

Bis-naphthobipyrrolylmethene derived BODIPY complex: an intense near-infrared fluorescent dye†

Tridib Sarma,^a Pradeepta K. Panda^{*a} and Jun-ichiro Setsune^bCite this: *Chem. Commun.*, 2013, **49**, 9806Received 27th June 2013,
Accepted 25th August 2013

DOI: 10.1039/c3cc44834g

www.rsc.org/chemcomm

Synthesis of a novel π -extended BODIPY derived from naphthobipyrrole is presented. This dye molecule displays very intense near-infrared (NIR) absorption ($\epsilon > 400\,000\text{ M}^{-1}\text{ cm}^{-1}$) and emission bands ($>700\text{ nm}$), accompanied by high quantum yield ($\phi_f = 0.65$) owing to its extended π -conjugation along with imposed structural rigidification.

4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene dye **1** commonly known as BODIPY or 'porphyrin's little sister' represents a unique class of fluorophores that display strong absorption in the UV-Vis region and sharp emission with high quantum yield.¹ These attributes have made BODIPYs attractive for a variety of applications including laser dyes,² luminescent devices,³ chemical sensors,⁴ biological labeling,⁵ and photovoltaic devices.⁶

However, most of the compounds in this potential class of fluorophores absorb and emit below 600 nm and have relatively low extinction coefficients (ϵ around $80\,000\text{ M}^{-1}\text{ cm}^{-1}$), which makes them undesirable for applications in biotechnology and imaging. In order to overcome this deficiency, several synthetic modifications have been performed on the parent BODIPY moiety, which includes extension of π -conjugation,⁷ introduction of the intramolecular charge transfer (ICT) character⁸ and replacement of carbon with a nitrogen bridge-head in the BODIPY skeleton.⁹ The extension of the π -conjugation has so far been achieved *via* introduction of ethynyl and vinyl groups or fusion of BODIPY with aryl groups at its periphery.

Recently NIR dyes (*i.e.* absorbing in the range of 700 to 1000 nm) have drawn wide attention from researchers, owing to their effective use in visualization and investigation of molecular targets in biomolecules (transparent in this region) *via* autoabsorption and auto-fluorescence. However, there are only very few reports in this regard.¹⁰ Towards this, BODIPYs with fused aromatic polycyclic or

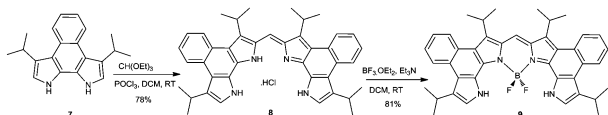
heteroaromatic rings have gained much attention.¹¹ Fused BODIPY systems are generally synthesized by oxidative fusion of BODIPY with the aryl moiety at the periphery or by condensation of a π -extended fused pyrrole with an aldehyde and subsequent conversion to the desired target. However, efforts in the latter direction are limited, owing to the associated synthetic challenges involved in preparing π -extended fused pyrroles.^{11a-h} So far, fusion of an aromatic ring has resulted in a significant red shift in the absorption and emission properties of the BODIPY dyes, owing to the extended π -conjugation. However, an efficient dye in addition needs to show sharp absorption and emission bands with high extinction coefficient and quantum yield simultaneously, in order to find practical application. Most of the NIR dyes synthesized so far have lacked one or more attributes. For instance, the very recently reported benzo-fused bis-BODIPY **4** shows emission around 940 nm, which is very attractive yet displays arguably very weak emission ($\phi_f < 1\%$).^{11g} On the other hand, bis-BODIPY **6** with absorption and emission above 840 nm is highly labile under aerobic conditions.^{11h} Similarly, perylene-fused BODIPY **5** shows aggregation dependent emission at 830 nm but possesses a moderate extinction coefficient and very low quantum yield.¹¹ⁱ Very few derivatives possess these qualities, especially beyond 700 nm.^{9c,11a,b} Therefore, quest for new efficient NIR dyes, endowed with intense absorption and greater fluorescence quantum yield still continues.

