

Taking the Road Less Travelled – the Downing Legacy

Sharon G. Wolf¹*

¹. Dept. Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel.

* Corresponding author: sharon.wolf@weizmann.ac.il

This special session honoring Ken's life and work provides an opportunity to reflect on his legacy. I arrived in Ken's lab in 1991 where he had recently demonstrated information beyond 4 Å resolution in TEM images of glucose-embedded tubulin zinc-sheets [1], moving forward from previous intriguing negative stain studies [2, 3]. Despite intimidating technical limitations, Ken was certain that the goal of an atomic-resolution tubulin structure was achievable by electron crystallography. Years later, that goal was achieved, guided by Ken's fearless leadership [4]. He taught by example the best things one can learn about the scientific life; deep curiosity, lack of fear to try new things, and simple joy in doing good work.

Ken's list of publications is fascinating (Fig. 1). Besides his huge contribution in tubulin and microtubule structures, Ken was interested in far-ranging subjects ranging from materials sciences to biology, and in technique development. Particularly interesting for me is to find his long-term interest in spectroscopy [5-7], and his pioneering attempts to reveal chemical content in cryogenically preserved cells [6]. At a Symposium held in Ken's honor in 2014 (Fig. 2) [8], he talked about the privilege of being able to study whatever interested him, and he touched on some of his more unusual projects, including a decelerator for CCD cameras [9], polymer studies for energy applications [7], and more.

I will present previous results [10, 11] and new studies of mineral storage deposits in the mitochondria of mammalian and other eukaryotic cells, by cryoSTEM tomography (CSTET) [12, 13] and on-the-spot chemical characterization by EDX. STEM imaging mode allows for quantification of elemental content in intact cells [14, 15], and it is fundamental to development of aloof spectroscopy techniques [16, 17], which hold great promise for biological materials. The development of this work, in my mind, is a natural extension of the important lessons learned from my wonderful mentor, Ken Downing.

References:

