

Early days

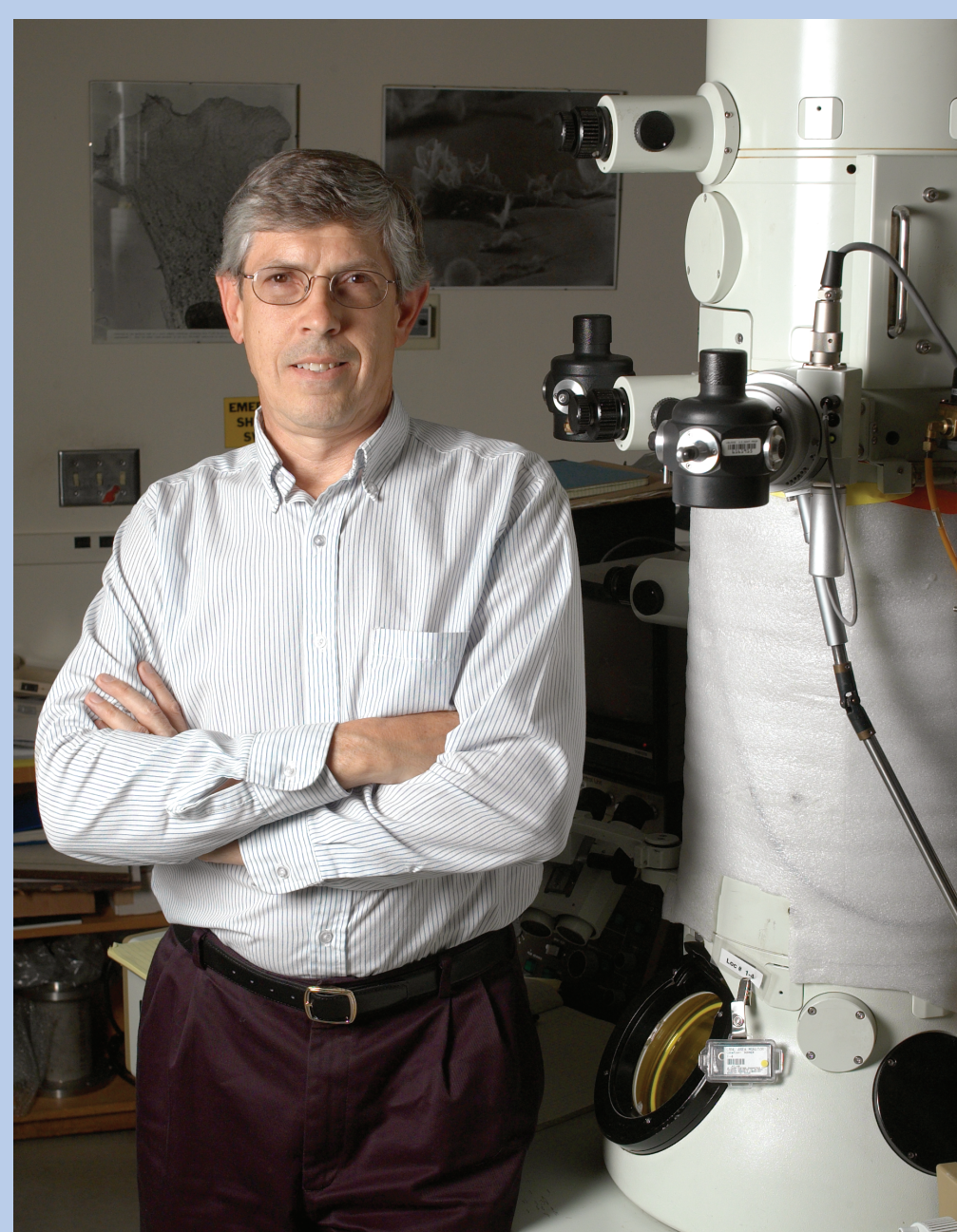
Kenneth Downing

1945 - 2018



From the MSA 2016 Distinguished Scientist interview

Biography

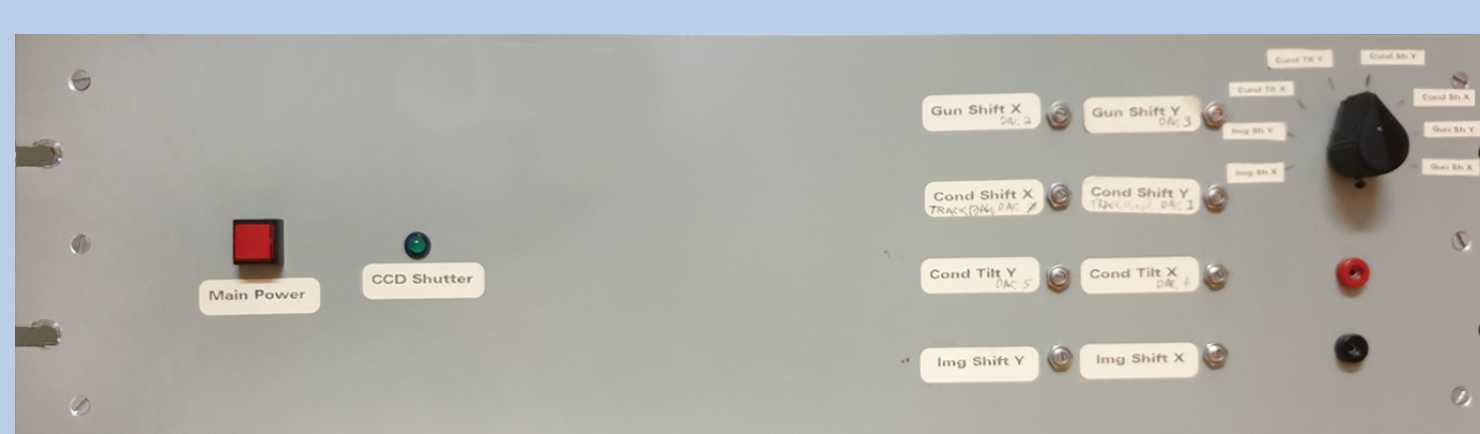
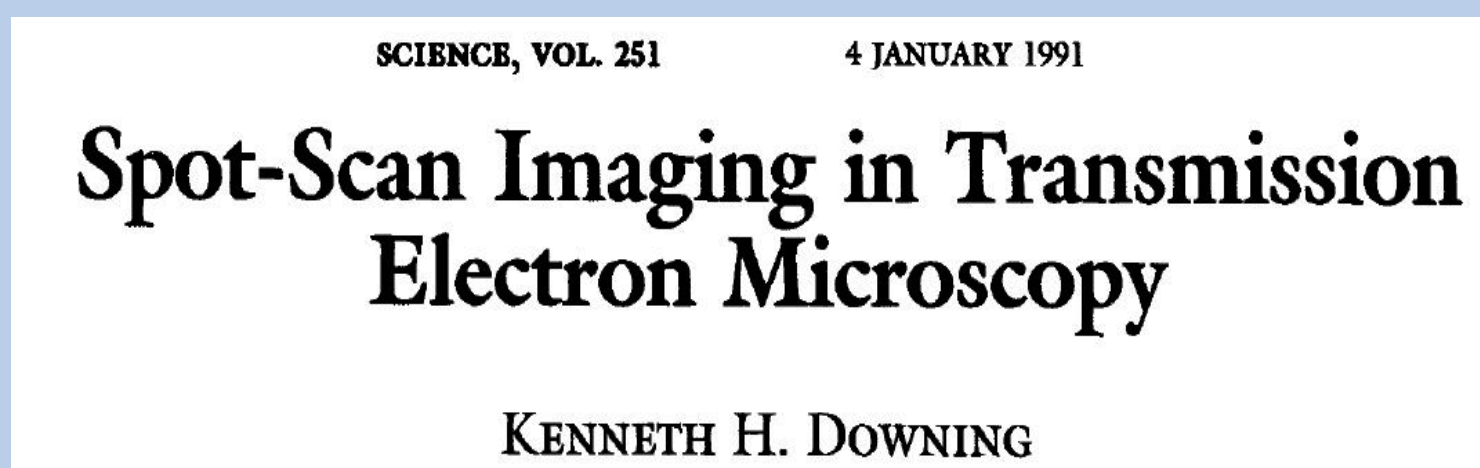


Ken Downing earned both BS and PhD in Physics at Cornell University. After his postdoc at Cornell in 1973, followed by a stint at the ETH in Switzerland, he went to the Donner laboratory at Lawrence Berkeley National Laboratory, where he remained until retirement as a Senior Scientist. Over 41 years at LBNL, papers on the atomic structures of two membrane proteins by means of electron crystallography, and research by his own group in determining the structure of tubulin gained him fame in both structural biology and in development of TEM technology, which made it possible.

