

In tribute of our fond Bioinformatics colleague - Late Prof. N. Srinivasan (1962-2021)

N. Srinivasan (NS) was born in 1962 in Triplicane, Madras to Mr K Narayanaswamy and Ms. N. Jayalakshmi. After his Bachelors degree in Physics, he pursued Masters in Biophysics in the Madras University (1982-84). He learnt about Prof GN Ramachandran (GNR) and his great works with his student C. Ramakrishnan (CR) through Drs R. Srinivasan, N. Gautam and Vasantha Pattabhi at the University. NS's thoughts towards polypeptide stereochemistry and to follow the legacy of GNR-CR school had been initiated by them.

Hence, it was no surprise that NS joined MBU of IISc in 1984 after few rounds of interviews there. But young NS was not used to being away from home. The short distance between Bangalore and Madras was a consolation that he could visit home often and spend some time with his aging parents. Besides, he was strongly encouraged by his eldest brother to pursue his interests in the prestigious Indian Institute of Science.

NS's interests on polypeptide stereochemistry and computer programming were nurtured under the excellent guidance of CR. CR carried a good blend of scientific rigour as GNR, great teaching skills and tons of patience for his students! Towards the late '80s, CR's group collaborated with Prof P Balaram of the same Department and who was highly regarded for his expertise in peptide design. The next five years turned out to be highly productive for NS due to this collaboration and he was studying stereochemistry of disulphide bonds (Srinivasan et al., 1990) and backbone torsion preferences in 20 amino acids (Sowdhamini et al., 1992; Ramakrishnan and Srinivasan, 1992). He also found his wife, R Sowdhamini (RS), in front of the computer during this collaboration. People in the Department had remarked how they were-made-for-each-other-couple with similar passion for research.

After their PhD and marriage, NS and RS both moved to the United Kingdom, working in the well-known protein crystallography lab of Prof Tom Blundell (TLB). TLB and the then Chairperson of MBU, Prof M Vijayan know each other well since they come from the Dorothy Hodgkin's school of protein crystallography. Whilst at TLB's lab (initially in London and later in University of Cambridge), NS applied his mind on homology modelling (Srinivasan and Blundell, 1993; Emsley et al., 1994), protein mutations (Topham et al., 1997) and particularly on domains in signal transduction (Srinivasan et al., 1994; 1996). NS's sharp intellect and collaborative frame of mind were highly appreciated by TLB and together they produced nearly 16 publications. NS was growing more and more confident and fluent in research ideas. NS and RS were blessed with their daughter, Jayashree, whilst in Cambridge. NS had developed a strong wish to return to India and was offered a faculty position in the same MBU department of IISc. Luckily, both NS and RS could get independent positions in Bangalore in 1998. As his well-wisher, TLB was happy to support this move, but TLB and NS continued their interactions and collaborations. Indeed, NS was eagerly waiting for TLB's visit in 2020, which had to be postponed due to COVID lockdown restrictions.

Once NS established his laboratory in IISc, using the start-up funds and a timely Senior Research Fellowship by the Wellcome Trust, U.K., he contributed to areas such as protein families (Sujatha et al., 2001; Pandit et al., 2002; Sandhya et al., 2005) and in particular on protein kinases (Krupa et al., 2004; Anamika et al., 2005) in genomes. He also analysed protein domain architectures and how such understanding could enable host-pathogen interactions. NS's lab was highly collaborative within IISc (for example, Bandari et al., 2001; Reddy et al., 2014) and across Institutes (for example, Talla et al., 2006; Jhingran et al., 2008). NS developed collaborations with few French laboratories – Dr Bernard Offmann (initially in Universite de la ReUnion and later in Univeristy of Nantes), Dr Frederic Cadet (in Universite de la ReUnion) and Dr Alexandre de Brevern (INSERM, Paris) – which led to strong friendships. He had enjoyed the support of CEFIPRA grants with Dr Brevern and been Visiting professor

