BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Schnapp, Bruce J.	Professor
eRA COMMONS USER NAME (credential, e.g., agency login) SCHNAPP	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Connecticut, Ct.	B.S.	06/72	Biology
University of Connecticut, Ct.	Ph.D.	06/78	Neurobiology
Harvard Medical School, MA.	Postdoctoral	11/80	Neurobiology

A. Personal Statement

I have a publication track record of 29 years in the motor protein field, especially in the area of imaging and biophysically analyzing organelle and motor protein motility. My lab has also worked and published in the field of maternal mRNA localization in oocytes. Most recently I have been using the zebrafish model system to investigate how cytoskeletal motor proteins are regulated in the context of pigment granule transport.

Biographical narrative. As a Ph.D, student in the 1970s, I trained in a leading neurocytology laboratory, and became expert in electron microscopy of the nervous system, especially freeze-fracture and, later, the rapid freeze technique, both very new at the time. As a postdoctoral fellow in the Department of Neurobiology at Harvard Medical School I gained expertise in neurophysiology and learned electronics, disciplines that I expanded on as a Multiple Sclerosis Society Fellow at the Institute of Neurology, London, England. It was during these postdoctoral years that I developed my interest in axonal transport, about which little was known.

In my first independent position (1983-89), with the NIH (within the Division of Structural Cell Biology headed by Dr. Tom Reese at the Marine Biological Laboratory, Woods Hole, MA), I elucidated the mechanism of axonal transport. These studies took place primarily in my lab and depended on a singular collaboration that I initiated with two biochemists, Dr. Michael Sheetz and his postdoc Ron Vale. They were investigating axonal transport in squid axons from a biochemical standpoint that complemented the structural one Dr. Reese and I were pioneering, also in squid axons. I was the microscopy specialist for our collaborative studies. My principal contributions were to make technical improvements in computer enhanced light microscopy that capitalized on my electronics and instrumentation background, and to develop a reliable method to dissociate squid axoplasm on a coverglass. Thus, I obtained real-time images of organelle movements along isolated "filaments", which I identified in the EM, using Reese's rapid freeze technique, as single microtubules. This work established the basic role of microtubules in intracellular transport. Using the instrumentation and methods I had pioneered for real time imaging of single microtubules, Drs. Vale and Sheetz, still collaborating with Drs. Reese and I in our Woods Hole labs, pioneered the next phase of the work. These studies entailed reconstituting vesicle transport biochemically. Using purified microtubules and subcellular fractions from squid axoplasm, Ron Vale and I devised in vitro motility assays that revealed the existence and polarity of cytoplasmic microtubule motor proteins. We established that distinct motors promote transport toward opposite ends of the microtubule. The in vitro motility assays we developed enabled us to purify the plus-end motor, kinesin, led by Ron Vale, and the minus-end motor, cytoplasmic dynein, by myself.

I subsequently (1986-1993) produced a body of biophysical work that harnessed the in vitro motility assays to elucidate the mechanism of kinesin motility. My initial experiments, using nucleotide inhibitors, provided the first evidence that the two heads of kinesin work in alternate fashion, i.e. that kinesin walks along the microtubule. Prominent in the next phase of my work was the development and use of advanced light optical methods that revealed the molecular mechanics of kinesin walking. These studies depended on a series of collaborations. Initially, Dr. Michael Sheetz, his postdoc Jeff Gelles, and I used a novel centroid-tracking program (developed by Dr. Gelles) to compute the displacement of beads carrying multiple kinesins. This work

demonstrated that kinesin tracks along single protofilaments of the microtubule. To determine whether bead movement could be driven by a single kinesin, I collaborated with Dr. Steven Block, who at that time was investigating bacterial motility with optical tweezers. Guided by Dr. Block, I interfaced optical tweezers to the microtubule imaging equipment in my lab. I then developed a reproducible single kinesin motility assay that utilized optical tweezers to place onto microtubules individual beads, each carrying a single kinesin. These studies demonstrated that a single kinesin is processive. A direct outgrowth of this work was the demonstration that a single kinesin walks along the microtubule in a step-wise manner, pausing at 8 nm intervals – the tubulin dimer repeat. Karel Svoboda, a biophysics Ph.D. student guided by Dr. Block and I led this work.

Upon moving my laboratory to Harvard Medical School I switched my focus to the question of how motors are linked to cargo. This culminated in publications establishing that motors like kinesin are auto-inhibited through folding, linked to cargos by scaffold proteins, such as JIP1 and spectrin, and transport signaling pathways such as the c-Jun N-terminal kinase pathway. In addition to continuing my organelle transport research I expanded my lab to work on the transport and localization of maternal mRNAs in oocytes. This work culminated in publications that identified conserved localization signals in maternal mRNAs such as Vg1 in frogs and oskar in Drosophila, and purified the protein that interacts with these motifs.

I moved my laboratory to OHSU in 2001 and turned my attention to the problem of how cargo transport is regulated in the cell, settling on zebrafish melanosome transport as the best way to crack this problem. Initially I pursued this project with a graduate student, resulting in the publication (Sheets et al, 2007) that validates the utility and feasibility of using zebrafish to dissect the mechanisms of organelle transport and its regulation. Over the past years I have worked at the bench, performing follow up studies on the mutant *mlpha*^{j120} (Sheets et al 2007), and identifying and characterizing a collection of additional melanosome transport mutants. I also teach extensively in the medical and graduate schools in the areas of cell and tissue biology.