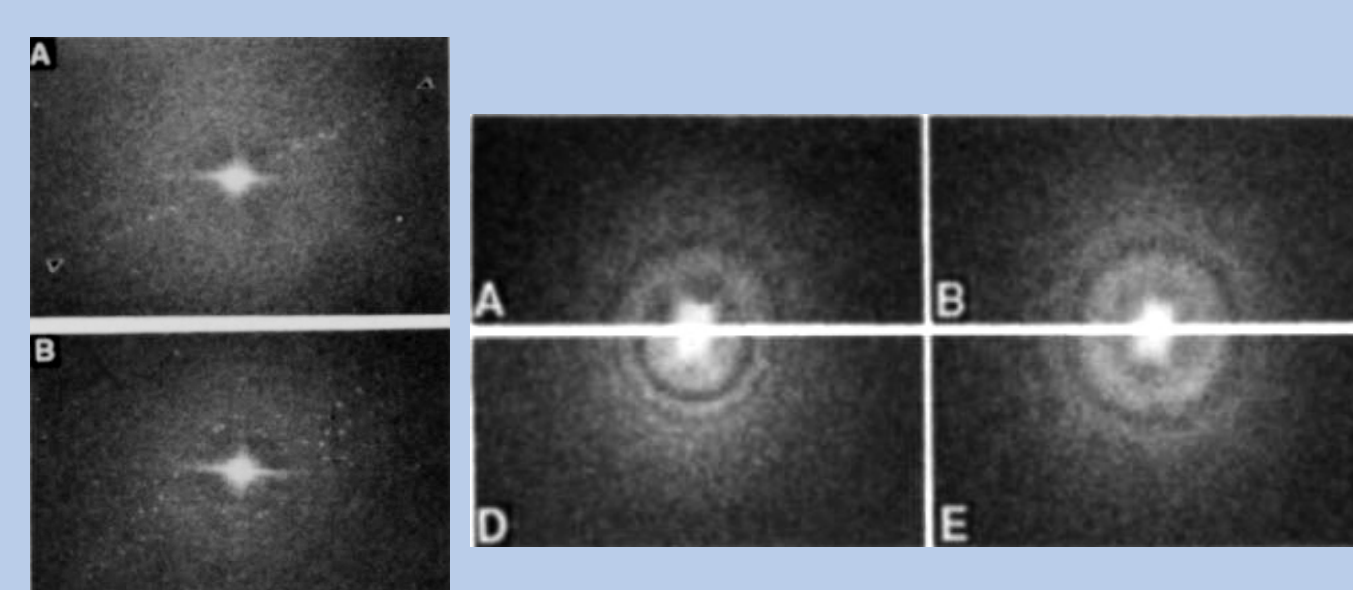
Instrumentation

Ken was well-known for advances in TEM instrumentation as well as in structural biology which was thereby made possible. The titles of his related NIH grants in this area provide a brief summary of this work:

- High Resolution Imaging
- Reduction of Specimen Charging
- Electron deceleration for CCD camera
- Improvement to CCD Camera Performance on IVEM
- CCD Camera for Intermediate Voltage Electron Microscopes



The control box for "Beam-e", which directly controlled the deflection coils of the JEM-4000 for spot-scan and low-dose imaging.



