CHEMICAL HERITAGE FOUNDATION

# KAREL SVOBODA

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

William Van Benschoten

at

Cold Spring Harbor Laboratory
Cold Spring Harbor, New York

on

19 and 20 August 2004

Karel Svoboda

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Date


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# KAREL SVOBODA

| | |
|---|---|
| 1965 | Born in Prague, Czechoslovakia, on 30 December |

## Education

| | |
|---|---|
| 1988 | B.A., Physics (*cum Laude*), Cornell University |
| 1994 | Ph.D., Biophysics, Harvard University |

## Professional Experience

| | |
|---|---|
| | Bell Laboratories, Lucent Technologies |
| 1994-1997 | Postdoctorate, Neuroscience, under D.W. Tank and W. Denk |
| | Cold Spring Harbor Laboratory |
| 1997-2003 | Assistant, Associate Professor |
| 2004-present | Professor |
| | State University of New York at Stony Brook |
| 1997-present | Affiliated Professor |
| | Howard Hughes Medical Institute |
| 2000-present | Investigator |
| 2006-present | Group Leader, Janelia Farm Research Campus |

## Honors

| | |
|---|---|
| 1994-1995 | Society of General Physiology Scholar |
| 1998-2002 | Pew Scholars Award |
| 1998-2001 | Klingenstein Award |
| 1999 | *Science* Magazine, Runner-up, Breakthrough of the Year |
| 1999-2002 | Mathers Foundation Award |
| 1998-2001 | Whitaker Foundation Award |
| 2000-present | Howard Hughes Medical Institute, Assistant Investigator |
| 2002-2003 | McKnight Technological Innovations in Neuroscience Award |
| 2003 | Eppendorf and Science Prize for Neurobiology, Runner-Up |
| 2004 | Popular Science Brilliant 10 |
| 2004 | Society for Neuroscience, AstraZeneca Young Investigator Award |

Selected Publications


Holtmaat, A., Wilbrecht, Knott, G., Welker, E. and Svoboda, K. (2006). Experience-dependent and cell-type specific spine growth in the neocortex. *Nature in press.*

Yasuda, R., Harvey, C. D., Zhong, H., Sobczyk, A., van Aelst, L., and Svoboda, K. (2006). Supersensitive Ras activation in dendrites and spines revealed by two-photon fluorescence lifetime imaging. *Nat Neurosci 9,* 283-291.

De Paola, V., Holtmaat, A., Knott, G., Song, S., Wilbrecht, L., Caroni, P., and Svoboda, K. (2006). Cell type-specific structural plasticity of axonal branches and boutons in the adult neocortex. *Neuron 49,* 861-875.

Karpova, A. Y., Tervo, D. G., Gray, N. W., and Svoboda, K. (2005). Rapid and Reversible Chemical Inactivation of Synaptic Transmission in Genetically Targeted Neurons. *Neuron 48,* 727-735.

Sobczyk, A., Scheuss, V. & Svoboda, K. NMDA receptor subunit-dependent [Ca2+] signaling in individual hippocampal dendritic spines. *J. Neurosci.* 25, 6037-6046 (2005).

Portera-Cailliau, C., Weimer, R. M., Paola, V. D., Caroni, P. & Svoboda, K. Diverse Modes of Axon Elaboration in the Developing Neocortex. *PLoS Biol* 3, e272 (2005).

Shepherd, G. M. G. & Svoboda, K. Laminar and columnar organization of ascending excitatory projections to layer 2/3 pyramidal neurons in rat barrel cortex. *J. Neurosci.* 25, 5670 (2005).

Shepherd GMG, Stepanyants A, Bureau I, Chklovskii DB, Svoboda K. 2005. Geometric and functional organization of cortical circuits. *Nature Neurosci.,* 8:782-790.

Egger V, Svoboda K, Mainen ZF (2005) Dendrodendritic synaptic signals in olfactory bulb granule cells: local spine boost and global low-threshold spike. *J Neurosci* 25:3521-3530.

Holtmaat AJ, Trachtenberg JT, Wilbrecht L, Shepherd GM, Zhang X, Knott GW, Svoboda K (2005) Transient and persistent dendritic spines in the neocortex in vivo. *Neuron* 45:279- 291.

Harwell, C., Burbach, B., Svoboda, K. & Nedivi, E. Regulation of cpg15 expression during single whisker experience in the barrel cortex of adult mice. *J Neurobiol* 65, 85-96 (2005).

Cristo GD, Wu C, Chattopadhyaya B, Ango F, Knott G, Welker E, Svoboda K and Huang ZJ. 2004. Subcellular domain-restricted GABAergic innervation in primary visual cortex in the absence of sensory and thalamic inputs. *Nat Neurosci* 7, 1184-1186.

Chklovskii DB, Mel BW and Svoboda K. 2004. Cortical rewiring and information storage. *Nature* 431, 782-788.

Zito K, Knott G, Shepherd GM, Shenolikar S and Svoboda K. 2004. Induction of spine growth and synapse formation by regulation of the spine actin cytoskeleton. *Neuron* 44, 321-334.

Pologruto TA, Yasuda R and Svoboda K. 2004. Monitoring neural activity and [Ca2+] with genetically encoded Ca2+ indicators. *J Neurosci* 24, 9572-9579.

Bureau I, Shepherd GM and Svoboda K. 2004. Precise development of functional and anatomical columns in the neocortex. *Neuron* 42, 789-801.

Wang Y, Guo HF, Pologruto TA, Hannan F, Hakker I, Svoboda K and Zhong Y. 2004. Stereotyped odor-evoked activity in the mushroom body of Drosophila revealed by green fluorescent protein-based Ca2+ imaging. *J Neurosci* 24, 6507-65 14.

Maravall M, Stern EA and Svoboda K. 2004. Development of intrinsic properties and excitability of layer 2/3 pyramidal neurons during a critical period for sensory maps in rat barrel cortex. *J Neurophysiol* 92, 144-156.

Maravall M, Koh IY, Lindquist WB and Svoboda K. 2004. Experience-dependent changes in

basal dendritic branching of layer 2/3 pyramidal neurons during a critical period for developmental plasticity in rat barrel cortex. *Cereb Cortex* 14, 655-664.
Nimchinsky EA, Yasuda R, Oertner TG, Svoboda K. 2004. The number of glutamate receptors opened by synaptic stimulation in single hippocampal spines. *J Neurosci* 24(8):2054-64.
Egger V, Svoboda K and Mainen ZF. 2003. Mechanisms of lateral inhibition in the olfactory bulb: efficiency and modulation of spike-evoked calcium influx into granule cells. *J Neurosci* 23, 755 1-7558.
Yasuda R, Sabatini BL and Svoboda K. 2003. Plasticity of calcium channels in dendritic spines. *Nat Neurosci* 6, 948-955.
Pologruto T, Sabatini BL and Svoboda K. 2003. Flexible software for operating laser-scanning microscopes. *BioMedical Engineering OnLine* 2:13-22.
Shepherd GM, Pologruto TA and Svoboda K. 2003. Circuit analysis of experience-dependent plasticity in the developing rat barrel cortex. *Neuron* 38, 277-89.
Takahashi T, Svoboda K, Malinow R. 2003. Experience strengthening transmission by driving AMPA receptors into synapses. *Science* 299:1585-1588.
Trachtenberg JT, Chen BE, Knott GW, Feng G, Sanes JR, Welker E and Svoboda K. 2002. Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature* 420, 788-94.
Oertner TG, Sabatini BS, Nimchinsky EA and Svoboda K. 2002. Facilitation at single synapses probed with optical quantal analysis. *Nat Neurosci* 5, 657-664.
Sabatini BS, Oertner TG and Svoboda K. 2002. The life-cycle of $Ca^{2+}$ ions in spines. *Neuron* 33, 439-452.
Nimchinsky E, Oberlander B and Svoboda K. 2001. Abnormal development of dendritic spines in FMR1 knockout mice. *J Neurosci* 21:5139-5146.
Koh IYY, Lindquist WB, Zito K, Nimchinsky E and Svoboda K. 2002. Automated three-dimensional dendritic spine detection and analysis. *Neural Computation* 14, 1283-13 10.
Stern E, Maravall M and Svoboda K. 2001. Rapid development and plasticity of layer 2/3 maps in rat barrel cortex in vivo. *Neuron* 31, 305-3 15.
Wang Y, Wright NJ, Guo H, Xie Z, Svoboda K, Malinow R, Smith DP and Zhong Y. 2001. Genetic manipulation of the odor-evoked distributed neural activity in the Drosophila mushroom body. *Neuron* 29, 267-76.
Sabatini BL and Svoboda K. The number and properties of calcium channels in single dendritic spines determined by optical fluctuation analysis. *Nature* 408:589-593 (2000).
Cox CL, Denk W, Tank DW and Svoboda K. 2000. Action potentials reliably invade axonal arbors of rat neocortical neurons. *Proc Natl Acad Sci U S A* 97:9724-8.
Chen BE, Lendvai B, Nimchinsky EA, Burbach B, Fox K and Svoboda K. 2000. Imaging high-resolution structure of GFP-expres sing neurons in neocortex in vivo. *Learn Mem* 7:433-41.
Lendvai B, Stern E, Chen B and Svoboda K. 2000. Experience-dependent plasticity of dendritic spines in the developing rat barrel cortex *in vivo*. *Nature* 404:876-881.
Maravall M, Mainen ZF, Sabatini B, and Svoboda K. 2000. A method to estimate intracellular calcium concentrations without wavelength ratioing. *Biophys J* 78:2655-2667.
Helmchen F, Svoboda K, Denk W and Tank DW. 1999. In vivo dendritic calcium dynamics in deep-layer cortical pyramidal neurons. *Nat Neurosci* 2:989-96.
Shi SH, Hayashi Y, Petralia RS, Zaman SH, Wenthold RJ, Svoboda K and Malinow R. 1999. Rapid Spine Delivery and Redistribution of AMPA Receptors After Synaptic NMDA

Receptor Activation. *Science* 284:1811-1816.
Mainen ZF, Malinow R and Svoboda K. 1999. Synaptic calcium transients in single spines indicate that NMDA receptors are not saturated. *Nature* 399:151-5.
Maletic-Savatic M, Malinow R and Svoboda K. 1999. Rapid dendritic morphogenesis in CA1 hippocampal dendrites induced by synaptic activity. *Science* 283:1923-7.
Svoboda K, Helmchen F, Denk W and Tank DW. 1999. Spread of excitation in the dendrites of layer 2/3 pyramidal neurons *in vivo. Nature Neurosci* 2:65-73.
Svoboda K, Denk WD, Kleinfeld and Tank DW. 1997. *In vivo* dendritic calcium dynamics in neocortical pyramidal neurons. *Nature* 385:161-165.
Svoboda K, Denk W, Knox WH and Tsuda S. 1996. Two-photon excitation scanning microscopy with a compact, mode locked, diode-pumped Cr:LiSAF Laser. *Opt Lett* 21: 1411-1413.
Svoboda K, Tank DW, Denk W. 1996. Direct measurement of coupling between dendritic spines and shafts. *Science* 272:716-719.
Yin H, Wang MD, Svoboda K, Landick R, Block SM, Gelles J. 1995. Transcription against an applied force. *Science* 270:1653-1657.
Block SM and Svoboda K. 1995. Analysis of high resolution recordings of motor movement. *Biophys J* 68:230-241.
Svoboda K, Mitra PP and Block SM. 1994. Fluctuation analysis of motor protein movement and single enzyme kinetics. *Proc Natl Acad Sci* 91:11782-11786.
Svoboda K and Block SM. 1994. Force and velocity measured for single kinesin molecules. *Cell* 77:773-784.
Svoboda K and Block SM. 1994. Optical trapping of metallic Rayleigh particles. *Opt Lett* 19:930-932.
Latour LL, Svoboda K, Mitra PP and Sotak CH. 1994. Time-dependent diffusion of water in a biological model system. *Proc Natl Acad Sci* 91:1229-1233.
Svoboda K, Schmidt CF, Schnapp BJ and Block SM. 1993. Direct observation of kinesin stepping by optical trapping interferometry. *Nature* 365:721-727.
Schmidt CF, Svoboda K, Lei N, Petsche IB, Berman LE, Safinya CR and Grest G. 1993. Existence of a flat phase in red cell membrane skeletons. *Science* 259:952-954.
Svoboda K, Schmidt CF, Branton D and Block SM. 1992. Conformation and elasticity of the isolated human red blood cell skeleton. *Biophys J* 63:784-793.
Luvalle M, Welscher T, Svoboda K. 1988. Acceleration transforms and statistical kinetic models. *J Stat Physics* 52: 3 11-330.
Svoboda K, Zettl A, Sherwin MS. 1989. A novel switching phenomenon in quenched NbSe3. *Solid State Comm* 70:859-862.

## ABSTRACT

**Karel Svoboda** was born in Prague, Czechoslovakia, though he and his family immigrated to western Germany—the Ruhr Valley—during the Cold War era, in stages: first, his father, then his mother, Svoboda, and one sister, and then, finally, his youngest sister. Both of Svoboda's parents studied chemical engineering, though only his father received his degree since his mother focused on raising their children; later, his mother became a teacher in Germany and then, when the family immigrated, the United States as well. In Germany, Svoboda attended an alternative school that focused much more on the arts, like music, chorus, and theater, which he enjoyed tremendously. He always performed well in his mathematics and science classes, and developed prowess in chess.

Not wanting to stagger his education for time in Germany's military service, Svoboda applied to several universities in the United States and chose to matriculate at Cornell University. He capitalized on the work-study program while there, working in a number of research labs throughout his undergraduate career, initially as a computer programmer. The summers he spent at Bell Laboratories, where he worked in statistics and then in physics, and the semester he spent at the Lawrence-Berkeley National Laboratory, where he worked full-time in a physics laboratory focused on high-temperature critical superconductors, were significant in his scientific development. After applying to and being accepted at Harvard University for graduate studies Svoboda deferred for a year in order to teach physics in Katmandu, Nepal. At Harvard, he started his doctoral work with Howard Berg but then also worked with Steven M. Block at the Rowland Institute for the Sciences. His love of Bell Laboratories during his undergraduate years brought him back there for postdoctoral research on synapses with Winfried Denk and David Tank, and gave him the opportunity to take what became a very influential course on neural systems at the Woods Hole Oceanographic Institute. Svoboda left Bell for a position at the Cold Spring Harbor Laboratory, studying biophysical neuroscience in neocortical circuits and their plasticity, with the intent of expanding his work to ensembles of neocortical circuits.

As the interview came to a close, Svoboda discuss some of the general issues associated with being a principal investigator and a scientist working in the United States, like the issue of patents; the origin of his ideas; the process of conducting scientific research; becoming familiar with the history of a particular field of research; competition and collaboration in science; setting the national scientific agenda; and the role of the scientist in educating the public about science. The interview concluded with his thoughts on the Pew Scholars Program in the Biomedical Sciences award.

## UCLA INTERVIEW HISTORY

INTERVIEWER:

William Van Benschoten, Interviewer, UCLA Oral History Program; B.A., History, University of California, Riverside, 1990; M.A., History, University of California, Riverside, 1991; C.Phil., History, University of California, Los Angeles, 1995.

TIME AND SETTING OF INTERVIEW:

**Place:** Svoboda's office at Cold Spring Harbor Laboratory.

**Dates of sessions:** August 19, 2004; August 20, 2004.

**Total number of recorded hours:** 4.5

**Persons present during interview:** Svoboda and Van Benschoten.

CONDUCT OF INTERVIEW:

This interview is one in a series with Pew Scholars in the Biomedical Sciences conducted by the UCLA Oral History Program in conjunction with the Pew Charitable Trusts's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The project has been designed to document the backgrounds, education, and research of biomedical scientists awarded four-year Pew scholarships since 1988.

To provide an overall framework for project interviews, the director of the UCLA Oral History Program and three UCLA faculty project consultants developed a topic outline. In preparing for this interview, Van Benschoten held a telephone preinterview conversation with Svoboda to obtain written background information (curriculum vitae, copies of published articles, etc.) and agree on an interviewing schedule. He also reviewed documentation in Svoboda's file at the Pew Scholars Program office in San Francisco, including Svoboda's proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members.

ORIGINAL EDITING:

Carol Squires edited the interview. She checked the verbatim transcript of the interview against the original tape recordings, edited for punctuation, paragraphing, and spelling, and verified proper names. Words and phrases inserted by the editor have been bracketed.

Svoboda reviewed the transcript. He verified proper names and made a minor number of corrections and additions.

Carol Squires prepared the table of contents and TechniType Transcripts compiled the guide to proper names.

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**INTERVIEWEE:** **Karel Svoboda**

**INTERVIEWER:** **William Van Benschoten**

**LOCATION:** **Cold Spring Harbor Laboratory**
**Cold Spring Harbor, New York**

**DATE:** **19 August 2004**

**VAN BENSCHOTEN:** It is August 19th, 2004, and correct me if I'm mangling your name, but I'm with Karel Svoboda.

**SVOBODA:** That's right.

**VAN BENSCHOTEN:** At Cold Spring Harbor [Laboratory, Cold Spring Harbor, New York]. Is that your full name?

**SVOBODA:** That is my full name, right.

**VAN BENSCHOTEN:** Where were you born, and when?

**SVOBODA:** I was born in Prague, Czechoslovakia, at the end of 1965, on the thirtieth of December.

**VAN BENSCHOTEN:** Oh, so you just got in, in that year.

**SVOBODA:** Right. I just got in that year.

**VAN BENSCHOTEN:** Did you spend most of your childhood, then, in Prague?

**SVOBODA:** When I was about five years old, my parent**s** left in a couple of stages, to essentially escape to West Germany, so my whole immediate family ended up there, by 1971, I think. I did most of my schooling in Germany and then went on to be a college student in the U.S. [United States]

**VAN BENSCHOTEN:** This process of leaving Czechoslovakia, when did they undertake that? Was that after ‘68 or before?

**SVOBODA:** This was in the aftermath of ‘68. So my father had an opportunity to leave, and left and stayed out of the country. Then after some negotiations, mother, with myself and one of my siblings [Helena Svoboda Dechant], was allowed to visit him, and they stayed. Then after another year or so, my youngest sister [Ludmila Svoboda] was able to join us, stayed with relatives. This was Cold War stuff. Nothing too dramatic, but yes.

**VAN BENSCHOTEN:** When you lived in Germany, did you live at various places, or was there one particular place?

**SVOBODA:** We lived mostly in the Ruhr Valley, which is *this Industrie-gebiet* in German, it’s Essen, Dortmund, a whole bunch of big—a whole bunch of big cities [*Industrie-städte*]—an urban area of about five million people. That’s where we lived for most of that time.

**VAN BENSCHOTEN:** I’ve heard of it. I’ve heard of the Krupp armaments. I don’t know if they’re still there. Are they?

**SVOBODA:** Krupp was, in fact, a major steel manufacturer in the 1980s, and they still may very well be, but I think now the state has a majority ownership stake. As a matter of fact, at one point my father worked for Krupp. He worked on emission control. That’s his thing. He worked for Krupp itself, or a subsidiary actually of Krupp. I think they were called Krupp Wilputte.

**VAN BENSCHOTEN:** Looking back at history, it’s a much contested piece of land, isn’t it? That whole area of the Ruhr Valley is so strategic.

**SVOBODA:** Yes, it is strategic. Certainly in the Second World War it was very important, and then it was, of course, rich in coal, so it was the energy source for the Third Reich. Basically, when the Allies essentially took that—conquered that—the war was over.

**VAN BENSCHOTEN:** For someone who hasn’t been there, how would it [where you grew up] compare, say, to someplace like Cold Spring Harbor? You say it’s heavily industrial.

**SVOBODA:** Oh, it's heavily industrial, and by the time we got there, the coal mining had ground to, essentially, a halt and stopped being profitable. I must have been about ten, fifteen when the last coal mine in the region stopped. Right at the River Ruhr there was still some very big steel manufacturers, but even that had shifted to specialized steel manufacturing. The basic stuff—the really polluting industries— were moving to places like Korea already at that point, and Japan and Taiwan, probably more Taiwan, actually, at that time.

So the place, famous for its particulate matter in the air, cleaned up the air pollution, and service industry moved in. You couldn't put laundry out to dry because it would end up all gray, uniformly gray.

**VAN BENSCHOTEN:** That's incredible.

**SVOBODA:** Yes, and it really changed quite a bit over the last twenty, thirty years. It's very different. It's now a modern urban center mostly dominated by banking and service industry and so on.

