BIOGRAPHICAL SKETCH	
NAME **Howard D. White**	POSITION TITLE **Professor**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Colorado, Boulder Colorado	B.S.	1964-1968	Chemistry/Engineering
Brandeis University, Waltham, Massachusetts	PhD	1968-1973	Biochemistry
Kings College, London	Postdoctoral	1973-1978	Biophysics

A. Personal Statement.

The principal focus throughout my scientific career has been to determine how the motor protein, myosin, converts the free energy from ATP hydrolysis into movement and work. My initial work on muscle myosin began during a postdoctoral fellowship in Ed Taylors's laboratory at Kings College in London. I have a broad background in presteady state biochemical kinetics with an emphasis on the mechanism of myosin function. Work from my laboratory has been fundamental in determining the important roles of phosphate and ADP dissociation with respect to the powerstroke and limiting shortening velocity of actomyosin. A sabbatical in John Trinick's laboratory sponsored by a Fogarty fellowship has resulted in an extensive collaboration which combined the rapid kinetic methods from my laboratory with the electron microscopy expertise in Trinick's laboratory to develop various approaches to time resolved electron EM, which have been utilized in our work and by the wider scientific community. Current work in my laboratory is focused on the molecular mechanism of contraction of non-muscle myosins V and VI and the mechanism of calcium regulation of vertebrate thin filaments. The goal of the research in this application is to obtain preliminary data on the structure and function of myosin VI using state of the art stopped flow fluorescence, single molecule kinetic studies and cryo-EM. Myosin VI is less well understood than the extensively studied myosins II and V, but has attracted great interest because it moves in the opposite direction on actin filaments relative to all other myosin classes so far examined. It also takes much longer steps than predicted for its two calmodulin lever arm. A key question in the molecular motors field of how binding to actin changes myosin structure has remained unresolved because of the difficulty in obtaining crystals of actomyosin for crystallography. The recent high resolution structures of F-actin show the feasibility of obtaining this information by cryo-EM and image processing as described in this proposal. This is a truly exciting time in the molecular motors field in which we now have the technology and incite to truly understand function at the molecular level. Throughout my career I have collaborated with a number of laboratories in the US and the UK and currently have active collaborations with Eva Forgacs (EVMS), Jim Sellers (NIH), Take Sakamoto (Wayne State University), David Heeley (Memorial University, Newfoundland), Martin Webb at the NIMR (Mill Hill, London), John Sleep (Kings College, London) and the molecular motility group at Leeds including John Trinick, Peter Knight, Michelle Peckham and Stan Burgess. These collaborations and the special expertise and insights of the various investigators have been critical to my research endeavors.

B. Positions and Honors.

1. Positions and Employment:
   Postdoctoral Fellow: Department Biophysics, Kings College, University of London, 1973-1976
   Scientific Staff: Medical Research Council Cell Biophysics Unit, London, 1976-1978
   Assistant Professor: Department of Biochemistry, University of Arizona, 1978-1985
   Associate Professor: Department of Biochemistry, Eastern Virginia Medical School, 1986-1990.
   Professor: Department of Physiological Sciences, Eastern Virginia Medical School, 1990-present.

2. Other Experience and Professional Membership
Advisory Committee: Resource for the Visualization of Biological Complexity, New York Public Health Department: (2001-present)
NIH Molecular Structure and Function C Study Section, October 2005
NIH Skeletal Muscle Biology and Exercise Physiology, June 2006
NIH Biochemistry and Molecular Biophysics Special Study Section, October 2007
NIH Molecular Structure and Function C Study Section, February 2008
NIH Biochemistry and Molecular Biophysics Special Study Section, May 2009.
NIH ARRA panel, July 2009.
NIH Biochemistry and Molecular Biophysics Special Study Section, June 2011.

3. Honors and Awards:
Regents Scholarship, University of Colorado, 1964-1968
Helen Hay Whitney Foundation Postdoctoral Fellow, 1973-1976
Fogarty Senior International Fellowship - NIH (1993-1994)
Research Award - Eastern Virginia Medical School, 1997
Fogarty Senior International Fellowship - NIH (2001-2002)