Herein, we report on the synthesis, structure and photophysical properties of a naphthobipyrrole derived BODIPY based NIR dye **9**. The salient features of this molecule are: it displays extremely sharp absorption and emission bands with exceptionally high extinction coefficient ($\log \epsilon = 5.61$ to 5.37) as well as possesses high quantum yields ($\phi_f = 0.65$ to 0.44) in the range of 715–730 and 733–755 nm respectively, depending on the solvents used for the measurement. From the synthetic point of view, two bipyrrole units had never been employed directly as a precursor for BODIPY and utilization of the fused bipyrrole moiety to extend the π -conjugation is also a completely new approach. This mode of fusion leads to structural rigidification thereby reducing non-radiative emissive pathways and hence increasing the fluorescence quantum yield. In addition, it also imparts a greater stability to the resultant target molecule. Exploration of naphthobipyrrole as a BODIPY precursor was inspired by our

^a School of Chemistry, University of Hyderabad, Hyderabad-500046, Andhra Pradesh, India. E-mail: pradeepta.panda@uohyd.ac.in, pradeepta.panda@gmail.com

^b Department of Chemistry, Graduate School of Science, Kobe University, Kobe 657-8501, Japan

† Electronic supplementary information (ESI) available: Synthetic procedures and characterization data for new compounds, crystal data for **8** and **9** (CIF). CCDC 946926 and 946927. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3cc44834g



Scheme 1 Synthetic route to BODIPY 9.

recent findings related to various π -extended porphyrinoids derived from it, which displays unprecedented optical and structural properties.¹² Synthesis of alkylated naphthobipyrrole has been reported recently by our group and Sessler's group independently.^{12a,b}

Scheme 1 depicts the synthetic route to BODIPY 9. Bis-naphthobipyrrolyldipyrromethene hydrochloride **8** was originally obtained as an unexpected by-product in an FeCl_3 mediated oxidative coupling reaction of naphthobipyrrole to yield cyclo[4]naphthobipyrrole.^{12d} Initially, it was presumed to be a higher analogue, cyclo[n]naphthobipyrrole ($n > 4$) and could not be characterized unequivocally owing to the very low yield (due to the presence of a *meso*-like proton signal at 8.16 ppm and the absence of a molecular ion peak in HRMS). Interestingly, this compound was first characterized using single crystal X-ray diffraction analysis and found to be a hydrochloride salt of bisnaphthobipyrrolylmethene **8** (Fig. 2a) and subsequently other spectroscopic data complied with (ESI^+). Since neither any formyl equivalent (as the carbon source) nor HCl were used in the reaction, the source of *meso* carbon can be attributed to the solvent dichloromethane, which under the reaction conditions, probably oxidized to a formic acid derivative liberating HCl. Compound **8** appeared to be an interesting building block for the synthesis of novel π -extended porphyrinoids, owing to its interesting structure, photophysical properties and stability. However, the yield of the product obtained using this route was very low (*ca.* 2%). Subsequently, we adopted the rational synthetic approach,¹³ where the reaction of naphthobipyrrole **7** and triethylorthoformate in the presence of POCl_3 led us to isolate **8** in 78% yield, again as the mono-hydrochloride salt (Scheme 1). The ^1H NMR spectrum of **8** in CDCl_3 shows two NH-signals at 12.59 ppm and 11.69 ppm. Treating compound **8** with triethylamine and $\text{BF}_3 \cdot \text{OEt}_2$ furnished the desired BODIPY **9** in 81% yield.

The X-ray structure of compound **8** (Fig. 2a) displayed its almost planar nature owing to the β - β fusion of the constituent bipyrrolic moieties. Two outer pyrrolic nitrogens N1 and N4 lie above the mean plane (0.22 Å) defined by the dipyrromethene unit. The outer fused *o*-phenylene moieties lie below the mean plane at a maximum distance of 0.30 Å. The chloride ion was found at 0.38 Å above the mean plane and hydrogen bonded to four pyrrolic NH groups with the N-H...Cl distance in the range of 3.17–3.18 Å. On the other hand, the X-ray structure of compound **9** (Fig. 2b) shows comparatively more deviation from planarity than compound **8**, in an otherwise near planar structure. The two outer pyrrole nitrogens N1 and N4 were found to be above the mean plane defined by the BODIPY core at a distance of 0.37 and 0.14 Å respectively. Furthermore, the two fused *o*-phenylene moieties lie below the mean plane with maximum deviations of 0.55 and 0.58 Å. Interestingly, we noticed good face to face π - π stacking interactions in compound **8** (interplanar distance of 3.94 Å), where the two molecules lie in adjacent planes that face in the opposite direction. In the case of its BODIPY derivative **9** π - π stacking interaction is reduced (interplanar