**VAN BENSCHOTEN:** Do you get back there very often?

**SVOBODA:** I barely ever get back there. I still have some friends there, actually, from high school, and I see them on occasion, maybe every three years or so. I have very few relatives there, actually no relatives there. The only relatives I have in Germany live in Munich, so I go there more frequently.

**VAN BENSCHOTEN:** Let's talk a little bit about your family, if you would, and maybe start with your grandparents. If you could, start with your mother's mother, mother's father, maternal grandparents.

**SVOBODA:** You want to know what they did and where they came from?

**VAN BENSCHOTEN:** Their education, yes.

**SVOBODA:** They were both teachers, and they were both from, essentially, farming families. But they were both teachers. Their farms were expropriated in 1948, in the aftermath of the Communist takeover in the Czech Republic. They're from what is called Moravia, which is now the eastern Czech Republic. It's rural and farming country. Then they made their living as teachers and taught, I think, the gamut: language and stuff like that. They both taught German,

for example. My grandparents passed away over the last ten, fifteen years. They spent their entire lives within a radius of a couple of villages. Their families have known each other for generations. It's a typical eastern European rural place.

My parents met at university. My mother and her brothers all went to university in Prague, and my father's family actually are long-term Prague residents, much more cosmopolitan. They tend to be by profession what we would call professionals: physicians and lawyers and that kind of stuff—urbanites—which in the Czech Republic has some saliency. Although it's not as important as, perhaps, in Northern Ireland, but my mother's parents are Protestants and my father's parents are Catholics. So when they married, that was a little bit of an issue.

**VAN BENSCHOTEN:** Did that have anything to do with geography, with being in a city?

**SVOBODA:** Yes, it's a good question. I actually don't know whether or not there's this division, but what is now the Czech Republic, the first [Protestant] Reformation played itself out there, and still some people take these things more seriously than others. It's largely now, after forty years of Communist rule, more or less a secular society, but my father's parents, in particular, are very active nowadays in Catholic politics. For example, the Christian Democratic Party, a Catholic party, they're quite active in that, and then lots of politicians, parliamentarians and then even ministers and so on and so forth.

So, yes, my parents met at university, and that's how that came about in Prague.

**VAN BENSCHOTEN:** So which set of grandparents did you tend to see more frequently?

**SVOBODA:** It was very symmetrical. Well, of course when I was very young, mostly my grandparents in Prague. For one thing, we lived in the same house as they. My grandparents had a very large house in a nice—what was then—a suburb. Now it's really relatively close to the center of Prague, simply because Prague has grown. But they had a nice big house in a district of Prague that they were allowed to keep because they had seven children, many of whom had children, and they all lived together in this, in what really was a villa, but in quite cramped quarters. So of course, because of that, I saw my grandparents frequently. The grandfather was the patriarch there.

But I still have memories of visiting my maternal grandparents in Moravia, actually Bystrice, it's called, and where, of course, this was more rural, where one could go play in the fields and so on and so forth. So there were different kinds of experiences. There were farm animals around and so on. It was a completely different experience even for a kid of four years. I actually remember that reasonably vividly.

**VAN BENSCHOTEN:** They've gone through quite a bit of history: World War II, the Communist takeover, '68. Were they politically active or not?

**SVOBODA:** The grandparents in Prague, they were politically active in the sense that they were active Catholics. They weren't perhaps radicals, but the family suffered because of that. These were petty things, but the children were not allowed to study what they wanted to study, and that kind of thing. Minor things.

Similarly, my grandparents in Moravia were also—shall we say—not collaborators, were never party members, so many of the privileges of party membership and so on were never open to them. But they were not openly rebellious, I would say.

The Czech psyche is such that there were relatively few people that were openly rebellious, but people withdrew from public life, and so in the privacy of one's home, people would bitch and moan and criticize, but it was kept fairly within the family, so to speak.

**VAN BENSCHOTEN:** There wasn't much of a public sphere anymore, I guess, to participate in.

**SVOBODA:** Exactly. It was dangerous, frankly.

**VAN BENSCHOTEN:** Let's talk about your father and mother. You've already talked a little bit about them. Your father, I take it, then, was one of seven children.

**SVOBODA:** That's right.

**VAN BENSCHOTEN:** Describe his growing up, his education, and his work.

**SVOBODA:** Well, so he's a chemical engineer, that's what he studied at university. So did my mother. Actually, the state made that decision for you unless you had strings that you could pull. That's where they met. He worked on process engineering. This was the kind of chemical engineering that one could apply to steel manufacturing and manufacturing of coke, which is the fuel for steel manufacturing.

I think he became an expert—as far as I understand—in making filter systems and retrofitting filter systems of old polluting steel plants and coke plants to essentially conform to modern emission control. Essentially, the Clean Air Act was probably the main reason why he

ultimately came to the U.S.

**VAN BENSCHOTEN:** That's interesting.

**SVOBODA:** That's what he's still doing. So the progression was that he went to study some of that stuff in western Germany, where the state of the art was a bit more advanced. He took that as an opportunity to essentially escape the Czech Republic. Then he worked in engineering firms, including that subsidiary of Krupp [Wilputte] that I mentioned earlier. In the end, there was more and more business in the U.S., and that's one reason he ended up moving to the U.S.

In the end, he started his own company. Actually, most of his clientele are in newly industrialized countries, because that technology has run its course—as far as I understand it—in the U.S. Now the markets are in Turkey, in former Soviet Republics, and even in Iran through collaborators—the U.S. doesn't do business there—in South America, and there's still some business in Canada, but pretty much nothing in the U.S.

**VAN BENSCHOTEN:** Anything in China?

**SVOBODA:** Actually, he had the promise of a large job in China, but that never came through. I don't think he's actually had a project in China. But that would be a natural place. They might be looking elsewhere for expertise. I don't know the details.

**VAN BENSCHOTEN:** If you were to describe him in three words, or maybe a few more, but if you were to describe him briefly, how would you describe his temperament, his personality?

**SVOBODA:** My father. Some people think he's a bit like myself, fairly strong-willed or argumentative. He's very interested in lots of things. He really understands science, for example, remarkably well, at the level of *Scientific American* but quite impressive. He's interested in lots of things.

They were very good parents also, which is important and difficult to describe in detail, but always very involved in our lives. There were problems, of course. We moved a lot and were relatively poor, of course, especially in the beginning when we were in West Germany, but nothing tragic. They were always trying to allow us to do the things that we wanted to do and so on and so forth, so the usual good immigrants.

**VAN BENSCHOTEN:** Making that move from the Czech Republic to Germany, was that a dangerous undertaking at the time that he did that?

**SVOBODA:** It could have been dangerous. Certainly, if he had gone back, it would have been dangerous. It resulted in, again, petty punishment of my family back in the Czech Republic, and there were some conflicts based on that. But, no, he was sanctioned to leave and didn't return, and then my mother was sanctioned to visit him. They probably knew that she wouldn't come back, and she was only allowed to take a little bag of stuff and then had to leave her youngest daughter behind. There were all kinds of negotiations between the German State Department and the Czech Foreign Ministry about how to get that poor girl out, and there were all these tits-for-tats. Willy Brandt, the German Chancellor, made all these deals. I'm not sure if a particular swap was involved here, but it was all having to do with aid and all these kinds of things. This was not, of course, restricted to my family. There were many such cases. But in West Germany, one immediately got asylum and very rapidly. If one actually escaped from the Eastern Bloc, one could get citizenship in Germany relatively quickly, which was otherwise a relatively homogenous society. So if you came as a guest worker, it would be much harder; until very recently, it was almost impossible to become a German citizen any other way.

**VAN BENSCHOTEN:** Let's talk about your mother. Again, the same question. What is her work? You've already talked about her education. Talk a little bit about her character, her personality.

**SVOBODA:** She had a very similar education to my father. They were in similar secondary school, of course, identical university program, but then she actually had trouble in this kind of business. She never finished, mostly because, actually, I was born. I'm the oldest of three, and then my sisters came in quick succession, so she didn't finish her studies. But she was still a fantastic student, always straight As, a legend almost. So she had a lot of job opportunities after we moved to Germany, and she worked in chemical engineering, more technical jobs. She hadn't finished her diploma in engineering. That was a very male-dominated world. Essentially, people climbed around these steel plants and so on and so forth, and really, I think the harassment she had to endure there made her change careers, at least in part.

As you probably know, in the Eastern Bloc countries, everyone had to learn Russian the way in the Western Bloc countries everyone would learn English. She knew Russian very well, so she became a Russian teacher for a while, because that actually caught on in Western Germany as an important secondary language, competing with French and Latin, the second spot after English. So there was a market for that [teaching Russian].

But in the end, she became certified as a teacher. She went through university education, went back to university, actually, in Germany, and became a special education teacher. That's what she's been doing for the last, probably—let's see— twenty-five years. Here [in the U.S.] she had to be recertified again, so she had to go through another year of courses, even though she had already been an experienced teacher in Germany. So she struggled to get going each time we moved.

That's how it is. In the previous generation, the woman adjusted much more to the man than it would be today, I suspect. But I think she's been quite happy doing this. She's very effective, and she's worked with mentally retarded kids, mentally disabled—I'm not sure what the latest PC [politically correct] word is—so, serious developmental abnormalities. Then more recently, she's focused on children with difficult homes. She teaches them, often, really basic stuff that they should have learned a long time ago, but she's very well known as a reading specialist.

We're actually benefiting from that. Our son [Benjamin Svoboda] is only three and a half, and he can do three- or four-letter words pretty well, because she knows how to get kids motivated and interested in reading. So that's what she's been doing.

Her temperament is, she's also very lively and she's always been very involved in our lives and a bit more combustible than my father and also interested in lots of things and likes to travel and has lots of friends.

Actually, one of the distinguishing features of my father is he's more of a loner. He doesn't have a large circle of friends. It's his family and a couple of people, often from long ago. He really likes his family in the Czech Republic and really likes to go back. My mother has very little connection to that past, and she has a very elaborate network of friends and is very socially gregarious, and so they're quite different in that way.

**VAN BENSCHOTEN:** So they live here in the U.S.?

**SVOBODA:** Yes, yes. Anywhere she was, she has friends. They go traveling and bump into people and the next thing, they're friends for life or they e-mail each other for the next fifteen years, that kind of stuff. I don't take after her in that department.

**VAN BENSCHOTEN:** You say that you're the oldest of three children.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** If you could, describe your siblings as well, briefly, what they do, where they live.

**SVOBODA:** So we all came to the U.S. independently: my parents for professional reasons and my sisters with my parents, because they were younger than I was. I had finished school in Germany, more or less, and came here for college. One of the reasons was that this allowed me to avoid the compulsory military service in Germany. I'd just become a citizen, and so I didn't

feel too enthusiastic about spending eighteen months in the German military or twenty-four months doing civil service. It's really a large time commitment, was at that point. It's much reduced since then.

My sisters are one and a half and three years younger, and most people say that we're very different. My middle sister lives in Alexandria, Virginia, now, and she's essentially a businesswoman who's in the hotel industry. She works for Hilton and is essentially a salesperson for Hilton Hotels. She's fairly—what one could perhaps say—conservative, not politically, but she lives in the suburbs and is married and all the usual things that one does. She's actually just about to become a mother. My youngest sister lives in the Lower East side in Manhattan [New York] and has a very different temperament. She's single, and she has lots of friends. She's part of many activist groups. She's politically very active in progressive politics, as a matter of fact, very much preparing for the Republican National Convention right now. She's in any kind of political issue you can imagine, and also arts stuff. Her profession is she's an oncology nurse, the younger sister. Oh, actually, what am I saying? She was an oncology nurse, but she got her master's in public health, and now she runs a patient education program at a major hospital in Manhattan, but related to family education—outreach—related to oncology. So it's an oncology program. She's actually a cancer survivor, so she had cancer relatively early on, my youngest sister. Well, she was unusually young, and so that really drove her into this field.

Although we're very different, we're fairly close. We see each other quite a bit, and we have kids, and they come quite a bit and hang out and take an active interest. We see each other at least once a month—the three of us—even though we don't live in the same place.

**VAN BENSCHOTEN:** When you were growing up together, younger, what was the relationship that you had with them?

**SVOBODA:** Yes, it evolved. It went through many stages. I was the oldest boy. Both of our parents worked, so in the early days we played with each other quite a bit, naturally, but then there was a period where we lost interest in each other. I have to speak for myself. I can't quite remember how they interacted. They were probably closer and probably also competed with each other more that I did with them.

Only after we went away for college did we become close again. That's a relationship that's really matured over the last ten, fifteen years. The older we get, the more we appreciate each other. So it's gone through a couple of phases. It's probably not atypical, I would think.

My middle sister, the one who works in the hotel industry, she spent many years abroad, right, with Hilton, so she just wasn't around. It's only recently also that we are—even though we're not in the same town—within a manageable distance, so that it's reasonable to see each other on a time scale of a day or two, for a weekend. So that facilitates, of course, growing closer.

**VAN BENSCHOTEN:** Let's turn to you and your schooling. What were some of your earliest memories of school when you were growing up?

**SVOBODA:** The earliest memories of school. Well, I remember, actually, school fairly well from day one, learning to read. I went to an alternative school that emphasized the arts quite a bit. My strongest memories, probably throughout my schooling precollege, have to do with music, chorus, plays, that kind of stuff. That was really an important part of the education.

We had, for example, school on Saturday, which was a bit unusual, and it was only orchestra and chorus for six hours: three hours this, three hours that. That is still something I remember very vividly, because it's a very powerful thing to play in a large ensemble. Even though I was never very good, but I was part of some reasonably good ensembles, so it's still something that I would like to pick up at some point. It takes time, of course, but singing with a hundred people is really a very vivid memory going way back.

Yes, there are lots of memories of school, of course, and I was there for twelve years.

**VAN BENSCHOTEN:** Were you predisposed at any particular age toward any subject?

**SVOBODA:** I was actually a pretty good student. I was misadjusted early on because I was a foreigner, and that, actually, in Germany is a tricky thing, back then at least it was. It's not so much that there was bigotry or anything, but that the kids would poke fun at you, at your funny name, even though my name is not really that funny, but in a very homogenous society where you're not Christian, Schmidt, or something generic, it became an issue. I had an accent for at least the first year or two, and so I hung out with more of the riffraff—the more difficult kids—early on.

But mastering the school material was really never a problem. It came to me with very little effort, and very little effort I always put into it. I always did well on exams and stuff like that. But that really until eleventh, twelfth grade didn't play much of a role.

I don't think I really gravitated towards any subjects in particular. I really liked German and literature and stories and books. Very early on, I had a friend whose father was politically active in the Social Democratic Party, and very early on we started to read the local newspaper and then also this newsmagazine, *Der Spiegel.* I don't know if you know it. It's like a lower-quality version of *The Economist,* but it's thicker and has a lot of, also, news pieces and analysis pieces, and it's leftliberal—liberal in the European sense—so economically liberal, but, of course, socially liberal also. So we devoured these things and discussed these things at a really very early age. I remember my parents actually had to buy me this thing every week. It's actually a weekly newsmagazine. We just loved this thing and then discussed it and so on.

So if anything, I was really always interested in social issues, political issues. I had always strong opinions on who should be in office, who shouldn't be in office long before most kids. That was really initiated by a couple of friendships.

Another thing that I did a lot of, I really played a lot of chess; that I was fairly good at. But again, it came relatively easy, and I never got to be, perhaps, top fifteen in my age group in Germany. But to improve, one would have to really study openings and so forth, and I always did that fairly superficially. I lost interest in that, actually, pretty much when I was fifteen or sixteen, when it became incompatible with the kinds of social dynamics that one is interested in at fifteen, sixteen: going to parties and so on.

**VAN BENSCHOTEN:** That's not very chesslike.

**SVOBODA:** Yes, exactly. I still really like to play chess, but my skill level is so hung up, and it's probably decayed quite a bit. So now I'm trying to teach my son chess, but he's really too young.

**VAN BENSCHOTEN:** How old is your son again?

**SVOBODA:** Three and a half. He can set up the pieces, and that's good enough for this year.

**VAN BENSCHOTEN:** Did you play any tournaments?

**SVOBODA:** Oh, yes. I played lots of tournaments. Yes, I was serious. By the time I left, I could have probably been paid for playing chess, so I could have been the second. They had the top leagues. It's all clubs, right? You didn't do it through schools; you had clubs. It's different in western Europe. You don't really play sports as much with the school. You have sports education, but you went to clubs, local clubs.

So the club that I was in had a team that played in the second, maybe like triple-A baseball, something like that.

**VAN BENSCHOTEN:** A different team or something.

**SVOBODA:** Right. And they would pay you travel expenses and a stipend, that kind of thing. So it was a fairly serious business. Even in my district, I remember there was first one kid, and

then that guy became a punk and dropped out of chess, and then another kid who became really serious about chess and always played better than I did. It really does take a lot of work, a very deep commitment, and it's probably not, at that point, time wisely spent, in some sense.

**VAN BENSCHOTEN:** I'm a big fan of chess, too. When you were talking about playing it and being good, [Anatoly] Karpov was the world champion, as you know.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** I was wondering, did you have any particular favorite chess player?

**SVOBODA:** Oh, yes. Karpov is a guy I hated. Yes. This is something we can talk about for four or five hours if you want. No, I was a purist. The kinds of guys I liked were [Alexander] Alekhine, among the Russians, [Mikhail] Tal. Do you know Tal?

**VAN BENSCHOTEN:** Oh, yes.

**SVOBODA:** Okay, so now we're talking. Yes, and then, obviously, Bobby [Robert] Fischer. Bobby Fischer. And I think [Garry] Kasparov is an absolutely fantastic player. Actually, probably the last time I followed a chess event was when he lost against Deep Blue [computer]. Of course, I had the luxury of a board in front of me and could play things out. But I remember where he made a blunder against Deep Blue.

**VAN BENSCHOTEN:** Yes, he had trouble with Deep Blue.

**SVOBODA:** Yes. It was really uncharacteristically weak, because he shouldn't have lost that.

So, Kasparov I really like. This book, I know, was available in Germany. There was a guy called [Vladimir] Vukovic.

**VAN BENSCHOTEN:** Oh, yes.

**SVOBODA:** You know him?

**VAN BENSCHOTEN:** The combination. He wrote a book on tactics.

**SVOBODA:** Two books *[The Art of Attack in Chess* and *The Chess Sacrifice: Technique, Art and Risk in Sacrificial Chess],* right. One of them is *The Art of the Sacrifice,* and I knew that book very well, and that is *not* the right approach to winning tournaments, but it's really the fun way to play, helter-skelter. Even if the sacrifice ultimately is not sound, the complexities tend to be such that if you're comfortable with really complex situations, the other guy will blunder, and so that's really how I try to play. I try to never let it become an even endgame.

**VAN BENSCHOTEN:** End it earlier, before you hit the endgame.

**SVOBODA:** Yes, exactly.

**VAN BENSCHOTEN:** That's the mark of a better player, too, probably.

**SVOBODA:** Well, I'm not sure. I actually don't think so. A really good player like Kasparov obviously commands all phases of the game, and they can convert a small positional advantage in the endgame to victory. There're just so many facets to the game. And, of course, you need to know openings. That's one thing I never really mastered. I played King's-Pawn to a head. I never really had a good opening repertoire. If someone didn't play the Caro-Kann [Defense] and the Sicilian [Defense] or something, if someone just played the King-Pawn to a head, I never felt comfortable with that, with a Ruy Lopez [Opening], or something like that. Probably a week of studying would have alleviated that. I was never committed enough, you know.

**VAN BENSCHOTEN:** My last question on chess, then we'll move on. I realize this interview isn't about chess. But I know they have ChessBase software, and a lot of people have said that has made study of the opening easier, because it has a database and you can go through trees and whatnot. Have you used any of that software?

**SVOBODA:** That was after my time. I tested chess computers early on, and they were a complete joke, and it was not until they had this program called *Mephisto.* When I was an undergrad [undergraduate student] at Cornell [University], they were dealing it, essentially; these computer geeks were pirating it, and that's where I got it for five dollars. That was a Mac [Apple Computer] program, and that could play some pretty reasonable chess games. That must have been around 1986 or something. Obviously, the Bell Labs [Laboratories] computer, which was specialized hardware— this was early eighties—where they had a master-level playing computer; that was a serious piece of hardware and software that couldn't be run on ordinary hardware. But there was one for the Mac. As soon as the Mac came out, there was this German

program called *Mephisto* that was surprisingly strong. Of course, now you can't beat these things.

