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G N Ramachandran– A Nobel Prize Nominee and Nominator

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Abstract

The Nobel Prizes are one of the most prestigious awards in the scientific community. G N Ramachandran is the only Indian nominated for the Chemistry Nobel Prize. The documents, such as nomination letters, expert's and the Nobel Committee's reports were obtained from the Royal Swedish Academy of Sciences, Stockholm. The results of their analysis are given in the present communication.

Key words: Collagen, Chemistry Nobel Prize, Indian scientists, Nobel Laureate C V Raman, G N Ramachandran.

1. Introduction

Gopalasamundram Narayana Ramachandran, better known as G N Ramachandran is famous for the plot named after him. It deals with the torsional angles-phi (Φ) and psi (Ψ)-of the residues (amino acids) contained in a peptide. Different aspects of his life have been dealt by various authors (Sarma, 1998; Anonymous, 2016; Mahanti, 2004; Balaram & Ramaseshan, 2001, pp.908–991; Vijayan, 2001, pp.81-97; 2001, p.544; Ramakrishnan, 2001, pp.1689-1691; Rose, 2001, pp.1691-1693; Subramanian, 2001, pp. 489-491;Vijayan & Johnson, 2005). Unfortunately the book by the author *Chemistry and Physics Nobel Prizes-India's Contribution*, Shaker Publisher Aache 2016, is not available in India and I think it will be worthwhile to write an article for the readers of the *Indian Journal of History of Science*. So far as I am aware the existing literature does not discuss the following:

1. G N Ramachandran's nomination for the Chemistry Nobel Prize
2. Opinion of the Chemistry Nobel Prize Committee's as well as its expert's on Ramachandran's researches
3. Ramachandran's role as a Nobel Prize nominator.

The present communication intends to explore the above points in detail.

G N RAMACHANDRAN
(Courtesy: INSA)

To start with Ramachandran's short biography is based on the above referred literature is given below.

2. G N Ramachandran FRS

1922: Born on 8th October

1938: Joined BSc (Hons) course in Physics in St. Josephs College, Trichy

1942-1947: Studied at the Indian Institute of Sciences (IISc), Bangalore

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1947: DSc, University of Madras

1949: PhD, University of Cambridge

1949: Assistant Professor, IISc.

1952-1969: Head and Professor, Department of Physics, Madras University

1954: Published the famous paper "Structure of Collagen" (Ramachandran, Kartha, 1954, pp. 269-270)

1955: Published the modified "Structure of Collagen" (Ramachandran, Kartha, 1955, pp. 593-595)

1962-1970: Director, Centre of Advanced Study in Biophysics & Crystallography

1963: Elected, Fellow of the INSA.

1964: Nominated for the Chemistry Nobel Prize by C V Raman

1967-1978: Part-time Professor of Biophysics, University of Chicago

1970-1978: Head, Molecular Biophysics Unit, IISc.

1977: Elected FRS. Fellow of Royal Society London

1978-1981: Head, Mathematical Philosophy Group, IISc.

1982-1984: CSIR - Distinguished Scientist

1984-1989: INSA - Albert Einstein Research Professor

2001: Expired

3. G N Ramachandran and the Fellowship of the Royal Society of London

G N Ramachandran is one of the very few Indian scientists to be elected for the Fellowship of the Royal Society of London. According to the record of the Royal Society, he was nominated in 1973. His nomination certificate reads:

> "G N Ramachandran has made significant contributions to the field of crystal structure analysis. These include: the technique of determining the phases of X-ray reflections from anomalous dispersion effects; and the development of novel types of Fourier synthesis for revealing the full structure from partial knowledge concerning it. Recently, he has developed a convolution method, which is a modification of the standard Fourier technique, but faster and as accurate as the Fourier method, which has got good prospects of application to radiographs and electron micrographs"
>
> (Archive Royal Society London, GB 117, Ref. No.EC/1977/29).