Left side: A: No spot scan – diffraction spots seen in one direction only; B: With spot scan – isotropic diffraction spots. Right side: aC film at edge of a tilted sample – defocus seen in D is corrected by spot-scan in A; aC film in center of tilted sample – correction of E, shown in B, has no effect. All images from the *Science* paper.

Downing KH (1991) Spot-scan imaging in transmission electron microscopy. *Science* 251:53–59.

Downing KH (1992) Automatic focus correction for spot-scan imaging of tilted specimens. *Ultramicroscopy* 46:199–206.

Downing KH and Mooney PE (2008) A charge coupled device camera with electron decelerator for intermediate voltage electron microscopy. *Rev Sci Instrum.* 79(4):043702.

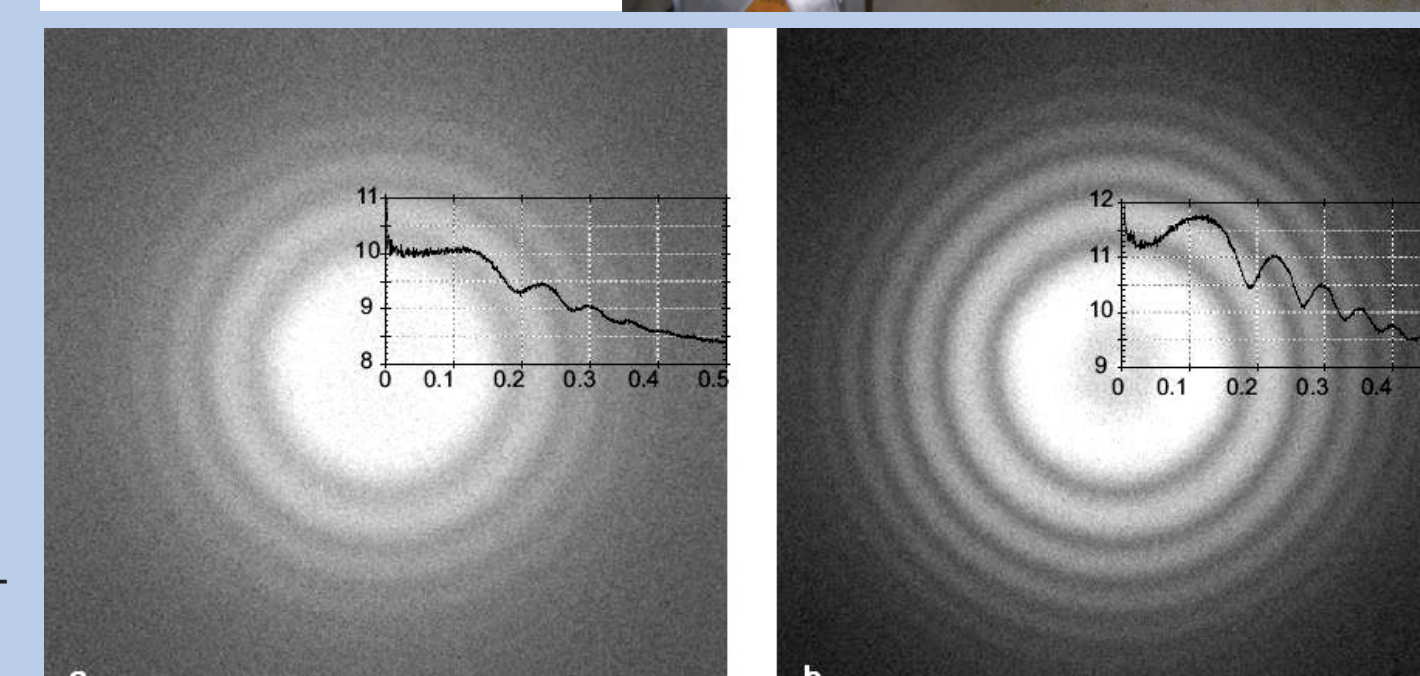
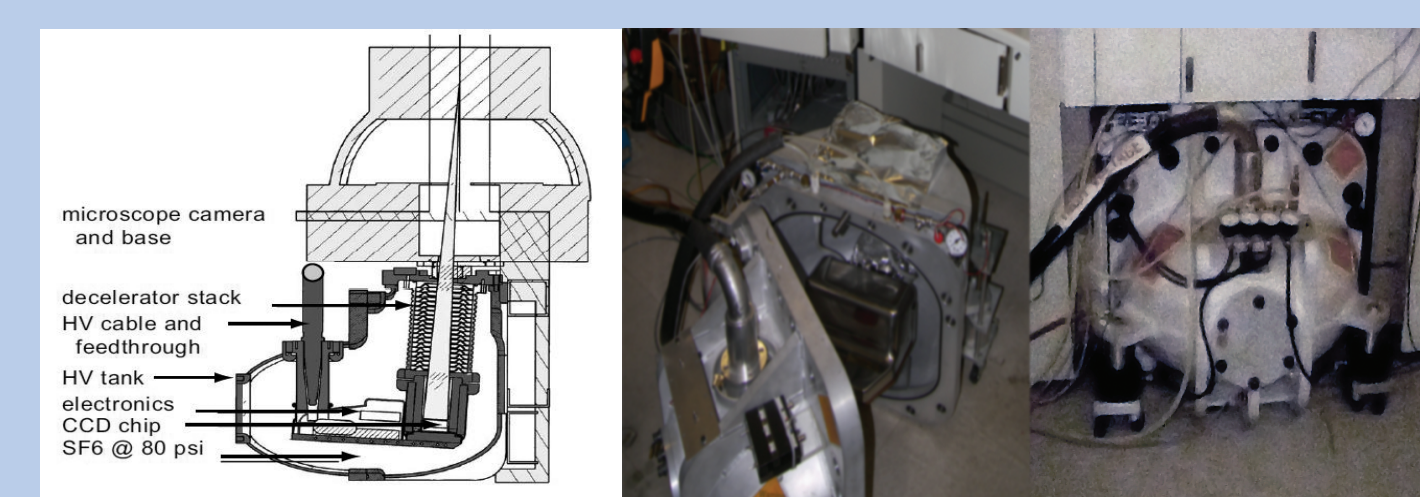
Downing KH (1992) Automatic focus correction for spot-scan imaging of tilted specimens. *Ultramicroscopy* 46:199–206.