**VAN BENSCHOTEN:** They're monsters.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** All right. We talked about your schooling. We talked about some of the things that you liked to do. You talked about chorus, plays, and music. When you say plays, acting in plays, I assume.

[END OF TAPE 1, SIDE 1]

**VAN BENSCHOTEN:** This is tape one, side B.

We were talking about hobbies, interests that you had as a child. You mentioned chorus, music. Did you play an instrument?

**SVOBODA:** Yes, I played flute, mostly, in the orchestra. I also took piano lessons. I dabbled in the saxophone. But flute was the instrument I played in the orchestra. But we also had a chorus that sang the *Matthew Passion* and *Messiah* and big choral music for religious holidays and stuff. It was quite ambitious, what they put on.

**VAN BENSCHOTEN:** Do you still play an instrument now, or have you given up?

**SVOBODA:** I really just pick it up once a week, that kind of thing. In grad [graduate] school, I still played chamber music, but not really since then. Now I pull it out just to expose the kids to it a bit.

**VAN BENSCHOTEN:** When you were going through elementary school all the way up to high school, were there any influential teachers that you met?

**SVOBODA:** Good question. There were influential teachers. Really, the most influential teachers were these art teachers. I'm not sure if that's really relevant, but I remember this guy [Matthiessen], a very influential teacher, but the way he was influential is that he ran a group

that met after school and worked on projects. It was social, political things. That was a few students, but also former graduates of the school and newly minted university students, a couple of them. He didn't set himself as the guy to lead this group, but he was a part of the group, but he was intellectually trendsetting.

He called this action art, and so we'd do little happenings in the shopping street on Saturdays. The kinds of things we'd do is roll up one of us in a wire mesh and just put him—right on Saturday morning—dump him in the shopping street, completely full of people. And he was untangling himself. No one knew what this guy was doing, and a circle formed. People didn't know if they should help him, because it was very, very strange and he was in wire mesh, clearly. Then some of us would be in the group and agitate with, "Wow, look! He's uncomfortable! We should help him!" and, "Oh, it's just a weirdo," and so on and so forth, and try to see what kinds of things would develop.

We put up theater for the fiftieth anniversary of [Adolf] Hitler's taking power. This was a big event, coming to grips with that, for Germans in particular. Fortunately, some people think about that. It was just fifty years ago, and we see Rwanda [genocide] and so on and so forth, but this is really in us, and how did it happen? So we had a whole bunch of events that we organized that tried to deal with these issues in a sort of artistic sense, and that was actually quite influential in the sense that I spent a lot of time developing these projects. It's actually political street theater that has a long tradition in various places, in Brazil and also in Europe.

**VAN BENSCHOTEN:** It reminds me of Dada, in a way, too.

**SVOBODA:** Yes, it is Dada, but it's really much more. The texts were really quite political and sensical, but, yes, the props were sort of Dada. It's difficult to explain, because I really haven't thought about it for a while, but every prop had a very weighty meaning.

**VAN BENSCHOTEN:** So was this something that you did for how long?

**SVOBODA:** Two years, perhaps. But I was one of the younger members, quite impressionable. But it was really quite fun. I got to read a lot of interesting stuff, and there were just a lot of creative people that were a part of it. It had very little to do with science.

**VAN BENSCHOTEN:** This was before college. How much did science impinge on your consciousness?

**SVOBODA:** Well, it did because I was actually hungry for it. The school I was in, as may have become obvious, didn't really emphasize that, and the science was always very easy for me. The

math we did was very easy. The physics, I already knew all of that, and I'd read quite a few pop—well, not actually pop—biographies, autobiographies, all sorts of descriptions of key figures and their discoveries. Nothing particular comes to mind. For example, I read [Werner] Heisenberg's autobiography and science, astronomy, astrophysics, stuff for the layperson. I was quite interested in science.

So when I went to college, that was something that I really wanted to pursue simply because I hadn't been exposed to it. I knew it was very important, very significant. I had very little exposure to it. I had actually relatively little math. I took all the math I could, but for Germans of secondary education, I had relatively little background. Compared to many of the people who were my contemporaries freshman year in college who were seriously interested in science, I was a year behind, but that was really not much of a problem because you can overcome that relatively quickly.

**VAN BENSCHOTEN:** What you had said earlier is that these subjects came fairly easily to you. Is that holding true as we get into junior high and high school, too?

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** You didn't have to study very hard?

**SVOBODA:** No, I was very lazy. Yes, and a couple of times, actually, I had real close calls, because they asked you to do reports, which just meant essentially handing something in, and I couldn't be bothered doing that. That was an absolute requirement to actually pass. So on a couple of occasions I was excused—allowed to submit something with a significant delay, which was against the rules—where clearly I had mastered the subject. I was perhaps quite immature in terms of discipline. Actually, I think I had much better work habits by the time I was in college.

**VAN BENSCHOTEN:** Getting back to extracurricular activities, was sports important at all?

**SVOBODA:** Yes. I've always liked sports. I was never very good at sports, so I played what they call team handball. Again, I was really not very good. I have a lot of slow-twitch muscle. I discovered I'm actually a fairly good long-distance runner. I really enjoy a lot of stuff. I play basketball. I actually do a lot of sports now, compared to most people, but it's really at a very real hobbyist's level. I've run a marathon, but barely four hours. I run and I play basketball. I swim. I do all kinds of stuff, but it's really just more to clear—to reset—the brain, that sort of thing.

Actually, I really like the social interactions, also. I really don't like running alone. I'm much more motivated running with three or four friends and shooting the breeze and catching up and so on and so forth. It really has a very important social element for me.

**VAN BENSCHOTEN:** I have a question, too, about religion. What impact, if any, did religion have on you and your family?

**SVOBODA:** That's a good question. I've been skeptical about religion very early on, and my parents never pushed it very hard, even though my father comes from a Catholic family. My parents have actually gotten more religious as they've become older, not perhaps that unusual. My parents actually are different on that front. My mother is probably fairly religious. My father is quite more appreciative of the traditions. He grew up with them, and they're meaningful to him. They're actually meaningful to me, more as I grow older. One has to reevaluate all of that stuff now that one has kids. But I think I was an atheist probably by the time I was twelve. Not just an agnostic, but I had made up my mind. Never tempted, so to speak.

**VAN BENSCHOTEN:** What was your parents' attitude towards church? Did you have to go to church?

**SVOBODA:** Well, we essentially went to church on occasion on Sundays. Then, as we became older, they forced the issue less and less. Even now we still go to church on Christmas Eve when we visit them. That's a core part of the tradition. But now they're part of a very liberal Lutheran church, and it's a very different experience than when I was ten. The Catholic church in Germany or in the Czech Republic was, of course, a much more strict affair and much more difficult, actually, to become a part of and to feel a part of, I think.

**VAN BENSCHOTEN:** Do you believe that science and religion are compatible, or can you be a good scientist and also be a believer in a deity?

**SVOBODA:** Oh, absolutely. There are lots of examples that prove that point. Do I think that they're intellectually compatible? I think no, but there are, of course, many definitions of what religion may or may not be. The question is, is it religion that is incompatible with natural law in some sense and something that can violate natural law. I've known, actually, a professor, who shall remain unnamed, but he's a Mormon and a very, very good atomic physicist. His scientific goal is essentially to test the fundamental laws of nature to ten orders of precision, and yet he's part of this very strange belief system that seems to me completely incompatible, but he's clearly a good scientist, and he's a believer. So what can you do? It wouldn't work for me, but it's certainly possible.

A lot of people need religion, of course, just for their own stability, to put everything into context and so on. There might be a strong psychological dimension to it. That's how I rationalize it. There are lots of people who draw a great and impressive strength from religion, and I think that's a perfectly fine way to do it.

**VAN BENSCHOTEN:** As you're finishing up high school, eleventh, twelfth grades—I don't know the German system, so you can correct me—how would you assess your education in that system?

**SVOBODA:** It's compatible to, essentially, the high school in the U.S. [United States]. Of course, in the U.S., the system is very heterogeneous.

**VAN BENSCHOTEN:** In your high school years, do you feel that your parents had any expectations about your going to college or about what direction your life might take?

**SVOBODA:** Yes. Actually, they must have had expectations, but they certainly didn't think that I would be a scientist, because that wasn't part of their experience. From both sets of the family there's a very strong practical bent, and science is a bit on the impractical end. They certainly don't have any problems with me. Of course, they're now very much proud of what I'm doing, and so on and so forth, but I think at some point they were like, "Well, why not do this kind of thing, work for Dupont or something like that?" There was a little bit of a disconnect.

You really asked about high school, actually. They were certainly expecting me to go to college or to university, but I don't think they had any particular expectations of what I would end up doing.

**VAN BENSCHOTEN:** How did you know that there was the expectation you'd go to college?

**SVOBODA:** That's a good question. I couldn't point to any one thing, but that was fairly standard in both of our families. Even my mother and her siblings were expected to go. This was a generational move, and in the Prague [Czechoslovakia] family virtually everyone had higher educations. They were fairly well educated as a clan, and my grandparents from Moravia, they were also well educated. Education was very important.

**VAN BENSCHOTEN:** Part of a family tradition, really.

**SVOBODA:** Yes, that's right, on both sides.

**VAN BENSCHOTEN:** When high school is about to finish up, what directions— what possibilities—were you looking at where to go to college and what you would study?

**SVOBODA:** Of course I came to the U.S. I applied to a few places. I think the way it started is that, if I look back, there was this political streak that I had, or have, perhaps, that drove me. I think I probably came to college thinking I would be doing some kind of engineering or applied science or something like that. So I felt that that was probably a very good way to make a difference.

But I was interested in lots of things. I actually took a lot of writing classes in college, but I think then what really happened is when I started taking serious science stuff, which were these honors classes in physics and chemistry, I really just liked it, and again it came relatively easy, and the professors were fantastic.

I was an undergrad [undergraduate student] at Cornell [University]. It was really a fantastic place to be an undergrad, because there were lots of undergrads. They took undergrads pretty seriously. I was an undergrad in physics, and the physics department was very, very good. I didn't even know it when I went to Cornell, but in hindsight, it was really a very, very good place. I still have friends there, faculty friends who knew me from there, and there were a couple of individuals who really took an interest in undergraduates, and it was a very, very rich experience.

**VAN BENSCHOTEN:** Why Cornell? Why Cornell in particular?

**SVOBODA:** I just applied there and got in, basically. I had a checkered transcript, fairly good SAT [Scholastic Aptitude Test] scores, and also I probably would have gone to MIT [Massachusetts Institute of Technology] if I had gotten in; I didn't. That's a place that I remember I was rejected. I got into Cornell and UPenn [University of Pennsylvania] or something like that, and they both had strong engineering schools. I just liked Cornell.

**VAN BENSCHOTEN:** Had you been to the U.S. before?

**SVOBODA:** Yes. I visited those places, of course.

**VAN BENSCHOTEN:** Had you been there often?

**SVOBODA:** I'd been an exchange student in tenth grade.

**VAN BENSCHOTEN:** You said that when you get to Cornell, this was when you— you didn't say this, but I'm assuming this—had your first laboratory experience.

**SVOBODA:** Yes, that came even later. Now you're talking about research, right? I had my first real—I would call it—science education that is worth remembering. I could have probably skipped everything that we'd done. Probably I learned more just reading popular science than I learned in high school, and I learned a lot of the process of thinking about science, about using mathematics in science. The power of mathematics became really clear to me, and I took a lot of math, and I really took as much math as I could until I really stopped understanding what they were teaching. So I had to find my way, because I was quite inexperienced.

The first thing that attracted me was mathematical things, but then in the end, abstract math is dissociated. I always have this practical streak, and it's quite dissociated from any applications. So that started being less satisfying than physics, and that's what I really focused on.

They had also a work-study program. Part of my financial-aid package was to work twenty hours a week. So the first year I worked in the library, but then I figured out that you could actually work in a lab, that professors would only have to pay a small fraction of your salary, like five dollars an hour, but they'd pay only one dollar-fifty, and the rest came from the state or something like that. I don't remember. So from then on I worked in labs, and that was actually very, very important. I didn't do much the first year, just helped out, and then some computer programming and then some electronics, just by osmosis picked up the doing of science in a number of labs, actually well-known labs. That was very, very useful. It was a very vibrant place, and you got the sense that this was actually not just very interesting, but also fun. The students were excited about what they were doing. They all had rich lives. So, that part of it.

Then a very important thing was, I got a summer job at Bell Labs [Laboratories] as a programmer, which was very, very important, because I actually worked there for four summers, and two in a statistics group where I did mostly programming. So I learned a lot and was really part of a research effort. My code was used in some software toolbox and so on. So I was really pretty serious about it.

Then later on I was in a basic physics research lab, where I did experiments for the summer. They had the summer program which was very hard to get into, but I got my foot in sideways, because I started as a programmer and then I learned about who does what, and I approached them directly and said, "Next summer, can I come into your lab?" That was important also.

**VAN BENSCHOTEN:** So this was all while you're an undergrad, then?

**SVOBODA:** Yes. Yes. They paid money, and it was great. I had to finance part of my [education]. Although my parents obviously supported me quite a bit, they weren't really prepared. This was incredibly expensive, these private universities. I could make $5,000 in the summer and do really very, very interesting things.

**VAN BENSCHOTEN:** Of that research you did over the summers, what stands out? Were there any projects that were particularly memorable?

**SVOBODA:** First of all, after my sophomore year the research that I did was the first paper that I was on. It was just real research, where there was a problem, you had to set up equations and you had to solve them. Then down the hall was someone who was really good at that, so you went and talked to them. They'd give you references to read, and then you would go into depth. This was applied math and statistics. It really was all about reliability testing: how do you extrapolate to normal conditions for failures for computer chips and stuff like that, that you test at extreme conditions, because you want to design things that last thirty years, but you don't want to test them for thirty years. So this whole field of reliability testing is very complicated extrapolation procedures, essentially, based on physical models of what the failure process would be.

**VAN BENSCHOTEN:** Is this connected with this paper, "Statistical Kinetic Models"?

**SVOBODA:** Exactly. So how did you dig that up?

**VAN BENSCHOTEN:** That was in, actually, your application, your Pew [Scholars Program in the Biomedical Sciences] application.

**SVOBODA:** Oh, yes? Interesting.

**VAN BENSCHOTEN:** That was your first paper, then.

**SVOBODA:** Well, yes, and then there, of course, was mostly stuff that Mike [Michael] LuValle, one of the authors, did, but I did a little piece of that, yes. Historically, the first. It may not have been the first that was published.

So I had these great jobs also at Cornell, and then another important thing was, I actually had acquired enough credits that I was able to do a semester at Lawrence-Berkeley [National] Lab [Laboratory]. Namely, the DOE [Department of Energy] was funding this semester research program, and I could do that because I had taken enough classes to graduate. So I went to [University of California,] Berkeley for a semester. That was a very important stint for me, where I worked in a physics lab pretty much full-time. That was very exciting, because this was a lab that really was in the midst of working on high-Tc [temperature critical] superconductors, which was a very important discovery. Do you know about that?

**VAN BENSCHOTEN:** I don't.

**SVOBODA:** It's not biology, but in the late eighties, these guys discovered—[J. Georg] Bednorz and [K. Alexander] Müller won the Nobel Prize two or three years later; it was very, very important—a completely new class of materials could be superconducting.

**VAN BENSCHOTEN:** I do remember that.

**SVOBODA:** And the mechanisms were unclear, and since these things were conducting at high temperatures, experiments were relatively easy so an undergrad could actually do fairly nice experiments. It turns out I actually didn't work on highTc superconductors directly, but on something related, but the whole lab was just very exciting.

This was in Alex Zettle's lab at Berkeley. So that was a place where I put together experiments with rubber bands and tape and wires and all kinds of things, again; where an undergrad could really get involved. It was a lot of fun. So it became clear that I wanted to try to do science, even though it was pretty clear that it would still be a long road.

**VAN BENSCHOTEN:** Nonscience questions, but maybe important ones, nonetheless: What about your extracurricular activities again? What are you doing outside of the classroom when you're at Cornell, or really focusing? Did you belong to clubs?

**SVOBODA:** Yes. What did I do? Let's see. Did I belong to any clubs? I belonged to clubs, intramural sports teams, that kind of thing. I would, of course, go to lots of events, and there were some political things that were relatively minor. But, yes, that was a time where I really took advantage of the university as an academy, just libraries and courses and learning how to write. That's something that I really learned. I think I learned how to write there, which—I noticed, writing papers with postdocs [postdoctoral fellows] of mine—it's really happy I did. I took expository writing classes, quite a few, and classes that were designed to teach you skills in

writing essays and so on. I took a lot of courses, at least five courses a semester.

I have lots of friends from there. We had, of course, the usual fun and so on, but I didn't play any organized sports beyond intramural clubs, which we never practiced.

**VAN BENSCHOTEN:** Just showed up.

**SVOBODA:** Yes. Winged it. All kinds of stuff: squash and running and soccer and basketball, but all at a very modest level.

**VAN BENSCHOTEN:** What was your social life like?

**SVOBODA:** Oh, I had tons of friends and girlfriends and all that kind of stuff. It was very rich. At Cornell, there was this what they called the Greek scene, and that was very strong. I don't think I ever was at a frat [fraternity] party. I actually met my wife [Sarah Ali] there [at Cornell], but very briefly, and we bumped into each other five years later in Cambridge [Massachusetts] when we were both grad students at Harvard [University]. But the first time I glimpsed her was at Cornell.

**VAN BENSCHOTEN:** Had you been formally introduced?

**SVOBODA:** Oh, yes. Sure, sure, sure. We knew each other, yes. But we didn't keep in touch.

**VAN BENSCHOTEN:** So it would seem, then, if you were assessing your education at Cornell, that it was rich.

**SVOBODA:** Yes, it was very, very rich, yes. I think, in hindsight, I really made a lot of it. I learned a lot and just made great connections. Yes, it was very good.

**VAN BENSCHOTEN:** In evaluating your development as a scientist, it seems to me that the way you describe it, you're learning almost as much outside of Cornell, really, with these summer jobs and this trip to Berkeley, as you are within its walls.

**SVOBODA:** Right. Absolutely, and it's almost complementary because the work-study stuff was important to get me exposed to different things, but it's very difficult when you're taking a

full load of courses—fifteen, twenty hours a week—to really get anything done. First of all, it's not a long time; but also, you're whipped, and you're cutting corners because if you have five courses, homework, all that kind of stuff, and a social life; then you just show up and do the minimum.

But it was important to get exposed to the excitement of doing science and going to group meetings and things like that where people discuss projects and all. But I think the opportunities to do stuff myself were mostly during the summers and during that semester in Berkeley, a cohesive project. Good stuff.

**VAN BENSCHOTEN:** So you graduate. You get your degree in physics, your B.A. [Bachelor of Arts] at Cornell, and then you head out to Katmandu in Nepal. Describe why you ended there.

**SVOBODA:** Well, I was already accepted to grad schools, and I chose to go to Harvard for various reasons, because I was interested in biophysics. My last semester at Cornell, I explored that a bit, but I just deferred. It turns out that there was a friend of mine from high school who was Nepalese, and through her I found out that there was a possibility to perhaps help out with some teaching in Katmandu, and that's what I did. I just said, "Well, let's do something else for a year." I worked in this school in Katmandu for a few months, really, only because the physics teacher had fallen sick with hepatitis, and I basically took his spot. I taught A-level physics, and then traveled a bit, did some trekking and went around India, and then came back, basically.

**VAN BENSCHOTEN:** With every intention, like you say, you'd already been accepted at Harvard.

**SVOBODA:** Right. Every intention to come back. There was no question about that.

**VAN BENSCHOTEN:** When you were applying to graduate schools, you get in at Harvard. Where else did you apply?

**SVOBODA:** Let's see. Where else did I apply? I applied to Berkeley, and probably the only reason I didn't go there is because I had already been there. I was tempted to go to [University of California,] Santa Barbara because another topic that I was interested in was fluid dynamics, classical physics. But then some wise people talked me out of going to Santa Barbara, because, although everyone agreed that for the particular thing I was interested in it was very good, it was a bit unwise to go to a place like that; it was a bit spotty otherwise.

I may have applied to two or three other places, but I just can't remember. At that point,

with all the experiences I had, I was pretty much accepted everywhere, but right now I can't remember. I may have applied to Stanford [University].

**VAN BENSCHOTEN:** You accepted Harvard, and there's obviously the Harvard name, clearly, but were there other things that attracted you?

