

CURRICULUM VITAE

Name Frederick J. Sigworth

Born October 20, 1951 in Berkeley, California

Nationality American Citizen

Marital Status Married; three children.

Education Stanford University (1969-1971), Electrical Engineering

California Institute of Technology (1971-1974), Applied Physics. Concentrated on semiconductor physics with Professor C.A. Mead as advisor. Received B.S. with honor, 1974.

Graduate study at the University of Washington (1974-1975) and at Yale University (1975-1979) under C.F. Stevens, working on conductance fluctuations in nerve membrane. Received Ph.D. from Yale in 1979.

Post-Doctoral Fellow of the Alexander von Humboldt Stiftung (1979-1981), and continued as a Research Associate (1981-1984) in the laboratory of E. Neher at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany.

Faculty positions at Yale University

Assistant Professor, Department of Physiology, 11/1984 to 6/1989.
Associate Professor with Tenure, Department of Cellular and Molecular Physiology, 7/1989-6/1991.
Professor, Department of Cellular and Molecular Physiology, 7/1991 to present.
Professor, Department of Biomedical Engineering, 7/2002 to present.
Professor, Molecular Biophysics and Biochemistry, 7/2015 to present.

Honors

Alexander von Humboldt Fellow, 1979-1981
Jacob Javits Neuroscience Investigator Award, 1992
Yale Science and Engineering Award, 1996
K. C. Cole Award, Biophysical Society, 1997
Bohmalk Teaching Prize, Yale School of Medicine, 2002
Member-Elect, National Academy of Sciences, 2016

Other experience

Chairman, 1994 Gordon Conference on Ion Channels
Editorial Boards, *Neuron*, *Journal of General Physiology*, *European Biophysics Journal*.
Invited lecturer in the Shanghai Ion Channel Workshop, 1987; Ion Channels course at Cold Spring Harbor Laboratory, 1990-1994; Computational Neuroscience course 1994-7 and the Neurobiology Course, 1996-2005 at the Marine Biological Laboratory. Invited lecturer in the Membrane Biophysics course, Rockefeller University, 1999-2007. Member, BPNS Study Section, NIH, 2010-2013; chairman 2011-2013.

Research interests

My main interest has been in the areas of gating and ion permeation in the ionic channels of excitable cell membranes, and how the structure of channel proteins give rise to these properties. The original approach in my laboratory has been to develop techniques for sensitive electrical measurements of ion channel currents, and to apply these techniques along with biochemical and molecular biology tools to the study of the function of ion channel proteins. More recently, my laboratory has been working on structural studies of ion channels using high-resolution electron microscopy. We have been developing new techniques for cryo-EM imaging of ion channels and other membrane proteins as reconstituted into lipid bilayer membranes.

Current teaching

Medical Physiology. For the medical school physiology course I developed and have delivered since the 1990s the segment of the course (7-10 lectures) on excitable cells and cardiac electrophysiology.
BENG 410a/ ENAS 510a, Physical & Chem Basis of Biosensing. I am an instructor, contributing 4 lectures.
C&MP 560b/ MCDB 560b/ ENAS 570b/ PHAR 560b/ MCDB 415b, Molecular Machines in Human Disease. I teach about half of this course.
C&MP 620/ NBIO 610/ NSCI 610, Fundamentals in Neurophysiology. I am one of three organizers of this course.
C&MP 710b/ MB&B 710b: Electron cryo-microscopy. I am course director of this half-semester course.

Department committees

CMP Graduate Education Committee (2000-present)
 CMP Core facility committee (past years)
 BME and CMP faculty search committees (past years)

Thesis advisory committees

At any given time I am a member of several committees; in the past year I have been a member of the following students' committees: Enping Hong (BME), Yanbin Wang (CMP), Grace Kim (CMP), Muhamed Hadzipsic (INP/Genetics), Brandon Gassaway (CMP)

University committees

YSM electron microscopy core committee (2008-present)
 Provost's advisory committee on students with disabilities 2009-2012
 Several YSM committees investigating academic misconduct (past years)
 Provost's advisory committee on cryo-EM facilities

