Hyderabad, collaborating with other organic chemists and biologists. The result is there for all to see.

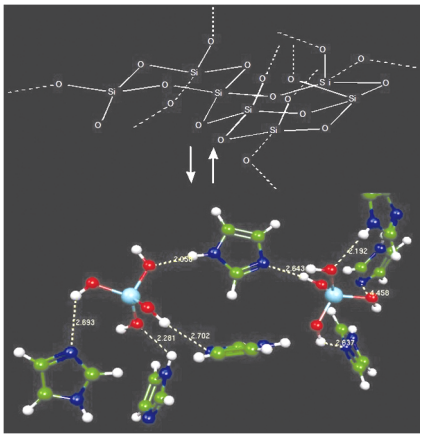

Figure 3. Solubilization of silica: an energy minimized profile of the imidazole centred H-bonded network with embedded $Si(OH)_4$.

Figure 4. Fractal formation of silicic acid in aqueous tetrahydrofuran medium: an SEM image of the imidazole initiated fractal structure of silica.

Study of science, along with an appreciation of beauty in science became a way of life for Ranga. It appears that Woodward was the role model for Ranga, who remained a passionate teacher and a researcher, who combined art with organic synthesis. His love for 'art in organic synthesis' was reflected in his book co-authored by Anand and Bindra[10]. The second edition of the book was published nearly two decades later[11]. The Ranganathans published a book on *Art in Biosynthesis* as well[12].

Ranga's research contributions have been duly recognized by his peers. He has received a large number of awards and honours. He received the prestigious Bhatnagar Prize in Chemical Sciences for the year 1977 from the Council of Scientific and Industrial Research, New Delhi. He is a Fellow of all the three Science Academies in India. He received the Silver Medal from the Chemical Research Society of India in 2000 and the Lifetime Achievement Award in 2006. He has been an Honorary Professor of the Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore since 1998. He continues to work as a Distinguished Scientist in IICT, Hyderabad.

Ranganathan was a passionate teacher, with a sense of humour. His cleaning of the blackboard and drawing structures meticulously, starting at one end of the blackboard and finishing at the other by the end of the hour is legendary. He did not believe in the usual one hour tests. He would give open book exams and let the students work on them as long as they wished. He was never in a hurry and yet, at the end of the semester, he would have covered the subject as expected.

He taught several courses, starting from the general chemistry to frontiers in biology at IITK. Along with Balasubramanian, he taught a course on biochemistry and biophysics. He has authored/co-authored several books as mentioned earlier.

Ranga travelled around the country giving seminars on his research and also giving lectures of pedagogical interest. He always carried models, be it ball and stick molecular models or the double-helical structure of DNA. Mischievously, he would illustrate the double-helical structure by superposing it on the figurine of Yakshi from Bhopal (Figure 5). He would go on to discuss the major groove and the minor groove as well!

Ranga was keen to popularize chemistry. For a while, he travelled around giving chemical demonstrations, ably assisted by his son Anand. He was always fond of talking to children and enthusing them to pursue science. One of his demonstrations of chemiluminescence is reproduced in Figure 6. In spite of his other activities, Ranga found time to write articles in the *Journal of Chemical Education*. In recent years, he has written several articles of pedagogical interest, *Resonance*, published by the Indian Academy of Sciences, Bangalore. Very recently, he edited a special issue of the journal[13] on Woodward, depicting his spirit of adventure and the art of creation in organic synthesis. Befittingly, the Academy decided to bring out an e-collection

Figure 5. Side-by-side positioning of an 8th century Yakshi and one turn of DNA.

Figure 6. Illustration of chemiluminescence by Ranga.

of his articles in *Resonance* under the title, *Organic Chemistry Master Classes*[14].

Ranga is very good in origami. I still remember the way he would make Platonic solids by folding paper (Figure 7). The construction of both the left-handed and right-handed DNA double helix was published by him in *Resonance* (Figure 8). Soon after fullerene was discovered, he had his paper folded buckyball ready (Figure 9)! My second daughter Anjana was an immediate beneficiary of his artful paper folding. She would go with me to Ranga uncle's lab, eat pizza and ice cream, and return with a handful of flying birds, horses, jumping frogs and so on.

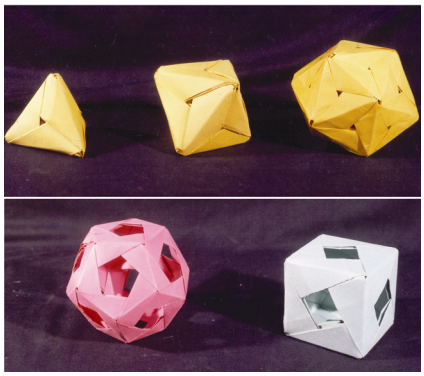

Figure 7. Paper folded models of Platonic solids by Ranga.