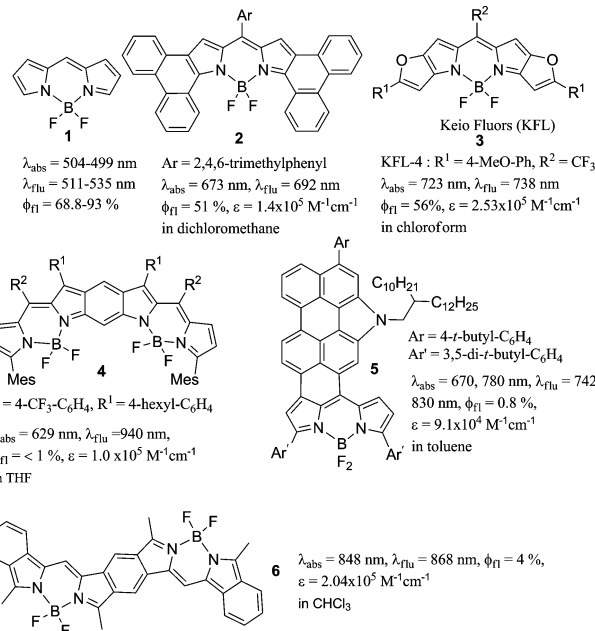


Fig. 1 BODIPY and some of its important π -extended analogues.

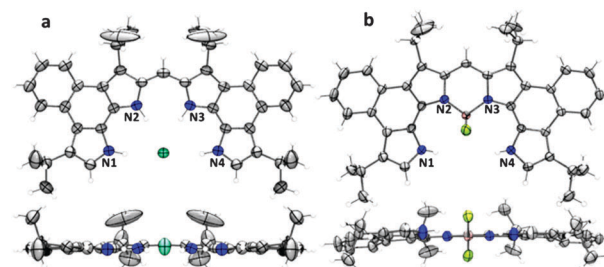


Fig. 2 POV-Ray ORTEP of (a) **8** and (b) **9**. Top: front view, bottom: side view. Thermal ellipsoids are scaled to 35% probability level.

distance of 4.29 Å), with a ladder-like arrangement of the molecules facing in the same direction (Fig. S11 and S12, ESI^+).

The absorption and emission properties of compound **9** were studied in different solvents (Fig. 3) and Table 1 summarizes the data. Compound **9** displayed substantially red shifted absorption (727 nm) and emission maxima (744 nm) in chloroform compared to the recently reported biphenyl fused BODIPY **2** (Fig. 1).^{11j} In addition, compound **9** exhibited a very high extinction coefficient with an ϵ value of $327\,000\ \text{M}^{-1}\ \text{cm}^{-1}$ and reasonably high fluorescence quantum yield (0.63). To the best of our knowledge, a BODIPY dye having a higher extinction co-efficient than **9** is not known, the

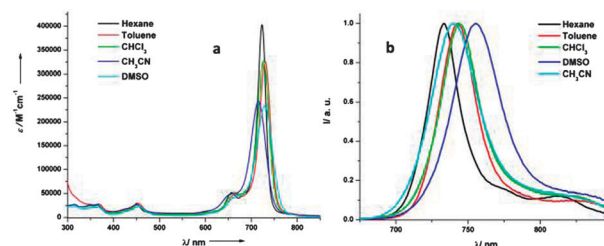


Fig. 3 (a) UV-Vis-NIR absorption and (b) normalized emission spectra of compound **9** in different solvents.