And further:

> 'The most significant scientific results obtained by G N Ramachandran have been in the field of bio-molecular structure. These include: (i) the proposed triple helical structure of collagen which is now universally accepted and is being widely applied in chemical and biological studies on collagen; (ii) development of an important technique whereby the mutual orientations of two peptide units, which are allowed, can be determined from a knowledge of the limiting contact distances to which two non-bonded atoms can approach each other; a plot of the regions of allowed and disallowed conformations is often referred to as the 'Ramachandran map'; (iii) application of the latter for examining the allowed and disallowed regions of the conformations of side groups of proteins, of linked nucleotides, and of polysaccharide chains, energy minimisation of the collagen triple helix and conformation of anti-biotics. He is now working on the application of NMR to the determination of peptide structure.'
>
> (Archive Royal Society London, GB 117, Ref. No. EC /1977/29).

For the above contribution, in 1977, G N Ramachandran was elected a Fellow of Royal Society of London.

Ramachandran belongs to the list of five Indian F.R.S. physicists (C.V. Raman, M N Saha, H J Bhabha, S N Bose), who were nominated for the Nobel Prize. However, the exception is, that

he was nominated for the Chemistry Nobel Prize (detail below).

4. C V Raman Nominates G N Ramachandran for the Chemistry Nobel Prize

The Nobel Laureate C V Raman, in his life nominated only five persons. Out of them four were from abroad - Three from the USA. (O Stern, E O Lawrence, S Chandrasekhar) and one from Italy (E Fermi). G N Ramachandran remains the only one Indian to be nominated by C V Raman (Singh, 2016, p.21).

C V Raman on December 11, 1963, proposed G N Ramachandran, for the Chemistry Nobel Prize

> 'on the basis of his discovery of the structure of Collagen and his elucidation of its properties in terms of the structure of that substance (C.V. Raman to Nobel Committee, Dec. 11, 1963).'

Raman reasoned the nomination in a long letter. To start with he emphasized the application of the Collagen in the field of medicine and biochemistry.

> "…, from the physical and chemical points of view, the properties of collagen are quite different from those of other protein molecules and set a challenging problem to the structure analyst to explain these at the molecular level",

wrote Raman (C V Raman to Nobel Committee, Dec. 11, 1963).

Raman argued that since 1930s a lot of work was done on the structure of collagen. However,

> "The first attempt to work out a structure based on the observed chemical data, particularly that one-third the number of residues are glycine and a good proportion are the amino-acid residues of proline and hydroxyl proline, is due to Ramachandran and co-workers (Ramachandran, Kartha, 1954, pp.269-270)."

Further, Raman stated that on the basis of stereo chemical criteria that structure proposed by Ramachandran's school was criticised in 1955. This was refuted by him (Ramachandran, Kartha, 1955, pp.593-595)."A new set of criteria for contact distances between atoms were developed and reported in a Symposium in 1960 (…) and in terms of these the 1955 structure was revised and perfected (…) (C V Raman to Nobel Committee, Dec. 11, 1963)."

Raman supported his case by mentioning the organisation of an "International Symposium on Protein Structure and Crystallography" in Madras, by Ramachandran. It was attended by renowned scientists in the field. Raman reproduced the testimony of some of the scientists as follows:

> "Dr. M F Perutz, Nobel-Laureate, Cambridge: 'The holding of an international conference of this kind in Madras is symbolic … of the international fame attained by your laboratory as a result of your inspired leadership in teaching and research.' Prof. J D Bernal, F R S., London: 'I have felt for a long time that the Madras School has made a great contribution to protein studies.' Professor K H Gustavson, Stockholm: 'This symposium is a signal token of the international recognition of the high scientific standard of research of the Madras School.' …(C V Raman to Nobel Committee, Dec. 11, 1963)"

On December 13, 1963, Raman sent another letter, in which he stated that with registered post he is sending: Two books which are edited by Ramachandran, a bound volume of G N Ramachandran's and his collaborators' publications, and a brochure regarding the International Symposium (organised by G N Ramachandran) on Protein Structure and Crystallography (C V Raman to Nobel Committee, Dec. 11, 1963).

