Curriculum Vitae

CHARLES V. SINDELAR

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ACADEMIC POSITIONS AND AFFILIATIONS

2011-2017	Assistant Professor, Department of Molecular Biophysics and Biochemistry, Yale University
2017-present	Associate Professor, Department of Molecular Biophysics and Biochemistry, Yale University

EDUCATION

Date	Institution/Location	Degree	Subject
1995-2002	University of California, San Francisco Robert Fletterick, professor	Ph.D.	Biophysics
1987-1992	Massachusetts Institute of Technology	B.S.	Mechanical Eng.

RESEARCH AND PROFESSIONAL EXPERIENCE

1992 – 1995	Massachusetts Institute of Technology. Research Technician, computational biophysics (Bruce Tidor, professor)
2003 – 2008	Lawrence Berkeley National Laboratory. Postdoctoral Fellow (Ken Downing, Principle Investigator)
2008 – 2010	Brandeis University. Research Scientist (Nikolaus Grigorieff, professor)

Research Statement

My group uses high-resolution structural tools, with a special emphasis on cryo-electron microscopy (cryo-EM), to unravel the mechanism of vital biological processes. The fundamental question that drives our work is how complex formation with a partner filament triggers the functional activity of molecular motors and other cytoskeletal proteins. In our cryo-EM work, we develop and apply novel state-of-the-art image-processing techniques to chemical intermediates and mutant forms of enzyme complexes in order to directly visualize key conformational changes. We synthesize such data with other biochemical and biophysical data to derive mechanistic models that explain how these

molecular machines work. I have assembled a research group with diverse expertise in cryo-EM, X-ray crystallography, optical spectroscopy, computational analysis, molecular dynamics simulation, and other biophysical approaches. My laboratory has also teamed up with a number of groups within and outside of Yale to study a diverse set of biological processes, including cofilin-mediated actin disassembly (Enrique De La Cruz, MB&B department), filamin-mediated actin cross-linking (David Calderwood, Pharmacology), mechanics of the myosin motor protein (Michael Ostap, U. Penn), and synaptic vesicle fusion (James Rothman, Cell Biology).

OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS

Honors and Awards

2001	Monbu Kagakusho Japan Summer Research Fellowship
2007	Japan Society for the Promotion of Science Research Fellowship
2007	Biophysical Society Discussions Meeting Postdoctoral Travel Award
2011	Kingsley Award in Medical Research, Yale University School of Medicine

Invited Talks

2007	Gordon Research Conference: Three-Dimensional Electron Microscopy, New London, NH
2008	Biophysical Society Annual Meeting, Motility Subgroup, Long Beach, California
2009	Session Chair, Biophysical Society Annual Meeting, Boston, MA
2011	Microscopy & Microanalysis Conference, Nashville, TN
2013	American Chemical Society National Meeting, New Orleans, LA
2013	McGill University, Montreal, Quebec
2013	Pennysylvania Muscle Institute, University of Pennysylvania, Philadelphia, PA
2014	Indiana University, Bloomington, IN
2014	Distinguished Guest Speaker, Cell Biology and Physiology Center, NIH, Bethesda, MD
2015	Yale YINQE seminar series
2015	Gordon Research Conference: Three-Dimensional Electron Microscopy, New London, NH
2015	Biophysics Seminar Speaker, University of Michigan, Ann Arbor, MI
2016	Molecular Structure & Function Special Seminar, University of Toronto, CA
2016	Alpbach Motors Workshop, Alpbach, Austria
2016	Dept. of Biological Sciences Seminar, Carnegie Mellon University, Pittsburg, PA
2017	Caspar Structural Biology Symposium, Tallahassee, FL
2017	New England Structural Biology Symposium, Hartford, CT
2017	University of Chicago, Chicago, IL
2018	University of California, San Francisco, San Francisco, CA
2018	National Institutes of Health, Bethesda, MD
2018	Janelia Farm Research Campus, Ashburn, VA
2018	Biochemistry&Biophysics Seminar, Brandeis University,
2018	Gordon Research Conference: Three-Dimensional Electron Microscopy, Newport, RI
2018	University of Oregon, Eugene, OR
2019	Gordon Research Conference: Motile and Contractile Systems, New London, NH
2019	Microscopy & Microanalysis annual meeting, Portland, OR
2019	University of Delaware, Wilmington, Newark, DE
2019	Washington University, St. Louis, MO
2020	Florida State University, Tallahassee, FL
2020	Gordon Research Conference: Spirochetology/Spirochete Disease Pathogenesis, Italy
2020	National Institutes of Health, Bethesda, MD
2020	Microscopy & Microanalysis annual meeting, Milwaukee, WI

