Journal of
Nanoscience and Nanotechnology
Vol. 7, 2253–2259, 2007

Looking Beyond Carbon Nanotubes: Polypeptide Nanotubes as Alternatives?

G. Praveena[1], P. Kolandaivel[1,*], N. Santhanamoorthi[1], V. Renugopalakrishnan[2,3], and Seeram Ramakrishna[3]

[1] *Department of Physics, Bharathiar University, Coimbatore, Tamil Nadu 641046, India*
[2] *Children's Hospital, Harvard Medical School, Boston, MA 02115, USA*
[3] *Division of Bioengineering and Department of Mechanical Engineering, NUS Nanotechnology Initiative (NUSNNI), National University of Singapore, Singapore-117576*

Since the discovery of CNT by Iijima, *Nature* 354, 56 **(1991)**. CNT's have surged to the forefront as a versatile nanostructured material in nanoelectronic applications. Polypeptides nanotubular structures with tunable properties offer a challenging alternative to CNT. Earlier experimental studies on L-Alanyl-L-Valine (AV) and L-Valyl-L-Alanine (VA) have demonstrated their potential as novel porous materials, which form channel-like structure (Soldatov et al., *Angew. Chem. Int. Ed.* 43, 6308 **(2004)**). In the study reported here, DFT calculations on two closely related cyclic dipeptides cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ and on their linear correlates, [L-alanyl-L-valine]$_3$ and [L-valyl-L-alanine]$_3$ have been performed. This paper presents the general structural and electronic properties of cyclic and linear correlates of the nanotubular oligomeric dipeptides constructs, AV, and VA. We have compared the energy gaps of these cyclic rings and their linear correlates with that of other nanotubular constructs. The calculated HOMO–LUMO gap of these isolated ring structures is significantly larger than CNT's. Further research is required to reduce the band gaps to be comparable to CNT's and other inorganic tubular structures. Polypeptide design promises to be a major tool in engineering desirable band gap for the creation of novel nanostructured polypeptide nanotubes.

Keywords: Cyclic Peptides, Nanostructures, Self-Assembly, Quantum Chemical Study, Band Gap, DFT.

RESEARCH ARTICLE

1. INTRODUCTION

Single wall carbon nanotubes (SWNTs) have unique electronic, mechanical, and structural characteristics. Since its discovery by Iijima[1] promising applications of CNT's as chemical sensors or nano-scale electronic devices have been exponentially growing. Structurally altered nanotubes with appropriate addends should facilitate utilization by improving solubility, processability, and ease of dispersion, as well as by providing sites for chemical attachment to CNT surfaces (Makala, Ramanath, Renugopalakrishnan et al., from our laboratories). Unfortunately CNT's are chemically sluggish and are difficult for covalent attachment to proteins. Besides CNTs, boron nitride,[2] gallium selenide,[3] silicon,[4] MoS2,[5] boron carbonitride,[6] and tungsten disulfide[7] have also emerged as interesting nanotubular structures. These quasi one dimensional nanotubular constructs have opened an exciting field of research because of their unique properties. The exceptional electronic property, metallic versus semi conducting behaviour of carbon nanotubes depends on the diameter and the chirality i.e., on the way the graphene sheet is rolled,[8] whereas in contrast boron nitride nanotubes display a more uniform behaviour with a wide band gap ∼4 eV almost independent of diameter and chirality.[9]

One of the biggest challenges in nanotechnology is the synthesis of pure, monodispersed nanotubes with identical structure and with tunable physical and functional properties. Inorganic nanotubes partially fulfil this goal as it is difficult to synthesize them in a controlled manner to produce identical nanotubes in bulk. Therefore the need to design organic or biological nanotube structures has been raised in the literature. Peptide materials are non toxic and may be used in biological and medical context such as in chiral recognition, preservation, and storage of drugs. Recent studies have focused on polymeric lipid-based tubules,[10] carbohydrate based nanotubes,[11–13] and DNA

*Author to whom correspondence should be addressed.

based nanotubular structures.[14] A series of papers in this series have discussed peptide, protein, lipid based nanotubular structures, and their decoration with semiconductors (De Santis et al.,[15] Hayes et al.,[15] Kumara et al.,[15] and Banerjee et al.[15]).

Specifically, synthesis of polypeptides in the form of nanotubular structures, Ghadiri et al., 1993[16] has drawn considerable interest owing to their applicability in the design of solid state porous materials,[17, 18] biologically relevant ion channels,[18, 19–22] and soluble cylindrical supramolecular structures.[23, 24] Moreover, peptide nanotubes may also find applications in optical and molecular electronic devices,[16, 19, 25] as the internal diameter and surface properties can be tailored by Merrifield solid-phase polypeptide synthesis.