According to the Rules and Regulations of the Nobel Foundation, after getting the proposals the Nobel Committee makes a list of the nominated candidates. The Committee

prepares a general report in which all nominated candidates are reviewed in short. Before that the Nobel Committee asks it experts to prepare detailed reports on the newly nominated candidates. If the N C thinks a person, who was previously nominated, might be a "potential" candidate to win the award; his report is complimented. The expert of the Nobel Committee was Gunnar Hägg.

5. Expert's Opinion of G N Ramachandran's Contribution

According to the summarized and translated report of June 8, 1964 (original is Swedish), Gunnar Hägg wrote that G N Ramachandran has been proposed by Sir C V Raman, for his discovery of the structure of Collagen, and elucidation of its properties in terms of the structure of that substance.

Hägg noted that the Fiber proteins collagen is found in bones, tendon and skin. It is very essential for the body. Knowledge of its structure and properties is of utmost importance. It should be recalled that the fiber protein's special form makes the determination of its structure difficult.

After giving short introduction on the structure and the technical difficulties in studying the structure, G Hägg stated that a major advance in collagen studies was made by P M Cowan, ACT North and J T Randall (1953, p.241).

Hägg then turned to the historical aspect, namely, since W T Astbury's pioneering work of fibrous proteins in the 1930s, many structural suggestions are given for collagen. It was perfectly clear that collagen consists of polypeptide chains extending along the fiber axis. In 1951, L Pauling and R B Corey adopted a structure with three polypeptide-spiral. This, as well as several other proposed structure were soon abandoned. An impressive progress was made by P M Cowan and R S Bear (Cowan & Bear, 1953, pp.2783-2784), and P M Cowan, ACT North and J T Randall (1953). They demonstrated the presence of a screw shaft with repetition after a non-integer number of turns. In 1954 G N Ramachandran and G Kartha suggested a structure of three parallel chains, each containing a three-membered screw shaft (Ramachandran, Kartha, 1954, pp.269-270). After criticism from others, they modified the model of the structure (Ramachandran, Kartha, 1955, pp.593-595).

Shortly after that A Rich and FHC Crick published the collagen structure (Rich and Crick, 1955, pp.915–916). They indicated Ramachandran's and Kartha's idea "to be basically correct but the actual structure suggested by them to be wrong." Rich and Crick found the Indian researchers' structure unreasonable, because the distance between carbon-carbon and carbon-oxygen bonds is too-short; and quite unusual hydrogen bond angles. Also, their model was not compatible with amino acid sequences found in collagen. Rich and Crick themselves proposed two possible collagen structures, which they termed as I and II. Almost simultaneously P M Cowan, S McGavin and ACT North reported that they have come to similar results (Cowan, Gavin and North, 1955, pp.1062-1064).The English scientist R S Bear also came to the building of a structures I and II (Bear, 1956, pp.363-368).

In 1958 Rich and Crick estimated space for the side chains of the structures I and II. They found alternative II most likely (Rich and Crick, 1958, p. 20).This chimed R E Burge, P M Cowan and S McGavin and L Pauling (…). Two other structural proposals were published at about the same time by M L Huggins (1957, pp.209-213), and M I Millionova and N S Andreeva. They are probably not correct.

G Hägg further stated that later, that is, in 1963, Ramachandran has changed some details. He claims to have eliminated most of the aforementioned critics, but topologically the structure is same as in 1955 (Ramchandran, 1963, p.39).The two restructuring proposals, which are

proposed by various research groups, indicate that, it is very likely, that Ramachandran's and Karth's structure from 1955 with some modifications, as well as the Rich and Crick from the same year, rendered the structure II. These two structures are very closely related. They differ in the way in which the three chains are "beveled" in relation to each other and particularly through which the hydrogen bonds holding together the three chains. However, as Rich and Crick say, these differences are not trivial (Rich and Crick, 1961, pp.483-506).

G Hägg concluded that it is obvious that under these conditions it is not possible to award Nobel Prize for Ramachandran's collagen work. But even if his proposed structure would later prove to be the right, his effort in this area is hardly more prominent than other researchers, to be considered worthy of a reward.