Downing KH and Hendrickson FM (1999) Performance of a 2k CCD camera designed for electron crystallography at 400 kV. *Ultramicroscopy* 75:215–233.

REVIEW OF SCIENTIFIC INSTRUMENTS 79, 043702 (2008)

A charge coupled device camera with electron decelerator for intermediate voltage electron microscopy

Kenneth H. Downing^{1,3} and Paul E. Mooney²
¹Life Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, USA
²Gatan, Inc., Pleasanton, California 94588, USA

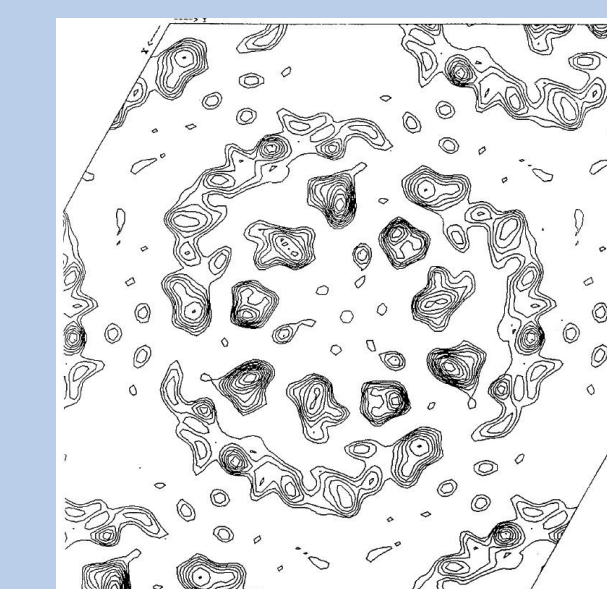
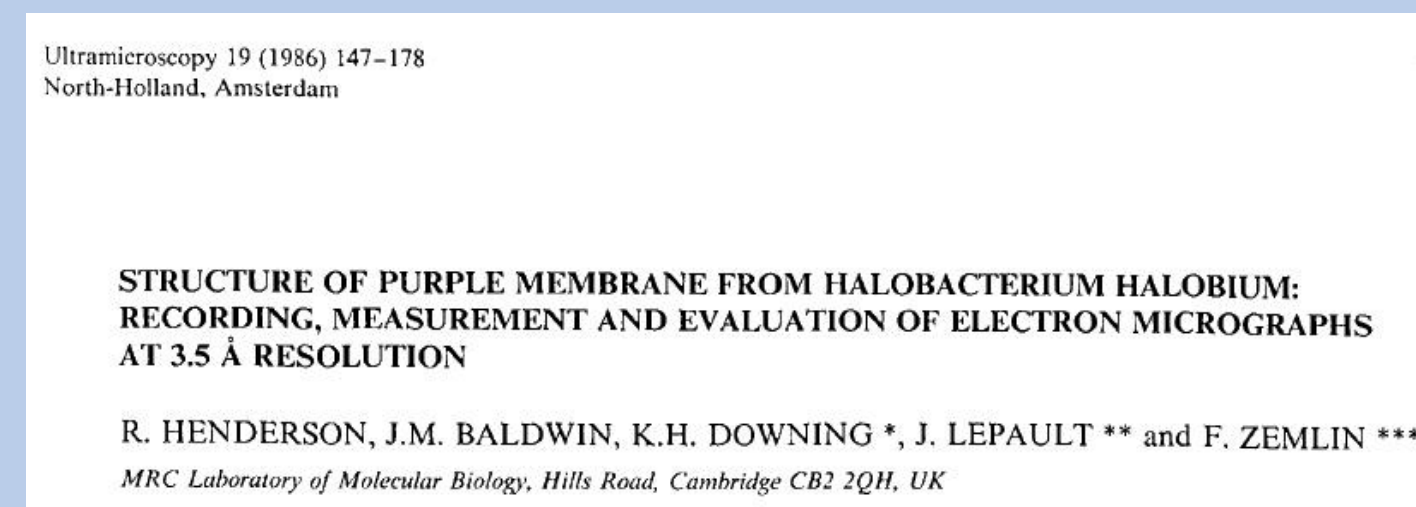


Improved Thon rings at 400 keV when using camera deceleration down to 100 keV.