Oligomers of dipeptides may be generated to form an entire family of bioorganic host and micro porous solids. The lower oligomeric dipeptides being simpler model systems appear to be useful as practical porous materials to host small organic and biomolecules.[26, 27] Previous experimental studies[28] on nanotubular assemblies of dipeptides L-alanyl-L-valine (AV) and L-valyl-L-alanine (VA) have indicated their potential as promising novel porous materials. The channels in AV and VA with molecular diameter of 5.13 and 4.90 Å were found to possess minor surface irregularities and are essentially hydrophobic thus exhibiting molecular sieving property. In the present study, we have investigated by DFT calculations the structural and electronic properties of oligomers of L-alanyl-L-valine (AV) and L-valyl-L-alanine (VA). The above peptide oligomers are now being synthesized in our laboratories for characterization of bands gaps by photoelectron spectroscopy and I–V characteristics.

2. COMPUTATIONAL STUDIES

The geometries of monomeric rings cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ and their respective linear forms have been optimized employing DFT calculations. Hybrid functionals are in widespread use for calculations in molecular systems due to their higher accuracy compared to pure functionals.[29] From these family of functionals, we have chosen B3LYP (Becke'3 parameter for the exchange and Lee, Yang, and Parr for the electronic correlation) hybrid exchange correlation functionals.[30–32] The basis set with polarization function 6-31G* has been used through out our calculation. Also single point energy calculation at HF/6-31G*//B3LYP/6-31G* level is carried out for the optimized geometries. A topological analysis for the electron density ρ, and the Laplacian of the electron density, $\nabla^2\rho$, for the bonds were obtained through the wavefunction calculation using Morphy98.[33]

Calculation of the energy band gap requires energy of the *Frontier orbitals: HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital)*, [Fukui[34]] which are largely responsible for

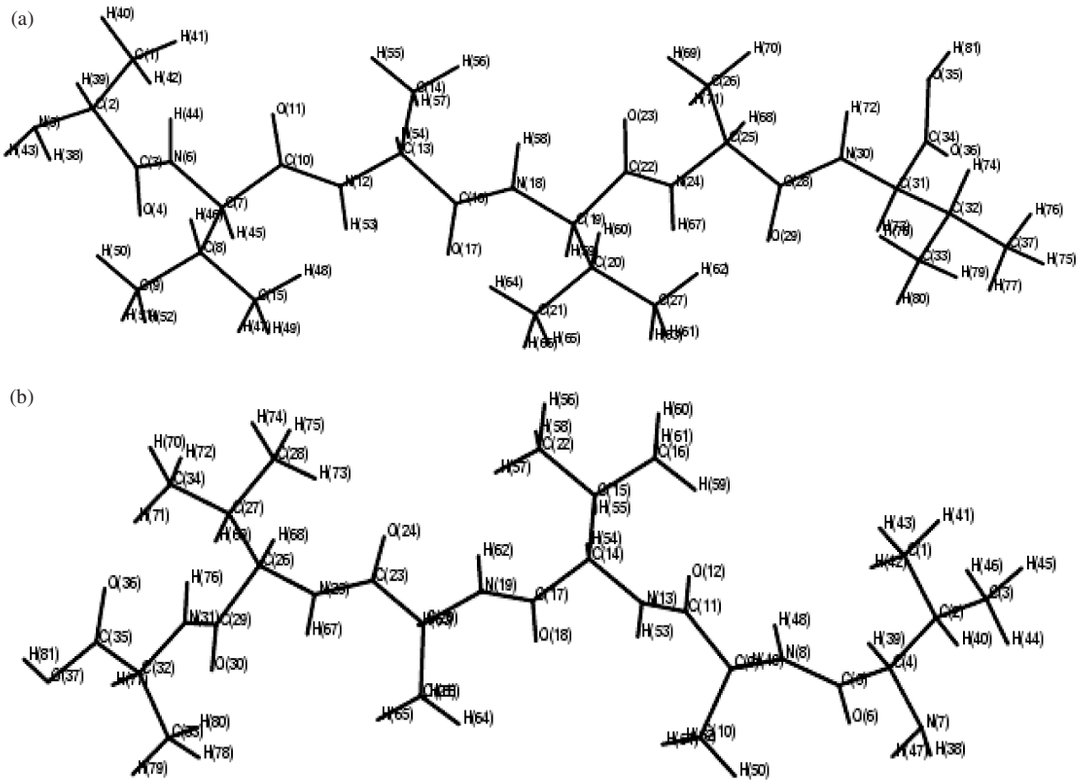

Fig. 1. Linear structures of (a) [L-alanyl-L-valine]$_3$ (AV) and (b) [L-valyl-L-alanine]$_3$ optimized at B3LYP/6-31G* level of theory.