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1	HENDERSON, R; BALDWIN, JM; CESKA, TA; ZEMLIN, F; BECKMANN, E; DOWNING, KH	JOURNAL OF MOLECULAR BIOLOGY	MODEL FOR THE STRUCTURE OF BACTERIORHODOPSIN BASED ON HIGH-RESOLUTION	1990	2551
2	Nogales, E; Wolf, SG; Downing, KH	NATURE	Structure of the alpha beta tubulin dimer by electron crystallography	1998	1547
3	Nogales, E; Whittaker, M; Milligan, RA; Downing, KH	CELL	High-resolution model of the microtubule	1999	823
4	Grigorieff, N; Ceska, TA; Downing, KH; Baldwin, JM; Henderson, R	JOURNAL OF MOLECULAR BIOLOGY	Electron-crystallographic refinement of the structure of bacteriorhodopsin	1996	812
5	Low, J; Li, H; Downing, KH; Nogales, E	JOURNAL OF MOLECULAR BIOLOGY	Refined structure of alpha beta-tubulin at 3.5 Å resolution	2001	768
6	HENDERSON, R; BALDWIN, JM; DOWNING, KH; LEPAULT, J; ZEMLIN, F	ULTRAMICROSCOPY	STRUCTURE OF PURPLE MEMBRANE FROM HALOBACTERIUM-HALOBIVM - RECORD	1986	648
7	Giannakakou, P; Gussio, R; Nogales, E; Downing, KH; Zaharevitz, D; Bollback, B; Poy, G	PROCEEDINGS OF THE NATIONAL ACADEMY	A common pharmacophore for epothilone and taxanes: Molecular basis for drug	2000	398
8	Nogales, E; Downing, KH; Amos, LA; Lowe, J	NATURE STRUCTURAL BIOLOGY	Tubulin and FtsZ form a distinct family of GTPases	1998	349
9	Nettles, JH; Li, HL; Cornett, B; Krahn, JM; Snyder, JP; Downing, KH	SCIENCE	The binding mode of epothilone A on alpha,beta-tubulin by electron crystallogra	2004	328
10	Snyder, JP; Nettles, JH; Cornett, B; Downing, KH; Nogales, E	PROCEEDINGS OF THE NATIONAL ACADEMY	The binding conformation of Taxol in beta-tubulin: A model based on electron cr	2001	296
11	Li, HL; DeRosier, DJ; Nicholson, WV; Nogales, E; Downing, KH	STRUCTURE	Microtubule structure at 8 angstrom Resolution	2002	271
12	NOGALES, E; WOLF, SG; KHAN, IA; LUDUJENA, RF; DOWNING, KH	NATURE	STRUCTURE OF TUBULIN AT 6.5 ANGSTROM AND LOCATION OF THE TAXOL-BINDING	1995	287
13	Downing, KH	ANNUAL REVIEW OF CELL AND DEVELOPME	Structural basis for the interaction of tubulin with proteins and drugs that affect	2000	257
14	Hud, NV; Downing, KH	PROCEEDINGS OF THE NATIONAL ACADEMY	Cryo-electron microscopy of lambda phage DNA condensates in vitreous ice: The	2001	209
15	Henderson, Richard; Sali, Andrej; Baker, Matthew L.; Carragher, Bridget; Devkota, Bats	STRUCTURE	Outcome of the First Electron Microscopy Validation Task Force Meeting	2012	192
16	BUTT, HJ; DOWNING, KH; HANSMA, PK	BIOPHYSICAL JOURNAL	IMAGING THE MEMBRANE-PROTEIN BACTERIORHODOPSIN WITH THE ATOMIC FOR	1990	178
17	Downing, KH; Nogales, E	CURRENT OPINION IN CELL BIOLOGY	Tubulin and microtubule structure	1998	177
18	Bowman, Grant R.; Comolli, Luis R.; Zhu, Jian; Eckart, Michael; Koenig, Marcelle; Dow	CELL	A polymeric protein anchors the chromosomal origin/ParB complex at a bacteri	2008	173
19	Park, Moon Jeong; Downing, Kenneth H.; Jackson, Andrew; Gomez, Enrique D.; Minor, J	NANO LETTERS	Increased water retention in polymer electrolyte membranes at elevated tempera	2007	158
20	Gomez, Enrique D.; Panday, Ashoutosh; Feng, Edward H.; Chen, Vincent; Stone, Gregor	NANO LETTERS	Effect of Ion Distribution on Conductivity of Block Copolymer Electrolytes	2009	137
21	HUD, NV; DOWNING, KH; BALHORN, R	PROCEEDINGS OF THE NATIONAL ACADEMY	A CONSTANT RADIUS OF CURVATURE MODEL FOR THE ORGANIZATION OF DNA IN TI	1995	137
22	Downing, KH; Nogales, E	CURRENT OPINION IN STRUCTURAL BIOLOG	Tubulin structure: Insights into microtubule properties and functions	1998	130
23	HUD, NV; ALLEN, MJ; DOWNING, KH; LEE, J.; BALHORN, R	BIOCHEMICAL AND BIOPHYSICAL RESEARCH	IDENTIFICATION OF THE ELEMENTAL PACKING UNIT OF DNA IN MAMMALIAN SPERM	1993	127
24	MCEWEN, BF; DOWNING, KH; GLAESER, RM	ULTRAMICROSCOPY	THE RELEVANCE OF DOSE-FRACTIONATION IN TOMOGRAPHY OF RADIATION-SENSIT	1995	105
25	Sindelar, Charles V.; Downing, Kenneth H.	JOURNAL OF CELL BIOLOGY	The beginning of kinesin's force-generating cycle visualized at 9-Å resolution	2007	101
26	Sui, Haixin; Downing, Kenneth H.	NATURE	Molecular architecture of axonemal microtubule doublets revealed by cryo-elect	2006	100