Graduate students, and their degree-granting institutions or departments

Stefan Heinemann (Uni. Göttingen)
 Jiuying Zhou (CMP)
 Scott Shenkel (CMP)
 Nathan Schoppa (CMP)
 Jie Zheng (CMP)
 Theodore Cummins (INP)
 Lalitha Venkataramanan (EE)
 Qiu-Xing Jiang (CMP)
 Leon D. Islas (CMP)
 Christoph Cantener (INP)
 Puey Ounjai (Mahidol Univ.)
 Fiona E. Müllner (Uni. Freiburg)
 Andrew Barthel (BME)
 Pujitha Weerakoon (BME)
 Brian Goldstein (EE)
 Yi Chen (CMP)

Postdoctoral fellows

Steven Sine
 Hubert Affolter
 Ken McCormack
 Serge C. Crouzy
 Richard Ayer
 David Chester
 Shumin Bian
 Youshan Yang
 Kathryn G. Klemic
 Theresa Giraldez
 Ligu Wang
 Yunhui Liu
 Hideki Shigematsu

PUBLICATIONS

Research Articles

1. Sigworth, F.J. Sodium channels in nerve apparently have two conductance states. *Nature* 270, 265-267 (1977).
2. Sigworth, F.J. Sodium current fluctuations in frog myelinated nerve. Thesis, Yale University (1979).
3. Sigworth, F.J. and Spalding, B.C. Chemical modification reduces the conductance of sodium channels in nerve. *Nature* 283, 293-295 (1980)
4. Sigworth, F.J. and Neher, E. Single Na-channel currents observed in cultured rat muscle cells. *Nature* 287, 447-449 (1980).
5. Sigworth, F.J. The variance of sodium current fluctuations at the node of Ranvier. *J. Physiol.* 307, 97-129 (1980).

6. Sigworth, F.J. The conductance of sodium channels under conditions of reduced current at the node of Ranvier. *J. Physiol* 307, 131-142 (1980).
7. Sigworth, F.J. Covariance of nonstationary sodium current fluctuations in the node of Ranvier. *Biophys. J.* 34, 111-133 (1981).
8. Sigworth, F.J. Interpreting power spectra from nonstationary membrane current fluctuations. *Biophys. J.* 35, 289-300 (1981).
9. Hamill, O.P., A. Marty, E. Neher, B. Sakmann and F.J. Sigworth. Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches. *Pfluegers Arch.* 391, 85-100 (1981).
10. Sigworth, F.J. Electronic design of the patch clamp. In: *Single Channel Recording*, B. Sakmann and E. Neher, eds. Plenum (1983).
11. Colquhoun, D. and Sigworth, F.J. Fitting and Statistical analysis of single-channel records. In: *Single Channel Recording*, B. Sakmann and E. Neher, eds. Plenum (1983).
12. Sigworth, F.J. An example of analysis. In: *Single Channel Recording*, B. Sakmann and E. Neher, eds. Plenum (1983).
13. Sigworth, F.J. Open channel noise. I. Noise in acetylcholine receptor currents suggests conformational fluctuations. *Biophys. J.* 47, 709-720 (1985).
14. Sigworth, F.J. Open channel noise. II. A test for coupling between current fluctuations and conformational transitions in the acetylcholine receptor. *Biophys. J.* 49, 1041-1046 (1986).
15. Sigworth, F.J. and S.M. Sine. Data transformations for improved display and fitting of single-channel dwell time histograms. *Biophys. J.* 52: 1047-1054 (1987).
16. Sigworth, F.J., D.W. Urry and K. U. Prasad. Open channel noise. III. High-resolution recordings show rapid current fluctuations in Gramicidin A and four chemical analogues. *Biophys. J.* 52:1055-1064 (1987).
17. Claudio, T., W.N. Green, D.S. Hartman, D. Hayden, H.L. Paulsen, F.J. Sigworth, S.M. Sine and A. Swedlund. Genetic reconstitution of functional acetylcholine receptor channels in mouse fibroblasts. *Science* 238: 1688-1694 (1987).
18. Heinemann, S.H. and F.J. Sigworth. Open Channel Noise IV. Estimation of rapid kinetics of formamide block in Gramicidin A channels. *Biophys. J.* 54: 757-764. (1988)
19. Sigworth, F.J. and Shenkel, S. Rapid gating events and current fluctuations in Gramicidin A channels. *Curr. Topics in Membranes and Transport* 33: 113-130. (1988).
20. Shenkel, S., E.C. Cooper, W.S. Agnew and F.J. Sigworth. Purified, modified Na channels are active in planar bilayers in the absence of Batrachotoxin. *Proc. Natl. Acad. Sci. U.S.* 21, 1989.
21. Trimmer, J., S. Cooperman, S. Tomiko, J. Zhou, S. Crean, M. Boyle, R. Kallen, Z. Sheng, R. Barchi, F. Sigworth, R. Goodman, W. Agnew and G. Mandel. Primary structure and functional expression of a mammalian skeletal muscle sodium channel. *Neuron* 3:33-49, 1989.
22. Stankovic, C.J., S. H. Heinemann, J.M. Delfino, F.J. Sigworth and S.M. Schreiber. Transmembrane channels based on tartaric acid-gramicidin A hybrids. *Science* 244: 813-817, 1989
23. Heinemann, S.H. and F.J. Sigworth. Estimation of Na⁺ dwell time in the gramicidin A channel. Na⁺ ions as blockers of H⁺ currents. *Biochim. Biophys. Acta* 987: 8-14, 1989.
24. Heinemann, S.H. and F.J. Sigworth. Open Channel Noise V. Fluctuating barriers to ion entry in gramicidin A channels. *Biophys. J.* 57: 499-514, 1990.
25. Sine, S.M., T. Claudio and F. J. Sigworth. Activation of Torpedo acetylcholine receptors expressed in mouse fibroblasts: single channel current kinetics reveal distinct agonist binding affinities. *J. Gen. Physiol.* 96: 395-437, 1990.
26. Crouzy, S. and F. J. Sigworth. Yet another approach to the dwell time omission problem of single channel analysis. *Biophys. J.* 58: 731-743, 1990.