Structural Biology

Ken also had excellent NIH support for structural biology. Again, a listing of grant titles provides a concise summary:

- Tubulin Structure by Electron Crystallography
- Structure and Interactions of Tubulin
- Chemical Bonding Effects in Protein Structures by Electron Crystallography
- High-resolution structure of bacteriorhodopsin
- Structure of G protein coupled receptors
- Macromolecular Surfaces by Scanning Tunneling Microscopy



Conferences and service

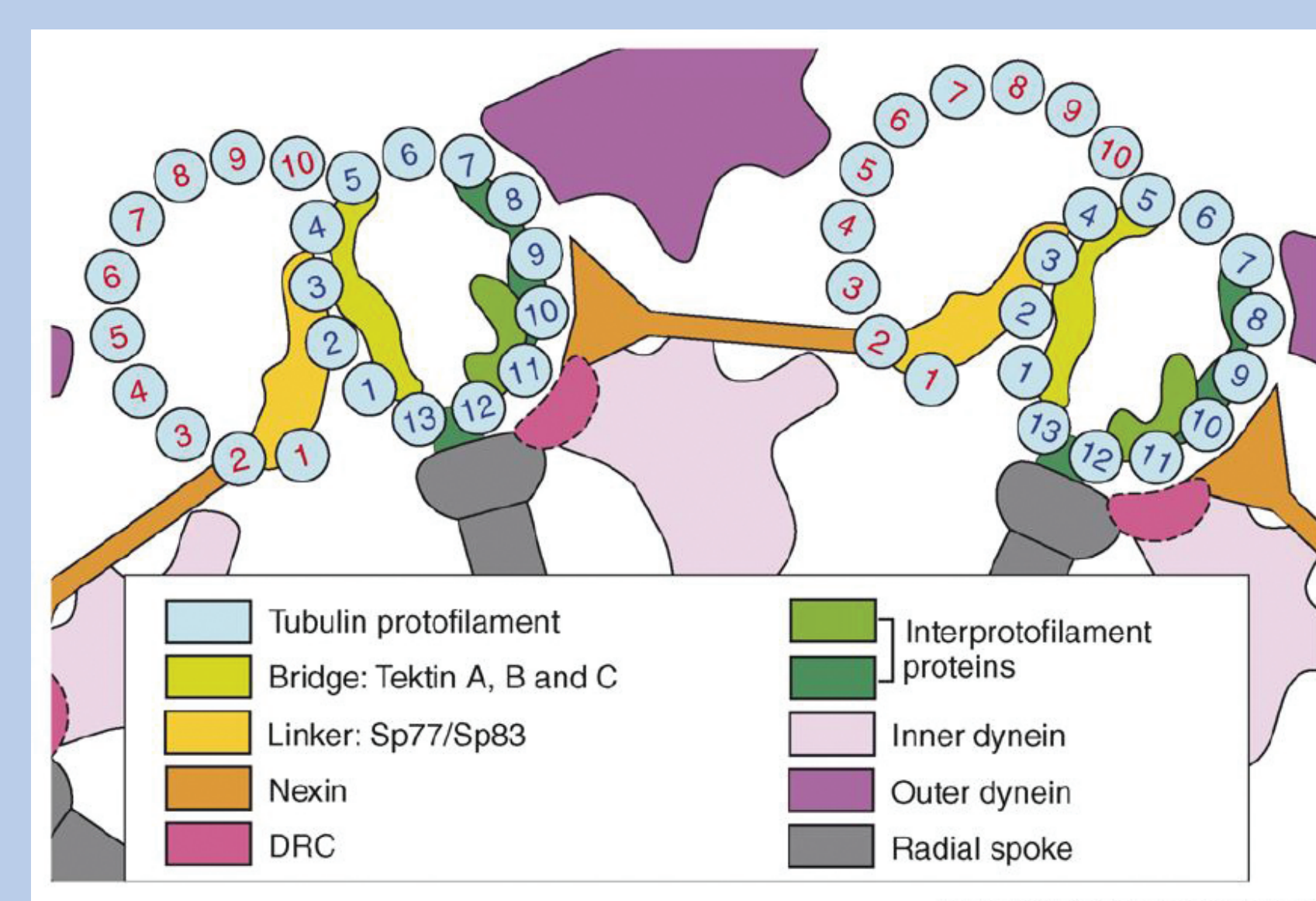
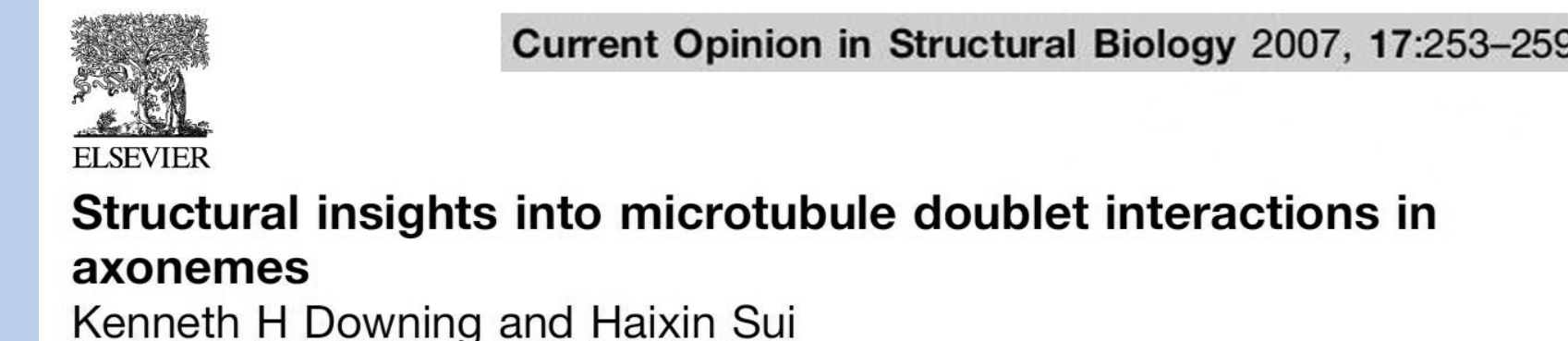
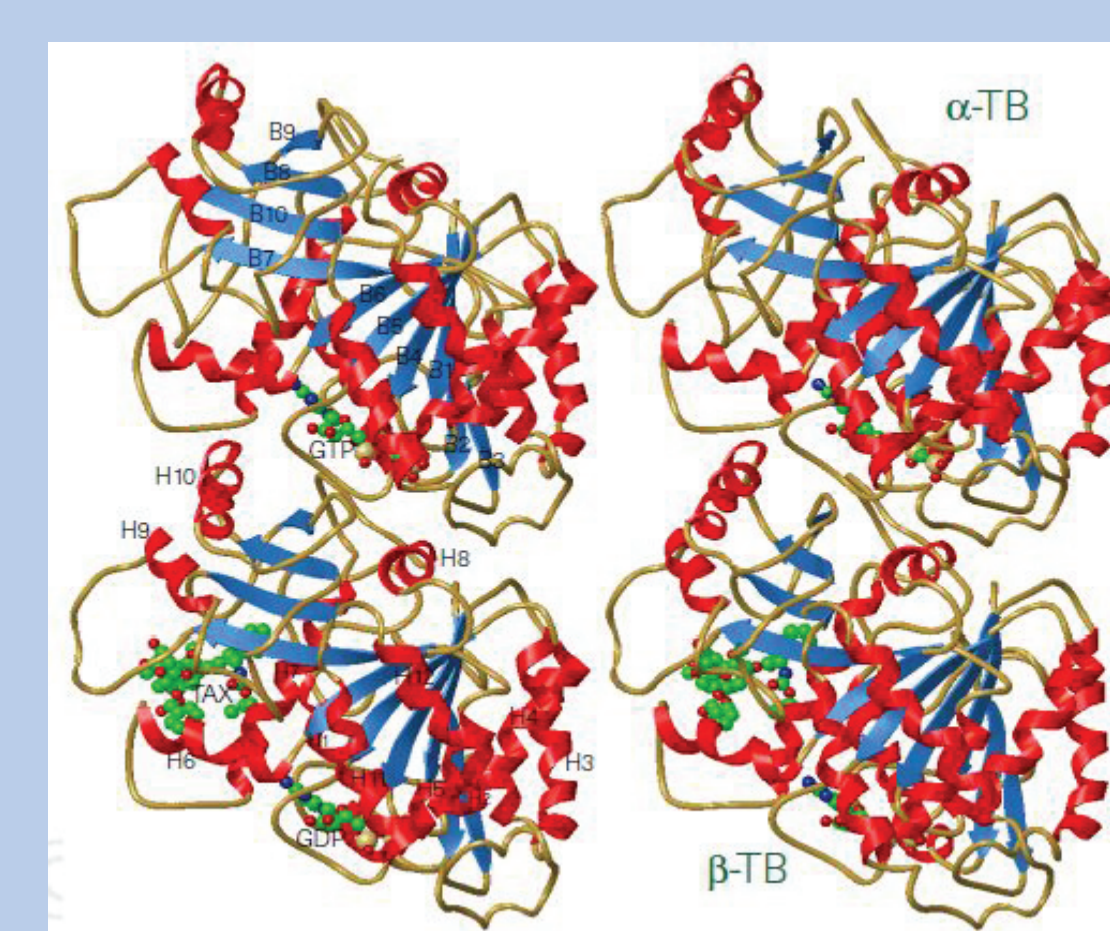
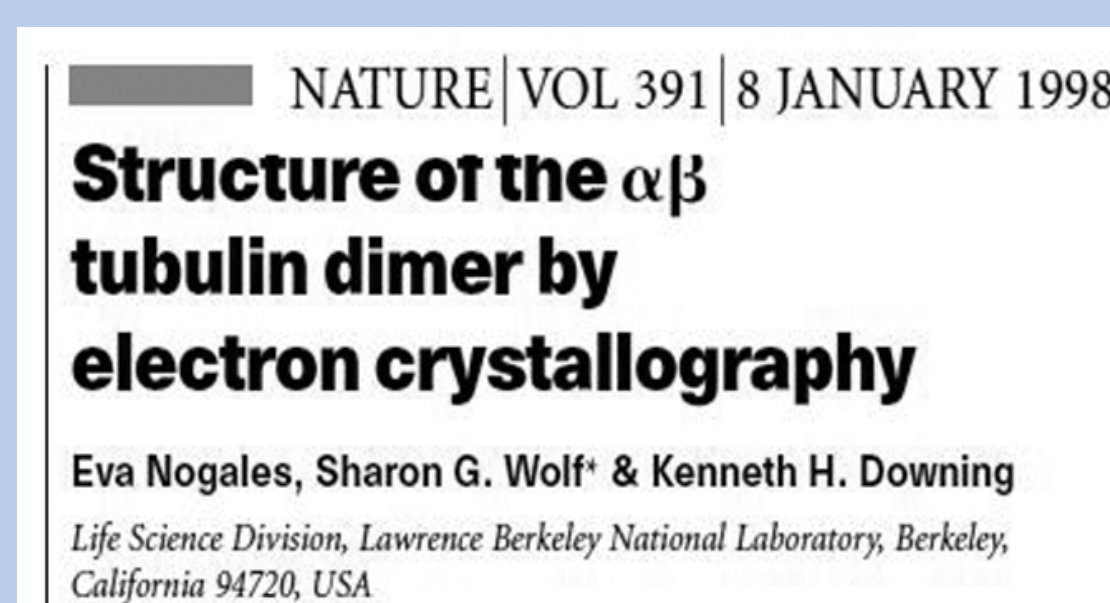
BERKELEY LAB
LAWRENCE BERKELEY NATIONAL LABORATORY