RESEARCH ARTICLE

chemical and spectroscopic properties of the molecules. The HOMO–LUMO energy difference represents the energy band gap that provides the basis for electrical conduction. All calculations have been performed using Gaussian 98W package.[35]

3. RESULTS AND DISCUSSION

DFT results of the properties of isolated monomeric ring structures of dipeptide systems [L-alanyl-L-valine]$_3$ (AV) and [L-valyl-L-alanine]$_3$ (VA) along with their linear correlates are discussed. A feature that distinguishes AV and VA from most of the other tubulates is that their channels are essentially chiral.[28] The optimized geometries of the linear and cyclic forms of [L-alanyl-L-valine]$_3$ (AV) and [L-valyl-L-alanine]$_3$ (VA) are shown in Figures 1 and 2. The total energies of all the optimized structures are presented in Table I. Even though the isolated ring structures of AV and VA have not been synthesized experimentally, it is interesting to investigate these systems as a basis for the larger nanotube systems. Further, these isolated ring structures can be stacked through an extensive network of hydrogen bonding to form nanotubular structures. The crystal structure for these two dipeptide nanotubular constructs have been determined experimentally[28] and demonstrated that both the crystal systems are hexagonal and assembles through hydrogen bonds spirally to form a channel. Ramachandran angles ϕ, ψ, and peptide deformation angle, ω determine the secondary structure of polypeptides. The resulting Ramachandran angles (Table II) of both the dipeptides cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ show that these cyclic systems, typical of cyclic peptides, do not maintain the perfect peptide planarity due to ring strain and the remaining angles ϕ and ψ deviates abruptly. This feature is found to be caused by the intra-ring hydrogen bond of N–H$\cdots$O induced by the cyclization of the peptide chain.[36]

Due to greater flexibility of the peptide backbone larger ring structures will not sample in the flat ring shaped conformational state to effectively take part in the nanotube self assembly process.[18] It could be seen from Figure 2 that there is a large backbone strain on the isolated ring structures of cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ due to the presence of intramolecular hydrogen bonds. Studies reported in the literature[37] have suggested that the formation of hydrogen bond is associated with the appearance of a bond critical point between hydrogen and acceptor atoms, which are linked by the concomitant bond path. This critical point has typical properties of a closed-shell interaction: the value of electron density at the bond critical point, ρ, is relatively low, and the Laplacian of the electron density, $\nabla^2\rho$, is positive indicating that the interaction is dominated by the contraction of charge away from the interatomic surface towards each nuclei. As seen in Table III, these conditions are fulfilled for the N–H$\cdots$O