**SVOBODA:** It was really the biophysics program. The physics I was interested in was, again, this more classical—classical in the sense that it's not quantum mechanical—fairly complicated statistical mechanics and fluid dynamics, and that was very strong.

There was a guy who I ended up working with for a while there, David Nelson, who I don't think I've ever written a paper with but was there, who was the best guy in the field. There's the Harvard name. That didn't really play such a big role for me. As I said, I probably would have gone to Berkeley if I hadn't been there. I know Berkeley is probably equally famous. But the really strong biophysics program was attractive to me. So they had a relatively early biophysics program that was mostly about structural biology, but where they try to draw physics students into biology, and that's what I actually ended up being in. And it's just, of course, an incredibly broad and rich university.

I have to say I had, again, a fantastic time as a graduate student. It was really very rich, but I think it was not uniformly so. It probably wasn't the best place to be a grad student. The situation I got myself into was very good, but it was—it has changed a bit since then—still the old Harvard, where there were lots of big professors who rarely interacted, and there were empires and lots of politics and not really the kind of thing that students really flourish in. Students flourish more in places where there's lots of interaction, lots of collaborations, and so on. But anyway, I really liked it for other reasons.

[END OF TAPE 1, SIDE 2]

**VAN BENSCHOTEN:** This is tape two, side A.

You were talking about graduate school and why you accepted at Harvard [University]. I assume you did rotations; you went from lab to lab. Is that how they work it there?

**SVOBODA:** That's what I did, but they didn't have that, actually. I came in and looked around and asked someone, "Can I do a project with you?" and then did some experiments. That wasn't really going anywhere. I just didn't like the project. Then what I did is I essentially, effectively, ended up doing rotations.

I worked for a year on a project that was working with biological materials but doing

essentially physics. That was a self-designed project, which is a dangerous thing to do in graduate school, I think, unless you're an exceptionally mature student. But that turned out okay. It was with a postdoc [postdoctoral fellow] [Christoph F. Schmidt] who was sort of an independent postdoc there, and together we worked on the structure and fluctuations of the red-blood-cell cytoskeleton. That sounds like a slightly strange topic, but it turns out that there were some important, interesting theoretical issues there that we were pursuing, really only peripherally related to the biology of these things.

That's really how I got into biology, because I noticed that as I learned these biochemical preps [preparations], and I worked in Dan [Daniel] Branton's lab, did the preps in Dan Branton's lab, who—Gosh, he must have been already sixty then—had invented freeze fracture. He was an old-time molecular biologist, really.

Then next door was Larry [Lawrence S.B.] Goldstein, who had cloned kinesin. Howard Berg was in the same building, who turned out to be my thesis advisor, who actually was a biophysicist. He also had studied physics as an undergrad [undergraduate] and grad [graduate] student, and who did absolutely beautiful work on the chemotaxis of *E. [Escherichia] coli* and the biophysics of the rotary motor of *E. coli.*

I actually finished a couple of papers on the red-blood-cell cytoskeleton with Christoph [F.] Schmidt, who was my collaborator, and we're still friends. Christoph was actually just here. He's now a professor in Amsterdam [the Netherlands]. In the physics community they were reasonably well-respected papers, and it was clear to me that biology was the more interesting place to be. Physics was a bit in a crisis. That whole high-Tc [temperature critical superconductors] thing had died down, and it wasn't so clear what the open, solvable questions were; whereas in biology, with the kind of thinking that a little bit of physics background provided, it was really quite obvious that there were lots of things to be picked and really right in the neighborhood.

So what I did is I asked Howard Berg if he would take me as a student—and he's really still one of my heroes—but he said he didn't really have a project for me. Basically, at that time what most of those guys were doing was two hybrids, to figure out who binds to whom in the motor, and that's something I didn't want to do. It was very important to understand the motor complex, but if I wanted to do two hybrids, I'd probably go to Mark Ptashne's lab or something down the hall. But he suggested that I work with this guy Steve [Steven M.] Block, who had been a student of Howard's and now had a lab at this Rowland Institute for Science. Have you heard of this place?

**VAN BENSCHOTEN:** No.

**SVOBODA:** It was a not-for-profit institute that was founded by Edwin [H.] Land. No one knows why it was called the Rowland Institute. Some people thought it was because they were all into crew and it was "row, land." But other people thought it was after the optician, the

optical physicist [Henry A.] Rowland, who was on the [Johns] Hopkins [University] faculty in the turn of the century. Who knows?

Edwin Land, of course, was the founder of Polaroid and sort of the Bill Gates of the sixties and so on, and a very, very big benefactor to Harvard. So he essentially built himself a retirement home, this Rowland Institute, where he surrounded himself with friends and good scientists, some perhaps not so good scientists.

Howard Berg came to Harvard from Caltech [California Institute of Technology], in part because he also had a laboratory at the Rowland Institute, which was fully funded, spectacular facilities, machine shops, and so on. Steve Block had moved there from Stanford [University] to be a full-time Rowland scientist, who also had an affiliation with Harvard. So Howard [Berg] became my thesis advisor, but I did most of my work with Steve [Block] subsequently. That was great, because I was the only student, and Steve was fairly hands-off and very enthusiastic. Do you know him?

**VAN BENSCHOTEN:** I don't.

**SVOBODA:** He's a phenomenon of nature, very funny and broadly educated. We had our fights, but it worked out very well. What we set out to do—what a couple of groups, including a group that involved Steve had figured out was how to essentially measure the movement of individual kinesin molecules, of individual molecular motors—was to measure the steps and forces of individual motors. This is a little bit like the single-channel patch clamp. This would be essentially a second single-molecule functional assay.

It really happened all very quickly. But we thought about how to do it, and we basically combined optical tweezers to apply forces on the kinesin molecule. Then you had to measure movement of the molecule with nanometer precision. So we used a technique developed by a guy named Winfried Denk, called dual-beam interferometry. Then we combined the two and made, essentially—perhaps a little bit luckily—the perfect tool to measure both the forces and steps of kinesin molecules.

I built this thing. We bought the laser. We designed the optics. We modified a microscope—that's really the stuff that I did, and that was the core of my Ph.D. thesis—and did a couple of measurements that really only took a few weeks to collect the data because it just worked so well. I could have graduated in four years. Until that time, it was amazing, I'd never known failure. It was just very lucky. It was just being at the right place at the right time and making decisions that, in hindsight, were very, very clever, but we really didn't know it.

There were people who were perhaps, in terms of fire power and depth in the subject matter, better poised to solve the problem, which was a big deal—to measure the steps and forces of single molecular motors—but who made the wrong choices and, in hindsight, really dumb choices. It took us all years to figure out how exactly to do force measurements at the

level of single molecules and steps and measurements of movements on the order of the size of a single protein. Now it's a cottage industry. There are dozens of labs doing it, but there was a lot of luck involved, actually.

**VAN BENSCHOTEN:** It's a very productive time. I may have counted wrong, but I count maybe about ten publications in a little over three years.

**SVOBODA:** Right. Very productive, yes.

**VAN BENSCHOTEN:** You're working in several areas of biophysics, too, and your work's shifting around quite a bit.

**SVOBODA:** Right. I've always had this tendency. I had a roommate, Partha Mitra. We had this little co-op in Cambridge [Massachusetts], and we collaborated quite a few times. Actually, there are a couple of papers that I did in grad school pretty much independently with him—one on kine sin and one on MRI [magnetic resonance imaging] of biological membranes—which really came about from dinner conversations, and both of them [are] actually highly cited papers now. We didn't pursue them, but other people built up on that and so on and so forth. We were really interested in science. We were just talking about it all the time, thinking about it all the time. Both Partha and I went to Bell Labs [Laboratories]; we overlapped at Bell Labs. He's now a faculty here, although I hardly ever see him because he's never here. He's traveling all the time.

**VAN BENSCHOTEN:** Why were you so productive? You were putting out a lot of papers. What is the secret to your success?

**SVOBODA:** That's a good question. And I've sort of been able to keep it up; I think the quality is fairly high, too. I think; I hope at least. It really struck me back then that there were people who were much smarter than I, or certainly who I perceived to be much smarter, who had trouble with productivity, and it has to do—again, I don't think about this much, so I'm searching here a little bit—with being disciplined and organized, recognizing significant but doable problems. In brain research, for example, the stuff that we work on, there are lots of very important problems, and 95 percent of them we just don't know how to begin to address. I would say 90 percent of them we wouldn't know what shape the answer would have. There are really deep conceptual and experimental issues that make it beyond reach.

I think, too, there's a real sense that might it be the genes: That it comes from lawyers and doctors and farmers and teachers, that there's a practical sense. I like to work on problems that are doable on a scale of five years that are difficult, but where I can at least know what has

to be done and there's a clear set of steps that are also well matched to our skills. Certain problems I may be interested in, but they require incredible biochemical expertise that I haven't developed, and I'd rather collaborate if need be, or I wouldn't pursue them. But, of course, technique rarely stops a good scientist. It's obviously something that if the problem is important enough, you learn any technique you need.

Acquiring a technique wouldn't scare me away, but if it wasn't clear it could be done and if there were some real fundamental uncertainties, I'd probably be too risk-averse to pursue it. I do like problems, but it's also now for the sake of students and postdocs and other considerations that creep in. So it's, I think, a practical sense. I've learned that I'm fairly good with my hands. That's another thing. You can be very smart, but you can be a klutz and break stuff.

**VAN BENSCHOTEN:** A poor experimentalist.

**SVOBODA:** Right. Not conceptually, but practically. Part of it is like cooking or like juggling or something.

**VAN BENSCHOTEN:** Before we get you to Bell Labs, I wanted to ask, you said that in your last year, I think, at Cornell [University], you had explored biophysics.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** What did that amount to? Why did you explore biophysics?

**SVOBODA:** Because it was sort of in the air. There was this guy named Watt [W.] Webb, who is a very important figure. He's been a big supporter of mine. My last semester at Cornell, I worked in his lab.

Actually, an interesting story. Years later, I was invited back to give a talk— give a lecture—at his seventieth, I think, birthday party. There was a symposium, and I was invited as the typical undergraduate. Even though I had worked there five, six years earlier, he didn't remember. It was a huge operation, and he was very distracted. He had a couple of really good people in his lab that are still friends of mine. One of them is Winfried Denk, who I actually ended up working with at Bell Labs, who's a giant in science, one of the real giants, and will be appreciated as such. You know, he's still quite young. Then Tim [Timothy] Ryan, who is also a very, very good scientist, who is now at Cornell, and we talk quite a bit. Both of them were doing biophysics projects for their theses, and they were doing interesting things and solving interesting problems, perhaps not as interesting as they might have been—and I think both of

them wouldn't disagree—if Webb had been in a biology department, but interesting problems.

So Winfried Denk, for example, worked on hair cells—the cells that make hearing work—and showed that hair cells sense the Brownian motion of the tip link. So you can hear, in some sense, the Brownian motion of your ear. That's a cool experiment. It might not really set the limits of hearing, but it's just a very cool experiment. So it was actually one of the more exciting groups, even in the physics department. That was a very, very exciting physics department; even in that physics department, it was really one of the more exciting groups. The Cornell physics department at that time, the experimental part, was very, very exciting. Everyone loved being there.

**VAN BENSCHOTEN:** There was enthusiasm. There was a spirit to it.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** Between 1994 and '97, you do something that is not common. You've done three-plus years in your Ph.D. You say that you were all but finished with your Ph.D.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** Then you go to Bell Labs. Explain that transition. What gets you into Bell Labs?

**SVOBODA:** I had been at Bell Labs. I loved the place. Again, it was a place where the spirit was just incredible. You should read *Three Degrees Above Zero* [by Peter L. Bernstein] and the accounts of science at Bell Labs. Everyone who's been there has been shaped by it, and that was perhaps already after the heyday when I got there. When I was there as an undergrad, it was really *the* place to do experimental physics, for sure. There was actually a biophysics group there that was very small, but incredibly good, and that morphed into a neuroscience group.

So towards the end of my Ph.D., I was looking for things to do, and I actually did another project with Partha. I went on to explore MRI because I wanted to study the brain. My advisor, Steve [Block], my main mentor, had moved to Princeton [University], and I was there, and I wanted to take that summer course at Woods Hole [Oceanographic Institute], but I had a half a year. Actually, historically, it's a little bit different, because I did this—already started this—earlier, to play with MRI.

Partha and I had some ideas about how to maybe do very high-resolution MRI, so we teamed up with these guys at Worchester [Polytechnic Institute] who were interested in these

experiments. Basically we were thinking about them, and they were running the magnet. They were fairly rare, these machines—research magnets— so you had someone to run it for you. So Larry [Lawrence] Latour ran the magnet. But we did some experiments, and those experiments turned out to be interesting, but they showed me that that wasn't really a good way to study the brain. The reasons, I don't know if you want to get into them. For me, the relevant length scale and time scale in neuroscience is microns and milliseconds, and it's just much too coarse and low sensitivity by many, many orders of magnitude.

So I said, well then, the right way to study the brain is with light. I had actually followed Winfried Denk's work, whom I'd met as an undergrad, and he had invented in a short postdoc in Webb's lab—one of a couple of inventions he's made— this two-photon excitation microscopy, which still almost everyone in my lab uses to some extent or another. But I thought, well, wouldn't that be a great way to study synapses? I had also gone to some lectures in neuroscience and got interested in synapses, how synapses change with learning, from a very superficial standpoint. I understood that this was a very important problem. I also understood that it would be very, very significant if one were to be able to study individual synapses. No one has been able to do that in the mammalian brain the way perhaps [Eric R.] Kandel has been able to do it in *Aplysia*. So I thought that it would be possible with light and particularly with two-photon excitation microscopy.

So it was a very natural thing to go to Bell Labs for the following reasons: that this two-photon excitation microscopy was unheard of in biology labs, and it required lasers that would be very difficult to hook up in your standard biology lab. Even if I could convince someone to allow me to build a thing like that, which involves dye lasers, hundreds of thousands of dollars of equipment, and so on, that you had to build and maintain, whereas at Bell Labs, Winfried already was setting this stuff up, and the infrastructure was there. That really became a no-brainer.

Then the other guy that I was really attracted by was David Tank, who really ended up hiring me, who was a very inspiring and thoughtful guy doing really meaningful physiology experiments and using an intellectual approach that really appealed to me.

So I worked with those two guys, and the experiments I came there to do didn't work, but I ended up doing other things quite related. Many of the things that I learned there from David and Winfried are still core technologies in my lab and core experimental approaches. It was also very productive, although I have to say the first half year there was very, very difficult, because this is the first time I really encountered something that was a complete failure, even though I don't think I ever worked as hard, because I moved to New Jersey; there was nothing to do. I just worked probably six, seven days a week, sixteen-hour days, trying to get this experiment to work, trying to essentially read out the strengths of individual synapses using two-photon uncaging.

It didn't work for technical reasons that were fairly subtle. It turns out that the absorption cross-section of the compound was too small and at the same time, the absorption cross-sections of endogenous chromophores in the tissue that led to photo damage were too large. So the

window of opportunity was just too small. Before you did the relevant number of experiments, you just killed your prep, and it was pretty fundamental. Only now, ten years later, are we doing those experiments. As a matter of fact, a student right now is doing the kinds of experiments I wanted to do back then. It had to do with, actually, better caged compounds. But it was, again, a very easy place to work and a good, nice place to work.

**VAN BENSCHOTEN:** If we could just back up briefly to the Steven [M.] Block lab, how big was that? How many people were in it?

**SVOBODA:** So I was the only student, and then there was Christoph [F.] Schmidt, the postdoc that I had collaborated with, also joined the lab for about a year, but that's it. He worked on related stuff, but not the same stuff.

**VAN BENSCHOTEN:** Did Block give you a lot of leeway?

**SVOBODA:** Oh, yes. It was incredible, because he was really very, very interested in this project. At the same time, he had become the guru of optical tweezers, so he was away a lot, and so he didn't really micromanage things as much as he might have. We really had a great time. Of course, he was negotiating moving to Princeton, so that took some of his focus away, but it was a very good time, just the right level of inspiration, and he knew a lot and so on, so I learned a lot.

**VAN BENSCHOTEN:** When it came to writing up your results, how did that process work? Did you come up with a first draft and then present it to him?

**SVOBODA:** The first paper that we wrote, Steve wrote, and he was very interested in that, because this was a very important paper for him, and actually won him the Young Investigator Award of the Biophysical Society. So as soon as I had the results, he wrote it, and he wrote it in a few days. I made the figures, and that actually taught me a lot, because he's a very effective writer. The other papers I wrote, and then the writing of the thesis was essentially writing an introduction and putting it all together. That's it.

**VAN BENSCHOTEN:** I'll ask the same question as with Bell Labs. How big was that lab? How big was the Winfried Denk lab?

**SVOBODA:** It was very small, unusually small. It's unheard of in biology. So let's see. The whole department was about five PI's [principal investigators] and probably another five people,

including postdocs. So two techs and maybe three postdocs. So three postdocs between five PIs. It was small, and that was actually a major problem. It was a bit of a problem because in biology it actually sometimes pays to have manpower. But in experimental physics, it worked fairly well. So it wasn't optimal for all kinds of biology, I think, and many people left because of that.

**VAN BENSCHOTEN:** In 1994, you took a course at Woods Hole on neural systems. In the great scheme of things—in your research and everything—how important was that course?

**SVOBODA:** Well, it was important because I switched fields again, so to speak. For example, this field of molecule motors was very new. Actually, at Cornell, they really wanted me to apply for jobs straight out of grad school, a faculty job in applied physics. So I had the option of doing either that or perhaps doing a postdoc in a highly related field, maybe for a year or a year and a half, then getting a faculty job.

The trajectory was pretty clear. You'd refine the measurements for two or three years. It was pretty clear how to do that. I was probably in the optimum position to really be successful at it. Then one would have to do structure-function studies the way the channel field went. Instead, I chose to switch fields and do something else, and that was perhaps a good thing in hindsight, but was greatly facilitated by this course, because I hadn't really taken neuroscience classes. I actually took one in my last year in grad school while writing my thesis, essentially. But this was a very nice course, because it's long and takes most of the summer, and you get a crash course in some of the basics of cellular and systems neuroscience, and at the same time you do experiments on selected model systems.

Again, I met people in the course. A good number of them are now serious scientists at various places. As a matter of fact, three people in my lab took similar courses, and they really benefited greatly. So these are recognized to be very, very effective courses for the right kind of student, and I think it's most effective for people changing careers between grad school and postdoc level.

**VAN BENSCHOTEN:** Why don't we leave it there.

**SVOBODA:** That sounds good.

[END OF TAPE 2, SIDE 1]

[END OF INTERVIEW]

**INTERVIEWEE:** **Karel Svoboda**

**INTERVIEWER:** **William Van Benschoten**

**LOCATION:** **Cold Spring Harbor Laboratory**
**Cold Spring Harbor, New York**

**DATE:** **20 August 2004**

**VAN BENSCHOTEN:** Today is August 20th, 2004. I'm with Karel Svoboda.

Where we had left off, I believe, is with you at Bell Labs [Laboratories]. We had done a rather quick overview of the research that you do. I was hoping that you could go into it again, maybe in more length and the evolution of your research at those labs.

**SVOBODA:** I went there after this summer course in Woods Hole [Oceanographic Institute], which was an important piece of my neuroscience education, and yet I was still quite, when I got there, naïve on some fronts in what the important questions in neuroscience were. I had a good idea of what some of the important questions were, but, of course, in neuroscience in particular, one always has to think about questions that are also addressable in some way, that are tractable, perhaps. I think that is an important aspect of choosing a problem: not just to be able to identify significant questions, but significant questions that are amenable to currently available experimental approaches.

So, early on, I got interested in synapses and how synapses could underlie learning and memory and stuff like that in the mammalian cortex. The idea I had was to distinguish myself. Lots of people, of course, study synapses, but the thing that I wanted to do was study individual synapses, which would teach me a lot about the basic biology of synapses. I think that is absolutely essential to learning about the relationship between synapses and the properties of synapses and learning and memory, because there are lots of theoretical and all kinds of circumstantial data that suggest that the properties of individual synapses in some ways encode memories. That's something that is very indirect and really begs to be tested and probed more directly.

The idea was to use optical tools to study synapses, as opposed to electrodes, which was the classical way. That's optical tools in addition to electrodes, because electrodes, when one records from a neuron, a neuron—that's part of its job— integrates input from many synapses. So when one records from a neuron, one averages over the response of multiple synapses, but with optical methods, one can really, perhaps, look at individual synapses.