Editorial Work

Reviewer for: Current Biology, *Science, Cell, PNAS*, *Nature Communications, eLife, Journal of Biological Chemistry, Journal of Molecular Biology, Journal of Structural Biology, Biophysical Journal, PLOS One, iScience, Journal of Theoretical Biology*

Thesis Examination Committees

External examiner, Ph.D thesis of Jianhua Zhao, University of Toronto

Meeting Organization

2009	Biophysical Society Annual Meeting, minisymposium co-chair
2016	Co-chair, Motility Subgroup (Biophysical Society Annual Meeting)
2016	Co-chair, Motors Structure & Dynamics Section (Alpbach Motors Workshop, Alpbach, Austria)
2018	Session co-chair, Cryo-EM Subgroup (Biophysical Society Annual Meeting)

Scientific Societies

2001-present	Member, Biophysical Society
2007-2008	President, LBNL Life Sciences Postdoctoral Society

RESEARCH SUPPORT

COMPLETED

1. ACS-IRG #58-012-55 (Sindelar) 01/01/2013 – 12/31/2013
Title: Structural basis of action and inhibition of kinesin motor proteins involved in mitosis
Source: Yale Cancer Center Pilot Grant

ACTIVE

1. **R01 GM 110530 (PI: Sindelar)** 08/31/2019 – 08/31/2023
Title: Structural basis of motility by dimeric kinesin and myosin motor proteins
Source: NIH

2. **R37 GM057247-20 (PI: Michael Ostap; Sindelar, Collaborator)** 09/01/15 - 08/31/20
Title: Molecular function of Myosin-I
Source: NIH

IN REVIEW

1. **R01 AI 145326 Principal PI: Sindelar;** 05/31/2020 – 05/31/2024
Co-PI Albert Ko (Yale)
Co-PI Alejandro Busschiazzo (Institut Pasteur, Uruguay)
Title: Elucidating a novel flagellar architecture from the pathogenic spirochete Leptospira and its role in motility
Source: NIH

TEACHING

Yale University

Spring 2012:	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(6 lectures)**
Fall 2012:	MBB	720a	Macromolecular Structure and Biophysical Analysis **(4 lectures)**
	MCDB	630b	Biophysical Methods **(2 lectures)**
Spring 2013:	MBB	105b	An Issues Approach to Biology **(8 lectures)**
	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(6 lectures)**
	MBB	517 01	IGPPEB Methods & Logic in Interdisciplinary Research **(1 lecture)**
	MCDB	630b	Biophysical Methods **(4 lectures)**
Fall 2013:	MBB	435a/635a	Mathematical Methods in Biophysics **(6 lectures)**
Spring 2014:	MBB	302b	Principles of Biophysics **(10 lectures)**
	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(6 lectures)**
	Pharm Chem.	529b	Structural Pharmacology (**1 lecture**)
Spring 2015:	MBB	302b	Principles of Biophysics **(10 lectures)**
	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(1 lecture)**
	Pharm Chem.	529b	Structural Pharmacology (**1 lecture**)
Spring 2016:	MBB	302b	(**Course director)** Principles of Biophysics **(18 lectures)**
	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(2 lectures)**
	Pharm Chem.	529b	Structural Pharmacology (**1 lecture**)
Spring 2017:	MBB	302b	Principles of Biophysics **(10 lectures)**
	MBB	710b4	Electron Cryo-Microscopy for Protein Structure Determination **(2 lectures)**
	Pharm Chem.	529b	Structural Pharmacology (**1 lecture**)
Spring 2018:	Pharm Chem.	529b	Structural Pharmacology (**1 lecture**)