27. Bouzat, C., F. J. Barrantes and F. J. Sigworth. Changes in channel properties of acetylcholine receptors during the time course of thiol chemical modifications. *Pflügers Archiv* 418: 51-61, 1991.
28. Shenkel, S. and F. J. Sigworth. Patch recordings from the electrocytes of *Electrophorus Electricus*. Na currents and PNa/PK variability. *J. Gen. Physiol.* 97:1013-1041, 1991.
29. Heinemann, S. H. and F. J. Sigworth. Open channel noise. VI. Analysis of amplitude distributions to determine rapid kinetic parameters. *Biophys. J.* 60: 577-587, 1991.
30. Zhou, J., J. F. Potts, J. S. Trimmer, W. S. Agnew and F. J. Sigworth. Multiple gating modes and the effect of modulating factors on the $\mu 1$ sodium channel. *Neuron* 7: 775-785, 1991.
31. Ukomadu, C., J. Zhou, F. J. Sigworth and W. S. Agnew. $\mu 1$ Na⁺ channels expressed transiently in human embryonic kidney cells: biochemical and biophysical properties. *Neuron* 8: 663-676, 1992.
32. Schoppa, N. E., K. McCormack, M. A. Tanouye and F. J. Sigworth. The size of gating charge in wild-type and mutant *Shaker* potassium channels. *Science* 255: 1712-1715, 1992.
33. McCormack, K., L. Lin, L. E. Iverson, M. A. Tanouye and F. J. Sigworth. Tandem linkage of *Shaker* K⁺ channel subunits does not ensure the stoichiometry of expressed channels. *Biophys. J.* 63: 1406-1411, 1992.
34. Crouzy, S. and F. J. Sigworth. Fluctuations in ion channel gating currents. Analysis of nonstationary shot noise. *Biophys. J.* 64: 68-76, 1993.
35. Cummins, T. R., J. Zhou, F. J. Sigworth, C. Ukomadu, M. Stephan, L. J. Ptacek and W. S. Agnew. Functional consequences of a Na⁺ channel mutation causing hyperkalemic periodic paralysis. *Neuron* 10: 667-678, 1993.
36. McCormack, K., L. Lin and F. J. Sigworth. Substitution of a hydrophobic residue alters the conformational stability of *Shaker* K⁺ channels during gating and assembly. *Biophys. J.* 65:1740-1748, 1993.
37. Cascio M., Schoppa NE., Grodzicki RL., Sigworth FJ. and Fox RO. Functional expression and purification of a homomeric human alpha 1 glycine receptor in baculovirus-infected insect cells. *J. Biol. Chem.* 268(29):22135-42, 1993.
38. Jiang, C., F. J. Sigworth and G. G. Haddad. Oxygen deprivation activates an ATP-inhibitable K⁺ channel in substantia nigra neurons. *J. Neurosci.* 14:5590-5602, 1994
39. Sigworth, F. J. Design of the EPC-9, a computer-controlled patch clamp amplifier. 1. Hardware. *J. Neurosci. Methods* 56:195-202, 1995.
40. Sigworth, F. J., H. Affolter and E. Neher. Design of the EPC-9, a computer-controlled patch clamp amplifier. 2. Software. *J. Neurosci. Methods* 56:203-215, 1995.
41. Cummins, T. R. and F. J. Sigworth. Impaired slow inactivation in mutant sodium channels. *Biophys. J.* 71: 227-236, 1996
42. Andreose, J. S., G. Fumagalli, F. J. Sigworth and M. J. Caplan. Real-time detection of the surface delivery of newly synthesized membrane proteins. *Proc. Natl. Acad. Sci. U.S.A.* 93: 7661-7666, 1996.
43. Mathur, R., J. Zheng, Y. Yan and F. J. Sigworth. Role of the S3-S4 linker in *Shaker* potassium channel activation. *J. Gen. Physiol* 109: 191-200, 1997.
44. Ayer, R. K. and F. J. Sigworth. Enhanced closed-state inactivation in a mutant *Shaker* K⁺ channel. *J. Membrane Biol.* 157:215-230, 1997.
45. Yang, Y., Y. Yan and F. J. Sigworth. How does the W434F mutation block current in *Shaker* potassium channels? *J. Gen. Physiol.* 109: 779-789, 1997.
46. Zheng, J. and F. J. Sigworth. Selectivity changes during activation of mutant *Shaker* potassium channels. *J. Gen. Physiol.* 110: 101-117, 1997.
47. Schoppa, N.E. and F. J. Sigworth. Activation of *Shaker* potassium channels. I. Characterization of voltage-dependent transitions. *J. Gen. Physiol.* 111:271-294, 1998.