C. Selected Recent Peer Reviewed Publications (of 81)

1. Burgess S, Walker M, Wang F, Sellers JR, White, H.D., Knight PJ, Trinick, J. "The prepower stroke conformation of myosin V. **J Cell Biol**.159:983-91, 2002. PMID: 12499355; PMCID: PMC2173995
2. Sato O, White HD, Inoue A, Belknap B, Ikebe R, Ikebe M. Human deafness mutation of myosin VI (C442Y) accelerates the ADP dissociation rate. **J Biol Chem**. 279:28844-54, 2004. PMID: 15123708
3. Forgacs E, Cartwright S, Kovács M, Sakamoto T, Sellers JR, Corrie JET, Webb MR and White HD, " Kinetic Mechanism of MyosinV-S1 Using a New Fluorescent ATP Analogue", **Biochemistry,** 45, 13035-45 , 2006. PMID: 17059220
4. Forgacs E, Cartwright S, Sakamoto T, Sellers JR, Corrie JET, Webb MR and White HD, "Kinetics of ADP Dissociation from the Trail and Lead Heads of ActomyosinV Following the Powerstroke", **J Biol Chem** 283**,** 766-73, 2008. PMID: 17965414
5. Sakamoto T, Webb MR., Forgacs E, White, HD and Sellers JR. "Direct observation of the mechanochemical coupling in myosin Va during processive movement". **Nature** 455, 128-132, 2008. PMID: 18668042; PMCID: PMC2775414
6. Forgacs E, Sakamoto T, Cartwright S, Belknap B Kovács M, Tóth J, Webb MR, Sellers JR, and White HD The Switch-1 Mutation Ser^{217}Ala Converts MyosinV into a Low Duty Ratio Motor", **J Biol Chem.** 284, 2138-49, 2009. PMID: 19008235; PMCID: PMC2629086
7. Baboolal TJ, Sakamoto T, Forgacs E, White HD, Jackson WM, Takagi Y, Farrow RE, Molloy JE, Knight PJ, Sellers JR, Peckham M, "The SAH domain extends the functional length of the myosin lever", **PNAS**, 106:22193-8, 2009. PMID: 20018767; PMCID: PMC2794034
8. Oke O, Burgess S, Forgacs E, Knight PJ, Sakamoto T, Sellers JR, White H and Trinick J, "Influence of lever structure on myosin 5a walking" PNAS, 107:2509-14, 2010. PMCID: PMC2823865 PMID: 20133809
9. Song CF, Sader K, White H, Kendrick-Jones J, Trinick J. Nucleotide-dependent shape changes in the reverse direction motor, myosin VI. **Biophys J.** 99:3336-44, 2010. PMID: 21081082 [PubMed - in process]PMCID: PMC2980756 [Available on 2011/11/17].
10. Nicholson WV, White H, Trinick J. An approach to automated acquisition of cryoEM images from lacey carbon grids. **J Struct Biol**. 172:395-9. 2010. PMID: 20817100 [PubMed - indexed for MEDLINE]PMCID: PMC3001122 [Available on 2011/12/1]

More general contributions to the field.

1. Heeley DH, Belknap B, White HD, Maximal activation of skeletal muscle thin filaments requires both rigor myosin S1 and calcium. **J Biol Chem.** 281:668-76, 2006. PMID: 16186114
2. White HD and Ashcroft AE, "Real-time Measurement of Myosin – Nucleotide Noncovalent Complexes by Electrospray Ionization Mass Spectrometry" **Biophys. J.** 93, 914-9, 2007 PMID: 17483158; PMCID: PMC1913167.
3. Xu, S, White HD, Offer GW and Yu LC, Stabilization of helical order in the thick filaments by blebbistatin: further evidence of coexisting multiple conformations of myosin. **Biophys J.** 96:3673-81, 2009. PMID: 19413972; PMCID: PMC2711421
4. Houmeida A, Heeley DH, Belknap B, White HD Mechanism of regulation of native cardiac muscle thin filaments by rigor cardiac Myosin-S1 and calcium. **J Biol Chem.** 285:32760-9, 2010. PMID: 20696756 [PubMed - indexed for MEDLINE]PMCID: PMC2963418 [Available on 2011/10/22]
5. Haithcock J, Billington N, Choi K, Fordham J, Sellers JR, Stafford WF, White H, Forgacs E. The Kinetic Mechanism of Mouse Myosin VIIa. **J Biol Chem.** 286:8819-28, 2011.

C. Research Support

Completed Research Support

1. **"**Electron Cryo-microscopy of Acto-S1 ATPase Intermediates, NIH EB00209 Sept. 1, 1994 to August 1, 2009. (no cost extension until August 1, 2010) This grant supported work to determine the structure and function of actomyosin ATPase intermediates using site directed mutagenesis, rapid enzyme kinetics and time-resolved electron microscopy.

2. "Mechanism of Thin Filament Regulation of Cardiac Actomyosin ATP Hydrolysis", NIH HL84604, July 1, 2006 to June 30, 2010. The grant has a no cost extension until June 30, 2011. This grant supported a study of the mechanism of thin filament regulation of cardiac actomyosin ATP hydrolysis using transient kinetics and cryoelectronmicroscopy.

Pending

White H.D. Grant in Aid – AHA (PI)
"Effect of Myopathic TroponinI Mutations on the Mechanism of Regulation of Cardiac Thin Filaments. July 1, 2012 to June 30, 2014.