Table 1 Summary of the optical properties of compound **9**

Solvent	Absorption			Emission				
	λ_{max} in nm (log ϵ)	fwhm (cm ⁻¹)	λ_{exc} (nm)	λ_{max} (nm)	Stokes shift (cm ⁻¹)	fwhm (cm ⁻¹)	τ_f (ns)	ϕ_f^a
Hexane	723 (5.61)	402	655	733	189	487	4.70	0.65
Toluene	730 (5.51)	555	655	743	239	550	4.40	0.62
CHCl ₃	727 (5.51)	577	660	744	315	583	4.45	0.63
CH ₃ CN	715 (5.39)	775	655	739	454	715	3.80	0.48
DMSO	729 (5.37)	798	660	755	472	704	3.39	0.44

^a Quantum yields were measured using DOTC iodide as the reference.¹⁵

closest being the KFL-7 dye [$\epsilon = 316\,000\text{ M}^{-1}\text{ cm}^{-1}$, $\lambda_{\text{max}}(\text{abs}) = 662\text{ nm}$, $\lambda_{\text{max}}(\text{flu}) = 671\text{ nm}$ in CHCl₃].^{11b} The absorption and emission properties of compound **9** were not much affected by the nature of the solvent. However, in polar solvents like DMSO and acetonitrile a relatively larger Stokes shift was observed accompanied by a decrease in the fluorescence quantum yield and fluorescence lifetime. Nonetheless they are still quite high for this class of NIR dyes ($\phi_f > 0.4$). These values are better than or comparable with KFL-4 dye **3**, which is regarded as possessing the best optical properties among the BODIPY dyes [$\lambda_{\text{max}}(\text{abs}) = 723\text{ nm}$, log $\epsilon = 5.40$, $\lambda_{\text{max}}(\text{flu}) = 738\text{ nm}$, fwhm = 577 cm^{-1} and $\phi_f = 0.56$ in CHCl₃].^{11a} The absorption and emission properties of our BODIPY dye **9** also competes well with the cyanine dye Cy7 [$\lambda_{\text{max}}(\text{abs}) = 742\text{ nm}$, log $\epsilon = 5.38$, $\lambda_{\text{max}}(\text{flu}) = 772\text{ nm}$ and $\phi_f = 0.28$ in ethanol] which is one of the most widely used NIR dyes.¹⁴ Further, in spite of two additional unbound pyrrole derivatives with free α -positions, dye **9** (air saturated) shows quite good photostability [exposure to 365 nm (8 watt UV lamp) for 96 h shows an absorption λ_{max} decrease of 31%; an average of only 1% decrease per 3 h of irradiation].

In conclusion, an efficient synthesis of novel π -extended BODIPY **9** was demonstrated, which shows very intense NIR absorption (730 nm) and emission (744 nm) with efficient quantum yield ($\phi_f = 0.65$) and hence may find application as an efficient NIR dye. Presently we are trying to increase the robustness of this molecule *via* suitable derivatization, while extending our approach to synthesize new π -extended BODIPYs, which may possess more interesting photophysical properties.

This work was supported by CSIR, India. T. S. thanks CSIR for a fellowship. We thank Dr K. Santhosh, School of Chemistry, University of Hyderabad, for lifetime measurements.