48. Schoppa, N.E. and F. J. Sigworth. Activation of *Shaker* potassium channels. II. Kinetics of the V2 mutant channel. *J. Gen. Physiol.* 111: 295-312, 1998.
49. Schoppa, N.E. and F. J. Sigworth. Activation of *Shaker* potassium channels. III. An activation gating model for wild-type and V2 mutant channels. *J. Gen. Physiol.* 111: 313-342, 1998.
50. Venkataramanan, L., J. L. Walsh, R. Kuc and F. J. Sigworth. Identification of hidden Markov models for ion channel currents containing colored background noise. *IEEE Transactions on Signal Processing* 46: 1901-1915, 1998.
51. Venkataramanan, L., R. Kuc and F. J. Sigworth. Identification of hidden Markov models for ion channel currents containing state-dependent noise. *IEEE Transactions on Signal Processing* 46:1916-1929, 1998.
52. Zheng, J. and F. J. Sigworth. Intermediate conductances during deactivation of heteromultimeric *Shaker* potassium channels. *J. Gen. Physiol.* 112:457-474, 1998
53. Sigworth, F. J. A maximum-likelihood approach to single-particle image refinement. *J. Struct. Biol.* 122: 328-339, 1998.
54. Yang, Y. and F. J. Sigworth. Single-Channel Properties of I_{K_S} Potassium Channels. *J. Gen. Physiol.* 112: 665-678, 1998.
55. Baumgartner, W. and F. J. Sigworth. Two-Microelectrode Voltage Clamp of *Xenopus* Oocytes: Voltage Errors and Compensation for Local Current Flow. *Biophys J* 77:1980-1991, 1999.
56. Islas, L. D. and F. J. Sigworth. Voltage sensitivity and gating charge in *Shaker* and *Shab* family potassium channels. *J Gen Physiol* 114:723-742, 1999.
57. Venkataramanan, L., R. Kuc and F. J. Sigworth. Identification of hidden Markov models for ion channel currents, part III. Band-limited, sampled data. *IEEE Transactions on Signal Processing* 48:376-385, 2000.
58. Islas, L. D. and F. J. Sigworth. Electrostatics and the gating pore of *Shaker* potassium channels. *J. Gen. Physiol.* 117:69-89, 2001.
59. Cascio M, Shenkel S, Grodzicki RL, Sigworth FJ, Fox RO. Functional reconstitution and characterization of recombinant human alpha 1-glycine receptors. *J Biol Chem.* 276:20981-8, 2001.
60. Jiang, Q-X., D. W. Chester and F. J. Sigworth. Spherical reconstruction. A method for structure determination of membrane proteins from cryo-EM images. *J. Struct. Biol.* 133:119-131. 2001.
61. Zheng, J., L. Venkataramanan and F. J. Sigworth. Hidden Markov Model Analysis of Intermediate Gating Steps Associated with the Pore Gate of *Shaker* Potassium Channels. *J. Gen Physiol.* 118:547-562, 2001.
62. Klemic, K.G., Klemic, J.F., Reed, M.A. and Sigworth, F.J. Micromolded PDMS planar electrode allows patch clamp electrical recordings from cells. *Biosensors and Bioelectronics* 17:597-604, 2002.
63. Venkataramanan, L. and F. J. Sigworth. Applying hidden Markov models to the analysis of single ion channel activity. *Biophys. J.* 82: 1930-1942, 2002.
64. Jiang, Q.-X., E. C. Thrower, D. W. Chester, B. E. Ehrlich and F. J. Sigworth. Three-dimensional structure of the type 1 inositol 1,4,5-trisphosphate receptor at 24 Å resolution. *EMBO J.* 21:3575-3581, 2002.
65. Bhattacharjee A, Joiner WJ, Wu M, Yang Y, Sigworth FJ, L. K. Kaczmarek Slick (Slo2.1), a rapidly-gating sodium-activated potassium channel inhibited by ATP. *J Neurosci.* 17:11681-91, 2003.
66. Sigworth, F. J. Classical detection theory and the cryo-EM particle selection problem. *J. Struct. Biol.* 145:111-122, 2004.
67. Yang, Y., Yan, Y. and Sigworth, F. J. Can *Shaker* potassium channels be locked in the deactivated state? *J. Gen. Physiol.* 124:163-171, 2004.
68. Klemic, K. G., Klemic, J. F. and Sigworth, F. J. An air-molding technique for fabricating PDMS planar patch-clamp electrodes. *Pflugers Arch.* 449:564-572, 2005.
69. Sigworth, F. J. and Klemic, K. G. Microchip technology in ion-channel research. *IEEE Trans Nanobioscience.* 4:121-127, 2005.