Brandeis University

Spring 2010: Substitute lecturer, Biochemistry 153b
Spring 2009: Substitute lecturer, Biochemistry 100a

University of California, San Francisco

Winter, 2002: Teaching Assistant, Chemistry 112 (Chemical Kinetics)
Fall, 2001: Teaching Assistant, Chemistry 111 (Thermodynamics)
Spring 1999: Teaching Assistant, Biophysics 297 (Biophysical Methods)
Fall 1997: Teaching Assistant, Biophysics 241 (Statistical Mechanics)

PAST TRAINEES

2012-2014	Zhiguo Shang, postdoctoral associate (currently Senior Research Scientist, University of Texas Southwestern Medical Center; laboratory of Daniela Nicastro)
2012-2015	Xueqi Liu (postdoctoral associate; joint with David Schatz)
2012-2015	Jing Wang (postdoctoral associate; joint with James Rothman)

CURRENT TRAINEES

2012-2017	Daifei Liu (graduate student)
2014-present	Kimberley Gibson (postgraduate associate)
2015-present	Michael Cha (graduate student)

2015-present Andrew Huehn (graduate student)
2015-present Garrett Debs (graduate student)
2017-present Megan Brady (graduate student)

UNDERGRADUATE RESEARCHERS

2011-2012 Brian Mugo (Yale MBB; STARS fellowship, summer 2012)
2013 Angelo Morales (Peruvian exchange summer student)
2015 Max Knapp (Yale MBB)

YALE SERVICE

2011-present Web Consultant and Media (chair, 2011, 2016)
2012-2014 MB&B/BBSB Admissions committee
2012-2014,2016 MBB Retreat committee (chair 2014, 2016)
2012-2015 Undergraduate advisor for MB&B class of 2015
2015-present MB&B Cryo-EM committee
2015-present Faculty search committee (cryo-EM candidate)
2015-present Executive committee, Biophysics training grant
2018-2020 Undergraduate advisor for MB&B class of 2020

QUALIFYING EXAMS

2011 Vincent Yip
2012 Jessica Wiczar
2013 Anthony Schramm
2014 Shantao Li
2014 Yuhan Hu
2014 Grace Peters
2015 Jeremiah Johnston
2015 Ivy Huang
2015 Michael Cha
2016 Jonathon Powell
2016 Nakheira Christie
2016 Wanqing Lyu
2018 Carson Bryant
2018 Peter Niimi
2018 Sarah Prophet
2019 Cole Lewis

THESIS COMMITTEES

2011-2017 Vincent Yip
2012-2017 Daifei Liu
2012-2015 Ashley Schloss
2012-2017 Emily Wang
2014-present Yuhan Wu
2014-present Anthony Schramm

2014-present	Grace Peters
2015-present	Ivy Huang
2015-2016	Jeremiah Johnston
2015-present	Nandan Pandit
2015-present	Garrett Debs
2016-present	Jonathon Powell
2016-present	Meaghan Sullivan
2017-present	Megan Brady
2017-present	Wanqing Lyu

PUBLICATIONS (Total of 29)

PEER-REVIEWED PUBLICATIONS

Since arriving at Yale

1. Huehn, A., Cao, W., Elam, W. A., Liu, X., De La Cruz, E. M., & **Sindelar, C. V. (2020)**. Structures of cofilin-induced structural changes reveal local and asymmetric perturbations of actin filaments. PNAS 117:1478-1484. doi: 10.1073/pnas.1915987117. PMC6983403.

