NAME: William Shih

POSITION TITLE: Professor

# **EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Harvard College, Cambridge, MA	A.B.	06/1994	Biochemical Sciences
Stanford University School of Medicine, Stanford, CA	Ph.D.	06/2000	Biochemistry
Stanford University School of Medicine, Stanford, CA	Postdoctoral	12/2000	Biochemistry
The Scripps Research Institute, La Jolla, CA	Postdoctoral	07/2004	Chemistry and Molecular Biology

## A. Personal Statement

Our growing ability to shape matter with subnanoscale features and up to micron-scale global dimensions has opened a new era of research innovation. The field of structural DNA nanotechnology appears to offer the quickest route to mastery of self-assembly-based nanofabrication. I have spent the last twenty years in the field of structural DNA nanotechnology, and previously studied protein biochemistry and biophysics. My laboratory currently is a leading group in the world for developing multilayer DNA origami. We are continuing an active program in pushing the state-of-the-art in the field, including developing applications in tools for dissection of biophysical mechanisms and tools for future therapeutics, with special interest to nucleic acids such as DNA or RNA. As a mentor, I have trained 28 postdoctoral fellows, 16 of whom now are academic faculty members, and ten graduate students, two of whom now are academic faculty members.

## Select Citations:

- 1. Zeng YC et al. DNA origami vaccine nanoparticles improve humoral and cellular immune responses to infectious diseases. *Nat Biomed Eng*. Accepted. 2025.
- Zeng YC, Young OJ, Wintersinger CM, Anastassacos FM, MacDonald JI, Isinelli G, Dellacherie MO, Sobral M, Bai H, Graveline AR, Vernet A, Sanchez M, Mulligan K, Choi Y, Ferrante TC, Keskin DB, Fell GG, Neuberg D, Wu CJ, Mooney DJ, Kwon IC, Ryu JH, Shih WM. Fine tuning of CpG spatial distribution with DNA origami for improved therapeutic cancer vaccination. *Nat Nanotechnol* 19, 1055–1065, 2024.
- 3. Wintersinger CM, Minev D, Ershova A, Sasaki HM, Gowri G, Berengut JF, Corea-Dilbert FE, Yin P, Shih WM. Multi-micron crisscross structures grown from DNA-origami slats. *Nat Nanotechnol* 18, 281–289, 2023. (cover)
- 4. Shrestha P, Yang D, Tomov TE, MacDonald JI, Ward A, Bergal HT, Krieg E, Cabi S, Luo Y, Nathwani B, Johnson-Buck A, Shih WM\*, Wong WP\*. Single-molecule mechanical fingerprinting with DNA nanoswitch calipers. *Nat Nanotechnol* 16, 1362–1370, 2021. (\*co-corresponding authors)
- 5. Minev D, Wintersinger CM, Ershova A, Shih WM. Robust nucleation control via crisscross polymerization of highly coordinated DNA slats. *Nat Commun* 12, 1741, 2021. PMCID: PMC7979912.
- 6. Sun W, Shen J, Zhao Z, Arellano N, Rettner C, Tang J, Cao T, Zhou Z, Ta T, Streit JK, Fagan JA, Schaus T, Zheng M, Han SJ, Shih WM, Maune HT, Yin P. Precise pitch-scaling of carbon nanotube arrays within three-dimensional DNA nanotrenches. *Science* 68, 874-877, 2020.
- 7. Ponnuswamy N, Bastings MMC, Nathwani B, Ryu JH, Chou LYT, Vinther M, Li WA, Anastassacos FM, Mooney DJ, Shih WM. Oligolysine-based coating protects DNA nanostructures from low-salt denaturation and nuclease degradation. *Nat Commun.* 8, 15654, 2017.
- 8. Perrault SD, Shih WM. Virus-inspired membrane encapsulation of DNA nanostructures to achieve in vivo stability. *ACS Nano* 8, 5132–5140, 2014.
- 9. Ke Y, Ong LL, Shih WM, Yin P. Three-dimensional structures self-assembled from DNA bricks. *Science* 338, 1177–1183, 2012. (cover)