70. Giraldez, T., Hughes, T.E. and Sigworth, F. J. Generation of functional fluorescent BK channels by random insertion of GFP variants. *J. Gen. Physiol.* 126:429-438, 2005.
71. Zhang, P., Sigworth F. J. and Canessa, C.M. Gating of acid-sensitive ion channel-1: release of Ca²⁺ block vs. allosteric mechanism. *J Gen Physiol.* 127:109-117, 2006.
72. Li, X., Klemic, K. G., Reed, M. A. and Sigworth, F. J. Microfluidic system for planar patch clamp electrode arrays. *Nano Lett.* 6:815-819, 2006.
73. Yang B, Gribkoff VK, Pan J, Damagnez V, Dworetzky SI, Boissard CG, Bhattacharjee A, Yan Y, Sigworth FJ, Kaczmarek LK. Pharmacological activation and inhibition of Slack (Slo2.2) channels. *Neuropharmacology.* 51:896-906, 2006.
74. Wang, L., P. Bose and F. J. Sigworth. Using cryo-EM to measure the dipole potential of a lipid membrane. *PNAS* 103:18528-18533, 2006.
75. Chester DW, Klemic JF, Stern E, Sigworth FJ, Klemic KG. Holey carbon micro-arrays for transmission electron microscopy: A microcontact printing approach. *Ultramicroscopy.*107(8):685-91, 2007.
76. Stern E, Wagner R, Sigworth FJ, Breaker R, Fahmy TM, Reed MA. Importance of the Debye screening length on nanowire field effect transistor sensors. *Nano Lett.* 7:3405-3409, 2007.
77. Ounjai P, Unger VM, Sigworth FJ, Angsuthanasombat C. Two conformational states of the membrane-associated *Bacillus thuringiensis* Cry4Ba delta-endotoxin complex revealed by electron crystallography: implications for toxin-pore formation. *Biochem Biophys Res Commun.* 361:890-895, 2007.
78. Wang, L., Ounjai, P. and Sigworth, F.J. Streptavidin crystals as nanostructured supports and image-calibration references for cryo-EM data collection. *J. Struct. Biol.* 164:190-198, 2008.
79. Coifman RR, Shkolnisky Y, Sigworth FJ, Singer A. Graph Laplacian tomography from unknown random projections. *IEEE Trans Image Process.* 17:1891-1899, 2008
80. Weerakoon, P.; Sigworth, F.; Culurciello, E.. Integrated patch-clamp biosensor for high-density screening of cell conductance. *Electronics Letters*, 44:81-82, 2008.
81. Wang, L and Sigworth FJ. Structure of the BK potassium channel in a lipid membrane from electron cryomicroscopy. *Nature* 461:292-295, 2009. PMC2797367
82. Singer A, Coifman RR, Sigworth FJ, Chester DW, Shkolnisky Y. Detecting consistent common lines in cryo-EM by voting. *J Struct Biol.* 169:312-322, 2009. PMID: 19925867 PMC2826584
83. Chen H, Kronengold J, Yan Y, Gazula VR, Brown MR, Ma L, Ferreira G, Yang Y, Bhattacharjee A, Sigworth FJ, Salkoff L, Kaczmarek LK. The N-terminal domain of Slack determines the formation and trafficking of Slick/Slack heteromeric sodium-activated potassium channels. *J Neurosci.* 29:5654-65, 2009. PubMed PMID: 19403831. PMC3688047
84. Coifman RR, Shkolnisky Y, Sigworth FJ, Singer A. Reference Free Structure Determination through Eigenvectors of Center of Mass Operators. *Appl Comput Harmon Anal.* 28:296-312, 2010. PubMed PMID: 20436952; PubMed Central PMCID: PMC2860334.
85. Barmeyer C, Rahner C, Yang Y, Sigworth FJ, Binder HJ, Rajendran VM. Cloning and identification of tissue specific expression of KCNN4 splice variants in rat colon. *Am J Physiol Cell Physiol.* 2010 May 5. [Epub ahead of print] PMID: 20445171 PMC2928625