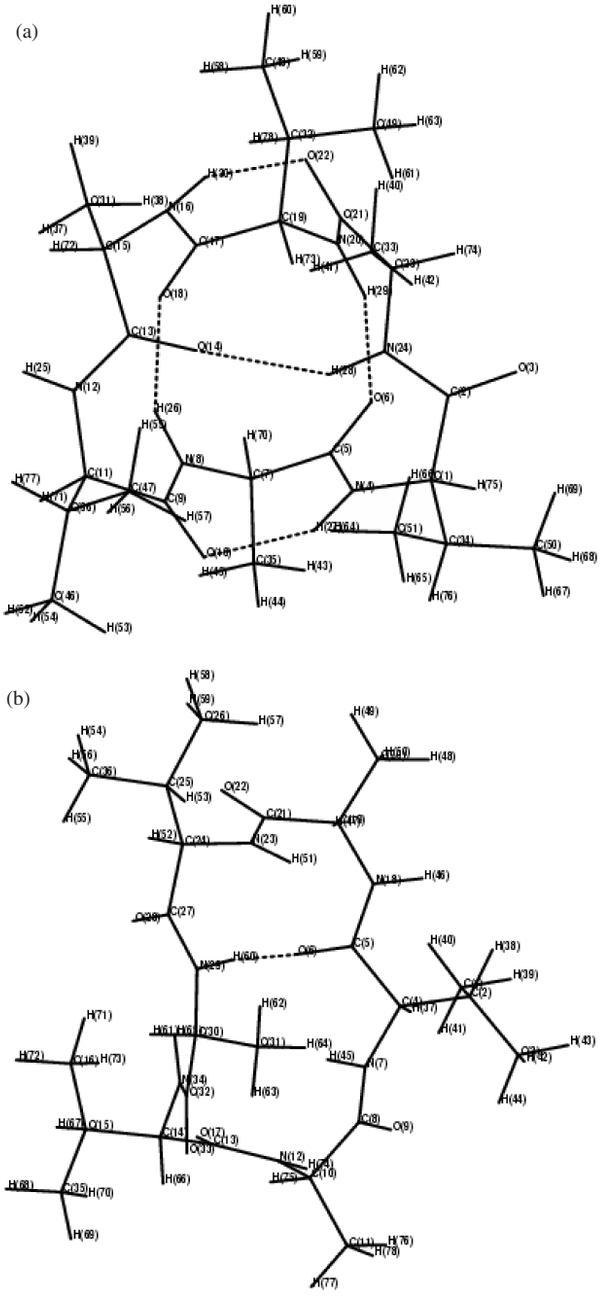

Fig. 2. The cyclic structures of (a) [L-alanyl-L-valine]$_3$ and (b) L-valyl-L-alanine]$_3$ optimized at B3LYP/6-31G* level of theory.

intra-molecular hydrogen bonds present in the cyclo[L-alanyl-L-valine]$_3$ (AV) and cyclo[L-valyl-L-alanine]$_3$ (VA) dipeptide systems. The electron density at the bond critical point ranges from 0.010 to 0.034 a.u., which compares fairly well with the values reported for different hydrogen bonded complexes where this quantity was found to vary from 0.002 to 0.034 a.u.[37c, e]

The diameters of experimentally[28] obtained channels of AV and VA are found to be small of the order of 5.13 and 4.90 Å compared to the theoretically calculated values,

Table I. Total energy (T. E in hartrees), E_{HOMO} and E_{LUMO} (in hartrees) and energy gap (in eV) of isolated [L-alanyl-L-valine]$_3$ and [L-valyl-L-alanine]$_3$ in linear and cyclic forms at B3LYP/6-31G* and HF/6-31G*//B3LYP/6-31G* levels of theory.

		B3LYP/6-31G*				HF/6-31G*//B3LYP/6-31G*			
	System	T. E	E_{HOMO}	E_{LUMO}	E_g	T. E	E_{HOMO}	E_{LUMO}	E_g
[L-Ala-L-Val]$_3$	Linear	−1796.257	−0.225	−0.019	5.61	−1785.316	−0.380	0.153	6.16
	Cyclic	−1719.844	−0.233	−0.014	5.96	−1709.291	−0.374	0.147	6.18
[L-Val-L-Ala]$_3$	Linear	−1796.261	−0.221	−0.022	5.42	−1785.320	−0.378	0.150	6.20
	Cyclic	−1719.826	−0.241	−0.021	5.99	−1709.278	−0.385	0.140	6.67

Table II. Ramachandran angles ϕ and ψ and peptide deformation angle ω (in degrees) of cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ at B3LYP/6-31G* level of theory.

Cyclo[L-alanyl-L-valine]$_3$	In degrees	Cyclo[L-valyl-L-alanine]$_3$	In degrees
Ramachandran angles (ϕ)			
C17-N16-C_α15(Ala1)-C13	−70.23	C21-N23-C_α24(Val1)-C27	−133.63
C21-N20-C_α19(Val1)-C17	−44.98	C5-N18-C_α19(Ala1)-C21	−63.99
C2-N24-C_α23(Ala2)-C21	52.438	C8-N7-C_α4(Val2)-C5	127.12
C5-N4-C_α1(Val2)-C2	−61.374	C13-N12-C_α10(Ala2)-C8	110.58
C9-N8-C_α7(Ala3)-C5	121.23	C32-N34-C_α14(Val3)-C13	125.29
C13-N12-C_α11(Val3)-C9	64.66	C27-N29-C_α30(Ala3)-C32	−144.22
Ramachandran angles (ψ)			
N16-C_α15(Ala1)-C13-N12	63.50	N23-C_α24(Val1)-C27-N29	34.73
N20-C_α19(Val1)-C17-N16	−40.25	N18-C_α19(Ala1)-C21-N23	−33.93
N24-C_α23(Ala2)-C21-N20	−132.75	N7-C_α4(Val2)-C5-N18	−177.47
N4-C_α1(Val2)-C2-N24	62.56	N12-C_α10(Ala2)-C8-N7	−0.22
N8-C_α7(Ala3)-C5-N4	−36.75	N34-C_α14(Val3)-C13-N12	−61.07
N12-C_α11(Val3)-C9-N8	25.40	N29-C_α30(Ala3)-C32-N34	0.54
Peptide deformation angle (ω)			
C_α15(Ala1)-N16-C17-C_α19(Val1)	−176.25	C_α24(Val1)-N23-C21-C_α19(Ala1)	177.30
C_α23(Ala2)- C21-N20-C_α19(Val1)	173.89	C_α4(Val2)-C5-N18-C_α19(Ala1)	−164.27
C_α23(Ala2)- N24-C2-C_α1(Val2)	−157.77	C_α4(Val2)-N7-C8-C_α10(Ala2)	−169.84
C_α7(Ala3)-C5-N4-C_α1(Val2)	163.91	C_α14(Val3)-C13-N12-C_α10(Ala2)	−4.37
C_α7(Ala3)- N8-C9 -C_α11(Val3)	−173.14	C_α14(Val3)-N34-C32-C_α30(Ala3)	170.13
C_α15(Ala1)-C13-N12-C_α11(Val3)	170.54	C_α14(Val1)-C27-N29-C_α30(Ala3)	−169.49