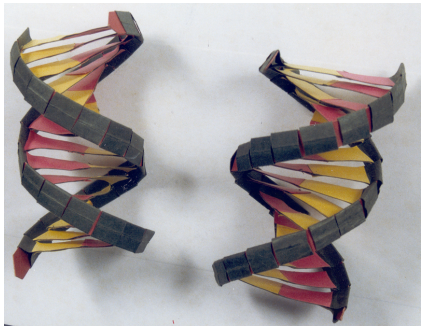

Figure 8. Origami constructed left- and right-handed helix of DNA.

Figure 9. Ranga with a paper-folded model of buckyball.

Ranga tried his hands in art too. Some of his paintings were appreciated by none other than M. F. Hussain, who awarded him the first prize in an all-India cultural competition for his painting on 'Cell', a copy of which is reproduced in Figure 10. He also held an exhibition of his paintings (40), inaugurated by Md. Sadiq, President of MODEUROPE. A brief write-up entitled 'Capturing of Science in Art' was

Figure 10. Ranga's painting of flagella of *Tricona nimpha*.

Figure 11. Group photograph taken on the occasion of Ranga's 80th birthday, 1 October 2014.

published in *The Hindu*. They are the property of the Vidyanantha, a registered society that he and Darshan founded in 2000.

Ranga realized that the future of organic chemistry lies in biology. So he was instrumental in founding the Indian Society of Bioorganic Chemists and served as its President from 1994 to 2002.

An artist by nature, Ranga sees art in organic synthesis and art in biosynthesis, art in life and art in everything. Origami and painting are the means of expression of his ideas. No work is too trivial for him and no subject is too mundane. He has a remarkable memory even at the age of 80. When prompted, he stood up and recited the famous Gettysburg speech of Abraham Lincoln on his 80th birthday!

Ranga is a voracious reader. He has read several classics. He would read anything that was printed and would comment on it. He had the quote from *Bhagavad Gita* put up on the wall of his lab: 'If I do not work, these worlds would perish'.

No wonder that his students, colleagues and admirers decided to celebrate Ranga's 80th birthday on 1 October 2014 in CSIR-IICT by delivering lectures on special topics in organic chemistry and paying glorious tributes to him and reminiscing his ways of dealing with his students and colleagues (Figure 11). It is befitting that the Indian National Science Academy, New Delhi has decided to present the INSA Best Teacher Award to Ranga for the year 2014.

1. Woodward, R. B., Recent advances in the chemistry of natural products. Nobel Lecture, 1965.
2. Woodward, R. B. *et al.*, *J. Am. Chem. Soc*., 1966, **88**, 852–853.
3. Ranganathan, S., *Fascinating Problems in Organic Reaction Mechanisms*, Holden Day, San Francisco, 1967.
4. Ranganathan, D. and Ranganathan, S., *Challenging Problems in Organic Reaction Mechanisms*, Academic Press, New York, 1972.
5. Ranganathan, D. and Ranganathan, S., *Further Challenging Problems in Organic Reaction Mechanisms*, Academic Press, New York, 1980.
6. Ranganathan, D. and Karle, I. L., *Patterns for Supramolecular Design* (ed. Ranganathan, S.), New Age International Pvt Ltd, Delhi, 2002.
7. Ranganathan, D., Biographical Memoirs of the Fellows of INSA, Indian National Science Academy, New Delhi, 2008, vol. 34, pp. 85–98.
8. Ranganathan, S., In *Lilavati's Daughters* (eds Godbole, R. and Ramaswamy, R.), Indian Academy of Sciences, Bangalore, 2008, p. 27.
9. Ranganathan, S., Ranganathan, D., Ramachandran, P. V., Mahanty, M. K. and Bamezai, S., *Tetrahedron*, 1981, **37**, 4171–4184.
10. Anand, N., Bindra, J. and Ranganathan, S., *Art in Organic Synthesis*, Holden Day, San Francisco, 1970.
11. Anand, N., Bindra, J. and Ranganathan, S., *Art in Organic Synthesis*, Wiley, New York, 1988, 2nd edn.
12. Ranganathan, D. and Ranganathan, S., *Art in Biosynthesis*, Academic Press, New York, 1976.
13. Ranganathan, S., *Resonance*, 2014, **19**(7), 585.
14. *Organic Chemistry Master Classes*, an e-Book, Indian Academy of Sciences, Bangalore, 2014.

ACKNOWLEDGEMENTS. I thank *Current Science* for giving me the opportunity to write about Ranga. I also thank Prof. Ranganathan for letting me reproduce some of the pictures from his collection; Dr G. N. Sastry, IICT Hyderabad for his assistance in getting the figures reproduced and Prof. D. Balasubramanian, L.V. Prasad Eye Institute, Hyderabad for his critical comments on an earlier version of the manuscript.

N. SATHYAMURTHY

Indian Institute of Science Education and Research Mohali,
Sector 81, SAS Nagar,
Manauli 140 306, India
e-mail: nsath@iitk.ac.in