B. Positions and Honors

Positions and Employment

1980-1982	Multiple Sclerosis Society Fellow, Institute of Neurology, Queen Square, London
1982-1988	Senior Staff Fellow, Division of Intramural Research, National Institute of Neurological, Communicative Diseases, and Stroke, N.I.H., Bethesda, MD.& Marine Biological Laboratory, Woods Hole, MA.
1988-1990	Associate Professor, Department of Physiology, Boston University School of Medicine, Boston, MA.
1991-1993	Associate Professor, Department of Cellular and Molecular Physiology, Harvard Medical School, Boston, MA.
1993-2001	Associate Professor, Department of Cell Biology, Harvard Medical School, Boston, MA.
2001-present	Professor, Department of Cell and Developmental Biology, Oregon Health & Science University, Portland, OR.

Other Experience and Professional Memberships

1976-Present	Member, American Society for Cell Biology
1980-Present	Member, American Society for Advancement of Science
1983 -1989	Faculty, Summer Neurobiology Course, Marine Biological Laboratory, Woods Hole, MA.
1985-1988	Member, Editorial Board, Journal of Neurocytology
1993-1998	Member, Molecular Cytology NIH Study Section ad hoc reviewer pool

Honors

2004	Award for best poster presentation (with L. Sheets), International Zebrafish Meeting, Madison, WI.
2013-2014	Faculty Excellence in Education Award OHSU School of Medicine

C. Selected Peer-Reviewed Publications

1. Schnapp, B. and Reese, T. (1982). Cytoplasmic structure in rapid frozen axons. J. Cell Biol. 94: 667-679.

2. Vale, R.D., Schnapp B.J., Reese T.S. and Sheetz M.P. (1985). Movement of organelles along filaments dissociated from the axoplasm of the squid giant axon. *Cell* 40:449-454. PMID: 2578324

3. Schnapp, B.J., Vale, R.D., Sheetz, M.P. and Reese, T.S. (1985). Single microtubules from squid axoplasm support bi-directional movement of organelles. *Cell* 40:455-462. PMID: 2578325

4. Vale, R.D., Schnapp, B.J., Reese, T.S. and Sheetz, M.P. (1985). Organelle, bead and microtubule translocations promoted by soluble factors from the squid giant axon. *Cell* 40:559-596. PMID: 2578887

5. Vale, R.D., Schnapp, B.J., Mitchison, T., Steuer, E., Reese, T.S. and Sheetz, M.P. (1985). Different axoplasmic proteins generate movement in opposite directions along microtubules in vitro. *Cell* 43:623-632. PMID: 2416467

6. Gelles, J., Schnapp, B.J. and Sheetz, M.P. (1987). Tracking kinesin-driven movements with nanometer-scale precision. *Nature* 331: 450-453. PMID: 3123999

7. Block, S.M. Goldstein, L.S.B. and Schnapp, B.J. (1990). Bead movement by single kinesin molecules studied with optical tweezers. *Nature* 348:348-352. PMID: 2174512

8. Svoboda, K., Schmidt, C.F., Schnapp, B.J. and Block, S.M. (1993). Direct observation of kinesin stepping by optical trapping interferometry. *Nature* 365:721-727. PMID: 8413650

9. Deshler, J.O., Highett, M., and Schnapp, B.J. (1997). Localization of Xenopus Vg1 mRNA by vera protein and the endoplasmic reticulum. *Science* 276: 1128-1131. PMID: 9148809

10. Verhey, K.J., Lizotte, D.L., Abramson, T., Barenboim, L., Schnapp, B.J.*, and Rapoport, T.A.. (1998) Light chain-dependent regulation of kinesin's interaction with microtubules. *J. Cell Biol*. 143: 1053-1066. *corresponding author. PMID: 9817761

11. Deshler, J.O., Highett, M., Abramson, T., and Schnapp, B.J. (1998). A highly conserved RNA-binding protein for cytoplasmic mRNA localization in vertebrates. *Current Biology* 8: 489-496. PMID: 9560341

12. Muresan, V. Stankewich, M.C., Steffen, W., Morrow, J., Holzbaur, and Schnapp, B.J. (2001) Dynactin-Dependent, Dynein-Driven Vesicle Transport in the Absence of Membrane Proteins: A Role for Spectrin and Acidic Phospholipids. *Molecular Cell* 7: 173-183. PMID: 11172722

13. Verhey, K.J., Meyer, D., Deehan, R., Blenis, J., Schnapp, B.J. *, Rapoport, T. A., and Margolis, B. (2001) Cargo of kinesin identified as JIP scaffolding proteins and associated signaling molecules *J. Cell Biol.* 152: 959-970. *corresponding author. PMID: 11238452

14. Kwon S, Abramson T, Munro TP, John CM, Kohrmann M, Schnapp BJ. (2002) UUCAC- and Vera-Dependent Localization of VegT RNA in Xenopus Oocytes. *Curr Biol* 12:558-64. PMID: 11937024

15. Munro, TP, Kwon, S., Schnapp, BJ, *St. Johnston, D. (2006) A repeated IMP-binding motif controls oskar mRNA translation and anchoring independently of Drosophila melanogaster IMP. *J Cell Biol*. 172:577-88. *corresponding author. PMID: 16476777

16. Jacobson, C, Schnapp, B, Banker, G.(2006) A change in the selective translocation of the Kinesin-1 motor domain marks the initial specification of the axon. *Neuron* 49:797-804. PMID: 16543128

17. Sheets, L, Ransom, DG, Mellgren, EM, Johnson, SL, Schnapp, BJ. Zebrafish melanophilin facilitates melanosome dispersion by regulating dynein. Curr Biol. 2007 17:1721-34. PMID: 17919909