There are several ways of doing that. One idea in particular I wanted to pursue at Bell Labs, which was to essentially excite individual synapses using uncaging and using,

particularly, this two-photon excitation technique that we still use quite a bit for a variety of purposes that essentially allows one to release—to photo-release— substances in a tiny focal volume on the order of a micron on the site and so essentially to probe and stimulate a single synapse.

For various reasons, that didn't work, and those reasons are mostly technical. I think I mentioned earlier, right now we're actually doing these experiments because some of the technical obstacles were overcome. In particular, now we have better cage compounds that are more amenable to two-photon excitation. But that experiment failed.

Then Winfried Denk at Bell Labs had basically figured out that two-photon excitation was a great way to image in scattering tissues. In particular, he had started to look at calcium influx into individual synaptic compartments. That, it turns out, is a different way to probe the function of single synapses. The compartments that I became interested in are called dendritic spines, which are the receiving ends of synapses. They're tiny cellular compartments, and there's one of these dendritic spines per synapse, and when the synapse is active, calcium comes in, but it's very local calcium accumulation. One can then use that calcium elevation as an indication of synaptic function, because it's the synaptic receptors that admit the calcium.

So that's one area of work that began at Bell Labs and that we're still pursuing today in a variety of ways. We've, for example, measured the properties of synaptic receptors. They, again, are inaccessible to other techniques, and we have learned a lot about calcium signaling. Calcium itself is also important, so we've used calcium to learn about receptors and synapses. But calcium by itself is an important variable in neurobiology because it couples the excitation provided by synaptic transmission to biochemistry, because it drives biochemical reactions. This is actually mostly since I left Bell Labs, so we've gotten interested in calcium signaling per se.

But at Bell Labs, the other thing we did: a lot of playing around, exploring what kinds of things were possible to do with these kinds of tools. Bell Labs is a very good place to do that. I set up a couple of lasers, and I played around with using these lasers for microscopy.

Then another important experiment was to use biophysical techniques—important for me, at least—something called fluorescence recovery after photo bleaching, to measure, in fact, to what extent dendritic spines are coupled to the rest of the neurons. So this is an example of microphysiology, really trying to understand the subcompartmental arrangement of neurons and synapses and so on.

Then we moved to the intact brain, and again, my interest was ultimately to relate these essential biophysical assays at the synapse to try to learn about the properties of synapses in the context of learning. So, in some way or another, these experiments had to be done in the intact animal. Again, the fact that these techniques allow imaging deep in the brain allowed us to do *in vivo* experiments. I spent probably half of my time at Bell Labs doing *in vivo* experiments. Also lots of that stuff has been continued here.

It was actually a relatively short postdoc [postdoctoral fellowship]—less than three

years—considering I had changed fields. The projects that I worked on in some sense lacked cohesion, but I certainly learned a lot and got exposed to several preparations and carried with me a big toolbox that I could apply to problems here.

Historically, I think it's interesting that I lived through a couple of important changes at Bell Labs. Bell Labs had been this fantastic place and was still a fantastic place, but a little bit in decline. It was actually part of AT&T [American Telephone and Telegraph] at that point. This was, of course, long after the breakup of the Bell companies. So now we were part of AT&T. But AT&T had turned into a service company, so this was all part of the physics research labs that traditionally had supported hardware development, chips and fiber optics communications and so on.

So the atmosphere, when I started off there, was a bit mixed. There was clearly an air of decline of the importance of the research labs and the support for the research labs. There was considerable excitement when, about halfway through, AT&T split off Lucent Technologies and another company, and Lucent became essentially a hardware company and took most of the chunk of the labs that I was part of with it. That was a company that would make switches and fiber-optic communications and so on. There was a lot of excitement.

They were decimated, unfortunately, during the technology slump a couple of years ago. It really came at a terrible time for them, and there were a couple of bad management decisions. So my time was really divided between AT&T and Lucent, and the latter part, the atmosphere improved considerably before it got much worse long after I left. I don't think there is basic research there anymore.

**VAN BENSCHOTEN:** So you were there in the last great days of Bell Labs.

**SVOBODA:** Pretty much, yes.

**VAN BENSCHOTEN:** Working under [Winfried] Denk and [David] Tank, what were their lab management styles?

**SVOBODA:** Well, they both had very small labs, and to some extent it was me, and Tank was the department head, so he had some other responsibilities. One of his responsibilities was to argue and explain why this was a worthwhile pursuit for a phone company. He was very effective at that.

But they were both hands-on, and Denk was really in the laboratory constantly. Hands-on in the sense that he did a lot of experiments and constructed a lot of instrumentation. Tank had a slightly bigger operation—maybe two or three people— and he basically mostly was turning his back on the kind of stuff that I was doing and started working on other things. So I interacted

with him less and less directly— scientifically, he was around all the time and so on—as I stayed on.

They are both intellectually very sharp and broadly educated and very unlike, I think, typical department heads. It was fairly helter-skelter—the whole place—and well supported. Of course, no grant writing, which was good, but there was a great sense of urgency, always, because the manpower was so short. They had very clear ideas of what they wanted to do—what they wanted to accomplish—and were very efficient at getting it done, again because, I think, there was very little manpower; there was very little effort to waste.

I earned a lot, also, from that. Actually, what looked wasteful on the surface, because they had a lot of equipment, they had many things that looked very expensive—one spare in case one broke—but when you do the calculation, it turns out to actually be an efficient thing to do, because the down time and the headaches you have. People often don't do that calculation correctly. Those are the kinds of things I learned there that would have been difficult to learn somewhere else: where you really think about the cost-benefit analysis of where to spend your money, the research funds you have, and how to really propel science forward efficiently. They were very acutely aware of that. I'm not saying that people at universities aren't, but not universally so, I would say.

And they were fairly fearless. That was another thing. It was a place where, really, risk was rewarded and where people were trying to tackle relatively big questions. Again, that happens on occasion at universities—the best people you have at universities—but they did that routinely at Bell Labs. It was the culture there.

**VAN BENSCHOTEN:** In '97, when you leave Bell Labs, why did you leave when you did? What went into that thinking?

**SVOBODA:** Well, it's interesting. I had, relatively early on, a job offer here [Cold Spring Harbor Laboratory], and so, as I mentioned earlier, I had some feelers about going to an applied physics department as a faculty member after grad [graduate] school. Those guys at Cornell [University], they kept in touch. That's a very good place for applied physics. Physics has its biophysics component. Then I published a paper, and then they asked me to apply to a job. I got a job offer there, and this was very, very early on. I had probably been at Bell Labs maybe nine months.

**VAN BENSCHOTEN:** So '94, maybe early '95?

**SVOBODA:** '95, yes. Perhaps. Although I liked the place a lot, I was a bit reluctant to go back to where I had been. That's not my style.

The other thing was that I really felt it would be better for me to be in a biology department, and that's where I wanted to be. But probably a biology department wouldn't give me a job as a neurobiologist at that time.

It turns out I'd met Roberto Malinow and Hollis Cline, who are scientists here at Cold Spring Harbor [Laboratory], who had just moved to Cold Spring Harbor, during that summer course at Woods Hole. These guys invited me to apply for a job here. I don't know how that came about. Oh, I think what happened is, I actually asked them for their advice. I said, "Look at this job. Do you think you can do neuroscience there?"

They said, "Well, look, there are openings here. There will be openings here. You would fit in well here." There actually wasn't lab space, it turns out, but that's a different story. They said, "Look, come over. Give a talk." And here at Cold Spring Harbor, things can go very quickly. You know, there are no FTEs [full-time equivalents] or anything like that, so you come, and you talk to a few people, and then if support builds, it can happen very quickly, especially back then, where there was a fair amount of slush money around. You know, the economy was good, private donors were giving, and so on.

This was in 1995, perhaps late '95. So I gave a talk here, and two weeks later I had a job offer that basically matched the very generous startup packages you can get in a physics department, which were unusual in biology departments then. That, together with the fact that I really liked the research institute atmosphere, and this place really did remind me a little bit of Bell Labs. There were some similarities, and some of the disadvantages weren't here. You could actually hire several people and run a normal biology lab, but you didn't have too many administrative loads. Well, the conclusion of this long story is that I had a job offer relatively early on during my postdoc, and so I had to, at some point, leave to take that position.

But the other thing is that at Bell Labs, postdocs—physics postdocs—are usually two years with one year renewable, and David wanted to hire someone else. He only had one slot—David Tank—and he really wanted to hire someone for his goldfish project. His interest had shifted, so he probably wouldn't have been too amenable. These guys are not soft there. They were not soft.

**VAN BENSCHOTEN:** Brutal, right?

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** Kick 'em out and get somebody in.

**SVOBODA:** Yes, exactly. We were friends, and there were no hard feelings, but it was not, "Oh, stay as long as you want," the way I do it here. Especially with someone who is, at that

point, very reasonably valuable because they can run by themselves and help other people and so on. But no, no. They needed that slot.

**VAN BENSCHOTEN:** So you were homeless.

**SVOBODA:** No, no. I wasn't homeless, because I had this job here for a year and a half, so I just moved here. I was lableless, in a sense.

**VAN BENSCHOTEN:** So they offered you a position in '95. You continued to work at Bell Labs.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** So you just simply said, "I'll be there."

**SVOBODA:** Exactly.

**VAN BENSCHOTEN:** When '97 came around, you started up your own lab.

**SVOBODA:** Right. It was one and a half years; one year is typical.

**VAN BENSCHOTEN:** So it wasn't too long of a period.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** You established your lab in '97. What was the startup package here?

**SVOBODA:** You're talking about Cold Spring Harbor now, I presume. I had list of stuff that I needed that I put together for this other job, and I basically went to Bruce [W.] Stillman, who was the director then, and now his title is CEO [chief executive officer] and president, I think. There was this title inflation, but he has the same job. There are no departments here. He really has a lot of influence, or you can call it power, to be direct. I said, "Look, this is what I get from them."

He actually was reluctant to sign something like that, but he said, "Look, pretty much everyone who's come here in your position has been supported at a substantially larger level than that. I can sign this, but don't worry about it."

I talked to a few people, and that actually was generally the perception: that especially young people are treated very well here. That turned out to be right.

Now, I actually don't know how much of the money I spent. I have never calculated it, but this was also a time where—as I mentioned—there was a fair amount of private money, and I had done fairly high-profile stuff, so I got a few of these Young Investigator Awards, like the Pew [Scholars Program in the Biomedical Sciences], that were incredibly helpful.

Then this is right when the federal government had committed itself to doubling the NIH [National Institutes of Health] budget over the next seven years. All of a sudden, the paylines in the NIH grants became thirtieth percentile or something like that. It made RO1 grants relatively easily available. So very quickly I got an RO1 grant. I never went back and checked how much of the money I spent; probably half a million dollars or something. I could have probably spent significantly more without them complaining. Friends of mine here have.

**VAN BENSCHOTEN:** Does Cold Spring Harbor pick up your salary, or do you need to get your salary out of the grants?

**SVOBODA:** The salary is done similar to most medical schools. There's no tenure here, but you have these five-year appointments of various types, and they essentially guarantee you the salary for those appointments, yet you are requested to get your salary from grants; so most people do. That's a big chunk of one RO1 grant, and that is fairly standard.

**VAN BENSCHOTEN:** Is there anything comparable to tenure here? Let's say you're here for ten years, fifteen years.

**SVOBODA:** Well, I've been here seven years, and about a half year ago, I became what is called a rolling-five. I got a rolling-five appointment. So that's an annually renewed five-year contract. So basically at any time you have five years to roll out, so to speak. There are people who are *de facto* tenured, they have endowments, but relatively few, and it's not the tradition. It has simply to do with the fact that it is a place where only research matters.

Now it's a little bit different with this new graduate school, where one needs some continuity—there are forty labs of modest size—and this cannot tolerate people [who] stop being interested in research and so on. So I can understand why the place is the way it is.

**VAN BENSCHOTEN:** As you mentioned off tape yesterday, the first graduating class actually was graduated this year, so it's been up and running for about four years.

**SVOBODA:** Yes, actually five years this week.

**VAN BENSCHOTEN:** You've mentioned the research you've done as a graduate student, as a postdoc. What are some of the projects that you have currently under way? What are you doing now?

**SVOBODA:** We have a fairly broad lab. We've branched out into a number of things, but the focus is the neocortex and how do cortical circuits work and how do cortical circuits rewire in response to experience. There we're focusing really on synapses, which are the connections between neurons, and we work mostly in the barrel cortex. Again, that's a system that I started to play with at Bell Labs.

So one of those systems was to study experience-dependent plasticity, because it is the part of the cortex that passes information from the whiskers, and just by making the animal do certain things to a subset of whiskers or just trimming a subset of whiskers, the cortex rewires. There are changes in the wiring that happen. That has been described using electrophysiological experiments, but all of the cellular mechanisms and circuit mechanisms are really unknown. There are lots of indication that what is happening in the barrel cortex is really quite intimately related to the kinds of changes that underlie more cognitive forms of memory.

We're looking at this from a number of standpoints. So from the most reductionist standpoint, we're still learning about how synapses in the cortex—these fundamental units of information processing, these synapses—work in the neocortex.

Then another project in the lab that has grown in prominence is trying to figure out the structure of cortical circuits: What is the pattern of connectivity of different neuronal types in the barrel cortex and which of these connections change in an experience-dependent manner. Now you're asking, cell type A to cell type B, cell type B to cell type C, which connections change with experience.

Then we try to look directly in the intact brain in experiments that take many months, often the entire life of the animal. What changes when an animal has novel experiences? What changes its synapses, and how does that fit into the changes at the level of circuits?

Then we're also developing tools in a couple of ways that allow us to analyze. For future work, it will be important to read out the function of collections of neurons in the brain that are anatomically identified. So we're thinking about ways to read out the function of populations of ensembles of neurons, and that technology development has to do with developing sensors—

activity-dependent fluorescent molecules—and also targeting them to the proper cellular populations in the cortex.

Another important aspect of understanding the cortex is trying to be able to perturb the function of specific cell populations. There are these diverse cell types. We don't know what these different cell types do, and so what we'd like to do is to be able to manipulate these neurons in such a way that we can turn them off, make genetically-modified neuron populations of these so that you can turn them off *in vivo* in a rapidly inducible and reversible manner. That's actually something that's recently started to work very nicely.

Those are, broadly, the areas that we're working in, the kinds of projects that are going on.

**VAN BENSCHOTEN:** Where do you see your lab maybe going in five to ten years?

**SVOBODA:** We've really just made over the last few years—last couple of years, I think—some real, for us, breakthroughs in the kinds of things that we can do in experimental approaches and so on that we really want to exploit, so there are clearly defined directions that will allow us to harvest these efforts in development of technology. We really want to understand what is stable and what is plastic at synapses in the adult brain. We'd like to understand the cell biology of synaptic plasticity in the adult brain *in vivo.* That is completely *terra incognita*, and we can do many of these things. We know how to image. We know how to do the biophysical measurements in the brain. We have to just get the probes to the right place at the right time, and then talented postdocs can do experiments and discover new things. So those kinds of analyses will be central to our work for a long time, for certainly five to ten years.

The new stuff is going to be to look at—rather than at synapses in this very myopic way—at ensembles of neurons. Ultimately it's the patterns of activities in neurons that, in some sense, are the most salient for information processing, and we'd like to be to read out the firing of populations of neurons in the intact brain. That will involve making these fancy reagents, but it will get us back to building microscopes, because we will need to be able to image faster in three dimensions. Right now with point-scanning microscopes it's much too slow, and there are some ideas we have, but it's really very poorly formed right now. But those are things that will happen over the next ten years, faster imaging for multi-unit optical recording in the intact brain.

**VAN BENSCHOTEN:** As you know, the NIH has been very big just recently on translational—on what can be translated—clinical uses of basic research. Do you see short- or long-term applications for any of the work that you do?

**SVOBODA:** We tend to not think about that when we think about starting a new project. I think that we are paid to some extent by the NIH, but I think that it's pretty clear that the NIH is

committed to basic research, and that's what we're good at. But the flip side is that I would be quite interested in working on neurodevelopmental and neural degenerative disease that I think is tractable in some rational way. So my kinds of contributions would, in fact, be able to contribute relatively directly to therapy.

I haven't really found that model. We're playing with a couple of things. We're, for example, very interested in fragile-X mental retardation. There's a good animal model. We've done some work that was, I think, fairly important, but then we went through a phase where we didn't make much progress, and now we've come back to it, using a new approach that we've developed in the lab, and it looks very promising. So we'll see how far we get, again trying to understand really the phenotype of fragile-X mental retardation protein, lack of fragile-X mental retardation protein on the circuits.

But it turns out that even though we don't design our projects with applications in mind, there often are. So, for example, the kinds of long-term imaging experiments that we've done *in vivo*, now people are looking at using very similar techniques to look at the dynamics of plaques in models of Alzheimer's disease and the dynamics of plaques with antibody therapy and stuff like that.

Actually, this project that I mentioned to you, silencing of neurons in an inducible manner, there's a lot of interest from neurologists, because, of course, silencing neurons is what deep-brain stimulation does, and it's relatively poorly controlled. So the alternative would be to infect neurons with the kinds of transgenes that we've developed, and then give the patient the drug. In that case, there's a dose-response curve; you can titrate; the effect is reversible and so on. That really wasn't clear to us when we started in this, but now, last year, it started working, we've told people about it, and then a number of people have expressed a lot of interest in it, a neurologist working on epilepsy, for example.

It actually happens remarkably often, relatively close encounters between translational and clinical research in the kinds of things that we're doing.

**VAN BENSCHOTEN:** Let's turn to the next part of the topic outline, which is, more or less, PI [principal investigator] duties that you have. This is a research institute. You have your first graduating class. Do you have teaching duties?

**SVOBODA:** Yes. I've taught the neuroscience course for a couple of years, which is really quite a small commitment—really a few weeks, a couple of weeks—of teaching. I've participated in committee meetings and things like that, and then I've also taught quite a bit in these summer courses that we have here. Every year I give several lectures in a variety of courses on imaging, on channels, on development. Actually, it's varied quite a bit. But the teaching here is minimal, comparable to most medical schools, a few lectures a year, essentially.

**VAN BENSCHOTEN:** So it doesn't take up too much time then?

**SVOBODA:** It doesn't take too much time. It's often related to one's research, so it's perhaps even less than in a medical school.

**VAN BENSCHOTEN:** A question about travel, job-related travel. How much of it do you do on average during a year?

**SVOBODA:** It's hard to say. It varies a bit. But I don't like traveling, so I travel as little as I can get away with. I'm probably away—I would guess, gosh—a month a year, something like that. So I give maybe ten seminars and three meetings, something like that. There's a minimal amount of travel that is necessary. I try to get senior postdocs to go if at all possible. There are commitments I have, so, for example, the Pew [Scholars Program in the Biomedical Sciences] meetings, and those tend to be very pleasurable, of course. McKnight [Doctoral Fellowships] has a meeting. [Howard] Hughes [Medical] Institute [HHMI], that I'm part of, has an annual meeting that one has to attend, and those often tend to be the best meetings, and then literally three or four other meetings where I try to attend as little as I can get away with.

I find it very distracting. I rarely learn. I've noticed that at many of these meetings, one only gets to hear already published work, which I find disappointing, frankly. I actually think one could cancel two-thirds of the meetings without any loss of flux of scientific information.

**VAN BENSCHOTEN:** Is that a growing trend: that you're getting more and more published information at these conferences?

**SVOBODA:** It may be the stuff that I'm working on more than a growing trend. So the closer you are into molecular biology, it's more the case. Ten years ago, cloning of a gene was a big thing, right? So, of course, you could easily be scooped. I'm only making this up. I really don't know if that's why that is so, but I imagine that could be a reason. You could easily get scooped, and so people rarely talk. And being second is completely worthless.

It's different in physiology, but molecular neurobiology and physiology are merging, so these traditions from molecular neurobiology, I think, are taking over a bit, and then also, meetings where physiology is discussed. However that may be, I perceive it more than I used to, and perhaps I read more than I used to and hear more published stuff and am cognizant of it, so less and less is new to me at these meetings. Perhaps I probably already have reviewed a good chunk of the papers that are presented.

**VAN BENSCHOTEN:** Let me flip this over.

[END OF TAPE 3, SIDE 1]

**VAN BENSCHOTEN:** This is tape three, side B.

Another duty you have is administrative responsibilities, things like search and theses committees. Or maybe you don't. I don't know. Do you have those things?