27	Sindelar, Charles V.; Downing, Kenneth H.	PROCEEDINGS OF THE NATIONAL ACADEMY	An atomic-level mechanism for activation of the kinesin molecular motors	2010	99
28	Facciotti, MT; Rouhani, S; Burkard, FT; Betancourt, FM; Downing, KH; Rose, RB; McDer	BIOPHYSICAL JOURNAL	Structure of an early intermediate in the M-state phase of the bacteriorhodopsin	2001	97
29	Detrich, HW; Parker, SK; Williams, RC; Nogales, E; Downing, KH	JOURNAL OF BIOLOGICAL CHEMISTRY	Cold adaptation of microtubule assembly and dynamics - Structural Interpretati	2000	96
30	Richards, KI; Anders, KR; Nogales, E; Schwartz, K; Downing, K; Botstein, D	MOLECULAR BIOLOGY OF THE CELL	Structure-function relationships in yeast tubulins	2000	95
31	Luef, Birgit; Frischkorn, Kyle R.; Wrighton, Kelly C.; Holman, Hoi-Ying N.; Bira	ENVIRONMENTAL MICROBIOLOGY	Diverse uncultivated ultra-small bacterial cells in groundwater	2015	88
32	Sui, Haixin; Downing, Kenneth H.	STRUCTURE	Structural Basis of Interprotofilament Interaction and Lateral Deformation of Mi	2010	85
33	DOWNING, KH	SCIENCE	SPOT-SCAN IMAGING IN TRANSMISSION ELECTRON-MICROSCOPY	1991	84
34	Amat, Fernando; Moussavi, Farshid; Comolli, Luis R.; Elidan, Gal; Downing, Kenneth H.	JOURNAL OF STRUCTURAL BIOLOGY	Markov random field based automatic image alignment for electron tomography	2008	83
35	Cambie, Rossana; Downing, Kenneth H.; Typke, Dieter; Glaeser, Robert M.; Jin, Jian	ULTRAMICROSCOPY	Design of a microfabricated, two-electrode phase-contrast element suitable for	2007	73
36	Dietrich, Kristen A.; Sindelar, Charles V.; Tyspe, Dieter; Glaeser, Robert M.; Cremo	PROCEEDINGS OF THE NATIONAL ACADEMY	The kinesin-1 motor protein is regulated by a direct interaction of its head and	2008	70
37	JAP, BK; DOWNING, KH; WALIAN, PJ	JOURNAL OF STRUCTURAL BIOLOGY	STRUCTURE OF PHOE PORIN IN PROJECTION AT 3.5 Å RESOLUTION	1990	69
38	DOWNING, KH; GLAESER, RM	ULTRAMICROSCOPY	IMPROVEMENT IN HIGH-RESOLUTION IMAGE QUALITY OF RADIATION-SENSITIVE SP	1986	64
39	Aquila, A.; Barty, A.; Bostedt, C.; Boutet, S.; Carini, G.; dePonte, D.; Drell, P.; Doniach, S	STRUCTURAL DYNAMICS	The linac coherent light source single particle imaging road map	2015	62
40	Comolli, Luis R.; Baker, Brett J.; Downing, Kenneth H.; Siegerist, Cristina E.; Banfield, J	JISME JOURNAL	Three-dimensional analysis of the structure and ecology of a novel, ultra-small	2009	62
41	DOWNING, KH; GRANO, DA	ULTRAMICROSCOPY	ANALYSIS OF PHOTOGRAPHIC-EMULSIONS FOR ELECTRON-MICROSCOPY OF TWO-C	1982	61
42	Bowman, Grant R.; Comolli, Luis R.; Gaietta, Guido M.; Fero, Michael; Hong, Sun-Hae;	MOLECULAR MICROBIOLOGY	Caulobacter PopZ forms a polar subdomain dictating sequential changes in pole	2010	60
43	Comolli, Luis R.; Spakowitz, Andrew J.; Siegerist, Cristina E.; Jardine, Paul J.; Grimes, S	VIROLOGY	Three-dimensional architecture of the bacteriophage phi 29 packaged genome ar	2008	60
44	KUHLBRANDT, W; DOWNING, KH	JOURNAL OF MOLECULAR BIOLOGY	TWO-DIMENSIONAL STRUCTURE OF PLANT LIGHT-HARVESTING COMPLEX AT 37-Å RI	1989	60
45	Shen, MR; Downing, KH; Balhorn, R; Hud, NV	JOURNAL OF THE AMERICAN CHEMICAL SOC	Nucleation of DNA condensation by static loops: Formation of DNA toroids with	2000	57
46	Downing, KH; Nogales, E	EUROPEAN BIOPHYSICS JOURNAL WITH BIO	New insights into microtubule structure and function from the atomic model of	1998	53
47	Murat, Dorothee; Falahati, Veesta; Bertinetti, Luca; Csencsits, Roseann; Koernig, Andr	MOLECULAR MICROBIOLOGY	The magnetosome membrane protein, MmsF, is a major regulator of magnetite bi	2012	52
48	Rosenberg, OS; Deindl, S; Comolli, LR; Hoelz, A; Downing, KH; Nairn, AC; Kuriyan, J	FEBS JOURNAL	Oligomerization states of the association domain and the holoenzyme of Ca2+/C	2006	51
49	Yeh, Yi-Chun; Comolli, Luis R.; Downing, Kenneth H.; Shapiro, Lucy; McAdams, Harley J	JOURNAL OF BACTERIOLOGY	The Caulobacter Tol-Pal Complex is Essential for Outer Membrane Integrity and	2010	50
50	DOWNING, KH; HU, MS; WENK, HR; OKEEFE, MA	NATURE	RESOLUTION OF OXYGEN-ATOMS IN STAUROLITE BY 3-DIMENSIONAL TRANSMISSIO	1990	48

Figure 1. Ken's 50 most cited papers showing an amazing range of interests and lasting influence.



Figure 2. Scientific Symposium celebrating Ken Downing in 2014.