2. Grushin, K., Wang, J., Coleman, J., Rothman, J.E., & **Sindelar, C. V. *,** Krishnakumar., S. S. Structural Basis for the Clamping and Ca2+ Activation of SNARE-mediated Fusion by Synaptotagmin (2019). **Nat Commun.** 10:2413. doi: 10.1038/s41467-019-10391-x. PMC6546687.
***Co-corresponding author**

3. Iwamoto, D. V., Huehn, A., Simon, B., Huet-Calderwood, C., Baldassarre, M., **Sindelar, C. V.***, & Calderwood, D. A. **(2018)**. *Structural basis of the filamin A actin-binding domain interaction with F-actin*. **Nat Struct Mol Biol**. 10:918-927. doi: 10.1038/s41594-018-0128-3. PMC6173970.
***Co-corresponding author**

4. Wunder, E. A., Jr., Slamti, L., Suwondo, D. N., Gibson, K. H., Shang, Z., **Sindelar, C. V.**, Trajtenberg, F., Buschiazzo, A., Ko, A. I., & Picardeau, M. **(2018)**. *FcpB Is a Surface Filament Protein of the Endoflagellum Required for the Motility of the Spirochete Leptospira*. **Front Cell Infect Microbiol**. 8: p. 130. doi: 10.3389/fcimb.2018.00130. PMC5953323.

5. Huehn, A., Cao, W., Elam, W. A., Liu, X., De La Cruz, E. M., & **Sindelar, C. V. (2018)**. *The actin filament twist changes abruptly at boundaries between bare and cofilin-decorated segments*. **J Biol Chem**. 293(15): p. 5377-5383. doi: 10.1074/jbc.AC118.001843. PMC5900768.

6. Mentes, A., Huehn, A., Liu, X., Zwolak, A., Dominguez, R., Shuman, H., Ostap, E. M., & **Sindelar, C. V. (2018)**. *High-resolution cryo-EM structures of actin-bound myosin states reveal the mechanism of myosin force sensing*. **Proc Natl Acad Sci U S A**. 115(6): p. 1292-1297. doi: 10.1073/pnas.1718316115. PMC5819444.

7. Elam, W. A., Cao, W., Kang, H., Huehn, A., Hocky, G. M., Prochniewicz, E., Schramm, A. C., Negron, K., Garcia, J., Bonello, T. T., Gunning, P. W., Thomas, D. D., Voth, G. A., **Sindelar, C. V.**, & De La Cruz, E. M. **(2017)**. *Phosphomimetic S3D cofilin binds but only weakly severs actin filaments*. **J Biol Chem**. 292(48): p. 19565-19579. doi: 10.1074/jbc.M117.808378. PMC5712599.

8. Wang, J., Li, F., Bello, O. D., **Sindelar, C. V.**, Pincet, F., Krishnakumar, S. S., & Rothman, J. E. **(2017)**. *Circular oligomerization is an intrinsic property of synaptotagmin*. **Elife**. 6. doi: 10.7554/eLife.27441. PMC5576491.

9. Bell, K. M., Cha, H. K., **Sindelar, C. V.**, & Cochran, J. C. **(2017)**. *The yeast kinesin-5 Cin8 interacts with the microtubule in a noncanonical manner*. **J Biol Chem**. 292(35): p. 14680-14694. doi: 10.1074/jbc.M117.797662. PMC5582858.

10. Liu, D., Liu, X., Shang, Z., & **Sindelar, C. V. (2017)**. *Structural basis of cooperativity in kinesin revealed by 3D reconstruction of a two-head-bound state on microtubules*. **Elife**. 6. doi: 10.7554/eLife.24490. PMC5459574.

11. Zanetti, M. N., Bello, O. D., Wang, J., Coleman, J., Cai, Y., **Sindelar, C. V.**, Rothman, J. E., & Krishnakumar, S. S. **(2016)**. *Ring-like oligomers of Synaptotagmins and related C2 domain proteins*. **Elife**. 5. doi: 10.7554/eLife.17262. PMC4977156.