Table III. Diameter and molarvolume of cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ at B3LYP/6-31G* level of theory.

	ρ	$\nabla^2\rho$	H···Y (Å)	X–H (Å)	Diameter (Å)	Molar volume (cm^3/mol)
Cyclo[L-Ala-L-Val]$_3$						
N4-H27···O10	0.028	0.088	1.948	1.020		
N24-H28···O14	0.010	0.039	2.324	1.015		
N16-H30···O22	0.034	0.112	1.840	1.023	5.84 (5.13)*	430.03 (109.39)*
N8-H26···O18	0.022	0.073	2.018	1.017		
N20-H29···O6	0.020	0.065	2.064	1.019		
Cyclo[L-Val-L-Ala]$_3$						
N29-H60···O6	0.012	0.040	2.315	1.015	5.05 (4.90)*	476.29 (109.98)*

*Experimental values are given in the parenthesis.

which are about 5.84 and 5.05 Å, respectively. It is confirmed both experimentally and theoretically that the range of nanotube diameters may confined between 7 and 13 Å.[17] The energetics of the two cyclic structures optimized at B3LYP/6-31G* level of theory (Table I) show that cyclo[L-alanyl-L-valine]$_3$ is more stable and facilitates the formation of channel with molar volume (Table III) of about 430.03 cm^3/mol compared to cyclo[L-valyl-L-alanine]$_3$. Moreover, it is noted that theoretical calculations on molar volume overestimates in comparison to the experimental one.

The energy band gap values, measured as the difference between the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are calculated for both the linear and cyclic forms of AV and VA and presented in Table I. Figure 3 gives the pictorial representation of HOMO and LUMO orbitals of the cyclic peptides. The values that are obtained for the