Notes and references

- (a) A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **107**, 4891; (b) R. P. Haugland, In *The Handbook: A Guide to Fluorescent Probes and Labeling Technologies*, Invitrogen Corp., Eugene, OR, 10th edn, 2005; (c) R. Ziessel, G. Ulrich and A. Harriman, *New J. Chem.*, 2007, **31**, 496; (d) G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem., Int. Ed.*, 2008, **47**, 1184; (e) I. J. Arroyo, R. Hu, G. Merino, B. Z. Tang and E. Pena-Cabrea, *J. Org. Chem.*, 2009, **74**, 5719.
- T. L. Arbeloa, F. L. Arbeloa, I. L. Arbeloa, I. Garcia-Moreno, A. Costela, R. Sastre and F. Amat-Guerri, *Chem. Phys. Lett.*, 1999, **299**, 315.
- (a) J. M. Brom, Jr. and J. L. Langer, *J. Alloys Compd.*, 2002, **338**, 112; (b) R. Y. Lai and A. J. Bard, *J. Phys. Chem. B*, 2003, **107**, 5036; (c) A. Hepp, G. Ulrich, R. Schmechel, H. von Seggern and R. Ziessel, *Synth. Met.*, 2004, **146**, 11; (d) C. Jiao, K.-W. Huang, C. H. Chunyan and J. Wu, *J. Org. Chem.*, 2011, **76**, 661; (e) C. Jiao and J. Wu, *Synlett*, 2012, 171.
- (a) K. Yamada, Y. Nomura, D. Citterio, N. Iwasawa and K. Suzuki, *J. Am. Chem. Soc.*, 2005, **127**, 6956; (b) J. Wang and X. Qian, *Org. Lett.*, 2006, **8**, 3721; (c) T. W. Hudnall and F. P. Gabbai, *Chem. Commun.*, 2008, 4596; (d) D. W. Domaille, L. Zeng and C. J. Chang, *J. Am. Chem. Soc.*, 2010, **132**, 1194; (e) E. Atilgan, E. Ozdemir and E. U. Akkaya, *Org. Lett.*, 2010, **12**, 4792; (f) N. Boens, V. Leen and W. Dehaen, *Chem. Soc. Rev.*, 2012, **41**, 1130; (g) S. Madhu, S. K. Basu, S. Jadhav and M. Ravikanth, *Analyst*, 2013, **138**, 299; (h) M. Formica, V. Fusi, L. Giorgi and M. Micheloni, *Coord. Chem. Rev.*, 2012, **256**, 170.
- (a) H.-G. Knaus, T. Moshhammer, K. Friedrich, H. C. Kang, R. P. Haugland and H. Glossmann, *Proc. Natl. Acad. Sci. U. S. A.*, 1992, **89**, 3586; (b) E. J. Merino and K. M. Weeks, *J. Am. Chem. Soc.*, 2005, **127**, 12766; (c) Q. Meng, D. H. Kim, X. Bai, L. Bi, N. J. Turro and J. Ju, *J. Org. Chem.*, 2006, **71**, 3248; (d) C. Peters, A. Billich, M. Ghobrial, K. Hoegenauer, T. Ullrich and P. Nussbaumer, *J. Org. Chem.*, 2007, **72**, 1842; (e) Z. Li and R. Bittman, *J. Org. Chem.*, 2007, **72**, 8376; (f) R. P. Haugland, *Handbook of Fluorescent Probes and Research Chemicals*, Molecular Probes, Eugene, OR, 6th edn, 1996.
- (a) T. Rousseau, A. Cravino, T. Bura, G. Ulrich, R. Ziessel and J. Roncali, *Chem. Commun.*, 2009, 1673; (b) D. Kumaresan, R. P. Thummel, T. Bura, G. Ulrich and R. Ziessel, *Chem.-Eur. J.*, 2009, **15**, 6335; (c) S. Kolemen, Y. Cakmak, S. Erten-Ela, Y. Altay, J. Brendel, M. Thelakkt and E. U. Akkaya, *Org. Lett.*, 2010, **12**, 3812; (d) T. Bura, N. Leclerc, S. Fall, P. Leveque, T. Heiser and R. Ziessel, *J. Am. Chem. Soc.*, 2012, **134**, 17404.
- (a) C. Thivierge, R. Bandichhor and K. Burgess, *Org. Lett.*, 2007, **9**, 2135; (b) Z. Dost, S. Atilgan and E. U. Akkaya, *Tetrahedron*, 2006, **62**, 8484; (c) T. Rohand, W. Qin, N. Boens and W. Dehaen, *Eur. J. Org. Chem.*, 2006, 4658; (d) Y. Mei, P. A. Bentley and W. Wang, *Tetrahedron Lett.*, 2006, **47**, 2447; (e) K. Rurack, M. Kollmannsberger and J. Daub, *Angew. Chem., Int. Ed.*, 2001, **40**, 385; (f) K. Rurack, M. Kollmannsberger and J. Daub, *New J. Chem.*, 2001, **25**, 289; (g) Y.-H. Yu, A. B. Descalzo, Z. Shen, H. Röhr, Q. Liu, Y.-W. Wang, M. Spieles, Y.-Z. Li, K. Rurack and X.-Z. You, *Chem.-Asian J.*, 2006, **1**, 176; (h) V. Lakshmi and M. Ravikanth, *J. Org. Chem.*, 2013, **78**, 4993.