86. Xu J, Sigworth FJ, LaVan DA. Synthetic protocells to mimic and test cell function. *Adv Mater.* 2010 22:120-127. PubMed PMID: 20217710; PubMed Central PMCID: PMC2845179.
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90. Müllner FE, Syed S, Selvin PR, Sigworth FJ. Improved hidden Markov models for molecular motors, part 1: basic theory. *Biophys J*. 99:3684-3695, 2010. PMC2998602
91. Syed S, Müllner FE, Selvin PR, Sigworth FJ. Improved hidden Markov models for molecular motors, part 2: extensions and application to experimental data. *Biophys J*. 99:3696-3703, 2010. PMC2998599
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93. Bian S, Bai JP, Chapin H, Le Moellic C, Dong H, Caplan M, Sigworth FJ, Navaratnam DS. Interactions between β -catenin and the HSlo potassium channel regulates HSlo surface expression. *PLoS One* 6:e28264, 2011. PMID: 22194818; PMC3237428
94. Barthel AC Tagare H Sigworth FJ. Surface-constrained 3D reconstruction in cryo-EM. *Proceedings of the 2011 IEEE Asilomar Conference on Image Processing*, 1026-1030, 2011.
95. Kucukelbir A, Sigworth FJ, Tagare HD. A Bayesian adaptive basis algorithm for single particle reconstruction. *J Struct Biol*. 179:56-67, 2012. PMID: 22564910 PMC3377842
96. Shang Z, Sigworth FJ. Hydration-layer models for cryo-EM image simulation. *J. Struct. Biol*. 180:10-16, 2012. PMC3577369
97. Yan Y, Yang Y, Bian S, Sigworth FJ. Expression, Purification and Functional Reconstitution of Slack Sodium-Activated Potassium Channels. *J Membr Biol*. 245:667-674, 2012. PMC3577369
98. Miranda P, Contreras JE, Plested AJR, Sigworth FJ, Holmgren, M, and Giraldez T. State-dependent FRET reports calcium- and voltage-dependent gating-ring motions in BK channels. *PNAS* 110:5217-5222, 2013. PMC3612663
99. Kim D, Goldstein B, Wei Tang, Sigworth FJ, Culurciello E. Noise analysis and performance comparison of low current measurement systems for biomedical applications. *IEEE Trans Biomed Circuits Syst*. 7:52-62, 2013.
100. Shigematsu H and Sigworth FJ. Noise models and cryo-EM drift correction with a direct-electron camera. *Ultramicroscopy* 131C:61-69, 2013.
101. Kucukelbir, A, Sigworth FJ, Tagare HD. Quantifying the local resolution of cryo-EM density maps. *Nature Methods* 11:63-65, 2014.
102. Liu Y, Sigworth FJ. Automatic cryo-EM particle selection for membrane proteins in spherical liposomes. *J. Struct. Biol*. 185:295-302, 2014.
103. Dvornek NC, Sigworth FJ, Tagare HD. SubspaceEM: A fast maximum-a-posteriori algorithm for cryo-EM single particle reconstruction. *J Struct Biol*. 190:200-214, 2015.
104. Tagare HD, Kucukelbir A, Sigworth FJ, Wang H, Rao M. Directly reconstructing principal components of heterogeneous particles from cryo-EM images. *J Struct Biol*. pii: S1047-8477(15)30004-6. doi: 10.1016/j.jsb.2015.05.007. [Epub ahead of print] 2015.
105. Jensen KH, Brandt SS, Shigematsu H, Sigworth FJ. Statistical modeling and removal of lipid membrane projections for cryo-EM structure determination of reconstituted membrane proteins. *J. Struct. Biol*. 194:49-60, 2016.