12. Ropars, V., Yang, Z., Isabet, T., Blanc, F., Zhou, K., Lin, T., Liu, X., Hissier, P., Samazan, F., Amigues, B., Yang, E. D., Park, H., Pylypenko, O., Cecchini, M., **Sindelar, C. V.***, Sweeney, H. L., & Houdusse, A. **(2016)**. *The myosin X motor is optimized for movement on actin bundles*. **Nat Commun**. 7: p. 12456. doi: 10.1038/ncomms12456. PMC5025751.
***Co-corresponding author**

13. Shang, Z., Zhou, K., Xu, C., Csencsits, R., Cochran, J. C., & **Sindelar, C. V. (2014)**. *High-resolution structures of kinesin on microtubules provide a basis for nucleotide-gated force-generation*. **Elife**. 3: p. e04686. doi: 10.7554/eLife.04686. PMC4383081.

14. Kang, H., Bradley, M. J., Cao, W., Zhou, K., Grintsevich, E. E., Michelot, A., **Sindelar, C. V.**, Hochstrasser, M., & De La Cruz, E. M. **(2014)**. *Site-specific cation release drives actin filament severing by vertebrate cofilin*. **Proc Natl Acad Sci U S A**. 111(50): p. 17821-17826. doi: 10.1073/pnas.1413397111. PMC4273407.

15. Wang, J., Bello, O., Auclair, S. M., Wang, J., Coleman, J., Pincet, F., Krishnakumar, S. S., **Sindelar, C. V.***, & Rothman, J. E. **(2014)**. *Calcium sensitive ring-like oligomers formed by synaptotagmin*. **Proc Natl Acad Sci U S A**. 111(38): p. 13966-13971. doi: 10.1073/pnas.1415849111. PMC4183308.
***Co-corresponding author**

16. Shuman, H., Greenberg, M. J., Zwolak, A., Lin, T., **Sindelar, C. V.**, Dominguez, R., & Ostap, E. M. **(2014)**. *A vertebrate myosin-I structure reveals unique insights into myosin mechanochemical tuning*. **Proc Natl Acad Sci U S A**. 111(6): p. 2116-2121. doi: 10.1073/pnas.1321022111. PMC3926069.

17. Bai, X., Bowen, J. R., Knox, T. K., Zhou, K., Pendziwiat, M., Kuhlenbaumer, G., **Sindelar, C. V.**, & Spiliotis, E. T. **(2013)**. *Novel septin 9 repeat motifs altered in neuralgic amyotrophy bind and bundle microtubules*. **J Cell Biol**. 203(6): p. 895-905. doi: 10.1083/jcb.201308068. PMC3871440.

18. **Sindelar, C. V.***, & Grigorieff, N. **(2012)**. *Optimal noise reduction in 3D reconstructions of single particles using a volume-normalized filter*. **J Struct Biol**. 180(1): p. 26-38. doi: 10.1016/j.jsb.2012.05.005. PMC3498508.
***Co-corresponding author**

19. Goulet, A., Behnke-Parks, W. M., **Sindelar, C. V.**, Major, J., Rosenfeld, S. S., & Moores, C. A. **(2012)**. *The structural basis of force generation by the mitotic motor kinesin-5*. **J Biol Chem**. 287(53): p. 44654-44666. doi: 10.1074/jbc.M112.404228. PMC3531780.

20. Shen, Q. T., Hsiue, P. P., **Sindelar, C. V.**, Welch, M. D., Campellone, K. G., & Wang, H. W. **(2012)**. *Structural insights into WHAMM-mediated cytoskeletal coordination during membrane remodeling*. **J Cell Biol**. 199(1): p. 111-124. doi: 10.1083/jcb.201204010. PMC3461504.

Prior to Yale

21. **Sindelar, C. V.**, & Grigorieff, N. **(2011)**. *An adaptation of the Wiener filter suitable for analyzing images of isolated single particles*. **J Struct Biol**. 176(1): p. 60-74. doi: 10.1016/j.jsb.2011.06.010. PMC3184790.

22. Fourniol, F. J., **Sindelar, C. V.**, Amigues, B., Clare, D. K., Thomas, G., Perderiset, M., Francis, F., Houdusse, A., & Moores, C. A. **(2010)**. *Template-free 13-protofilament microtubule-MAP assembly visualized at 8 A resolution*. **J Cell Biol**. 191(3): p. 463-470. doi: 10.1083/jcb.201007081. PMC3003314.