A Scientific Symposium in Honor of Ken Downing—
Celebrating Ken's Contributions to the Cryo-EM Field

PROGRAM
Friday, February 14, 2014
Scientific Symposium (Registration required)
Lawrence Berkeley National Laboratory, Bldg. 66 Auditorium

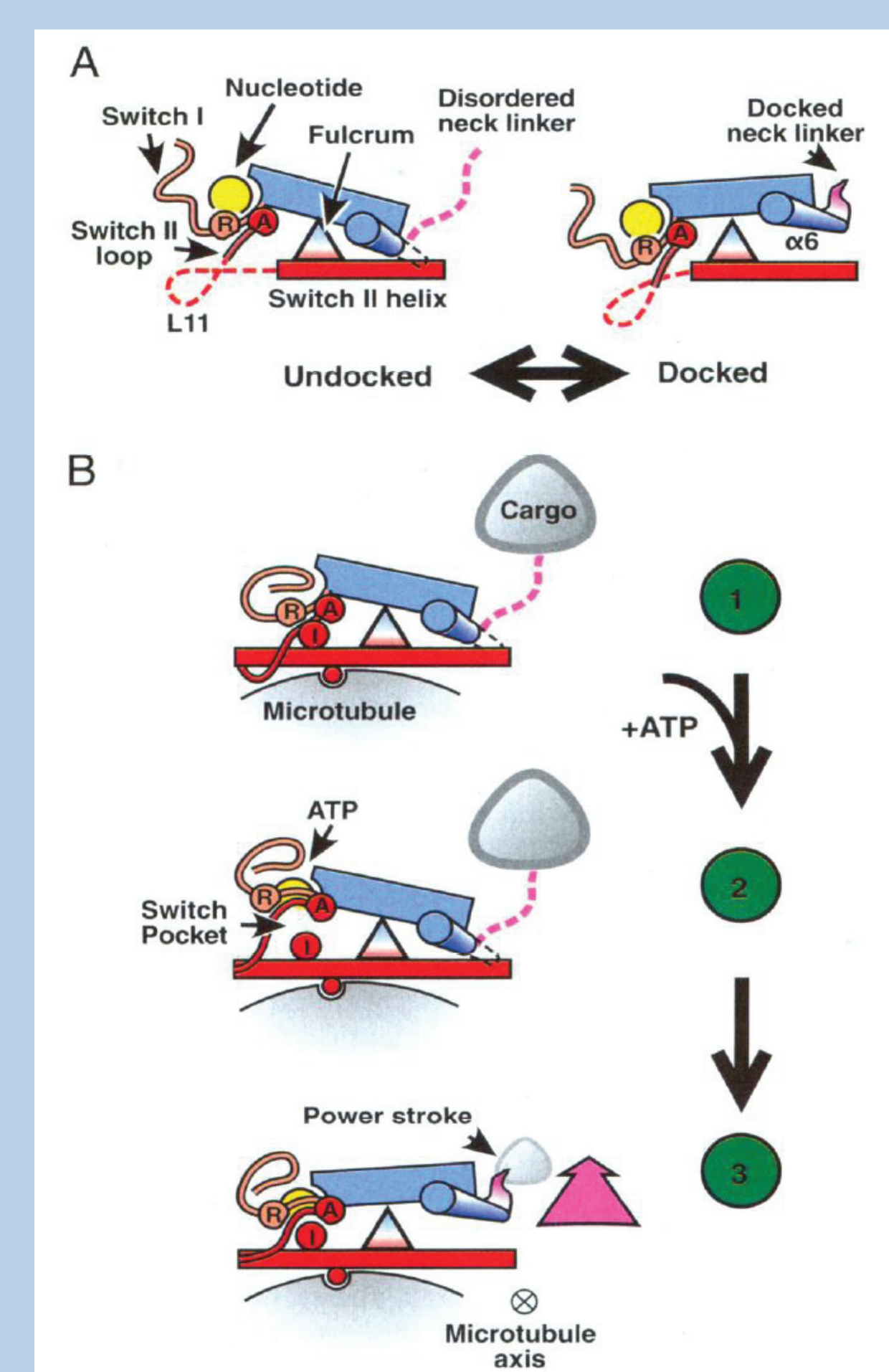
9:30 Check-in
10:00 Welcome
10:05 Chair: Eva Nogales
10:05 Single-Sideband Contrast: From the Early (Downing) Years to Today
10:30 Progress Towards Realizing the Full Potential of Single Particle Cryo-EM
10:55 Membrane Protein Structure and Function by Cryo-EM
11:20 Cryo-EM of Viruses
11:45 Lunch (lunch boxes served)
1:15 Chair: Grant Jensen
1:15 The Trouble with Ken
1:40 A Reverse Path through 3DEM: From 3 Angstrom to 3 nm Resolution
2:05 Atomic Structures of Assembled Tubulin: From Zinc-Induced Sheets to Microtubules
2:30 EM Reveals How the MCM2-7 Helicase Ring is Loaded onto the Replication Origin DNA
2:55 Break
3:20 Chair: Shuren Hui
3:20 Electron Cryotomography Past and Present
3:45 Cryo-Electron Tomography of Radial Spokes by Zernike Phase-Contrast Imaging
4:10 "Kneeling" Kinesin: Taking a Molecular Motor to the Next Level
4:35 My Perspective
5:00 Closing Remarks
5:05-6:00 Reception
6:30 Dinner (by invitation only)

Tubulin and microtubules



An atomic-level mechanism for activation of the kinesin molecular motors

Charles V. Sindelar^{1,2} and Kenneth H. Downing¹ PNAS | March 2, 2010 | vol. 107 | no. 9 | 4111–4116



In terms of professional friends and "family," Ken is "survived" by many co-workers, colleagues and peers around the world, who bonded deeply with him for his experimental skills, integrity, kindness and intellect, as well as by his many "scientific children" - students and postdocs trained in his lab.

Ken has served on several editorial boards of scientific journals, advisory committees, and was President of the Microscopy Society of America, from which he received the Distinguished Scientist Award in 2016. The previous year he received the Berkeley Lab Prize (Lifetime Achievement Award) from the Lawrence Berkeley National Lab.



Ken in earlier days with "academic offspring". All of these have become prominent scientists.



Group photograph with the attendees at the special symposium in Berkeley honoring Ken Downing (see the program at the left).