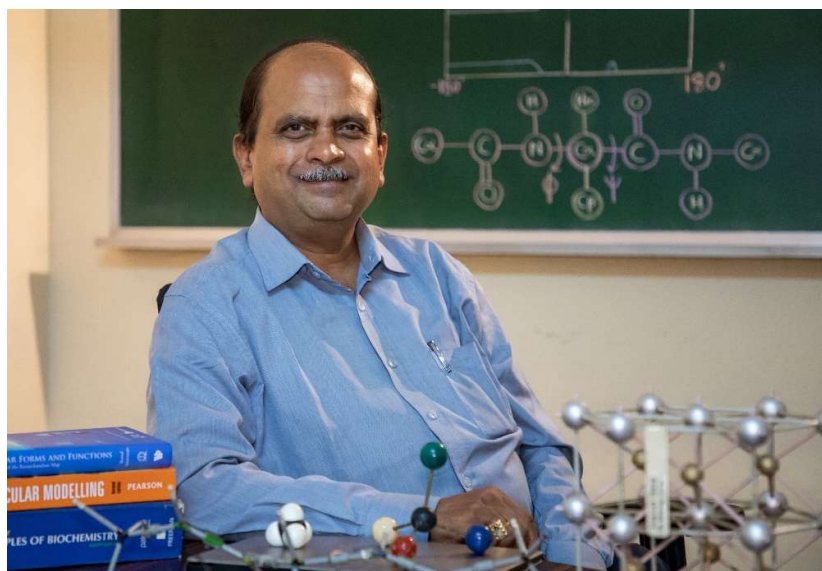
of ReUnion and Nantes University several times with Dr Offmann as the host. Together, they had analysed various aspects such protein structure comparison and prediction using amino acid alphabets (for example, Tyagi et al., 2006).

NS travelled extensively within India (to Institutes such as Alagappa University, Indian Institutes of Chennai, Roorkee, Kanpur, University of Pune, Dharmashala, IMTECH Chandigarh, IISER Pune, Mohali) and outside India (like Turku University in Finland, Auckland University in New Zealand), also to attend specialised meetings (in Hinxton, UK and Strasbourg, France) and conferences (like Asia Pacific Bioinformatics Conference in Beijing, Melbourne; Albany, USA; Indo-French Bioinformatics Conference in ReUnion, Montpollier). He had also visited other Institutes in places like Kollam, Trivandrum, Chandigarh and so on. He had also been instrumental in conducting conferences like IFBM and APBC in Bangalore. MBU had also celebrated in few occasions where NS had been a local organiser.


NS received Shanti Swarup Bhatnagar Award, the highest science prize in India, in 2008. He had been recognised as a Fellow in all three Indian Academies – Indian Academy of Sciences (Bangalore), National Academy of Science India (Allahabad) and Indian National Science Academy (Delhi). Yet, none of these awards made him behave less humble than he had always been.

During the COVID lockdown, alas, NS underwent a silent heart attack which he fought bravely for nearly eight months. His demise on 3rd September 2021 came as a huge shock to the bioinformatics and academic community in India. The fact that he continued to publish as many as 16 publications even after the heart attack is a testament to his commitment to science and his bravery.

NS leaves a lasting impression on people – whether he is attending a meeting, giving a lecture or an organiser of a conference. Many of us remember his description of the history behind Ramachandran map and their revisit of Ramachandran map (Ravikumar et al., 2019), highly appreciated by the Bioinformatics community. NS was an engaging speaker and a great communicator. His appreciation and encouragement for others' work would come from the heart and sporting a winning smile. He had the unique capacity to exhibit high scientific rigour, yet be highly approachable and simple at the same time. We believe that he leaves behind a huge legacy - his passion for science to follow and his courage to get inspired upon. The Indian bioinformatics community lost a valuable member, but his publications, collaborators, colleagues and students will continue to speak of his science.