It should however be noted that a final determination of the collagen structure is extremely important. It will give full clarity concerning much of the properties of collagen. In medicine, currently the "collagen diseases" caused or accompanied by changes in the collagen substance are of great interest. Among others, one hypothesis has been set to the aging of the collagenous tissues. It could be due to the occurrence of cross-linkages within the collagen fibers. A clarification of these problems would obviously deserve a Nobel Prize reward but would then fall in the Medical Nobel Prize area.

6. G N Ramachandran – Opinion of the Nobel Committee

In fact the Nobel Committee, in its report for the year 1964 (original is Swedish), in short, reproduced expert's opinion as follows: Mr. Hägg has reviewed Ramachandran's studies on the structure (…). The Indian researcher proposed a structure for Collagen - biologically an important substance. But other researchers have also suggested structure models. The two structures are admittedly quite similar but differ in the way in which the molecular chains are "beveled" in relation to each other and with respect to the hydrogen bonds that hold the chains together. The differences are thus not of much significance.

Mr. Hägg says that Ramachandran's collagen work cannot be awarded with the prize. He emphasizes that the exact knowledge of the structure is extremely important. Only then the much of the properties of collagen can be explained. In medicine, currently the "collagen diseases" caused or accompanied by changes in the collagen substance are of interest. One hypothesis has been set to the aging of the collagenous tissues would, inter alia, due to the occurrence of cross-linkages within the collagen fibers. A clarification of these issues would, of course, eminently deserve the Nobel Prize in the field of medicine.

From the forgoing we see that G N Ramachandran had no chance. Whether he was nominated after 1964 is difficult to say, as the rules and regulations of the Nobel Foundation allow to consult the documents, which are fifty or more than fifty years old. What we know for sure is that G.N. Ramachandran was asked to nominate candidate for the Nobel Prize (detail below).

7. G N Ramachandran as Nominator

Between 1901 and 1964 only ten Indian physicists were asked by the Nobel Committee to send proposals. G N Ramachandran was one of them (Singh, 2016, p.29). In 1959, Ramachandran nominated N Wiener, Massachusetts Institute of Technology; and C E Shannon, Bell Telephone Laboratories. The proposal, in part reads as follows:

> "The classical work of Shannon, although it was concerned mainly with telecommunication problems, has found application in many diverse fields – even as far away as linguistics, psychology etc. So also, Norbert Wiener, to whom is due the basic philosophy of modern information theory, was the first to recognize the essential similarity

between the problems of communication in mechanical systems and in living beings. This has led to the new discipline of cybernetics (G N Ramachandran to the Nobel Committee, Jan. 12, 1959)."

Ramachandran's proposal was not successful. In 1959, the Physics Nobel Prize was awarded to Emilio Gino Segrè and Owen Chamberlain "for their discovery of the antiproton."

8. Concluding Remarks

G N Ramachandran was the only Indian to be nominated by the Nobel Laureate C V Raman. It leaves no doubt about close relationship between the teacher Raman and his pupil Ramachandran.

The Chemistry Nobel Committee and its expert appreciated Ramachandran's scientific achievement. However, it was seen still incomplete; and also compared with other scientists working in the same field, Ramachandran's achievements were not seen as worth of the Nobel Prize.

The most important point to be noted is that the expert of the Committee saw the importance of the structure and the applications of the collagens in medicine. He saw Ramachandran's nomination for the Chemistry Nobel Prize as unfitting. G N Ramachandran's researches show the problematic of the interdisciplinary scientific work and its recognition by specialist from different fields.

Like M N Saha, H J Bhabha; Ramachandran did not nominate his own countrymen for the Nobel Prizes. Was it due to their international thinking? It remains an open question.

It is very probable that G N Ramachandran was nominee as well as nominator after 1964. For the time being it cannot be said definitely, because according to the Rules and Regulations of the Nobel Foundation, for research purposes, the documents older than fifty years can be consulted.

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