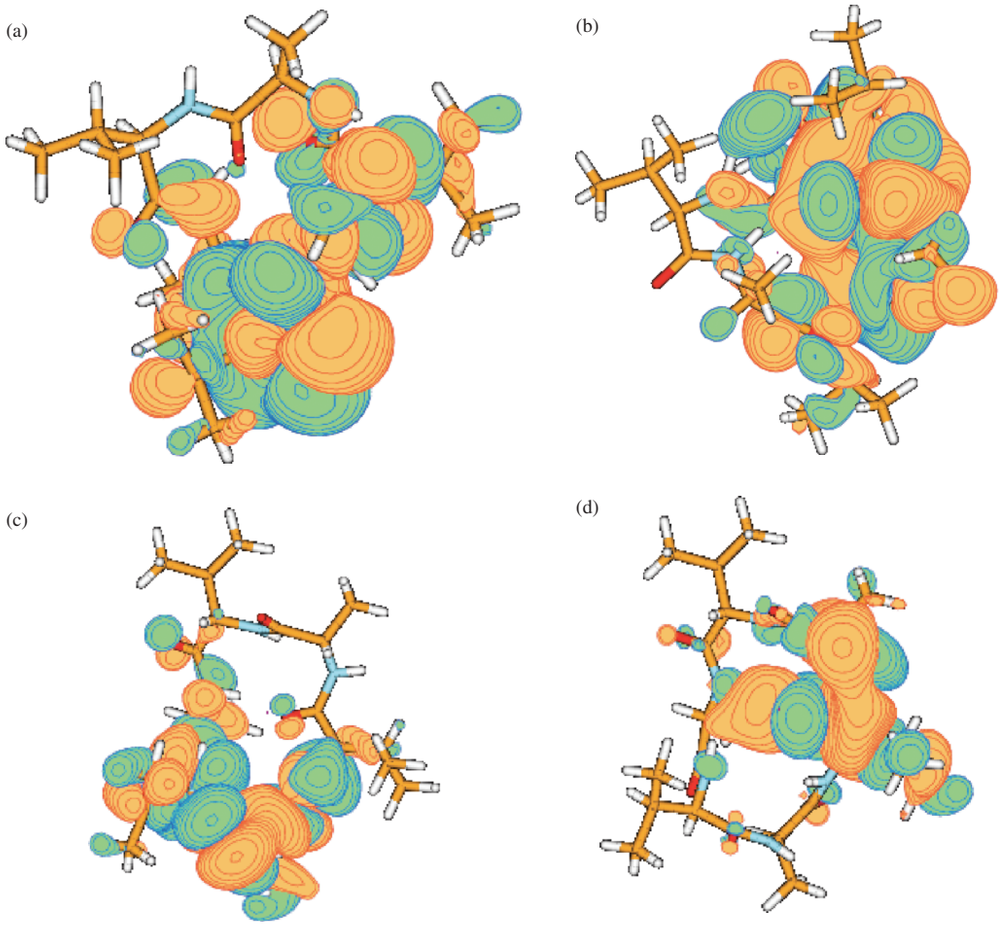

Fig. 3. Pictorial representation of HOMO and LUMO orbitals of cyclo[L-alanyl-L-valine]$_3$ (a and b) and cyclo[L-valyl-L-alanine]$_3$ (c and d) obtained at B3LYP/6-31G* level of theory.

energy gaps of these cyclic peptide systems are approximately 6.0 eV at both the B3LYP/6-31G* and HF/6-31G*//B3LYP/6-31G* levels of theory. The energy gaps are rather large. Almost all the peptide nanotubular constructs are found to have large band gaps, which have been experimentally supported in the earlier literature[23] that reports for the formation of colorless prismatic crystals. Here a comparison has been made over the energy gaps of these peptide nano constructs with that of inorganic nanotubes like CNT, BN, GaSe, Si, and BCN, which shows peptides nanotubes to be one of the most challenging and promising candidates in bioelectronic applications. It is well known that the smaller diameter CNTs are metallic while the larger diameter CNT's are semi conducting in nature[8] with BN tubes that show uniform band gap of 4 eV for an entire range of diameters.[9] As all the Si nanotubes are metallic,[4] the energy band gap of GaSe is found in between carbon and boron nitride nanotubes.[3] Boron-carbonitride nanotubes are the analogues of carbon and BN nanotubes that could be formed by the random replacement of carbon atoms with boron and nitrogen atoms and vice versa. It has been found that BCN tubes when formed by the substitution of B and N atoms in metallic CNTs causes level broadening but remains metallic in nature, whereas the energy gap of boron nitride nanotubes under random swapping of B-N atoms by carbon becomes

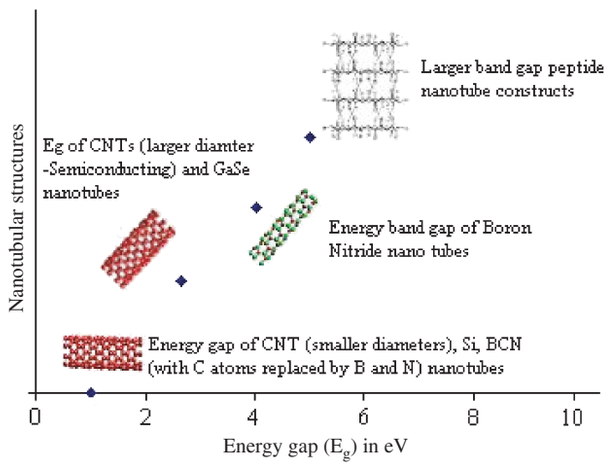

Fig. 4. The graphical representation of various nanotubular constructs with their corresponding energy gaps.

smaller than the original band gap.[38] Figure 4 depicts the comparison of the energy gaps of material nanotubes with that of the peptide nanotubes. The band gaps of peptide constructs are comparatively larger than any other material nanotubes which emphasize the use of these transparent biomaterials in the field of nanoelectronic devices and other materials science applications.