- (a) E. Deniz, G. C. Isbasar, O. A. Bozdemir, L. T. Yildirim, A. Siemiarzuck and E. U. Akkaya, *Org. Lett.*, 2008, **10**, 3401; (b) S. Rihn, M. Erdem, A. D. Nicola, P. Retailleau and R. Ziessel, *Org. Lett.*, 2011, **13**, 1916.
- (a) N. Adarsh, R. R. Avirah and D. Ramaiah, *Org. Lett.*, 2010, **12**, 5720; (b) M. J. Hall, S. O. McDonnell, J. Killoran and D. F. O'Shea, *J. Org. Chem.*, 2005, **70**, 5571; (c) W. Zhao and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2005, **44**, 1677; (d) W. Zhao and E. M. Carreira, *Chem.-Eur. J.*, 2006, **12**, 7254; (e) S. O. McDonnell and D. F. O'Shea, *Org. Lett.*, 2006, **8**, 3493.
- J. V. Frangioni, *Curr. Opin. Chem. Biol.*, 2003, **7**, 626.
- (a) K. Umezawa, Y. Nakamura, H. Makino, D. Citterio and K. Suzuki, *J. Am. Chem. Soc.*, 2008, **130**, 1550; (b) K. Umezawa, A. Matsui, Y. Nakamura, D. Citterio and K. Suzuki, *Chem.-Eur. J.*, 2009, **15**, 1096; (c) G. A. Samuel, J. Polreis, V. Biradar and Y. You, *Org. Lett.*, 2011, **13**, 3885; (d) A. B. Descalzo, H.-J. Xu, Z.-L. Xue, K. Hoffmann, Z. Shen, M. G. Weller, X.-Z. You and K. Rurack, *Org. Lett.*, 2008, **10**, 1581; (e) Z. Shen, H. Röhr, K. Rurack, H. Uno, M. Spieles, B. Schulz, G. Reck and N. Ono, *Chem.-Eur. J.*, 2004, **10**, 4853; (f) Y. Ni, W. Zeng, K.-W. Huang and J. Wu, *Chem. Commun.*, 2013, **49**, 1217; (g) A. Wakamiya, T. Murakami and S. Yamaguchi, *Chem. Sci.*, 2013, **4**, 1002; (h) M. Nakamura, H. Tahara, K. Takahashi, T. Nagata, H. Uoyama, D. Kuzuhara, S. Mori, T. Okujima, H. Yamada and H. Uno, *Org. Biomol. Chem.*, 2012, **10**, 6840; (i) C. Jiao, K.-W. Huwang and J. Wu, *Org. Lett.*, 2011, **13**, 632; (j) Y. Hayashi, N. Obata, M. Tamaru, S. Yamaguchi, Y. Matsuo, S. Saeki, Y. Kureishi, S. Saito, S. Yamaguchi and H. Shinokubo, *Org. Lett.*, 2012, **14**, 866.
- (a) T. Sarma, P. K. Panda, P. T. Anusha and S. V. Rao, *Org. Lett.*, 2011, **13**, 188; (b) V. Roznyatovskiy, V. Lynch and J. L. Sessler, *Org. Lett.*, 2010, **12**, 4424; (c) S. V. Rao, T. S. Prashant, D. Swain, T. Sarma, P. K. Panda and S. P. Tewari, *Chem. Phys. Lett.*, 2011, **514**, 98; (d) T. Sarma and P. K. Panda, *Chem.-Eur. J.*, 2011, **17**, 13987; (e) V. V. Roznyatovskiy, J. M. Lim, V. M. Lynch, B. S. Lee, D. Kim and J. L. Sessler, *Org. Lett.*, 2011, **13**, 5620; (f) S.-Y. Kee, J. M. Lim, S.-J. Kim, J. Yoo, J.-S. Park, T. Sarma, V. M. Lynch, P. K. Panda, J. L. Sessler, D. Kim and C.-H. Lee, *Chem. Commun.*, 2011, **47**, 6813; (g) M. Ishida, S.-J. Kim, C. Preihs, K. Ohkubo, J. M. Lim, B. S. Lee, J. S. Park, V. M. Lynch, V. V. Roznyatovskiy, T. Sarma, P. K. Panda, C. H. Lee, S. Fukuzumi, D. Kim and J. L. Sessler, *Nat. Chem.*, 2013, **5**, 15.
- S. Sepulveda-Boza and E. Breitmaier, *Liebigs Ann. Chem.*, 1983, 894.
- see <http://omlc.ogi.edu/spectra/PhotochemCAD/html/011.html>.
- S. Sanyal and M. S. Akseilrod, *J. Appl. Phys.*, 2005, **98**, 033518.