**SVOBODA:** Yes, we do have those things. We haven't had a search in a while. We have theses committees ongoing. There are a couple of other committees: admissions committee and information technology advisory committee, that kind of stuff. They're monthly faculty-type meetings that I attend, but it's really quite minor. This is as good as it gets in that realm.

On the other hand, here it's not clear how one would have influence, for example. Although one has few administrative responsibilities, there's really no clearly defined way to have influence. If there's no committee, then there's no formal way to communicate through a committee. So it goes both ways. In general, it's a good thing, I think.

**VAN BENSCHOTEN:** You talked about, when you started up your lab, getting an RO1. What is the source of your funding now?

**SVOBODA:** I have Hughes [Howard Hughes Medical Investigator Award] funding , which is a big chunk of my lab. Then I have some NIH [National Institutes of Health] grants, which is the other chunk. I also have a McKnight [Technological Innovations in Neuroscience Award] [Grant], a special award that's a technology development award, which is running out. I have some NIH grants and the Hughes funding. That's the huge bulk of my funding.

**VAN BENSCHOTEN:** You said earlier, too, that you travel to Hughes conferences. Those are good. You enjoy those. You look forward to those. Why those rather than others?

**SVOBODA:** What I actually like about them now is that they're a bit broader. So they're, really, now a bit more like the Pew [Scholars Program in the Biomedical Sciences] meetings used to be. They're not thematically organized, but rather they're organized by whatever your schedule allows and then equal numbers of people in each meeting, and one gets to hear a fairly broad range of stuff. Some of the talks are very, very good and pedagogical. That's the idea. Some are terribly technical. Especially immunologists have real problems with, I think, the culture, with communicating their work—of course, I'm generalizing here—to a general audience. But some of the people are making a great effort and being very effective. You learn

and you hear about things that you really wouldn't hear at these other meetings.

**VAN BENSCHOTEN:** This is off the beaten path, but we were talking about teaching. You were mentioning that there are these summer conferences or workshops.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** I've heard of them. They're constantly coming up. What is the function of those workshops? I know what it would be if I were a budding scientist, obviously. Cold Spring Harbor [Laboratory] has an incredible reputation, but what is the function of it for Cold Spring Harbor?

**SVOBODA:** What does it get out of it?

**VAN BENSCHOTEN:** What do you get out of it, yes.

**SVOBODA:** That's a question that I've asked myself sometimes. One thing that it gets out is virtually everyone comes through here once a year or once every two years. It is really true in most fields of modern biology.

So the meetings are clearly useful, and they have a long tradition, and they're *the* meetings. Especially the symposium tends to be a very important meeting. There is one annual meeting that is on a particular topic, like DNA replication or oncogenes or learning and memory, that kind of stuff, very focused, but the definitive meeting often of an era.

The courses are a little bit more difficult to understand, because the lab gets grant support for these courses. There are, in fact, lots of very, very good people who've learned their trade in these courses. I was a director of the "Imaging in Structure and Function of the Nervous System" course for three years, and I've taught in it for probably eight years now, and some of the graduates that I've seen are already beginning to have an impact in the field. So there's an impact. Rod [Roderick] MacKinnon learned crystallography here, right? We were just talking about him yesterday, but that's, of course, plastered all over the Cold Spring Harbor website. And David Baltimore took virology here, that kind of stuff.

But it is not a moneymaker, as far as I understand. I find the courses fairly disruptive, and they really take up a huge amount of space. They're only here three to four months of the year, but a lot of space is dedicated to them, the teaching facilities. So it's not so clear to me how much the courses add on balance, but it's a long tradition, of course.

Many of these courses are actually older than the permanent research program. The phage course, it's like early genetics, and it's been continuously running, I would guess for thirty or forty years.

**VAN BENSCHOTEN:** Cold Spring Harbor, maybe not directly, but it brings all these incredibly bright people, young, many of them. So do they use it as recruiting also?

**SVOBODA:** Yes. I think that happens naturally. There's just a huge flux of people through here. But I think the majority in terms of numbers is through the meetings. There are a dozen courses, but they're tiny. They bring like twelve students in and thirty faculty. The cost-benefit analysis is mind-boggling. But it has a long tradition. Just this summer, there are two applicants to my lab from the imaging course; two out of twelve. I won't be able to take them all, but it is a recruiting tool, and that is clearly very useful.

**VAN BENSCHOTEN:** We've taken a detour from funding. We had talked about your funding and the sources of it. How much concern do you feel day to day in your lab's funding?

**SVOBODA:** I've been very lucky this way. I have always had enough and some more. I don't foresee that to be the case always. One advantage that we have is that we have our foot also in technology development, and the stuff that we're doing is considered to be of interest to many people. So we have, for example, a project where we write lots and lots of software, and we have essentially agreed to make it open-source and give it away, and—boom!—NIH supports that, because there's a call for proposals on maintenance and distribution of open-source software. Then we got a whole bunch of letters from people who use our [software]. So I could have probably written two more of these, and then probably money would be coming out of my ears. There's a fair amount of money for imaging and for technology out there, and probably for good reason, but we can tap that if we want to, and we have on a couple of occasions.

Then I have two core R01s where I feel we are really leaders in the field, and I really hope that I have them for a couple of cycles. Then, of course, they have a natural life, and if we stop being topnotch in that field, it's time to probably do something else.

**VAN BENSCHOTEN:** How much does the source of your funding—Hughes, NIH, and others—shape the projects that you undertake?

**SVOBODA:** Well, it shapes the projects quite a bit. So, for example, mouse genetics for something, we use transgenic mice quite a bit. We make mice. We breed different mice. We get mice from other people. Mouse housing costs a certain amount per day. All these services cost a certain amount per day. It often is faster to do things on a larger scale. It's like that with many

things, right? You want to immediately order three sets of primers rather than one. You can do things faster when you have more money, and that is really the main issue.

That's often what we hear from Hughes people: that it has liberated them from having to constantly watch the bottom line, but rather than spend time on doing these kinds of calculations, just doing things in the fast track and ordering that extra antibody.

**VAN BENSCHOTEN:** So you can do it faster. Do you find that it leads to riskier science, people taking more risks?

**SVOBODA:** So there, NIH and Hughes are slightly differentiated. Under [Harold] Varmus, at least, the NIH has tried to emphasize innovation a bit more. At Hughes, that is very explicitly the primary category for evaluations. So risk is inherent. It's really a must. You have to do difficult, long-range projects. The idea is to really fund stuff that the NIH would have trouble to support.

Do lots of people do that? Does everyone do that, is a different question. Do we do that? It's borderline perhaps, but we're trying to do things that we wouldn't have otherwise done.

**VAN BENSCHOTEN:** This is going to elicit, no doubt, a subjective response, but I'll ask it anyway: Is there a correlation between those labs that are well funded and also good, solid science, maybe riskier science? Do you find that to be the case?

**SVOBODA:** Well, I think there's a correlation. It's by far not absolute. I've been on a few study sections, and every study section has a different culture. In general, I think that the system is admirable. It works very well. It's fair and relatively efficient.

But there are study sections that do not value as much as they should, perhaps, the track record of the investigator. They'd rather look at the proposal as such. Then there are very, very good scientists who can't put together a very effective grant. So there are people who are not very good and who write a very good grant, and if they land that grant in the right study section with the appropriate culture, they will get it funded. They may have a solid track record. So there are very wealthy individuals— or, rather, laboratories—I think, that are not, in my opinion, deserving of that wealth. Then there are absolutely fantastic scientists who live off one NIH grant, by choice or because they're terrible at writing grants.

But in general, I think, good science is rewarded. There is a category in the evaluations that describes the investigator, which means the track record of the investigator. In various places that's valued more or less.

Of course, there's positive feedback. If everything has been equal, if you have more

money, you can do things faster; you can try more things. In addition to your bread-and-butter things, you can do some riskier stuff and so on. Spent wisely, it can produce good science.

**VAN BENSCHOTEN:** It can?

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** The writing process is another duty that you have, getting out journal articles. What is the process here for originating those articles and then shepherding them through to publication?

**SVOBODA:** In my lab this varies a lot. It really depends on a number of factors. I don't have a clear set of criteria, but there are articles that I find that are very important to the lab, where I've been involved very intimately with the design and execution of the experiment, where I would keep a very close tab on the writing. You write the first draft and then we dominate the whole thing from beginning to the end. Unfortunately, that's sometimes necessary when I wouldn't like to do that.

There are, of course, foreign students and also people who should be writing better than they do. I really think that's actually sometimes surprising: how very, very highly educated people, how poorly they can write. Then, of course, sometimes you have people in the lab who write like gods, and you would like them to write all the papers. But that happens to be fairly rare.

I have one guy now who just writes wonderfully and where just writing together with him is just fun. Then grad [graduate] students, I tend to like to have at least try writing one paper completely from beginning to end and where I just really edit only if I absolutely have to, make general comments, "Go review your verb tenses and come back," and that kind of stuff.

**VAN BENSCHOTEN:** "Learn the subjunctive tense."

**SVOBODA:** Exactly.

**VAN BENSCHOTEN:** How do you know when you have a paper?

**SVOBODA:** Yes, that's a good question. That's actually something that we and other people struggle with a lot, because, of course, the science should drive that completely, right? If you

look back at the classics, it's absolutely clear. But then, of course, some types of science, it's absolutely clear. If you do crystallography, structure defines the paper—the coordinates—and then you write a little bit about the mechanism of the enzyme or of the channel or ion selectivity or what have you, what comes out of the structure. That's not so clear, always, in our work.

Putting something together like [Alan L.] Hodgkin and [Andrew Fielding] Huxley's papers on the action potential nowadays would be almost impossible. There are so many facets in that paper that would have almost certainly be broken up in five or six papers, probably to the detriment of the whole. But there is a need to break things up, and it's actually not me. It's usually more governed by the ambition and by the schedules of the people in the lab. They really come now for just a couple of years, and then they want to start applying for jobs, which is reasonable, and they want a paper in a good journal, and so you sometimes think a little bit too much about how to package it, rather than how to finish it. We, and I think probably many other people, have struggled with that.

So there are scientific concerns. Something has to be complete, and all the *t*'s have to be crossed and the *i*'s dotted in terms of controls and statistics and so on. But then there are larger scientific issues: Have you really addressed a sufficiently large question? That often falls short, I would say; to my taste, at least.

**VAN BENSCHOTEN:** Publications, as you know, play an incredible part in getting people positions and establishing your lab. Is that justified? Is that maybe the best way to do that? Do publications serve that purpose well?

**SVOBODA:** That's a good question. Yes, I think it serves the purpose reasonably well. A publication—it's essentially a fleshed out CV [curriculum vitae] in a way— should reflect your scientific style, your scientific taste.

The problem with publications—and not just the ones [problems] that I just mentioned, but another one—is that often lots of people are involved, and individual contributions get lost. That's especially true in some of the most interesting projects that develop that require expertise of many different skills: mouse genetics, electrophysiology, some anatomy and so on, where different groups collaborate, and often sometimes it's not so clear who did what and when and in what order and who conceived, who had the key insight.

Of course, letters of recommendation, therefore, play a very important role, which are also less, probably, useful than they might be, because they are nowadays so uniformly inflated. One very rarely reads a letter that has a useful critique in it, and then, of course, if it does, it's a horrible red flag, even though it might be the most useful thing in the letter.

**VAN BENSCHOTEN:** And the person who writes it can be branded as someone who's got an ax to grind or some ulterior motive or something of that sort.

**SVOBODA:** Something like that, yes.

**VAN BENSCHOTEN:** You described the lab management styles of [Winfried] Denk and [David] Tank and others. How would you describe your own lab management style?

**SVOBODA:** You're asking how would I describe my own lab management style, which is I clearly have a different view of that than the people in my lab, and I've noticed that a few times. I'm fairly involved with what's going on in the lab, and I think they would agree with that.

Well, yes, that will take some introspection. It is really, I think, more meaningful comparing myself to other people around, and I think I'm relatively hands-on, relatively often in the laboratory, and pretty much on top of the primary data in most projects, and to the point where some people would prefer me to be less involved. It's just something that, for my own sake, I would not do a project if I wasn't as involved in the data analysis aspect of it at least. So I'm less of a hands-off manager than many lab heads are, considering also the size of my lab, which is larger than ten people. So it's more a style that people with much smaller labs might have.

**VAN BENSCHOTEN:** You might have mentioned this already, but you say it's more than ten people. Do you know more or less how many?

**SVOBODA:** Well, right now it's fifteen people because there are a few people on their way out who are sticking around for a few extra months, so ten, twelve people is stable. Twelve people is a fairly stable number.

**VAN BENSCHOTEN:** How do you usually run your lab? Do you have things like weekly or biweekly lab meetings? Do you have journal clubs?

**SVOBODA:** Oh, yes. We run a very, very tight ship. Every week we have a lab meeting where someone presents, scheduled long in advance.

**VAN BENSCHOTEN:** You're looking at a chart that has people's names on it.

**SVOBODA:** Right. If I go to California, I'd rather take a red-eye than miss one of these, that kind of thing. We had one today.

Then coupled with that is a journal club. So the whole thing takes two and a half hours, and it's weekly, and pretty much everyone attends, I think it's fair to say. People submit essentially a presentation for everyone to look at so those who are interested before or after the meeting can actually peruse the data. It's all on the web. We use a lot of web-based tools to share protocols and software and stuff like that.

So you have a lot of management problems that challenge a bit, but we have a fair number of collective projects. I think programming is one of them, because we do a lot of instrument development, and a number of people write software.

It's a little bit like in a bioinformatics lab. One wants to ensure a certain style, a certain overall structure to the program so that they fit together, that other people can read each other's programs and are comfortable using each other's programs. So we have separate software meetings once a week for the four or five people who are doing software development, including myself. We have small meetings of two or three people who are working on related projects on a fairly frequent level. So we have probably four or five of these a week, that can last two or three hours.

**VAN BENSCHOTEN:** At these weekly meetings, people present their findings and is there a free-for-all? Whatever questions people have, they can suggest techniques?

**SVOBODA:** Right. Yes, yes. I think it's usually dominated by the people who are closest, who work on related subjects. It's very useful. People get useful feedback, and, of course, questions and answers are very much encouraged. That's the thing that makes it worthwhile. Yes, it's worked fairly well, and so there's a culture that's developed that I think is fairly effective.

**VAN BENSCHOTEN:** What do you think is your greatest strength as a PI [principal investigator], as the head of this lab?

**SVOBODA:** Again, it's difficult—very difficult—to have, of course, a dispassionate view of that, but looking at the track record and the kinds of things we have done and also the kinds of jobs people from my lab have gotten, I think I've matched people well with interesting projects that they were able to do and get recognition for.

I'm fairly effective, I think, at driving these things forward efficiently. I've been in labs where they have done that fairly efficiently, Bell Labs [Laboratories], as I mentioned, and also during graduate school. Just really thinking about what is the question here, what are the experiments that need to be done to address that question? Is it doable even? With the firepower that we have at our disposal, can we, in fact, address that question? And then, if so, how, and what are the different outcomes of different experiments? What's the strategy with outcome A,

outcome B? We're trying to really think through that. We don't dilly-dally. We're really trying to get stuff done, and people publish and move on. That, more than anything else, I think, has allowed me to attract very, very good people. People in my lab are very strong postdocs [postdoctoral fellows] and students because they see a culture where they see that other people are successful here.

**VAN BENSCHOTEN:** There's movement. There are results.

**SVOBODA:** Yes. Exactly. It's rare that they stick around for more than four years.

**VAN BENSCHOTEN:** Other duties that you have are professional services. Sometimes they're things like editorial boards, things like study sections.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** Do you provide any of those?

**SVOBODA:** Oh, yes. I'm fairly active on study sections. I think that's an incredibly important service. Obviously I've benefited from it, but I think that it's an opportunity to shape science. It's just an absolutely essential service. Everyone should do it averaging at least once a year, I think, review a few grants.

I've reviewed a lot for journals. I'm sort of an associate editor of the *Journal of Neuroscience,* but that only means that I'm on call as a reviewer. Beyond that, I've not been very active in editing journals, and I don't see that as really my future.

**VAN BENSCHOTEN:** You have two children [Benjamin and Tycho Svoboda]. You're married. How do you balance the demands of work here and family life as well?

**SVOBODA:** Yes, that's a constant struggle, and it's something that my wife [Sarah Ali] is fairly outspoken about, drawing lines and so on. So that's helped a lot, reminding me. I would definitely, if I could, spend more and more time here if left to my own devices. Of course, I really like to spend time with my children. There are so many things to do here. I drift to being here more and more.

So what I have now is a fairly fixed schedule that I've adjusted. It takes discipline, basically. Since I've had children, I've adjusted my schedule in various ways. The key change

that I've done is from being a complete night owl to essentially coming in now at six a.m. and then not returning after six p.m. That's been the key difference and really maintaining that. I come in maybe one night or something like that, and then really spending time with the family, those few hours in the evening. That's worked, I think, very well.

**VAN BENSCHOTEN:** Do you come in on the weekend at all?

**SVOBODA:** Yes, I come in, average one day, one normal working day a weekend, which could be one evening, one half day, or something like that.

**VAN BENSCHOTEN:** We haven't mentioned your wife. I was wondering, where did you meet her and when?

**SVOBODA:** I did mention that earlier. I did meet her originally when I was an undergrad [undergraduate student], very briefly, and then really bumped into her as one would into an acquaintance at Cambridge [Massachusetts].

**VAN BENSCHOTEN:** That was five years later, that second meeting?

**SVOBODA:** Well, probably six years later. Yes, five years later, actually. Probably four or five years later, actually. She was in a program there and I was in a program there, and we actually graduated the same day.

**VAN BENSCHOTEN:** That's amazing. When did you marry?

**SVOBODA:** We married six years ago exactly, last week, six years ago.

**VAN BENSCHOTEN:** An anniversary. Congratulations.

**SVOBODA:** Thanks.

**VAN BENSCHOTEN:** Is she a full-time mother, or does she continue to do science?

**SVOBODA:** She's not a scientist; she's a businessperson. She was a management consultant for a few years, and then she did some other stuff. Actually, she worked for Sloan-Kettering [Cancer Center] for a year, doing administrative work. But, yes, she's a freelancer now. She works from home, and she writes articles and so on, and she's just written a book. So she's clearly adjusted her schedule to suit family life much more than I have. But on the other hand, her job was very demanding. What we have is nothing compared to that.

**VAN BENSCHOTEN:** Really? That's hard to believe.

**SVOBODA:** They would travel for four days a week. This was completely standard, every week, and they would sometimes have to give six presentations in a week about six different topics to six different audiences that knew, really, much more about the topic than they did. So it's all these crazy pressure-cooker situations, to the CFO [chief financial officer] of this company and the COO [chief operating officer] of this company and so on, on manufacturing chocolate and about how to better do this. Of course, it was exciting, and it's a good baseline to do other things, but it's not maintainable. Five years is what most people do that for.

**VAN BENSCHOTEN:** And then to have a family on top of that.

**SVOBODA:** Right. Women, especially. It's impossible. They just drop out.

**VAN BENSCHOTEN:** What do you do when you want to relax a little bit and maybe get away from the science? What do you do for fun and leisure?

**SVOBODA:** Well, we have lots of friends. We have dinner parties, mostly with kids now, actually, so it's a different set of friends. That's important to us. Actually, almost every day I do some kind of sports, running mostly. That's very important.

**VAN BENSCHOTEN:** Do you run around here?

**SVOBODA:** Yes. As a matter of fact, they're running right now without me.

**VAN BENSCHOTEN:** Sorry to take you away from that. It's hot outside. You don't want to go.

**SVOBODA:** Oh, we do it pretty much every day.

**VAN BENSCHOTEN:** How far do you run?

**SVOBODA:** Anywhere from typically seven miles four or five times a week, maybe four miles once a week. But I also play basketball, so, depending. If I play basketball, I don't run that day.

**VAN BENSCHOTEN:** Are you a forward in basketball?

**SVOBODA:** No. I'm a point guard in my mind. [mutual laughter]

**VAN BENSCHOTEN:** Okay.

**SVOBODA:** No one else seems to agree.

**VAN BENSCHOTEN:** I like basketball, too. In my mind, I was a center, but I remained a forward, so I couldn't quite get those to correspond. But that's okay.

Anything else for leisure? You mentioned music earlier. You do that still.

**SVOBODA:** Yes, but it's on a really very, very low and inconsistent level. I read a lot. We're still politically a little bit active.

**VAN BENSCHOTEN:** Do you read politics, then?

**SVOBODA:** Yes, but we'll go register voters and stuff like that. But that's really occasionally. It's very important this year.