4. CONCLUDING REMARKS

We have demonstrated the structural and electronic properties of the monomeric rings of dipeptide nanotubular constructs cyclo[L-alanyl-L-valine]$_3$ and cyclo[L-valyl-L-alanine]$_3$ along with their linear correlates, which have been suggested as novel porous materials by Soldatov et al.[28] The energy gap of the cyclic constructs of [L-alanyl-L-valine]$_3$ (AV) and [L-valyl-L-alanine]$_3$ (VA) was found to be larger and approximately equals 6 eV consistent with a transparent material and suggesting their potential utilization towards bioelectronics applications. As AV and VA cyclic peptide systems have band gaps that are greater than even other peptide nano tubular structures, transport of various species may be independent of the channel diameter, allowing for a greater flexibility in applications.

Carbon Nanotubes discovered by Iijima[1] in NEC laboratories in early 90's have emerged as a versatile material in nanoelectronics. CNT's manifest excellent electrical conductivity and mechanical properties but are chemically poorly reactive. Synthetic polypeptide, protein, DNA, lipid nanotubes have been the subject of intense studies in recent times due to their potential utility in chemical, biological, and materials science applications. Single-wall carbon nanotubes (SW CNTs) are unique electronic structures. They are one-dimensional wires composed entirely of surface atoms yet exhibit transport properties superior to bulk single-crystalline silicon (Si). This high electron mobility makes them an ideal candidate for electronic device applications, while their virtually infinite surface-to-volume ratio offers extraordinary sensitivity for chemical and biological sensor applications. However, a major obstacle presently preventing their commercial implementation in new classes of electronic devices is the lack of a technique for the controlled assembly of large numbers of SW CNTs with precisely controlled position and orientation. Until this obstacle is overcome or circumvented. SW CNT-based devices and sensors will remain in the realm of impressive laboratory curiosities lagging behind in real-world applications. One of the biggest challenges in nanotechnology is the synthesis of pure, monodispersed nanotubes or nanowires with identical structure and with tuneable physical or functional properties. CNT's stops short of fulfilling this goal, partly because it is difficult to synthesise them in a way that produces identical nanotubes in bulk. Polypeptide nanotubes offer a promising alternative to CNT's and inorganic nanotubes.

Acknowledgments: PK is supported by CSIR, New Delhi, India. VR is supported by grants from NSF, NIH, Wallace H. Coulter Foundation. SR acknowledges support from AStar, Singapore.

ABBREVIATIONS

DFT Density Functional Theory
CNT Carbon Nanotube
AV L-Alanyl-L-Valine
VA L-Valyl-L-Alanine
HOMO Highest Occupied Molecular Orbitals
LUMO Lowest Unoccupied Molecular Orbitals

References and Notes

1. S. Iijima, *Nature* 354, 56 (**1991**).
2. N. G. Chopra, R. J. Luyken, K. Cherry, V. H. Crespi, M. L. Cohen, S. G. Louie, and A. Zettle, *Science* 269, 966 (**1995**).
3. M. Côté and M. L. Cohen, *Phys. Rev. B* 58, 4277 (**1998**).
4. J. Bai, X. C. Zeng, H. Tanaka, and J. Y. Zeng, *Proc. National Acad. Sci.* (*USA*) 101, 2664 (**2004**).
5. Y. Feldman, E. Wasserman, D. J. Srolovitz, and R. Tenne, *Science* 267, 222 (**1995**).
6. Z. Weng-Seih, K. Cherry, N. G. Chopra, X. Blase, Y. Miyamoto, A. Rubio, M. L. Cohen, S. G. Louie, A. Zettle, and R. Gronsky, *Phys. Rev. B* 51, 11229 (**1995**).
7. F. Tenne, L. Margulis, M. Genut, and G. Hodes, *Nature* 360, 444 (**1992**).
8. R. Saito, G. Dresselhaus, and M. S. Dresselhaus, Physical Properties of Carbon Nanotubes, Imperial College Press, London (**1998**).
9. A. Rubio, J. L. Corkill, and M. L. Cohen, *Phys. Rev. B* 49, 5081 (**1994**).
10. Y.-S. Lee, J.-Z. Yang, T. M. Sisson, D. A. Frankel, J. T. Gleeson, M. Aksay, S. L. Keller, S. M. Gruner, and D. F. O'Brien, *J. Am. Chem. Soc.* 117, 5573 (**1995**).
11. A. Harada, J. Li, and M. Kamachi, *Nature* 364, 516 (**1993**).
12. G. Gattuso, S. Menzer, S. A. Nepogodiev, J. F. Stoddart, and D. J. Williams, *Angew. Chem. Int. Ed. Engl.* 36, 1451 (**1997**).
13. K. Benner, P. Klüfers, and J. Schumacher, *Angew. Chem. Int. Ed. Engl.* 36, 743 (**1997**).
14. F. C. Simmel and W. U. Dittmer, *Small* 1, 284 (**2005**).
15. (a) P. De Santis, S. Morosetti, and A. Scipioni, *J. Nanosci. Nanotechnol.* 7, 2230 (**2007**); (b) M. A. Hayes, M. D. Pysher, and K. Chen, *J. Nanosci. Nanotechnol.* 7, 2283 (**2007**); (c) M. T. Kumara, S. Muralidharan, and B. C. Tripp, *J. Nanosci. Nanotechnol.* 7, 2260 (**2007**); (d) I. A. Banerjee, G. Muniz, S.-Y. Lee, and H. Matsui, *J. Nanosci. Nanotechnol.* 7, 2287 (**2007**).
16. M. R. Ghadiri, J. R. Granja, R. A. Milligan, D. E. McRee, and N. Khazanovich, *Nature* 366, 324 (**1993**).
17. N. Khazanovich, J. R. Granja, D. E. McRee, R. A. Milligan, and M. R. Ghadiri, *J. Am. Chem. Soc.* 116, 6011 (**1994**).
18. J. D. Hartgerink, J. R. Granja, R. A. Milligan, and M. R. Ghadiri, *J. Am. Chem. Soc.* 118, 43 (**1996**).
19. M. R. Ghadiri, J. R. Granja, and L. K. Buehler, *Nature* 369, 301 (**1994**).
20. J. R. Granja and M. R. Ghadiri, *J. Am. Chem. Soc.* 116, 10785 (**1994**).
21. M. Engles, D. Bashford, and M. R. Ghadiri, *J. Am. Chem. Soc.* 117, 9151 (**1995**).
22. H. S. Kim, J. D. Hartgerink, and M. R. Ghadiri, *J. Am. Chem. Soc.* 120, 4417 (**1998**).

