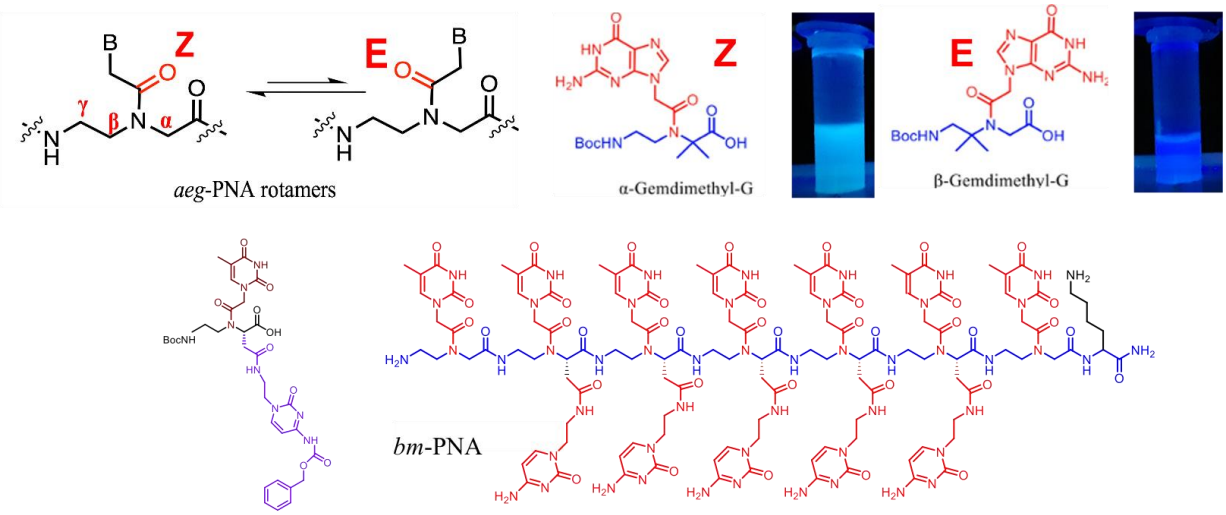
Structural control of peptide nucleic acid (PNA) rotamers: Serendipitous fluorescence in α, β and γ-gemdimethyl PNA monomers and DNA/RNA hybridization selectivity of PNA oligomers

Pradnya Kulkarni, Abdul Shiraz and Krishna Ganesh*
Department of Chemistry
Indian Institute of Science Education and Research (IISER) Tirupati and IISER Pune
(kn.ganesh@iisertirupati.ac.in)

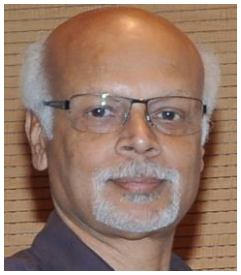
Abstract:
Rotamers are conformational isomers that differ by rotation around a single sigma bond, particularly in the hindered *t*-amides. Peptide nucleic acids (PNA) are achiral mimics of nucleic acids composed of a polyamide backbone with recurring units of 2-aminoethylglycine (*aeg*) to which nucleobases A, C, T and G are linked via a tertiary amide linkage.[1] Aminoethylglycyl (*aeg*) PNA monomers in solution exist as a mixture of Z (70%) and E (30%) rotamers, with preference for Z-isomer[1]. We have recently demonstrated that introduction of bulky gem-dimethyl group in the α, β and γ sites of *aeg*-PNA backbone in monomers introduces steric constraint on rotations of backbone bonds in backbone. This affects the relative Z/E-rotamer population and α-gemdimethyl PNA-T monomer showed exclusively the Z-rotamer, while β-gemdimethyl-T monomer exhibited only E-rotamer in solution. Thus it is possible to realise exclusive E or Z-rotamers in a rational way. It was serendipitiously observed that the gemdimethyl PNA monomers are fluorescent both in solution as well as in solid state: green fluorescence in E-rotamer and blue fluorescence in Z-rotamer. The influence of exclusive E and Z rotamers on biophysical and hybridization properties of derived gemdimethyl PNA oligomers and bimodal PNA will be presented.