**VAN BENSCHOTEN:** That's what I was about to say, but I'm glad you said it first.

Describe a typical workday from the time that you get up to the time that you go to bed. I think you, in some sense, have. You say you get in here, or do you get up at six?

**SVOBODA:** No, no, I get in here pretty much right after six.

**VAN BENSCHOTEN:** You get up fairly early, then.

**SVOBODA:** Yes, so I get up early. Basically, twenty minutes later, I'm here. Then I mostly work here on some writing or programming. Because very few people get in before nine or ten, it's actually very quiet in the mornings. Occasionally, also, I work in the lab early on, but that I almost never do by myself; I always work with someone. So the early time is always some writing, something that takes thinking, that doesn't really tolerate distractions too much. Then I might actually, on occasion, after the kids go to sleep, take the laptop home and continue that.

So then, after nine, ten, these meetings start, meetings with various people. I wander into the laboratory to see what's going on, bother a few people. There are seminars and such, meeting with speakers and visitors, and then working in the lab with people, mostly our new postdocs or new students and stuff like that.

**VAN BENSCHOTEN:** Let me put on a new tape, and we'll pick it up.

[END OF TAPE 3, SIDE 2]

**VAN BENSCHOTEN:** This is tape four, side A.

So you were talking about your typical day, and we'd gotten up, more or less, to mid-afternoon.

**SVOBODA:** Yes. Then, actually, somewhere between four and five, I go running, depending on where we are in the year and so on and so forth, typically early in the winter and later in the summer. So today, they're going early for some reason. Then I pack up, basically, and go home. I will pick up the kids [Benjamin Svoboda, Tycho Svoboda], who go to a daycare center right on campus here. Actually, I'm on the oversight committee, so I'm quite active on dealing with daycare issues here.

**VAN BENSCHOTEN:** You're plugged into the community here in many ways.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** How far do you live from here?

**SVOBODA:** Just a couple of miles, about four miles. If I didn't have to pick up the kids, it would be easy biking distance.

**VAN BENSCHOTEN:** What is the routine once you get home? Who tends to prepare the food? Who tends to help the children?

**SVOBODA:** Sarah [Ali] does most. Well, the children, we share that in equal measure. I cook maybe once a week, versus she'll prepare food three times a week, and that's probably the ratio. But I put the kids to bed about half the time or something like that.

**VAN BENSCHOTEN:** Do you take some work home, then? Do you work on it before you go to bed?

**SVOBODA:** Yes, I try. It really depends. Invariably, I take home a stack of stuff about two inches thick, and rarely do I make it through a tenth of that. Sometimes I don't do anything simply because I'm very tired. By the time ten o'clock rolls around, it's time to read some nonscience stuff and pack it in. I need six, seven hours of sleep. That's pretty important. More like seven, I think, over a longer time period.

**VAN BENSCHOTEN:** If you would, assess your efforts so far in achieving your professional goals. Are you more or less where you want to be professionally, or is there more to do?

**SVOBODA:** That's a good question. I'm certainly not dissatisfied. The horizon is always very far away, and there are always lots of things to do scientifically. We've achieved certain things intellectually that we've tried to achieve, even long-term goals. I'm fairly content with what we've gotten done, but it's a never-ending story. It's very exciting, and I really rarely look back, frankly.

Professionally, if you say about recognition from the community, certainly I don't have any reasons to complain. I think I get what I deserve and not too much more. I have options, with respect to where to go, from very, very good places. As I mentioned, I'm just thinking about moving. That's quite nice, to have options, and I think that's probably the most important thing to me, to have essentially options to work where you want to work and to live where you want to live. That's also, I think, the most important part of recognition, is to be desired.

**VAN BENSCHOTEN:** Be sought after.

**SVOBODA:** Sought after. Right.

**VAN BENSCHOTEN:** You're in the middle of that process now, deciding whether you're going to move?

**SVOBODA:** Right.

**VAN BENSCHOTEN:** Let's turn to the last part of the question set, which is more or less about public policy questions. It's a grab bag. I call them just big philosophical questions about ideas, where your ideas come from, inevitability of science, things of that sort. But let's start with, maybe, patents. Do you have any patents?

**SVOBODA:** I've applied for a couple of patents. One of them is fairly far along, and another one, which I'm much more really excited about, is actually this thing I mentioned to you earlier about silencing neurons in an inducive manner. That, we had a provisional application.

**VAN BENSCHOTEN:** So you don't have any patents now, but you have some under way.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** Are patents generally good for science, do you believe?

**SVOBODA:** It's probably not, actually. Are patents good for science? The answer is probably not, because very few of us do science for patents. We would be doing science anyway, and, of course, patents can have a devastating effect on doing science in some instances. That doesn't mean that patents aren't absolutely necessary for drug development and so on, because if you develop a drug, you need protection. Because if you have the drug, you need to profit from it.

No. My patenting some of the things that we do in the lab—and we haven't done it much; we could have done it much more—is really mercenary. It's something you can do. It doesn't cost me anything, and it may, in fact, yield financial benefit. But I wouldn't have done anything differently without being able to apply for patents.

**VAN BENSCHOTEN:** A question about ideas. Where do your ideas come from?

**SVOBODA:** That's a good question. Where do ideas come from? We have lots of ideas, and where do they come from? Ideas for projects usually come from data. You look at data and you see things that you don't understand, and the idea to pursue a certain experiment is to really understand some data that you've collected.

But I think the more fundamental question of what kind of research direction to pursue—which is not really an idea, it's defining what an important, open problem is—comes from, of course, reading and talking to people and so on. But once you have an area in a research program, I find that ideas for particular experiments and particular directions really immediately follow from previous experiments. It's one of these things where you do one experiment and you maybe address one experiment, you end up with ten other experiments. It's really wiring multiplication. And choosing the most important experiment is actually another skill that's quite important. I'm not sure if we've done that, actually, always as effectively as we should have. It's also a matter of taste, actually, to some extent.

**VAN BENSCHOTEN:** How important is creativity, let's say, to the doing of good science? When you're doing a study section and you pick up a grant, are there instances where you can say, here, clearly, creativity is coming out of the seams? If so how important is it, and then what is it?

**SVOBODA:** Yes. I really think it's really undervalued in science. What I see, I see creativity together with innovation, essentially doing something, putting things together that hadn't been put together. The longer you've been in this business, the rarer it is that one reads something where one is really surprised by the approach. Recently I read a grant where that was the case. It was just incredibly pleasurable. Usually that's such a drag, reading these grants, simply because many of them aren't very good and are really derivative. Then one reads the grant where it's not clear where this thing is going because it's so innovative and so different, but it's clearly incredibly rich. I think it's absolutely the best thing. It's the most important thing, I think, in science and also relatively undervalued. Yes, I think it's very important.

**VAN BENSCHOTEN:** Can creativity be cultivated? Can you learn it, teach it?

**SVOBODA:** That's a good question. I think it can be. I don't know. That's a good question. Perhaps by example, because creativity doesn't necessarily mean that you have to invent something. It doesn't mean that you have to calculate something that no one else can calculate. But it often means being on your toes and putting together things that haven't been put together. You can be creative through scholarship, if you make connections, if you know more, and if you know more in some depth, if you become more fluent in more techniques and more concepts.

So many of my—what I would call—most creative ideas are putting together things that other people haven't put together, because I have worked in many different fields in single-molecule biophysics. So I've applied single-molecule concepts to synapses, which in hindsight, maybe, was relatively natural to me, but to many other people it might have looked very creative because they would never have thought of it, and it's in the eye of the beholder to some extent.

We're doing also software design. It allows us to do complex experiments and creative experiments that are an order of magnitude more complex than what most people do with canned software: complicated sequences of stimuli and automation and all these kinds of things. In general, putting together techniques and insights from different fields and putting together chemistry, genetics, and neurobiology, and physiology, I think there are lots of interesting things that come together. I think that is one form of creativity, is putting these different things together.

**VAN BENSCHOTEN:** A question about serendipity. We talked about creativity and the deliberate search for new ways of doing things. Serendipity, where it sort of falls into your lap, what role has serendipity played in your research, if at all?

**SVOBODA:** Well, I think it has played some role in my research, especially early on. The first project I ever did in grad [graduate] school— well, not the first; I guess it was really the second project—the project on kinesin, which was the core of my thesis. In hindsight, we made a couple of very significant choices that were completely lucky, essentially.

First of all, we chose to work on kinesin, which is a molecular motor that turns out to be very well behaved biochemically and in the single-molecule assays. Myosin and dynein turned out to be much more difficult, and that can be the difference between doing and not doing the experiment, where you can be hung up because of uncontrolled problems for years and not get anything done. To this day, no one has really figured out how to really work with dynein in these single-molecule experiments. This is twelve years later. So that's really serendipitous.

If Steve [Steven M. Block] would have said, "Let's work on dynein," I would have said, "All right, let's work on dynein." And, of course, he didn't have any more information, except that we knew how to get kine sin, and there was local expertise around and so on.

Then the other thing was, the information wasn't around. We made the right choice in using optical trapping. That's, of course, something that Steve had already set up in his lab, so it was natural. But if we had used mechanical fibers—little microneedles—which other people had tried to use, that would have been a serious mistake, and there we could have done the calculation, the analysis, beforehand, but I only did that in chapter four of my thesis, after I had done the measurement and realized why it was really a dumb idea, because of something called the fluctuation dissipation theorem and the way noise is spectrally distributed for large probes

that have large viscous drag, versus small probes like a bead in an optical trap that are low viscous drag. It turns out to be much more favorable for signal-to-noise ratios to use these small probes. So there we were dumb and lucky.

**VAN BENSCHOTEN:** A question about scientific progress, and this is a horrifying prospect; I don't want to entertain it too long, but if your lab suddenly, let's say, had disappeared in the last year, would the work that you've done in the lab over the last year, would that have been done anyway by another lab at another time, do you feel?

**SVOBODA:** Yes, I ask myself that often. I really don't think so. In general, we've done pretty unusual things, and you could maybe criticize that, some things, not that many people care about, but we've done some things that a lot of people care about. And there are a couple of literal fields that have come out of the kinds of things that we're doing in the lab. So I think that probably is not the case. It's not like cloning some G-protein and being first, or doing structure of some kinase and being the first. I think here there's a lot of stuff to do in neuroscience. I think the important issue is to really be doing important stuff and to also do stuff that people are still interested in ten years from now, that survive in terms of still being interesting and central to neuroscience, and also, of course, being right ten years later.

**VAN BENSCHOTEN:** Which is also important.

**SVOBODA:** Yes. That's actually the one thing that keeps me up at night is that: making sure that what we're publishing is correct.

**VAN BENSCHOTEN:** A question about the literature in your field and really more about the history of science. Is it important, do you feel, or is it useful for the average, workaday scientist to know the history of his or her field? Is that necessary to do good science, or is that helpful to do good science?

**SVOBODA:** Yes. I'm not sure how important it is. It can be inspiring, for one thing, and also it can be humbling, and I think that's also an important thing. Lastly, in the history of science, very few of us will be remembered by the canon of history, right? Maybe through the Pew [Scholars Program in the Biomedical Sciences] work that will be a little broader, but probably if you look at all of the people that you do interviews with, how many of them will really be remembered a hundred years from now? Very few.

So what one can look at—what's been very useful for me—is to look at the kinds of people who did very significant things and ask how did they go about that and what made them successful. What kind of risks did they take? How did they choose their problems and their

preparations and their collaborators and so on? Of course, things are different now than they were in the forties and fifties, like [Alan L.] Hodgkin and [Andrew Fielding] Huxley, who are some of my heroes, but nevertheless, I think one can learn from them. Of course, it's not so clear that we know exactly how things were done back then and what went through their heads, except through autobiographical accounts, and who knows to what extent these are, in fact, accurate?

But are you thinking probably more about the history of scientific thought?

**VAN BENSCHOTEN:** Yes, that, too.

**SVOBODA:** See, there's very little actually written. I find very little written about that in neuroscience. It's really a relatively young field, and there are some pretty crazy ideas around still pretty recently, so I'm not sure how useful it is.

**VAN BENSCHOTEN:** But when you were in graduate school and doing your postdoc [postdoctoral fellowship], did you find people who stressed the history of a particular field as prologue to any particular experiment? I realize that it can be two years, three years; that's fairly normal. But let's say five, ten years.

**SVOBODA:** No, no. On that time scale, of course, yes, yes. I thought you were thinking a hundred years now.

**VAN BENSCHOTEN:** That's fine, too.

**SVOBODA:** Well, that's very different. Because molecular motors, that field was really ten papers. We knew every paper, and we knew who the players were and where they came from. Yes, this guy did mechano-transduction and was interested in adaptation, and that's how he got to work on molecular motors. This person worked on kinases and ATPases. It was pretty clear where the approaches came from, where their viewpoints came from, and that was over a five-year time scale, and we knew all of those things and knew where they came from and probably knew roughly where they were going. But then in these fields, there was no longer history.

Then there was, of course, the history of muscle research, which is a whole bunch of molecular motors, and that also you got exposed to, because, again, some of the key players came from muscle research, and they dominated the field intellectually in some sense or another because they had models of how motors might work. So you had to learn the history over time, because some of those papers were written in the fifties and sixties.

**VAN BENSCHOTEN:** So it really depended on the field, then.

**SVOBODA:** Yes, it really depends on the field, right. In neuroscience, it's actually quite useful. It is quite useful—now that I think about it—because neuroanatomy, for example, is an old field using essentially the same methods for about a hundred years, and in my opinion, neuroanatomy is a terrible backwater. It's really inexcusable, because I think it's very, very important to understand the structure of the biological substrate to understand its function, right? It's like the same way with DNA: The structure made biological meaning apparent. It's not always quite as miraculous as that, but it's always very informative.

The study of neuroanatomy of the brain is really very primitive, and most of the tools are a hundred years old. It's not clear why that is, actually, but it's entrenched methodologically and not very quantitative. It was a very powerful tradition that hasn't really evolved. So, understanding how that came about is, I think, quite interesting.

**VAN BENSCHOTEN:** Can you be a cutting-edge scientist, though, and pretty much bypass the history altogether, more or less, depending again on how old or new the field is?

**SVOBODA:** Can you be a good scientist and bypass the history?

**VAN BENSCHOTEN:** Yes.

**SVOBODA:** I'm not sure how you can be a good scientist and ignore the literature. The literature, in some sense, is the history, unless you have some kind of written history that supercedes that.

**VAN BENSCHOTEN:** How large that literature is depends, of course, on the newness or the oldness of the field.

**SVOBODA:** Exactly. Then, of course, you only read a tiny, tiny fraction of that, the stuff that survives, that is cited over generations and collected in reprint volumes and so on and so forth. But I think it is fairly important to understand what came before and try and understand the ideas and how they came about.

**VAN BENSCHOTEN:** Did you take a history of science class at any point?

**SVOBODA:** No.

**VAN BENSCHOTEN:** Were they offered, do you know?

**SVOBODA:** Let's see. Good question. I'm sure they were offered at Harvard [University] — history of science programs—and there were famous history of science professors. My education on that front, beyond reading the literature in my field, is really from autobiographical accounts and stuff like that.

**VAN BENSCHOTEN:** I want to ask a question about technology. It's fairly obvious to me—correct me if I'm wrong—technology plays an immense role in what you do in your research.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** I won't ask that, but what I will ask is: the fact that technology is so important in your science, does that change the way you think about your science? Has that changed? Can you see changes in your own thinking, let's say, over the last five, six, seven years because of the technological capabilities now that you have? Does that actually affect the way that you think about science?

**SVOBODA:** Oh, yes. Absolutely. Yes. If you look at the history of neuroscience, right, coming from that, it's intimately tied. The whole intellectual development is intimately tied to technological innovation. It's not surprising that that is so, I think, because the brain is very, very complicated. That's one thing everyone agrees on. And the tools that we have to study the brain are really limiting, fundamentally. I'm talking now about experimental tools. You have in your brain a million times a million neurons, and connected by a million times a billion synapses. The way people study neurons in an awake monkey is by sticking one wire into neurons, recording from one neuron. It's just very, very primitive compared to the complexity of the system.

If you look at the history of neuroscience, each time you have some kind of methodological breakthrough, it's immediately coupled to real insight. Hodgkin and Huxley really made use of that. They really benefited from the invention of the voltage-clamp amplifier, which allowed them to figure out how the action potential worked, and lots of really good experiments.

The same is true for anatomy. It's the Golgi method that allowed [Santiago Ramon y] Cajal to sort out the basics of cortical connectivity and that neurons are, in fact, cells and so on. There are several examples of that, I think.

I think on a more modest scale, it happens with us. We can do things now that we couldn't just a couple of years ago, that have completely changed the way we think about single synapses, and that also allows them a secondary analysis that we couldn't have done a couple of years ago. I mean, the examples like that are many on a day-to-day level, but also technology in neuroscience just moves entire fields. DNA arrays is another example; PCR [polymerase chain reaction]. There are so many of these.

**VAN BENSCHOTEN:** Are there drawbacks to technology?

**SVOBODA:** Are there drawbacks to technology? You mean for the doing of science or the fact of a mutually assured destruction? [mutual laughter] Well, there's a drawback, yes.

**VAN BENSCHOTEN:** That is a drawback, yes.

**SVOBODA:** That's not our fault.

**VAN BENSCHOTEN:** That's right. Science is neutral. Some people have made the case that technology is getting more and more expensive, that sometimes the people who have the biggest, the shiniest machines are now industry labs as well, and that there are sometimes restrictions on that kind of research. There are pros and cons to that as well. But I guess the point they're making is that as technology becomes, perhaps, more expensive, then there's a divide between the labs that can afford such technology and those that can't, and that there might be this growing division in science. Is that a perceived fear, a real fear?

**SVOBODA:** I don't think that makes a lot of sense. I think technology always comes with, of course, new machines. Let's take an example. Typically the same bit of scientific insight—you can think of it as a little bit or, literally, a bit, a piece of information—now is much more easily gained, right? You can think of, in a DNA array, as 20,000 Northern [RNA concentration measured], right? A Northern is a very wasteful thing if you can do it with a cDNA array, right? Of course, there was a time when very few labs could do cDNA arrays, and they deserved to be at the forefront because they developed the technology. Now everyone can make their own. They just have to get off their ass and do it, get together and buy the robots, buy the oligos [oligonucleotides], or whatever kind of arrays. Then there are, of course, commercial outfits that charge an arm and a leg, and they do it slightly better, and some labs are wealthier and would be able to benefit from that more.

But it really always has been like that, and it's not a function of technological advancement. It's really more related to the topic that we discussed earlier, that there are poor

labs and there are rich labs, and some labs deserve to be poor and some labs don't deserve to be rich.

**VAN BENSCHOTEN:** It does get back to that. My question about tenure. We already talked about tenure. You don't have tenure here.

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** We often hear that there's a biomedical revolution under way. Do you believe, in your own opinion, that we're going through this revolution?

**SVOBODA:** No. I think that's total bullshit.

**VAN BENSCHOTEN:** Oh, is it?

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** Why?

**SVOBODA:** In my opinion. Well, so we're going through a time of considerable discovery in biomedical research, but I can't see that it's any faster than over the last twenty, thirty years. Clearly, molecular biology started with genes, with DNA. It really didn't exist before the sixties, but it would be ludicrous to say that we're actually progressing faster than in the sixties and seventies and eighties when people worked out all of the basic stuff. There are a lot more people doing it now. But then, I find personally, there's a huge disconnect between—I should be careful here—the claims and the reality. If you really look at the number of drugs that have come out of basic biological discovery—it's now the medical part, and rational understanding of mechanism—these drugs are negligible. There are very few of them, and that's directly reflected in the fact that biotech [biotechnology] has been a horrible investment since its existence.

As a matter of fact, venture capital has poured $120 billion into biotech, and the whole biotech market, I think, is valued at 80 billion. It's been a black hole for venture capital. It really hasn't lived up to its promise, and I'm not sure it will any time soon, because we're learning a lot about basic mechanism, but putting that into the context of the system—people—and its complexity, that is, and we can't do high-throughput screening on mice or people, right? So it's *terra incognita.*

Many drugs that are approved by the FDA [Food and Drug Administration] for something were actually, quote, unquote, "designed" for something else. They just happened to have some beneficial side effect, right? The neuroreceptor blockers are now beginning to be used for pain, where they were developed for epilepsy, twenty years later. So there is progress, but it's really often disconnected from basic biomedical research and often connected. But I don't see the revolution, certainly. It's semi-blindly stumbling forward, and that's as good as we can do.