- Derr ND, Goodman BS, Jungmann R, Leschziner AE, Shih WM, Reck-Peterson SL, Tug of War in Motor Protein Ensembles Revealed with a Programmable DNA Origami Scaffold, *Science* 338, 662–665, 2012.
- 11. Berardi M, Shih WM, Harrison SC, Chou JJ. Mitochondrial uncoupling protein 2 structure determined by NMR molecular fragment searching. *Nature* 476, 109–113, 2011.
- 12. Dietz H, Douglas SM, Shih WM. Folding DNA into twisted and curved nanoscale shapes. *Science* 325, 725–730, 2009.
- 13. Douglas SM, Dietz H, Liedl T, Högberg B, Graf F, Shih WM. Self-assembly of DNA into nanoscale shapes. *Nature* 459, 414–418, 2009.
- 14. Shih WM, Quispe, JD, Joyce GF. A 1.7-kilobase single-stranded DNA that folds into a nanoscale octahedron. *Nature* 427, 618–621, 2004. (cover)
- 15. Shih WM, Gryczynski Z, Lakowicz JR, Spudich JA. A FRET-based sensor reveals ATP hydrolysis-induced large conformational changes and three distinct states of the molecular motor myosin. *Cell* 102, 683–694, 2000.

# B. Positions, Scientific Appointment, and Honors

<b>Positions</b>	and	Scientific	Αp	pointments

Positions and	<u>a Scientific Appointments</u>
2016-present	Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical School and
	Department of Cancer Biology, Dana-Farber Cancer Institute
2017–2019	President, International Society for Nanoscale Science, Computation, and Engineering
2015–2017	Vice President, International Society for Nanoscale Science, Computation, and Engineering
2010–2016	Associate Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical
	School and Department of Cancer Biology, Dana-Farber Cancer Institute
2009–2015	Secretary, International Society for Nanoscale Science, Computation, and Engineering
2009-present	Core Faculty Member, Wyss Institute for Biologically Inspired Engineering, Harvard University
2004–2010	Assistant Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical
	School and Department of Cancer Biology, Dana-Farber Cancer Institute
2004-present	Member, International Society for Nanoscale Science, Computation, and Engineering
2001–2004	Postdoctoral Fellow in the lab of Gerald F. Joyce, M.D., Ph.D. in the Departments of Chemistry
	and Molecular Biology and The Skaggs Institute for Chemical Biology, The Scripps Research
	Institute; Rational design of a clonable DNA nano-octahedron
1994-2000	Graduate Student (1994–2000) and Postdoctoral Fellow (2000) in the lab of James A. Spudich,
	Ph.D. in the Department of Biochemistry, Stanford University School of Medicine; Cysteine
	engineering studies on <i>Dictyostelium</i> myosin-II: nucleotide-induced myosin conformational
	changes monitored by disulfide crosslinking and by steady-state and time-resolved FRET
1991-1994	Undergraduate Student in the lab of Tom Kirchhausen, Ph.D. in the Department of Cell Biology,
	Harvard Medical School; Structural and functional characterization of recombinant fragments of
	clathrin associated AP-2 complexes

Summer intern in the lab of Amnon Altman, Ph.D. in the Division of Cell Biology, La Jolla Institute for Allergy and Immunology; Subcloning and *in vitro* assaying of chimeric tRNA-ribozymes

# **Honors and Awards**

1991

2018	The Rozenberg Tulip Award in DNA Computing
2017	Foresight Institute Feynman Prize in Experimental Nanotechnology
2014	Blavatnik National Award Finalist in Physical Sciences (Nanotechnology)
2010	Woodward Visiting Professorship, Harvard Chemistry & Chemical Biology
2008	New Innovator Award, NIH Office of the Director
2005	Claudia Adams Barr Program Investigator in Innovative Cancer Research, DFCI
2004	Finalist for the 2004 Foresight Institute Feynman Prize in Nanotechnology (Experimental)
2001-2004	Damon Runyon Postdoctoral Fellowship
2001	Harold M. Weintraub Graduate Student Award
1995-2000	Howard Hughes Medical Institute Predoctoral Fellowship
1994-1995	National Science Foundation Predoctoral Fellowship