Bioinformatics, 31(13), 2015, 2238–2239
doi: 10.1093/bioinformatics/btv218
Advance Access Publication Date: 22 May 2015
Message from the ISCB

Message from the ISCB: 2015 ISCB Accomplishment by a Senior Scientist Award: Cyrus Chothia

Christiana N. Fogg[1] and Diane E. Kovats[2,*]

[1]Freelance Science Writer, Kensington, MD, USA and [2]Executive Director, International Society for Computational Biology, La Jolla, CA, USA

*To whom correspondence should be addressed.

Abstract

The International Society for Computational Biology (ISCB; http://www.iscb.org) honors a senior scientist annually for his or her outstanding achievements with the ISCB Accomplishment by a Senior Scientist Award. This award recognizes a leader in the field of computational biology for his or her significant contributions to the community through research, service and education. Cyrus Chothia, an emeritus scientist at the Medical Research Council Laboratory of Molecular Biology and emeritus fellow of Wolfson College at Cambridge University, England, is the 2015 ISCB Accomplishment by a Senior Scientist Award winner.

Chothia was selected by the Awards Committee, which is chaired by Dr Bonnie Berger of the Massachusetts Institute of Technology. He will receive his award and deliver a keynote presentation at 2015 Intelligent Systems for Molecular Biology/European Conference on Computational Biology in Dublin, Ireland, in July 2015.

Contact: dkovats@iscb.org

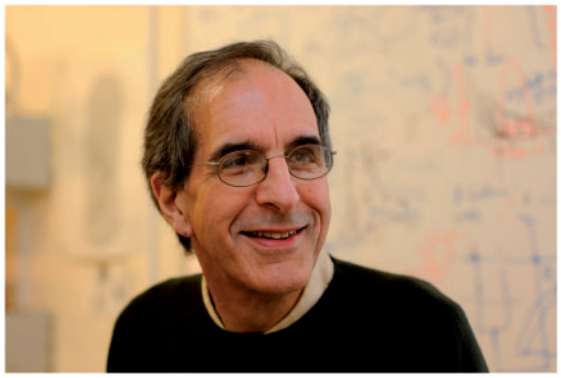
Cyrus Chothia: the structures and functions of proteins

Chothia was deeply interested in history as a young student in England but was discouraged from pursuing this subject by teachers. 'Because my foreign languages were so bad', Chothia recalled, 'my teachers said I couldn't be an historian. I turned to chemistry'. As a youth, Chothia remembers being fascinated by a hugely popular BBC television series by Nobel Laureate John Kendrew called 'The Thread of Life'. He said, 'I was enthralled by the series. I knew what I wanted to do, I wanted to be a molecular biologist and go Cambridge. I did it eventually in a roundabout way'.

Chothia completed his Bachelor of Science degree at Durham University in 1964 and his Master of Science degree at Birkbeck College, University of London, in 1967. He then pursued his PhD under the guidance of Peter Pauling at University College London. Chothia has fond memories of his time under Pauling's supervision. 'He was a generous supervisor and we got along extremely well', he said. His PhD research examined the conformations of molecules at nerve receptors. This marked the beginning of his lifelong research interest in protein structures.

After his PhD, Chothia went to the Laboratory of Molecular Biology (LMB) for postdoctoral training, during which time he got to know Joel Janin and Michael Levitt. His experience at LMB was quite different from his time under Pauling, and he and his new supervisor parted after 3 years. But this presented Chothia with an opportunity to travel abroad to different laboratories. '[Levitt and Janin] helped me find new places. Kendrew helped me get an EMBO fellowship to come to America to Fred Richards' lab at Yale. America was marvelous scientifically. People were excited about their work. I then went to the Weizmann Institute in Israel for six months and then to Paris to Joel's laboratory for two years. This was my "Grand Tour" and it was actually very valuable. I went to all these different labs and learned many things that I could use when I got back to Cambridge'. This was a very fruitful period for Chothia, and he published numerous articles with Levitt and Janin. Chothia and Levitt developed the 'all-a, all-b, a/b and a+b' classification of protein structures, and Chothia and Janin worked out the underlying principles required for protein– protein recognition and packing of protein secondary structures.

In 1976, Chothia came back to England and was affiliated with the University College London and the LMB. He was named the E.P.A. Cephalosporin Fund Senior Research Fellow of the Royal Society in 1980, which offered him stable funding to work as an independent researcher for 10 years. Chothia recollected, 'During that



The image was courtesy of the Medical Research Council

time, I met Arthur Lesk and we got on enormously well. Lesk was there for more than ten years. Working with him and others was very productive'. Their work covered a wide range of topics in structural biology, including how protein structures change to adapt to mutations, mechanisms by which proteins can transmit information to distant sites in a structure and the observation that a small repertoire of structures exist for the main chain conformation of immunoglobulin hypervariable regions, and these structures can be predicted from the amino acid sequences. By 1990, Chothia recalled how his laboratory work changed. 'I was given a permanent position at Cambridge and began to have students', he said. 'That made things somewhat different and I liked working with them. Before this, I worked with my contemporaries, and they would tell me when I was talking nonsense. Joel Janin and I used to have fierce arguments. When I started taking students the relationship became somewhat different: it was important to explain the terms of the argument'.

In 1992, Chothia's work on protein structures led him to propose that most proteins comprised domains that come from a limited number of families. Together with Tim Hubbard, Alexei Murzin and Steven Brenner, he created the Structural Classification of Proteins (SCOP) database. SCOP contains all entries in the Protein Data Bank and provides a detailed and comprehensive description of the structural and evolutionary relationships between all proteins whose structure is known (Hubbard *et al*., 1997). More recently, Chothia developed the SUPERFAMILY database with Julian Gough, which is a structural and functional annotation for all proteins and genomes (Gough and Chothia, 2002). The SUPERFAMILY annotation is based on a collection of hidden Markov models that represent structural protein domains at the SCOP superfamily level. Superfamilies group together domains with an evolutionary relationship.

Chothia is still active in the laboratory and is interested in questions related to biological complexity. His recent work has shown that a significant increase in the number of superfamilies in eukaryotes correlates with the complexity of organisms. But he is aware that there are further questions to answer. He said, 'The number of proteins about which we have good information as to function is small: we don't know what most proteins do'. These questions are sure to keep Chothia and other scientists in this field curious and busy for years to come.

Funding

Christiana Fogg was paid by the ISCB to write this article.

Conflict of Interest: none declared.

References

Gough,J. and Chothia,C. 2002. SUPERFAMILY: HMMs representing all proteins of known structure. SCOP sequence searches, alignments and genome assignments. *Nucleic Acids Res*., **30**, 268–272.

Hubbard,T. *et al*. 1997. SCOP: a structural classification of proteins database. *Nucleic Acids Res*., **25**, 236–239.