What worries me about this—especially neuroscience, because in neuroscience the development of drugs in neuroscience has been especially disappointing—is that all these claims about "the Decade of the Brain," what good it has done to treat this, to treat that; and then we won't be able to deliver. At some point the public has to stand up and say, "Well, you've been promising this for all these years, and what's going on here?" It's really lobbying at its best and its worst.

**VAN BENSCHOTEN:** Some people, when they make this claim, also point to the Human Genome Project, and they'll say, for the first time we have a plan, as it were, and we also have new technology like microarrays, where, instead of dealing with one particular gene, we can deal with massive amounts of genes and see how they interact.

**SVOBODA:** But you know what happened to these companies that were based on genome data, right? The market knows all this stuff. They don't fall for this bullshit. Those companies don't exist anymore.

Making a drug is the hard thing. In the Human Genome Project, there are plenty of targets. The human genome market will allow you to find targets, but we know lots of targets, but people don't have drugs. There is no easy way to make drugs that work. Nothing has advanced there, I think. High-throughput screening is great, but that's the first step. Everyone knows that, and Merck [Co.], Pfizer [Inc.], they've got lots of interesting stuff in their fridge that I'd like to get my hands on for laboratory work—blockers of this and blockers of that—but a tiny, tiny fraction ever make it out of the first clinical trials.

**VAN BENSCHOTEN:** Is competition generally good for the creation of good science?

**SVOBODA:** Yes, that's a good question. I think it is really. Yes, in balance, it's difficult to regulate competition, but I think it does keep you on your toes. It really does focus the mind. It reduces waste. I think it's a necessary evil.

**VAN BENSCHOTEN:** The other side to competition is collaboration. How important is collaboration in your science?

**SVOBODA:** It's fairly important. I'd like it to be more important. So we've had a few collaborations I'm quite happy with, that have given us a lot and where we've contributed a lot to other people's science. But I really think that the kinds of problems that we're dealing with—cortex, for example; the mammalian cortex—and part of the ten-year plan that I've described to you, that is not a single laboratory project. There are too many facets to it that, not just intellectual resources, but the financial resources of my laboratory are not large enough to do a good job of having transgenic mice that express, for example, activity-dependent reporters in all interesting cell classes in the cortex. And it would be ridiculous to make these mice only for myself, if that's what we actually did.

Ideally, I'd like to work with someone who is good at finding specific cell promoters, work with someone who is good in developing probes, then use our expertise in imaging technology and data mining for imaging data and apply them to interesting experiments in the barrel cortex, but at the same time have this consortium work with other people who study other problems in the cortex in different brain areas, and that would be the right way to do it.

The challenge is to get people involved and to establish it in a way that everyone gets credit for the piece that they do, and that still doesn't work quite right in biology, especially. It's not clear how these really collaborative projects will work when tenure comes up.

**VAN BENSCHOTEN:** In some cases have you found that collaborations are actually frowned upon when tenure discussions arise?

**SVOBODA:** Yes. I think they are. But if they're collaborations and you're the top dog, then it's not frowned upon. But if you somehow yell less loud and turn out not to be the top dog, they are authorless. There are people who are very collaborative, who are also very generous, who sometimes get the short end of the stick.

On the other hand, that happens relatively rarely, and good colleagues in the right places are rewarded for being good colleagues. So, in a wise place, that would be the case. You have to pull your weight. You have to be recognized; you have to publish enough to get grants and so on and so forth. That's very important. But if everyone knows that you're a very good colleague, very generous, and that you don't care whether or not you're last or next-to-last author, that won't really perturb your tenure decision.

On the other hand, there are these collaborations of necessity where you have these people who control. Now here is a place where resources are really a different matter. There are laboratories where they have a lot of resources to make mice, and we're now turning into one of these labs, and we have, at least, the resources. That is a very valuable resource—if you have an interesting genetically modified mouse—and there are some people who just want to be on every paper that's done with that mouse. That's not really a collaboration, but it's an aberration

and should be frowned upon. But it's routine, actually. It often happens.

[END OF TAPE 4, SIDE 1]

**VAN BENSCHOTEN:** We left off with a couple of public policy questions, collaboration and competition. Your lab's scientific agenda. Given the limited resources of your lab—and every lab—and the constraints sometimes attached to those resources, what are the criteria that you use to determine what projects you work on and what projects you don't?

**SVOBODA:** These criteria have changed in my mind over the last few years. When I first came here [Cold Spring Harbor Laboratory], there was a period where, sort of in hindsight and also sort of by design, we played around a bit with different things and then started a few projects that then took on a life on their own. Now I've become more disciplined, and I've figured out—and that is actually something I didn't and probably should have learned; would have learned, if I had done a more proper postdoc [postdoctoral fellowship] in a proper biology lab—that it really takes a lot of time and effort to address an important question, and it takes focus.

I've recently tried to terminate certain projects and to focus really on a core area of biology so that we can look at the same thing from a number of different standpoints, truly understand the biology a little bit more deeply. So that has become an important consideration in addition to does-it-fit-into-this-focus that I see the lab should have, intellectual focus in terms of neurobiology. But then, of course, the other things always were true: Is it exciting; is it new; is it significant; and then can we see it through to the end, at least conceptually; and do we think we'll be able to overcome most of the problems?

**VAN BENSCHOTEN:** A question about the nation's scientific agenda. As a nation, at least academic science is mostly overseen by the NIH [National Institutes of Health], as you know. The NIH is not entirely immune from political pressures. We know PAC [political action committee] groups, celebrities, rabbis, any number of forces can affect their decision, especially on controversial issues like stem cell and human cloning and the rest of it. If there were an imaginary commission, let's say, that was set up to oversee or to sign off on projects, controversial projects—and maybe on uncontroversial—but in any case, on important research, who do you believe generically should be on that commission? Who should mostly make it up?

**SVOBODA:** Well, obviously, I would think that it should be dominated by scientists, and that has traditionally been the case, of course, but there should be the religious leaders, ethicists, and so on should be, of course, represented. I would call this a matter of public relations more than anything else.

On these matters, I think that ethicists certainly have things to teach us. Cloning and so

on, there are very, very significant ethical issues involved. I think that religious leaders, as sort of ethicists, also have things to teach us. But in the end, these are scientific decisions, and these decisions should be dominated by scientists. I think scientists are well enough aware. There's very little controversy about what should be done and shouldn't be done with stem cells, for example, and it seems to me utterly uncontroversial what should be done and shouldn't be done. Yet it is an important debate that needs to be fostered, with the help of people who think about different things, including religion. So, for that reason, I think it should include religious leaders and ethicists and anyone else I've forgotten who should be on there.

**VAN BENSCHOTEN:** Interestingly, when I was at the Pew [Scholars Program in the Biomedical Sciences] annual meeting in San Juan [Puerto Rico] this past March, they had a speaker [Kathy Hudson] whose research was partly funded by the Pew [Scholars Program in the Biomedical Sciences], and she was connected with the Science and Society Project [Institute], and her talk was about the public image that scientists have. Part of the resistance, it seems, among the public at large, to stem-cell research and other types of research, in her view, was the public perception of scientists, scientists being seen as amoral, if not immoral at times, amoral at least. She had actually done interviews—face-to-face interviews—with a sample of people from across the country, and it was absolutely shocking, some of the things that she'd come up with. Of course, she was talking before a whole lot of scientists that had been painted by the people she interviewed, sometimes as monsters.

**SVOBODA:** Right.

**VAN BENSCHOTEN:** Not all, but certainly there were people who felt that scientists would almost do anything in order to make a finding, to be published, to be famous.

**SVOBODA:** Oh, really? Interesting. I see.

**VAN BENSCHOTEN:** To get ahead. There were all manner of reasons. They were almost all negative. But it was an incredible talk, if indeed the research is well founded.

**SVOBODA:** That's interesting. Is this somewhere published?

**VAN BENSCHOTEN:** It's Kathy Hudson's work.

**SVOBODA:** I'll have to contact her. Maybe I'll get it.

**VAN BENSCHOTEN:** She does have a website.

**SVOBODA:** Kathy Hudson. Like the river?

**VAN BENSCHOTEN:** Yes. I could give you the title of her talk as well. I assume they have that.

**SVOBODA:** Yes, that's really interesting. Of course, education and outreach, right, is something that we're terrible at. This place [Cold Spring Harbor Laboratory] is a real pioneer in this. I don't know if you knew that.

**VAN BENSCHOTEN:** No.

**SVOBODA:** We have a very, very strong and rich relationship with neighbors, and some of them are quite surprising. Of course, lots of wealthy people around, but very supportive of what's going on. Then they run this place called the DNA Learning Center, which is really an extraordinary place where they bus in tons of students who learn about PCR [polymerase chain reaction], about forensics and that kind of stuff, but also adults who can take essentially primer in molecular biology, do experiments, learn about what is involved. There are lectures of all kinds—the genetics of mental disease and all those controversial topics, SNPs sequencing, the human genome sequence—that are very, very well-attended and integrated into the community. It's the DNA Learning Center. It's actually in Cold Spring Harbor. It's a converted school. It's a year-round, full-time DNA science education center.

Clearly we do things wrong, right? I mean, because on that front there's no question. The thing is, what I find equally shocking is that just no one knows anything about science, really.

**VAN BENSCHOTEN:** Exactly.

**SVOBODA:** So what you just described is really a very sophisticated Machiavellian view of scientists, which is something I hadn't encountered. People who usually know about it are quite sympathetic in my experience, or at least express themselves sympathetically to me.

**VAN BENSCHOTEN:** I think it depends, too, on where you are in the country. It depends, I think, on class. It depends on a lot of different determinants. She goes through some of these, as

well, when she gave her talk.

**SVOBODA:** This is actually very interesting. It deserves study.

**VAN BENSCHOTEN:** The question of science literacy in America and people's image of science, I was wondering, is your own institution—obviously, in some respect it is—concerned with this?

**SVOBODA:** Yes, very concerned.

**VAN BENSCHOTEN:** Does it invite you—does it request other scientists—to attend town hall meetings or suggest that they do so, or is that completely voluntary?

**SVOBODA:** This place is very effective that way, good, and some of it self-serving. They make a big deal about cloning a breast-cancer gene in ways that perhaps I would see as almost inappropriate, [as] the link to cure and that kind of stuff. But in general, I've been very impressed with how that has been done, the outreach and interaction with the community, and this is really a very, very effective place. I wouldn't be surprised if the impact on public understanding of science from Cold Spring Harbor [Laboratory] is larger than most major research universities, and it's through the DNA Learning Center, it's through public lectures, but it's also through some other stuff.

For example, some of us have gone to give talks. There's this actually fantastic cinema in Huntington [Long Island, New York], like a repertory cinema. It's a not-for-profit institution. Cinema Art Center, it's called, and when they show movies about science, there's some arrangement. I actually don't know who does it on this end. They actually arrange for someone to give a talk about the topic there, which is kind of fun. About *Gattaca* [1997 film with Ethan Hawke], about cloning. There were a couple of films recently about amnesia, about memory, and so on. So that's another way to have exposure. Now, granted, this is a very educated public there at most of these things, but it's probably very sympathetic anyway.

Yes, I'm very curious to hear about this. And I think we could be doing more. Science shouldn't be viewed that way. Of course, many of the things that that person expressed, or the interviewee, through Hudson's—through your—interpretation are right. We are like any other people; we want to get ahead; we are ambitious. But I think there are clear limits, and there's a very important role for science. If people understood science and the role science plays and how little resources it actually swallows, I think there would be no question, that it's worthwhile.

**VAN BENSCHOTEN:** Part of that public image is created by the media. Do you believe that

the media overall—things like the *New York Times, New Yorker,* other avenues, websites—presents science fairly, in a balanced way?

**SVOBODA:** Well, it's a good question. I've read, actually, pretty good descriptions about the doing of science. The *New Yorker* has had a few stories, for example, about the human adult stem cells in the cortex. I don't know if you read that.

**VAN BENSCHOTEN:** No, I didn't.

**SVOBODA:** This was a year and a half ago, about the controversies and who the players are and so on and so forth. But even sophisticated publications have a hard time with describing science, with really pointing out the important issues and why something is important. I find it's best when they essentially just quote scientists. This is my particular perspective, right? I'm obviously fairly sophisticated compared to even the average *New York Times* reader, and it may just not be possible to do it justice. We do press releases, and it's just this constant battle with the writer here about how to cut corners, what to say and what not to say, and accuracy versus readability.

**VAN BENSCHOTEN:** Do you feel that they're dumbing it down too much, then, popularizing it to the point of incomprehensibility?

**SVOBODA:** Yes. Perhaps. I know the public less than I perhaps should. My wife [Sarah Ali], for example, we talk about these things, and she really understands. It could be more sophisticated for her. It could be more sophisticated for my father.

I think the *Scientific American* of ten, fifteen, twenty years ago is a great model. Actually, good people wrote good articles that could serve both as introductory material for an undergraduate biology course, but were also sufficiently well written and illustrated to be digestible by people who buy that stuff at an airport kiosk. I think that it's really gone downhill, *Scientific American.* No one would use an article from *Scientific American* in a course now, and nothing has filled the niche.

**VAN BENSCHOTEN:** Why do you think there has been that decline?

**SVOBODA:** I don't know. I really don't know. I don't know their economics. I browse through it. Recently I looked through lots of issues. They've asked me to write an article for *Scientific American,* and I was sitting on the fence for so long because of that issue, because I thought it was not worthwhile, that, in the end, the editor who asked me left and pursued another career, so

that was that.

**VAN BENSCHOTEN:** One final question, at least to public policy, about privatization, about the relationship between industry science and academic science. Some people have pointed up that this relationship has become more and more complicated and that the interconnections are blurring, maybe, the division between the two, a division that some people feel should be maintained, especially in terms of academic science and free inquiry and other things. What is your own view of that relationship?

**SVOBODA:** I'm actually fairly naïve on that front. We've been funded by private foundations, so there's never been any trouble, and we have on occasion consulted with companies, but I don't think that's ever had any effect on what we're doing in the laboratory. There are clearly important bounds that need to be maintained, in particular with respect to clinical science. But on the other hand, a close collaboration between private industry and academic science can be incredibly fruitful, especially when you talk about bringing something to the clinic. That's not something we're in the business of doing. So it might be very natural to collaborate or to become, essentially, the research arm of a company that works on a drug to solve a biomedical problem.

That actually exists at Cold Spring Harbor, where people are fairly project oriented. Of course, the company funds a lot of that research, and students can still get an excellent education, they can still publish, they can write their theses, and so on. Quality control, I think, is independent of that, but obviously it has to be open, and it has to be revealed. With clinical stuff there are a whole bunch of other issues that come into it.

**VAN BENSCHOTEN:** I think that gets sticky sometimes.

**SVOBODA:** Yes, that I'm not as familiar with, but they seem obvious.

**VAN BENSCHOTEN:** Final questions. You said your lab is about, more or less, fifteen people?

**SVOBODA:** Yes.

**VAN BENSCHOTEN:** What is the breakdown between men and women?

**SVOBODA:** There are five women in the lab right now; about a third.

**VAN BENSCHOTEN:** What is that breakdown, let's say, on the departmental level, among the PIs [principal investigators]? How big is your department?

**SVOBODA:** Well, we don't have departments. It's a little bit tricky, okay? I think that probably the fraction of women is probably a third on average. I work on a very "biophysics-y" field, so I'm proud of the women in my lab. I think it's more than average, and there are relatively few women in imaging. When there is a symposium, it's often a problem to find female contributors.

**VAN BENSCHOTEN:** Why do you think that is?

**SVOBODA:** Well, people who come from physics typically do well. There are relatively few women in physics graduate education. It may have to do with we build our own instruments, and women are less comfortable doing that. They have not had the same kinds of experiences and still not, right? And who knows why that is? I won't go there. But clearly, very few women have fixed motorcycles and read *Popular Mechanics* and built toy planes and these kinds of things, which for many tinkerers in the lab are part of a common experience. But it's possible to overcome that, I think, and people have, and women have in my lab but also men, of course. So this science is more amenable to the typical experiences that boys tend to have than girls tend to have. That's my explanation.

**VAN BENSCHOTEN:** Where do these people come from nationally? What countries are they coming from in your lab?

**SVOBODA:** Let's see. Netherlands, France, Italy, Japan, Norway, Argentina, Russia, Germany, Poland, China.

**VAN BENSCHOTEN:** That's a broad overview.

**SVOBODA:** Yes. There are a couple of Americans, but it's a fairly broad spectrum. In addition, we've had a Hungarian in the lab and maybe one or two other countries. It's pretty amazing.

**VAN BENSCHOTEN:** A couple more questions about gender. Do you believe that the playing field is level between men and women PIs who are doing science in the field?

**SVOBODA:** Well, I don't think it is. There's no question about that. Women are different than men in some instances in some sense, and women clearly are at a disadvantage, and the question really is, how do you fix that? The disadvantage is especially acute when—women drop out most at the end of grad [graduate] school, at first postdoc [postdoctoral fellowship]—people really have to make that decision about family, and women always carry more of a burden there and probably will always carry more of a burden there. It's very, very unusual where the man carries more of a burden.

We have one instance with friends where that's the case, and there are feelings of guilt that come with that. There are these couple of years where these kids are very important, where you just can't get as much done, where perhaps that should be recognized differently. I don't know, but there the playing field is really uneven, and that's probably the main reason, in my opinion, why women leave the sciences. That's a very challenging thing to deal with.

**VAN BENSCHOTEN:** How about actually doing science? Do you see that men and women approach science differently? Do they think differently, conceive of it differently? Do they shine in different parts of the scientific endeavor?

**SVOBODA:** No, I don't see that. I've had, of course, more men in the laboratory, so some things that men have done women haven't done, and it's less so vice versa. But the women I've had in the lab have really done a diverse set of things and have approached things in different ways, some where a couple of them really learned the real things that are typically more male, have built microscopes and programmed computers and stuff, and learned that, actually, pretty late, considering they're in their late twenties when they come here or for postdocs. And others, yes, it's been fairly mixed, I feel.

**VAN BENSCHOTEN:** What is the best part about having the job that you have? What's the best part about being a PI?

**SVOBODA:** Well, I think the best part of it is that it involves a huge number of diverse responsibilities that are interesting and involve the doing of science, which is rewarding. You get to work with lots of interesting people, the people in the laboratory, who are very smart and developing at a rapid pace. That's a very rewarding thing to witness. But then also just the science, the data coming forth, the understanding of biological phenomena that come about, discoveries, all of that stuff really makes it exciting.

I feel it's a job where I really look forward to going to work. That's the gold standard. We're very fortunate to be in a situation like that, and it's not universal. Most people count the hours to the weekend and so on. So it's a very, very good situation to be in. We have relative freedom. We're working on projects that we define within bounds, with a long-term vision and long- and short-term plans, and we just really control our destinies more than most people.

**VAN BENSCHOTEN:** What were the consequences on you and your lab of the Pew [Scholars Program in the Biomedical Sciences] grant?

**SVOBODA:** For me, this was really quite significant, because it was the first thing that came into the lab, that and the Klingenstein [Award], which is similar in some ways. It really is a great honor. Very, very good people have gotten the Pew [Scholars Program in the Biomedical Sciences award], so you look back and you say, "Look at this. I'm part of this group." So that's the first thing. It gives you a huge amount of confidence.

Then the money is actually more important than one would think because it essentially doesn't have strings attached, so you can bank it. We've bought big pieces of equipment from it that are just difficult to get. It's not something you write a grant for easily, especially if you're a beginning lab. Of course, I could have burned more of Cold Spring Harbor's money, probably.

Then there are these meetings, and I've actually met a fair number of people there at the Pew [Scholars Program in the Biomedical Sciences] meeting that I talk to fairly frequently, collaborate with. A research program that is quite vigorous in the lab was really initiated there. Did you interview Greg [Gregory] Hannon?

**VAN BENSCHOTEN:** No. I think it was someone else. We have his interview done.

**SVOBODA:** So he is a colleague of mine here. His entire research program was initiated there, essentially. So it was really scientifically quite rich.

**VAN BENSCHOTEN:** The final question, which is, I'll give the mic [microphone] entirely to you, and is there anything that you want to clarify, anything you want to add to the record that we haven't covered?

**SVOBODA:** I think not now. I'll look at the transcript and do it at that point. I don't remember what I've said.

**VAN BENSCHOTEN:** I want to thank you.

**SVOBODA:** Great. Well, thanks. It was fun.

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