Cited references

- N.Srinivasan, R.Sowdhamini, C.Ramakrishnan & P.Balaram (1990) **Conformations of disulfide bridges in proteins.** *Int. J. Pept. Prot. Res.*, 36, 147-155.
- R.Sowdhamini, N.Srinivasan, C.Ramakrishnan & P.Balaram (1992) **Orthogonal bb motifs in proteins.** *J. Mol. Biol.*, 223, 845-851.
- C.Ramakrishnan & N.Srinivasan (1992) **Conformational preference of glycol residues in proteins. A further confirmation.** *Proc. Ind. Natl. Acad. Sci.*, B59, 45-54.
- N.Srinivasan & T.L.Blundell (1993) **An evaluation of the performance of an automated procedure for comparative modelling of protein tertiary structure.** *Prot. Engng.*, 6, 501-512.
- J.Emsley, H.E.White, B.P.O'Hara, G.Oliva, N.Srinivasan, I.J.Tickle, T.L.Blundell, M.B.Pepys & S.P.Wood (1994) **Structure of pentameric human serum amyloid P component.** *Nature*, 367, 338-345.
- C.M.Topham, N.Srinivasan & T.L.Blundell (1997) **Prediction of protein mutant stability based on three-dimensional structure dependent aminoacid substitution and propensity tables.** *Prot. Engng.*, 10, 7-21.
- N.Srinivasan, H.E.White, J.Emsley, S.P.Wood, M.B.Pepys & T.L.Blundell (1994) **Comparative analyses of pentraxins: implications for protomer assembly and ligand binding.** *Structure*, 2, 1017-1027. 
- N.Srinivasan, M.D.Waterfield & T.L.Blundell (1996) **Comparative analysis of the regions binding bg-subunits in G alpha and PH domains.** *Biochem. Biophys. Res. Commn.*, 220, 697-702.
- S. Sujatha, S. Balaji & N. Srinivasan (2001) **PALI: a database of alignments and phylogeny of homologous protein structures.** *Bioinformatics*, 17, 375-376.
- S.B. Pandit, D. Gosar, S. Abhiman, S. Sujatha, S.S. Dixit, N.S. Mhatre, R. Sowdhamini & N. Srinivasan (2002) **SUPFAM - A database of potential protein superfamily relationships derived by comparing sequence-based and structure-based families: Implications for structural genomics and function annotation in genomes.** *Nucleic Acids Res.* 30, 289-293.
- S. Sandhya, S. Chakrabarti, K.R. Abhinandan, R. Sowdhamini & N. Srinivasan (2005) **Assessment of a rigorous transitive profile based search method to detect remotely similar proteins.** *J. Biomol. Str. Dyn.* 23, 283-298.
- A. Krupa, G. Preethi & N. Srinivasan (2004) **Structural modes of stabilization of permissive phosphorylation sites in protein kinases: Distinct strategies in Ser/Thr and Tyr kinases.** *J. Mol. Biol.*, 339, 1025-1039.
- Anamika, N. Srinivasan & A. Krupa (2005) **A genomic perspective of protein kinases in Plasmodium falciparum.** *Proteins Str. Fn. Bioinf.*, 58, 180-189.
- R.Bhandari, N. Srinivasan, Mahaboobi, K. Suguna & S.S.Visweswariah (2001) **Functional inactivation of the human guanylyl cyclase C receptor: Modelling and mutation of the protein kinase -like domain.** *Biochemistry*, 40, 9196-9206.
- U.B. Reddy, R. Mullick, A. Kumar, G. Sudha, N. Srinivasan & S. Das (2014) **Small molecule inhibitors of HCV replication from Pomegranate.** *Sci. Rep.* 4, 5411.
- V. Talla, C. Narayanan, N. Srinivasan & D. Balasubramanian (2006) **Mutations causing self-aggregation in human gamma-C crystalline leads to congenital cataract.** *Investigative Ophthalmology & Visual Science.* 47, 5212-5217.
- A. Jhingran, P.K. Padmanabhan, S. Singh, K. Anamika, A. A. Bakre, S. Bhattacharya, A. Bhattacharya, N. Srinivasan and R. Madhubala (2008) **Characterization of the Entamoeba histolytica Ornithine decarboxylase-like enzyme.** *PLoS NTD* 2, e115.
- M. Tyagi, P. Sharma, S. Swamy, F. Cadet, N. Srinivasan, A. de Brevern & B. Offmann (2006) **Protein Block Expert (PBE): A web-based protein structure analysis server using a structural alphabet.** *Nucl. Acids Res.* 34, W119-223.
- A. Ravikumar, C. Ramakrishnan & N. Srinivasan (2019) **Stereochemical assessment of (ϕ - ψ) outliers in protein structures using bond geometry-specific Ramachandran steric-maps.** *Structure* 27, 1875-1884. 