Honors

Awards

- Tau Beta Pi Engineering Honorary
- NIH Predoctoral Fellowship, 1969-1972
- Electron Microscopy Society of America Presidential Scholarship, 1972
- Northern California Society for EM: Council, 1981-84, President, 1982-83
- Advisory Committee, National Center for Electron Microscopy 1998 – 2008
- Microscopy Society of America: President 2000, Council, 1999-2002
- US National Committee for Crystallography, 2003 – 3005
- Center Advisory Committee, Cornell Physical Sciences – Oncology Center 2010-18
- Scientific Advisory Board, Max Planck Institute for Biophysics, Frankfurt 2010-18
- Elected Fellow, Microscopy Society of America, 2/2010

Patents

- U. S. Patent # 5,998,790: TEM CCD Camera
- U. S. Patent Application:
A Method for Identification, Selection, Design, Evaluation and modification of Compounds Binding to Tubulin; filed 2/4/02.

Editorial Boards

- Journal of Microscopy, 1993-1997
- Microscopy Research & Technique, 1997 – 2018 (Senior Associate Editor, 2003-09)
- Ultramicroscopy, 2001 – 2018

Acknowledgements

The MSA Archivist wishes to credit the information from the LBNL webpages and many of Ken's collaborators.

Selected publications

TEM/Imaging

- Downing KH (1991) Spot-scan imaging in transmission electron microscopy. *Science* 251:53–59.
- Downing KH (1992) Automatic focus correction for spot-scan imaging of tilted specimens. *Ultramicroscopy* 46:199–206.
- Li H, DeRosier D, Nicholson W, Nogales E, Downing K (2002) Microtubule structure at 8Å resolution. *Structure* 10:1317–1328.
- Downing KH. (1992) Automatic focus correction for spot-scan imaging of tilted specimens. *Ultramicroscopy*, 46:199-206.
- Downing KH and Hendrickson FM. (1999) Performance of a 2k CCD camera designed for electron crystallography at 400 kV. *Ultramicroscopy*, 75:215-233.

Membrane proteins

Henderson R, Baldwin JM, Downing KH, Lepault J, Zemlin F (1986) Structure of purple membrane from Halobacterium halobium: Recording, measurement and evaluation of electron micrographs at 3.5 Å resolution. *Ultramicroscopy* 19:147–178.

Henderson R, Baldwin JM, Ceska TA, Zemlin F, Beckman E, Downing KH (1990) Model for the structure of bacteriorhodopsin based on high-resolution electron cryo-microscopy. *J. Mol. Biol.* 213:899–929.

Killilea AN, Csencsits R, Le EBNT, Patel AM, Kenny SJ, Xu K, Downing KH (2017) Cytoskeletal organization in microtentacles. *Exp Cell Res.* 357:291-298.

Chiu W and Downing KH (2017) Editorial overview: Cryo Electron Microscopy: Exciting advances in CryoEM Herald a new era in structural biology. *Curr. Opin. Struct. Biol.* 46:iv-viii.

Tubulin

Downing KH, Jontes J 1992) Projection map of tubulin in zinc-induced sheets at 4 Å resolution. *J. Struct. Biol.* 109:152–159.

Nogales E, Wolf SG, Zhang SX, Downing KH (1998) Preservation of 2-D crystals of tubulin for electron crystallography. *J. Struct. Biol.* 115:199–208.

Nogales E, Wolf SG, Downing KH (1998) Structure of the alpha beta tubulin dimer by electron crystallography. *Nature*, 391:199–203.

Nogales E, Whittaker M, Milligan RA, Downing KH. (1999) High resolution model of the microtubule. *Cell*, 96:79–88.

Löwe J, Li H, Downing KH, Nogales E. (2001) Refined structure of alpha beta-tubulin at 3.5Å resolution. *J. Mol. Biol.* 313:1045–1057.

Snyder JP, Nettles JH, Cornett B, Downing KH, Nogales E (2001) The binding conformation of Taxol in beta-tubulin: A model based on electron crystallographic density. *Proc. Natl. Acad. Sci. USA*, 98:5312–5316.

Nettles JH, Li HL, Cornett B, Krahn JM, Snyder JP, Downing KH (2004) The binding mode of epithilone A on alpha-beta-tubulin by electron crystallography. *Science* 205:866–869.

Sui H and Downing KH (2006) Molecular architecture of axonemal microtubule doublets revealed by cryo-electron tomography. *Nature* 442:475–478.

Sindelar CV and Downing KH (2007) The beginning of kinesin's force-generating cycle visualized at 9-Å resolution. *J. Cell Biol.*, 177:377–385.

Nettles JH, Downing KH (2009) The tubulin binding mode of microtubule stabilizing agents studied by electron crystallography. In: Carlomagno T, editor. *Topics in Current Chemistry: Microtubule Stabilizing and Destabilizing Agents: Synthetic, Structural and Mechanistic Insights*. Springer; Heidelberg.

Sindelar CV and Downing KH (2010) An atomic-level mechanism for activation of the kinesin molecular motors. *Proc. Natl. Acad. Sci. USA*, 107:4111–4116.

Downing KH and Nogales E (2010) Cryoelectron Microscopy Applications in the Study of Tubulin Structure, Microtubule Architecture, Dynamics and Assemblies, and Interaction of Microtubules with Motors. *Methods Enzymol.* 2010; 483: 121–142.

Sui H and Downing KH (2010) Structural Basis of Inter-Protofilament Interaction and Lateral Deformation of Microtubules. *Structure* 18:1022–1031.

Han B-G, Watson Z, Cate JHD, Downing KH, Glaser RM (2017) Monolayer-crystal streptavidin support films provide an internal standard of cryo-EM image quality. *J Struct Biol* 200:307-313.

Kellogg EH; Hejab NMA, Howes S, Downing KH (2017) Insights into the Distinct Mechanisms of Action of Taxane and Non-Taxane Microtubule Stabilizers from Cryo-EM Structures. *J. Mol. Biol.* 429:633-646.