Chandrasekharan Ramakrishnan (1939–2019)

Professor C. Ramakrishnan who had made several seminal contributions over the last five decades in the area of conformational analysis of peptides and proteins passed away on 13 March 2019 in Bengaluru. He has left behind his lovely family, comprising his wife (Sakuntala), son (Pradeep) and daughter (Pavithra) and innumerable friends, colleagues and ex-students.

Ramakrishnan, fondly referred as 'CR' by many of us, was born in Madurai on 30 January 1939. He did his B Sc (Hons) in 1959, M Sc in 1960 and Ph D in 1965, all from the University of Madras. He then joined as a faculty in the University of Madras (Lecturer, 1964–67; Reader, 1968–72). In 1972, he moved to the Molecular Biophysics Unit, Indian Institute of Science, Bengaluru, first as Assistant Professor (1972–79), and then as Associate Professor (1979–84) and finally as Professor between 1984 and 2001. He was an Emeritus Professor of Institute of Genomics and Integrative Biology from 2001 to 2006 and finally as an INSA Senior Scientist from 2006 until his demise.

His Ph D work was on stereochemical analysis of peptides and proteins. His fundamental work on stereochemistry laid solid foundations to several developments in modern softwares on the analysis and assessment of complex three-dimensional architectures of proteins.

CR was the Ph D student behind the famous 'Ramachandran map' which is an important protein structure validation tool, used by structural biologists around the world on daily basis. This work is so fundamental that it is a textbook material on protein structures and has gone beyond the citations. (Do you cite a paper when you discuss Einstein's theory of relativity?).

How did Ramachandran map project start? In 1950s, working in University of Madras, Gopinath Kartha and G. N. Ramachandran (GNR) deciphered the triple helical structure of a fibrous protein, collagen, which was also studied by Crick and Rich in Cavendish Laboratory in Cambridge. The structural model proposed by Kartha and Ramachandran was criticized by the Cambridge group which reckoned that the distance between non-bonded atoms in the Madras model is shorter than the sum of the van der Waal's radii of non-bonded atoms. GNR, along with Sasisekharan and CR, decided to probe this matter mainly to validate the Kartha–Ramachandran model of collagen. They surveyed the crystal structures of small molecules and arrived at the data on shortest approach of non-bonded atoms. Indeed, this data, referred as 'contact criteria', clearly showed that

the shortest distance between two non-bonded atoms could be lower than the sum of their van der Waals radii. By considering a system of two-linked peptide units and considering all possible conformations characterized by rotations about N–C^{α} and C^{α}–C bonds (popularly referred as ϕ and ψ torsion angles), they worked out allowed and disallowed conformations that should be applicable to any protein system. Remarkably, much of the subsequent experimental observations of protein structures fell within the span of allowed conformations. Since then, the Ramachandran map has become a standard quality assessment approach to validate every protein structure determined by X-ray analysis or NMR, though it seems it was developed to validate collagen structure. As George Rose of Johns Hopkins University puts it, this is one of the very few instances in biological sciences where a discrepancy between theory and experiment raises doubt on the experimental result!

How was this work achieved in the early-60s? There were no computers accessible to CR at that time. He used a highly primitive calculator (Marchant calculator) which looks as big as a present day desktop and it can perform only addition, subtraction, multiplication and division and had no memory location. He used Clark's tables for trigonometric functions. CR had mentioned to us that the entire calculation took every single day from morning till evening for one year to get completed. Indeed, the meticulous and strict mentor (GNR) of CR, his own mathematical intellect and rigorous computing by hand has had a deep and life-long effect on CR! One could see his sheer joy and child-like enthusiasm when he deals with numbers and numerical patterns!!

CR continued to contribute to the structural science with many other interesting works. He had proposed an approach of learning about protein backbone structures through virtual bonds that enabled him to propose collagen like single helix in globular proteins. His contribution in the conformations of cyclic peptides is enormous, leading to generation of repertoire of stable conformations facilitating recognition of structures of some of the bioactive cyclic peptides. His work on hydrogen bond geometry impacted the area profoundly.

CR is well known for his crystal-clear classes and has appropriately been honoured with Best Teacher Award. No one goes out of his class with a half-baked knowledge. The clarity and passion with which he used to teach chirality in protein stereochemistry is so inspiring that even if we are woken up in the middle of the night, one can tell if we are looking at an L-amino acid or D-amino acid model! His trade mark in his teaching is that he used many of his hand-built plastic, wooden and metallic models of molecules. His own design of models to explain the concept of torsion angle is so impressive, almost every single student of CR's lectures acquires excellent understanding of fundamentals of conformational analysis. One cannot forget his amazing lecture at the International Conference on Biomolecular Forms and Functions in 2012 where he brought his metallic peptide bond model to demonstrate polypeptide stereochemistry and got surrounded by people, after his talk, to view his models closely!

CR as a mentor inspired many of us with his logical thinking and disciplined

approach to work. One feels privileged to learn computer programing from CR, which he used to teach with utmost patience. Sometimes, he motivates us to write a program and he himself codes using another approach to verify if the numbers match! He is one of the very few people we know, who did the work himself (despite being a Professor) for the sheer pleasure of doing science without expecting publications and grants. CR shies away from attention and is happy just doing his work.

Other than programing and numerical patterns, CR was often absorbed in hearing good music as his hobby. He used to play beat instruments – like the 'mridangam'. He was an ardent follower of Indian classical Carnatic music and cricket.

Despite being principled and disciplined, he was never intimidating. He has often gone out of the way to help students in need. He is one of the most supportive and understanding professors we know.

CR was an obedient student of his Guru GNR, a brilliant scientist, a superb teacher, an excellent mentor and a simple human being. He has set a high standard in work and culture – showed us how to research. We deeply mourn his death. Indeed, so long as CR's fundamental contributions in stereochemical analysis and Ramachandran map are in use, he will continue to live with us.

N. SRINIVASAN[1,*]
R. SOWDHAMINI[2,**]

[1]*Molecular Biophysics Unit, Indian Institute of Science, Bengaluru 560 065, India*
[2]*National Centre for Biological Sciences, Benglauru 560 012, India*
**e-mail: ns@iisc.ac.in;*
***e-mail: mini@ncbs.res.in*

Edited by S. K. Satheesh, and printed & published by G. Madhavan for Current Science Association, Bengaluru 560 080.
Typeset by WINTECS Typesetters (Ph: 2332 7311), Bengaluru and Printed at Lotus Printers Pvt Ltd, Bengaluru (Ph: 2320 9909)