RESEARCH ARTICLE

23. M. R. Ghadiri, K. Kobayashi, J. R. Granja, R. K. Chadha, and D. R. McRee, *Angew. Chem. Int. Ed. Engl.* 34, 93 **(1995)**.
24. T. D. Clark and M. R. Ghadiri, *J. Am. Chem. Soc.* 117, 12364 **(1995)**.
25. G. M. Whitesides, J. P. Mathias, and C. T. Seto, *Science* 254, 1312 **(1991)**.
26. S. N. Mitra and E. Subramaniam, *Biopolymers* 34, 1139 **(1994)**.
27. C. H. Görbitz, *Acta. Crystallogr.* B58, 849 **(2002)**.
28. D. V. Soldatov, I. L. Moudrakovski, and J. A. Ripmeester, *Angew. Chem. Int. Ed.* 43, 6308 **(2004)**.
29. J. Heyd and G. E. Scuseria, *J. Chem. Phys.* 120, 7274 **(2004)**.
30. C. Lee, W. Yang, and R. G. Parr, *Phys. Rev. B* 37, 785 **(1988)**.
31. B. Miehlich, A. Savin, H. Stoll, and H. Preuss, *Chem. Phys. Lett.* 157, 200 **(1989)**.
32. A. D. Becke, *J. Chem. Phys.* 98, 5648 **(1993)**.
33. P. L. A. Popelier and R. G. A. Bone, MORPHY98, UMIST, Manchester, England, EU **(1998)**.
34. K. Fukui, Nobel Lectures, Chemistry, 1981–1990, Editor-in-Charge, edited by T. Frangsmyr, Bo G Malmstrom, World Scientific Publishing Co., Singapore **(1992)**.
35. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, and J. A. Pople, *Gaussian98* Gaussian, Inc., Pittsburgh PA **(2001)**.
36. H. Okamoto, T. Nakanishi, Y. Nagai, M. Kasahara, and K. Takeda, *J. Am. Chem. Soc.* 125, 2756 **(2003)**.
37. (a) M. T. Caroll and R. F. W. Bader, *Mol. Phys.* 65, 695 **(1988)**; (b) M. T. Caroll, C. Chang, and R. F. W. Bader, *Mol. Phys.* 63, 387 **(1988)**; (c) U. Koch and P. L. A. Popelier, *J. Phys. Chem.* 99, 9747 **(1970)**; (d) R. F. W. Bader and H. Essén, *J. Chem. Phys.* 80, 1943 **(1984)**; (e) P. L. A. Popelier and R. F. W. Bader, *Chem. Phys. Lett.* 189, 542 **(1992)**.
38. T. Yoshioka, H. Suzuura, and T. Ando, *J. Phys. Soc. Jpn.* 72, 2656 **(2003)**.

Received: 1 November 2006. Accepted: 24 November 2006.