Review Articles

- R1. Sigworth, F.J. Sodium current fluctuations in myelinated axons. Chapter 4 in: *Abnormal Nerves and Muscles as Impulse Generators*, J. Ochoa and W. Culp, eds. Oxford University Press (1981).
- R2. Sigworth, F.J. Nonstationary noise analysis of membrane currents. In: *Membranes, Channels and Noise*, R.S. Eisenberg, M. Frank and C.F. Stevens, eds. Plenum Press, 1984.
- R3. Sigworth, F.J. The patch clamp is more useful than anyone had expected. *Federation Proc*. 45:2673-2677 (1986).

- R4. Sigworth, F.J. Rapid fluctuations in ionic current through membrane channels. Proceedings of the 9th International Symposium on Noise in Physical Systems. C. M. Van Vliet, Ed. (1987).
- R5. Claudio, T., H. L. Paulson, D. Hartman, S. Sine and F. J. Sigworth. Establishing a stable expression system for studies of acetylcholine receptors. *Current Topics in Membranes and Transport* 33: 219-247 (1988).
- R6. Sigworth, F.J. and Zhou, J. Analysis of nonstationary single-channel currents. *Methods in Enzymology* 207: 746-762 (1992).
- R7. Heinemann, S. H. and F.J. Sigworth. Fluctuations of ionic currents and ion channel proteins. In: *Thermodynamics of Cell Surface Receptors*, M. B. Jackson, ed., CRC Press (1993).
- R8. Sigworth, F. J. Voltage gating of ion channels. *Q. Rev. Biophys.* 27:1-40, 1994.
- R9. Sigworth, F. J. Charge movement in the sodium channel. *J. Gen. Physiol.* 106:1047-1051, 1995.
- R10. Schoppa, N. E., Y. Yang and F. J. Sigworth. How is voltage coupled to channel opening in Shaker K⁺ channels? *Progress in Cell Research* 6: 99-109, 1997.
- R11. Sigworth, F. J. Potassium Channel Mechanics. *Neuron* 32: 555-556, 2001.
- R12. Sigworth F. J. and Klemic, K. G. Patch clamp on a chip. *Biophys. J.* 82:2831-2832, 2002.
- R13. Sigworth, F. J. Life's transistors. *Nature* 423:21-22, 2003.
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