23. **Sindelar, C. V.**, & Downing, K. H. **(2010)**. *An atomic-level mechanism for activation of the kinesin molecular motors*. **Proc Natl Acad Sci U S A**. 107(9): p. 4111-4116. doi: 10.1073/pnas.0911208107. PMC2840164.

24. Cochran, J. C., **Sindelar, C. V.**, Mulko, N. K., Collins, K. A., Kong, S. E., Hawley, R. S., & Kull, F. J. **(2009)**. *ATPase cycle of the nonmotile kinesin NOD allows microtubule end tracking and drives chromosome movement*. **Cell**. 136(1): p. 110-122. doi: 10.1016/j.cell.2008.11.048. PMC2635066.

25. Dietrich, K. A., **Sindelar, C. V.**, Brewer, P. D., Downing, K. H., Cremo, C. R., & Rice, S. E. **(2008)**. *The kinesin-1 motor protein is regulated by a direct interaction of its head and tail*. **Proc Natl Acad Sci U S A**. 105(26): p. 8938-8943. doi: 10.1073/pnas.0803575105. PMC2449343.

26. Rice, S., Cui, Y., Sindelar, C., Naber, N., Matuska, M., Vale, R., & Cooke, R. **(2003)**. *Thermodynamic properties of the kinesin neck-region docking to the catalytic core*. **Biophys J**. 84(3): p. 1844-1854. doi: 10.1016/S0006-3495(03)74992-3. PMC1302753.

27. **Sindelar, C. V.**, Budny, M. J., Rice, S., Naber, N., Fletterick, R., & Cooke, R. **(2002)**. *Two conformations in the human kinesin power stroke defined by X-ray crystallography and EPR spectroscopy*. **Nat Struct Biol**. 9(11): p. 844-848. doi: 10.1038/nsb852.

28. Hendsch, Z. S., **Sindelar, C. V.**, & Tidor, B. **(1998)**. *Parameter dependence in continuum electrostatic calculations: A study using protein salt bridges*. **J Phys Chem B**. 102: p. 4404-4410.

29. **Sindelar, C. V.**, Hendsch, Z. S., & Tidor, B. **(1998)**. *Effects of salt bridges on protein structure and design*. **Protein Sci**. 7(9): p. 1898-1914. doi: 10.1002/pro.5560070906. PMC2144171.

INVITED REVIEWS AND EDITORIALS

1. **Sindelar, C. V.**, & Liu, D. **(2017)**. *Tracking down kinesin's achilles heel with balls of gold*. **Biophys J**. 112(12): p. 2454-2456. doi: 10.1016/j.bpj.2017.05.008. PMC5479109.

2. **Sindelar, C. V.**, & Huehn, A. **(2016)**. *Vinculin: an unfolding tale*. **J Mol Biol**. 428(1): p. 1-4. doi: 10.1016/j.jmb.2015.11.005.

3. **Sindelar, C. V. (2011)**. *A seesaw model for intermolecular gating in the kinesin motor protein*. **Biophys Rev**. 3(2): p. 85-100. doi: 10.1007/s12551-011-0049-4. PMC3117274.

SUBMITTED MANUSCRIPTS

1. Gibson K.H., Trajtenberg F., Brady M., San Martin F., Mechaly A., Wunder E., Picardeau M., Ko A. I., Buschiazzo A., & **Sindelar C.V.** *An asymmetric sheath controls flagellar supercoiling and motility in the Leptospira spirochete*.

2. Debs G., Cha H. K., Liu X., Liu D., & **Sindelar C. V.** *Dynamic and asymmetric fluctuations in the microtubule wall captured by high-resolution cryo- electron microscopy.*

3. Cha H. K., Debs G., Liu X., Liu D., & **Sindelar C. V.** *Structural Intermediates of the dimeric kinesin stepping cycle revealed by cryo-EM*.