References and Notes:

Pradnya Kulkarni, P.; Dutta, D.; Ramabhadran, R. O. and Ganesh, K. N. *Org. Biomol. Chem*. **2021**, *19*, 6534-6545

Bio-Sketch of Speaker



Krishna N. Ganesh
Professor & Director
IISER Tirupati

Founder & Ex-Director, IISER Pune

e-Mail: director@iisertirupati.ac.in; kn.ganesh@iiserpune.ac.in
Homepage: http://www.knganesh.in/

Krishna N Ganesh (born 1953) obtained his Ph.D (1976) in Chemistry at Delhi University. He was awarded a Commonwealth Fellowship to pursue higher studies University of Cambridge, UK that resulted in another Ph.D degree in 1980. He joined the Centre for Cellular and Molecular Biology (CSIR) at Hyderabad in 1981 where he established India's first DNA synthesis facility, initiating a vigorous research programme in DNA diagnostics, new motifs of DNA-protein interactions and PCR based diagnostics for then prevalent HIV. In 1987, he relocated to National Chemical Laboratory (NCL-CSIR) where he became the Head of Organic Chemistry Division in 1994. He was chosen as the First Director of the newly founded Indian Institute of Science Education and Research at Pune in 2006.

Dr Ganesh has made excellent research contributions to the chemistry and biology of nucleic acids, focusing on therapeutic and diagnostic applications of DNA analogues, structural biology of collagen peptides and the emerging area of DNA nanotechnology. He is internationally recognised for his original and creative contributions to design of Peptide Nucleic Acid (PNA) analogues for effective cell permeation. He has more than 170 publications in reputed international journals, 2 international patents and guided 45 students for their doctoral degrees.

Prof Ganesh is a Fellow of all the 3 Science Academies in India and also a Fellow of The World Academy of Sciences (TWAS). He served as the President of Division of Organic and Biomolecular Chemistry of IUPAC (2012-2013). Prof Ganesh has received innumerable professional awards, the most important ones being Shanti Swarup Bhatnagar award of Chemical sciences (CSIR) and TWAS Prize for Chemical Sciences, SASTRA-CNR Rao Award of SASTRA University (2015), H K Firodia Vijnan Bhushan Award (2015) and National Researcher Award in Nanoscience and Technology (2016).

He has served as a Member of the various policy making and Project Advisory Committees of Department of Science & Technology (DST) and Department of Biotechnology (DBT), Government of India and past Chairman of Indian Committee of Lady Tata Memorial trust. Among these are Member of Nanoscience Advisory Group of DST Nanoscience mission; Chairman, DBT Taskforce on Nanobiotechnology; Chairman, Finance Committee of India Alliance - Welcome trust DBT, Chairman, Past Chairman of Research Advisory Council of Institute of Nanoscience and Technology, Chandigarh.

He has served as a member of the Editorial Advisory Boards of various journals: Chemistry, An Asian Journal (Wiley), J Organic Chemistry (ACS), Beilsten J Organic Chemistry and Oligonucleotides. He is the Founding Editor for ACS Omega (since April 2016) - the first open

Access Journal from American Chemical Society and is currently leading its editorial team to achieve its IF of 3.51 within 4 years. He is a past member of Editorial Advisory Board (EAB) of J. Organic Chemistry and currently EAB member of ACS - Chemical reviews and Accounts of Chemical Research (2022).

In recognition of his scientific contributions, Prof Ganesh was conferred Degree of Doctorate of Science (honoris causa) by Vidyasagar University (West Bengal) in January 2017. Foremost, as the First and Founding Director of IISER Pune (www.iiserpune.ac.in, June 2006-October 2017), Prof Ganesh provided great leadership in Institution building to establish IISERs as brand science education and research institutes, now attaining international recognition. He was also the mentor Director of 6th IISER at Tirupati (www.iisertirupati.ac.in) since February 2015 and assumed charge of its full time Director in November 2017. He now has the rare and unique distinction of being the First and Founder Director of two IISERs - Pune and Tirupati